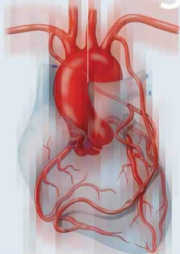


Guo-Wei He
Editor

Arterial Grafting for Coronary Artery Bypass Surgery



Second Edition

 Springer

Guo-Wei He (Ed.) Arterial Grafting for Coronary Artery Bypass Surgery
Second Edition

Guo-Wei He (Ed.)

Arterial Grafting for Coronary Artery Bypass Surgery

Second Edition

Foreword by Denton A. Cooley, Houston, USA

Contributions by

Floyd D. Loop, Cleveland, USA
Bruce W. Lytle, Cleveland, USA
Joseph F. Sabik, Cleveland, USA
Hendrick B. Barner, St. Louis, USA
Michael J. Mack, Dallas, USA
Hartzell V. Schaff, Rochester, USA
John Pym, Philadelphia, USA
Alfred J. Tector, Milwaukee, USA
David P. Taggart, Oxford, UK

Gianni D. Angelini, Bristol, UK
Antonio M. Calafiore, Torino, Italy
Christophe Acar, Paris, France
Brian F. Buxton, Melbourne, Australia
James Tatoulis, Melbourne, Australia
Hisayoshi Suma, Tokyo, Japan
Masashi Komeda, Kyoto, Japan
Anthony P.C. Yim, Hong Kong
and Other World Experts

With 148 Figures in 205 Parts and 77 Tables

Guo-Wei He (Ed.) Arterial Grafts for Coronary Bypass Surgery
First published by Springer-Verlag Ltd., Singapore, 1999

ISBN 3-540-30083-X Springer-Verlag Berlin Heidelberg New York

Library of Congress Control Number: 2005935948

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Printed in Germany

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Editor: Gabriele Schröder

Desk Editor: Stephanie Benko

Copy-editing: WS Editorial Ltd, Shrewsbury, UK

Production Editor: Joachim W. Schmidt

Cover design: eStudio Calamar, Spain

Typesetting: FotoSatz Pfeifer GmbH, D-82166 Gräfelfing

Printed on acid-free paper – 24/3150 – 5 4 3 2 1 0

THE EDITOR:

PROFESSOR GUO-WEI HE, MD, PHD, DSc

Clinical Professor of Surgery

Oregon Health and Science University (2002 –) and **Director**,
Cardiovascular Research, Albert Starr Academic Center for Cardiac Surgery,
Providence Heart and Vascular Institute (1994 –), Portland, Oregon, USA

Cardiac Surgeon-in-Chief

Department of Cardiac Surgery and **Director**,
Wuhan Heart Institute, The Central Hospital of Wuhan, China (2003 –)

Research Professor of Surgery and Director

Cardiovascular Surgical Research,
The Chinese University of Hong Kong, Hong Kong (2000 –)

Professor, Chair of Cardiothoracic Surgery

The University of Hong Kong, Hong Kong (1995 – 2000)

Foreword



Denton A. Cooley

Dr. Cooley is President and Surgeon-in-Chief, Texas Heart Institute, and Clinical Professor, University of Texas Medical School at Houston, Houston, Texas, USA

Ischemic heart disease is the leading cause of death in the world today, and its incidence is likely to increase as the average age of the population continues to rise, particularly in industrialized nations. In the 1950s, the prevalence and seriousness of ischemic heart disease and the advent of effective cardiopulmonary bypass technology spurred surgeons to develop coronary artery bypass grafting (CABG) procedures. Later, in the 1970s, percutaneous coronary interventions were devised as a less invasive alternative to CABG, and the number of these performed annually now surpasses that of CABG surgery. Nonetheless, CABG remains among the most common cardiac surgical procedures, with more than 500,000 performed each year in the United States alone.

For these reasons, advances in CABG techniques have tremendous potential to save lives and improve their quality. This is particularly true for improvements in the durability of arterial conduits, the use of which is the central and most technically demanding portion of the CABG procedure. This book is meant to be a comprehensive resource for cardiac surgeons concerning arterial grafting and graft materials in CABG.

Many renowned cardiac surgeons and cardiovascular researchers have contributed to this volume, which has been compiled by Guo-Wei He, MD, PhD, DSc. Dr. He has published a huge body of literature about arterial grafting in CABG, and his extensive experience in, and deep understanding of, this subject has earned him global recognition. He currently serves as Director of Cardiovascular Research Programs at the Chinese University of Hong Kong and the Providence Heart Institute in Portland, Oregon, and he is Clinical Professor of Surgery at the Oregon Health & Science University. Additionally, Dr. He directs the Wuhan Heart Institute in China, where he is also Chief of Cardiac Surgery.

The first edition of this book was written in 1999 to provide a detailed review of existing knowledge about the nature and selection of graft materials for CABG and the techniques used to harvest them and anastomose them to the coronary arteries. Rapid progress in this field during the last 5 years has stimulated Dr. He to publish this updated edition. Not only has new material been added to the existing chapters, but there are also new chapters on venous grafts, reoperative CABG, and the recently developed practice of internal thoracic artery and radial artery T-grafting.

Readers will find this book valuable both as a practical guide and as a stimulus for further improvement of arterial grafting techniques and technology. I commend Dr. He and the many authors of this volume for the diligence and expertise they have demonstrated in its creation and revision.

Houston, Texas, USA

Denton A. Cooley

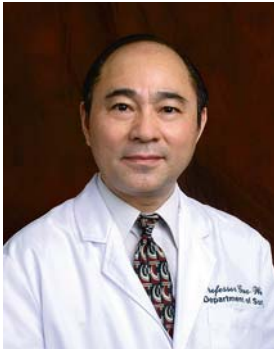
Preface

*“Some books are to be tasted, others to be swallowed,
and some few to be chewed and digested.”*

Francis Bacon (1561 – 1626)

“Isn’t it a pleasure to study and practice what you have learned?”

Confucius (551 – 479 b.c.)



Guo-Wei He

Coronary artery disease remains the major cause of mortality worldwide. Despite aggressive application of percutaneous coronary interventions, the surgical approach, namely coronary artery bypass grafting (CABG), remains a major approach for the treatment of coronary artery disease. Usage of arterial grafting has been well accepted as the main approach to increasing the long-term patency of the graft and long-term survival. However, the use of arterial grafts is not a simple issue. This is reflected by the diversity in practice among most experienced cardiac surgeons around the world as to the choice of conduit, the combined use of various arterial grafts, pedicle versus free grafting, etc. The issue is further complicated by the usage of these grafts during conventional cardiopulmonary bypass or on beating hearts, the usage of minimally invasive surgery in CABG, and, moreover, by the fact that most surgeons are still using vein grafts in combination with arterial grafts. With all these concerns, a comprehensive book on CABG using arterial grafts has become essential for cardiac surgeons and related professionals such as cardiologists, cardiac anesthesiologists, nurses, and other allied professionals for daily reference.

The first edition of this book was published in 1999 by Springer-Verlag. Since then, much experience has been obtained regarding arterial grafting in CABG. The principal role of the left internal mammary artery (IMA) as the first choice of arterial graft stands without argument and the use of alternative arterial grafts has become more mature in the hands of most cardiac surgeons. However, various methods of using the left IMA in combination with alternative grafts are being used since the role of the latter is defined differently among even most experienced cardiac surgeons. For example, use of the radial artery is routine practice by some surgeons but is ignored by others. A similar attitude is held by surgeons as to the use of the gastroepiploic artery and inferior epigastric artery. This issue exists in the use of the second IMA, namely the right IMA. In addition, the use of complex arterial grafts remains subject to diverse opinions. Furthermore, much attention has been paid to the logical use of the minimally invasive technique. For example, the roles of minimally invasive direct coronary artery bypass (MIDCAB) and port-access technology have been redefined.

This second edition is an effort to provide the reader with the most advanced knowledge regarding the issues such as those mentioned above from world-renowned experts. To best reflect the current status of arterial grafting worldwide, new contributors have been invited to write in their areas of expertise. I would particularly mention the contribution by these new authors and their colleagues in the second edition: Dr. Bruce Lytle and Joseph Sabik from the Cleveland Clinic; Dr. Hendrick Barner from St. Louis; Dr. Hartzell Schaff from the Mayo Clinic; Dr. Alfred Tector from Milwaukee; Dr. Matthew Slater from Portland; Dr. Piet Boonstra from The Netherlands; Professor Gianni Angelini, Professor David Taggart, and Dr. Jamie Jeremy from the UK; and Professors Masashi Komeda, Masami Ochi, and Tohru Asai from Japan. I would also acknowledge the contribution of my colleagues Professor Anthony Yim, Dr. Song Wan, and Dr. Qin Yang at the Chinese University of Hong Kong. In addition to all the contributors for the first edition, they have made the book more complete.

The successful use of arterial grafts, i.e., the arterial conduit with a diameter of around 2 mm, is largely related to the method of overcoming the vasospasm of the

graft in the perioperative period. With a more advanced understanding of the basic physiology and pharmacology of the arteries and veins used for grafting, this edition provides the newest information on the endothelial function and the method of overcoming vasospasm in the arterial grafts. The advancement of our basic knowledge of myocardial protection is also reflected in this edition.

There are a few chapters for which the original contributors are not contactable due to retirement or other reasons. In these cases where no new contributors could be identified, I did the relevant literature searches and updated the chapter myself. These chapters are „Histology and Comparison of Arterial Grafts Used for Coronary Surgery,“ „Splenic Artery Grafting,“ and „Use of Subscapular-Thoracodorsal Artery for CABG.“ There is no new literature about inferior mesenteric artery grafting and I therefore wrote an update note for the chapter.

For the chapter on the comparison of unilateral and bilateral IMA grafting, after discussion with the original author, I rewrote the chapter with updated information to better reflect the current view.

On the other hand, to best reflect the use of vein grafts in combination with arterial grafts in most surgeons' practice, this edition also includes a chapter on the role of vein grafts in CABG by myself, a chapter on gene therapy for vein graft disease, and a chapter on the prevention of vein graft failure. The use of arterial grafting in reoperative CABG is included by presenting the large experience from the Cleveland Clinic. In the minimally invasive technique of arterial grafting, Dr. Michael Mack has combined his three chapters in the first edition into a new concise one with updated information. Two chapters on port access of CABG have been reduced to one in order to reflect the new trend in this area.

As one of the most pressing and controversial issues in coronary surgery today, the indications and results of coronary intervention and CABG are attracting the attention of all cardiac surgeons and cardiologists. The second edition therefore includes a new chapter on the comparison between coronary intervention and CABG.

This edition also has an added section on quality control of arterial grafting by presenting the method of measuring the blood flow in the arterial graft. Furthermore, to better reflect the American experience at large in arterial grafting, in addition to the new chapter from Cleveland mentioned above on the use of arterial grafts in reoperative CABG, the experience on T-graft and internal thoracic artery-radial artery-T-graft from other centers is described in detail.

I would like to extend my great gratitude to the original contributors of the first edition who remain so in the second. These authors have made great efforts to provide updates to their experience and have kept the book in step with the advancement of science and medicine. They have made the book a valuable addition to the reference library of cardiac surgeons, cardiologists, anesthesiologists, and all other professionals and scientists working in cardiovascular science and medicine.

As I mentioned above, our aim with the second edition is to make this book one of the few to be chewed and digested, as Francis Bacon said, and to make it a pleasure to study and be helpful in practice, as indicated by Confucius. It is up to the reader to judge whether this goal has been fulfilled.

Finally, I am deeply indebted to Dr. Albert Starr for his continual support and encouragement to my work, not to mention that I have been the Director of Cardiovascular Research since 1994 at the Albert Starr Academic Center for Cardiac Surgery, the Providence Heart Institute, Portland, Oregon. I am also extremely grateful to Dr. Denton Cooley for the useful personal communications and for the foreword he warmly wrote for this edition. The secretarial assistance of Miss Ching-Yan Ng is greatly appreciated.

Portland, Oregon, USA
Wuhan and Hong Kong SAR, China

Professor Guo-Wei He

Contents

Foreword by Denton A. Cooley	VII	4 Clinical Classification of Arterial Grafts	
Preface	IX	G.-W. HE, C.-Q. YANG	31
I Biological Characteristics of Arterial Grafts		4.1 Introduction	31
1 Histology and Comparison of Arterial Grafts		4.2 Clinical Classification	31
Used for Coronary Surgery		References	34
J.A.M. VAN SON, F.M.M. SMEDTS, C.-Q. YANG,			
G.-W. HE	3	II Use of Vasodilators for Arterial Grafts	
1.1 Internal Mammary Artery	3	in Coronary Bypass Surgery	
1.2 Right Gastroepiploic Artery	7	5 Pharmacological Studies and Guidelines	
1.3 Inferior Epigastric Artery	8	for the Use of Vasodilators for Arterial Grafts	
1.4 Radial Artery	9	G.-W. HE, C.-Q. YANG	39
1.5 Intercostal Artery	10	5.1 Pharmacological Studies	39
1.6 Comment	11	5.2 Factors Determining the Effects of Vasodilator	
References	14	Substances	42
		5.3 Guidelines for the Use of Vasodilators	
		for Arterial Grafts in CABG	44
		References	44
2 Endothelial Function and Interaction			
Between the Endothelium and Smooth Muscle		III Myocardial Protection During Coronary	
in Arterial Grafts		Bypass Surgery Using Arterial Grafts	
G.-W. HE	17	6 Myocardial Management in Arterial	
2.1 Endothelium-Derived Relaxing Factors	17	Revascularization	
2.2 Endothelium-Derived Contracting Factors	17	B.S. ALLEN, G.D. BUCKBERG	51
2.3 Vasoconstrictors and Vasospasm in Arterial		6.1 Cardioplegic Prerequisites	51
Grafts	17	6.2 Cardioplegic Composition	52
2.4 Vasoconstrictor-Stimulated EDRF Release		6.3 Blood Cardioplegia	52
in Arterial Grafts	19	6.4 Operative Strategy	53
2.5 Endothelium-Dependent Relaxation		6.5 Cardioplegia Pressure	57
and Hyperpolarization in Arterial Grafts	20	6.6 Retrograde Cardioplegia	57
2.6 The Balance Between EDRFs and EDCFs	21	6.7 Specific Issues with all Arterial Conduits	59
References	22	6.8 Reperfusion	59
		6.9 Topical Hypothermia	60
		6.10 Conclusions	61
		References	61
3 Clinical Physiology and Related Biological			
Characteristics		7 Cardiac Protection from the Viewpoint	
G.-W. HE	24	of Coronary Endothelial Function	
3.1 Differences in Biological Characteristics		Q. YANG, G.-W. HE	63
Between Venous and Arterial Grafts	24	7.1 Possible Mechanisms Underlying the Damage	
3.2 Are There Any Differences Among Arterial		of Cardioplegia and Organ Preservation	
Grafts?	24	on Endothelial Function	64
3.3 Biological Characteristics	25		
References	29		

7.2	Influence of Cardioplegic and Organ Preservation Solutions on Individual EDRFs	65	11	Surgical Techniques for Internal Thoracic Artery Grafting	
7.3	Influence of Different Components in Cardioplegic and Organ Preservation Solutions on Endothelial Function	65	S. SEEVANAYAGAM, B. BUXTON	97	
7.4	Effect of Different Additives to Cardioplegic or Organ Preservation Solutions on Endothelial Function	66	11.1	Introduction	97
References		68	11.2	Anatomy	97
IV	Percutaneous Coronary Interventions Versus Coronary Artery Bypass Surgery		11.3	Harvesting	97
8	Needle or Knife? A Comparison Between Percutaneous Coronary Interventions (Including Plain Balloon Angioplasty and Coronary Stenting) and Coronary Artery Bypass Surgery		11.4	Histology	100
D.J. DRENTH, P.W. BOONSTRA	73		11.5	Goals of Arterial Grafting	100
8.1	Introduction	73	11.6	Grafting Strategy	101
8.2	Percutaneous Coronary Interventions	73	11.7	Grafting Techniques	101
8.3	Coronary Artery Bypass Grafting	73	11.8	Beating Heart Bypass Surgery	103
8.4	PCI Versus CABG	74	11.9	Less Invasive Surgical Techniques	103
8.5	Drug Eluting Stents	75	11.10	Conclusions	104
8.6	Revascularization Strategy	76	References	104	
References		76	12	Long-Term Results of Internal Thoracic Artery Grafting	
V	Clinical Choice of Arterial Grafts		J.F. SABIK III, E.D. LOOP	105	
9	Considerations in the Choice of Arterial Grafts		12.1	Introduction	105
G.-W. HE	81		12.2	History	105
9.1	General Condition of the Patient	82	12.3	Patency	105
9.2	Biological Characteristics	82	12.4	Survival	107
9.3	Anatomy of the Coronary Artery	84	12.5	Freedom from Recurrent Ischemic Events	109
9.4	Vessel Match Between the Graft and the Coronary Artery	84	12.6	Conclusions	110
9.5	Technical Considerations	84	References	110	
9.6	Conclusion	84	13	Bilateral Versus Unilateral Internal Thoracic Artery in Coronary Bypass Grafting	
References		84	E. BERREKLOUW, G.-W. HE	113	
VI	Internal Thoracic Artery Grafting		13.1	Introduction	113
10	History of Internal Thoracic Artery Grafting and Alternative Arterial Grafts		13.2	History	113
M. DURAIRAJ, B. BUXTON	89		13.3	Indications for Use of Bilateral ITAs	113
10.1	Early Direct Arterial Revascularization Techniques	90	13.4	Relative Contraindications	114
10.2	Coronary Arteriography	91	13.5	Early Mortality	114
10.3	Saphenous Vein Coronary Artery Bypass	92	13.6	Myocardial Infarction	115
10.4	Internal Thoracic Artery Grafting	92	13.7	Late Results	119
10.5	Expanded Use of the ITA Graft	92	13.8	Postoperative Flow Measurements	123
10.6	Alternative Arterial Grafts	93	13.9	Late ECG-Stress Testing	123
10.7	ITA Grafts and Minimally Invasive Coronary Artery Bypass Grafting	93	13.10	Late Blood Flow Studies	123
10.8	The Future	93	13.11	Late Patency Rates	124
References		94	13.12	Conclusions	125
			References	125	
			14	Left-Sided Myocardial Revascularization with Bilateral Skeletonized Internal Thoracic Artery	
			R. MOHR, A. KRAMER	130	
			14.1	Introduction	130
			14.2	Harvesting and Preparation of the Skeletonized ITA	131
			14.3	Strategies of Left-Sided Arterial Revascularization	132
			14.4	Clinical Results	137
			14.5	Comments	137
			References	138	

15 Free Compared with Pedicled Right Internal Thoracic Arteries for Coronary Artery Bypass Grafting	20.3 History	181
J. TATOULIS, B.F. BUXTON, J.A. FULLER	20.4 Harvesting Technique	184
15.1 Introduction	20.5 Preparation of the Artery	187
15.2 Materials and Methods	20.6 Routing the Pedicle	187
15.3 Indications	20.7 Anastomotic Technique	188
15.4 Surgical Technique	20.8 Perioperative Management	191
15.5 Follow-up	20.9 Conclusion	191
15.6 Results	References	191
15.7 Discussion		
15.8 Conclusion		
References		
VII Radial Artery Grafting		
16 History and Operative Technique	21 The Right Gastroepiploic Artery Graft	
C. ACAR	H. SUMA	193
16.1 History	21.1 Introduction	193
16.2 Preoperative Assessment	21.2 Clinical Results	193
16.3 Operative Technique	References	195
References		
17 Radial Artery Grafting: Clinical Antispastic Protocols	22 Technique and Results for Skeletonized GEA Using the Harmonic Scalpel in Combination with Other Arterial Grafts in Off-Pump Coronary Bypass Surgery	
G.-W. HE	T. ASAI	196
17.1 GWH Protocol (Previously University of Hong Kong Protocol)	22.1 History of GEA Skeletonization	196
17.2 Discussion	22.2 A Technique for Skeletonizing GEA Using the Harmonic Scalpel	197
References	22.3 Results of Skeletonized GEA in Combination with Skeletonized IMA in OPCAB	199
	22.4 Comments	200
	References	200
18 Radial Artery: Clinical Results	IX Inferior Epigastric Artery Grafting	
C. ACAR	23 Inferior Epigastric Artery Grafting: History, Anatomy and Surgical Techniques	
18.1 Early Results	L. BORO PUIG, S. ALMEIDA DE OLIVEIRA	203
18.2 Late Results	23.1 Historical Note	203
18.3 Conclusion	23.2 Inferior Epigastric Artery	203
References	23.3 Anatomy of the Epigastric Artery	203
	23.4 Surgical Technique	204
	23.5 Postoperative Angiography	206
	23.6 Remodeling of the IEA	206
	23.7 Clinical Experience	207
	References	207
19 Angiographic Studies of the Radial Artery Graft	24 Inferior Epigastric Artery Grafting: Clinical Results	
C.A. DIETL	F. DAGENAIS, L.P. PERREAULT, M. CARRIER	208
19.1 Introduction	24.1 Introduction	208
19.2 Patients and Methods	24.2 Indications, Perioperative Mortality and Myocardial Infarction Rate	208
19.3 Surgical Technique	24.3 Morbidity Related to IEA Harvesting	208
19.4 Results	24.4 Patency Rates	209
19.5 Angiographic Studies	24.5 Composite Grafts Using the IEA	210
19.6 Discussion	24.6 Conclusion	210
References	References	211
VIII Gastroepiploic Artery Grafting		
20 Right Gastroepiploic Artery Grafting: History and Operative Techniques		
J. PYM		
20.1 Introduction		
20.2 Anatomy		

X Rarely or Possibly Used Arterial Grafting

25 Splenic Artery Grafting	
B. BLAKEMAN, J. PICKLEMAN, G.-W. HE	215
25.1 Case Report	215
25.2 Technique	215
25.3 Use of the Splenic Artery Under Other Situations	216
25.4 Discussion	217
25.5 Conclusion	217
References	217
26 Use of the Subscapular-Thoracodorsal Artery for Coronary Artery Bypass Grafting	
G.-W. HE, N.L. MILLS	218
26.1 Anatomical Notes	218
26.2 Historic Notes	218
26.3 Harvest of the Subscapular Artery	219
26.4 Cannulation	220
26.5 Clinical Notes	220
26.6 Comment	221
References	222
27 Inferior Mesenteric Artery Grafting	
P. SHATAPATHY, B.K. AGGARWAL	223
27.1 Introduction and Anatomic Considerations	223
27.2 Physiopathologic Considerations	224
27.3 Harvesting of Inferior Mesenteric Artery	225
27.4 Clinical Experience	226
27.5 Closing Comments	226
References	226
28 Ulnar Artery as a Coronary Artery Bypass Graft: Five-Year Experience	
A. NEWCOMB, E. OQUELI, B.F. BUXTON	227
28.1 Introduction	227
28.2 Anatomy	227
28.3 Patterns of Arterial Supply to the Forearm and Hand	228
28.4 Surgical Technique	228
28.5 Results	230
28.6 Discussion	231
References	232
29 Descending Branch of Lateral Circumflex Femoral Artery Grafting	
T.O. TATSUMI, S. MINOHARA, K. KONDOH	233
29.1 Introduction	233
29.2 Anatomy	233
29.3 Surgical Procedure	234
29.4 Results	234
29.5 Comment	235
References	237

30 The Intercostal Artery: An "Ideal" Arterial Graft Awaiting Clinical Application	
L.C.H. JOHN	238
30.1 History	238
30.2 Potential Advantages of Intercostal Arteries	238
30.3 Feasibility Studies	239
30.4 The Future	239
References	240

XI Arterial Grafting Using Complex Grafts

31 Complex Arterial Grafts: Operative Techniques	
A.M. CALAFIORE, M. DI MAURO	243
31.1 Internal Mammary Artery	243
31.2 Right Gastroepiploic Artery	245
31.3 Inferior Epigastric Artery and Radial Artery	245
31.4 Inferior Epigastric Artery	245
31.5 Radial Artery	246
References	246
32 Complex Arterial Grafts: Clinical Results	
A.M. CALAFIORE, M. DI MAURO	248
32.1 End-to-Side	248
32.2 End-to-End	248
32.3 End-to-Side/End-to-End	248
32.4 BIMA Y Graft	249
32.5 Radial Artery	250
32.6 Inferior Epigastric Artery	252
32.7 Conclusion	252
33 Internal Thoracic Artery T-Grafting: Operative Technique and Long-Term Results	
A.J. TECTOR	253
33.1 Introduction	253
33.2 Developments Leading to T-Graft Technique	253
33.3 Advantages of ITA Grafts	253
33.4 Operative Technique	254
33.5 Failure of ITA Grafts	256
33.6 Demographics of T-Graft Patients	257
33.7 Results	257
33.8 Comparison of Results	259
33.9 Comment	259
References	260
34 Internal Thoracic Artery and Radial Artery T-Grafting: Operative Technique and Long-Term Results	
H.B. BARNER	261
34.1 Radial Artery	261
34.2 Technique	261
34.3 Harvest Complications	263
34.4 Hypoperfusion	263
34.5 Results	264
34.6 Conduit Patency	264
34.7 Conclusions	264
References	265

XII Arterial Grafting in Reoperative Coronary Artery Bypass Surgery

35 Role of Internal Thoracic Artery Grafts in Reoperative Coronary Artery Bypass Surgery J.F. SABIK III, B.W. LYTLE	269
35.1 Introduction	269
35.2 Perioperative Risk of Internal Thoracic Artery Grafting at Reoperation	269
35.3 Impact of Patent Internal Thoracic Artery Grafts on Perioperative Risk	271
35.4 Internal Thoracic Artery Grafts and Survival after Coronary Reoperation	273
35.5 Conclusions	274
References	274

XIII Quality Control of Arterial Grafting: Early Detection of Graft Patency and Flow

36 Flow Capacity of Arterial Grafts: Internal Thoracic Artery, Gastroepiploic Artery and Other Grafts M. OCHI	279
36.1 Internal Thoracic Arteries	279
36.2 Studies of Flow Reserve of the ITA	279
36.3 Effect of Competitive Flow on the ITA and Remodeling	280
36.4 Capability of ITA to Respond to Flow Demand	280
36.5 Effect of Skeletonization on the Flow Capacity of the ITA	281
36.6 Right Gastroepiploic Artery	281
36.7 Pressure Characteristics of GEA	281
36.8 Adequate Size of the GEA as a Graft	281
36.9 Effect of Skeletonization on the Flow Capacity of the GEA	283
References	283
37 Intraoperative Graft Evaluation in Coronary Artery Bypass Grafting Using a 15-MHz High-Frequency Linear Transducer: Maintaining the Comprehensive Quality of Coronary Surgery H. NAKAJIMA, M. KOMEDA	285
37.1 Routine Evaluation of Graft, Artery and Anastomosis	285
37.2 Troubleshooting with Anastomosis in OPCAB	286
37.3 Revascularization of Intramuscular Coronary Artery in OPCAB	286
References	288

XIV Role of Venous Grafts in Arterial Grafting

38 Role of Venous Grafts in Combination with Arterial Grafting G.-W. HE	291
38.1 Introduction	291
38.2 Recent Reports on the Long-Term Patency of SVG	291
38.3 Methods to Improve SVG Patency	292
38.4 Use of SVG in Combination with Arterial Grafts	293
38.5 Use of SVG in Minimally Invasive CABG ...	293
38.6 Surgical Strategy and Technique for the Use of SVG	293
References	296
39 Minimally Invasive Saphenous Vein Harvesting for Coronary Artery Bypass Grafting M.S. SLATER	298
39.1 Introduction	298
39.2 Minimally Invasive Techniques for Saphenous Vein Harvest	298
39.3 Limitations of Endoscopic Vein Harvest ...	299
39.4 Evolution and Technique of Endoscopic Technique at Our Institution	301
39.5 Conclusion	301
References	302
40 Novel Strategies for the Prevention of Vein Graft Failure S. WAN, A.P.C. YIM, G.D. ANGELINI, J.Y. JEREMY	303
40.1 Introduction	303
40.2 Mechanisms Underlying Neointima Formation, Graft Thickening and Atherogenesis ..	303
40.3 External Dacron Stents and Biodegradable Sheaths	305
40.4 Endothelin-1 _A Antagonists	306
40.5 Nitroaspirin	308
40.6 Antioxidant Therapy	308
40.7 Concluding Remarks	309
References	309
41 Gene Therapy for Vein Graft Disease D.G. CABLE, H.V. SCHAFF	311
41.1 Gene Therapy	311
41.2 Saphenous Vein Graft Disease	312
41.3 Vein Graft Gene Therapy	313
41.4 Candidate Genes	315
41.5 Future Directions	318
41.6 Conclusion	318
References	318

XV Minimally Invasive Techniques in Arterial Grafting**42 Minimally Invasive Coronary Artery Bypass Surgery and the Role of Arterial Conduits**

M.J. MACK	323
42.1 MIDCAB Procedure	323
42.2 Minimally Invasive CAB (Port Access)	324
42.3 Off-Pump Coronary Artery Bypass Grafting (OPCAB)	324
42.4 Multivessel Off-Pump Limited Access Surgery	327
42.5 Hybrid Procedure	327
42.6 Facilitating Technology for Minimally Invasive Arterial Grafting	327
References	329

43 Off-Pump Coronary Artery Bypass Grafting Using Arterial Grafts

E. BUFFOLO, L.R. GEROLA	331
43.1 Extracorporeal Circulation	331
43.2 When Can Myocardial Revascularization Without Extracorporeal Circulation Be Performed?	332
43.3 Arterial Grafts and Off-Pump Myocardial Revascularization	332

43.4 Operative Technique	333
43.5 Clinical Experience	334
References	335

44 Comparison of the Effect of On-Pump and Off-Pump Coronary Artery Bypass Grafting on Neurological Events

Y. ABU-OMAR, D.P. TAGGART	337
44.1 Introduction	337
44.2 Stroke	337
44.3 Delirium	338
44.4 Cognitive Impairment	338
44.5 Conclusions	339
References	340

45 Closed-Chest Cardiopulmonary Bypass and Cardioplegia for Coronary Artery Bypass Surgery: History and Development

J.I. FANN, T.A. BURDON	342
45.1 Introduction	342
45.2 History and Development	342
45.3 Closed-Chest Cardiac Surgery and Robotics	345
45.4 Conclusions	348
References	348

Subject Index	351

List of Contributors

Yasir Abu-Omar, MB, ChB, MRCS

John Radcliffe Hospital, Oxford, UK

Christophe Acar, MD

Department of Cardiac Surgery, Hôpital La Pitié Salpêtrière, Paris, France

Bhuvnesh Kumar Aggarwal, MS, MCh

Department of Cardiothoracic Surgery, Kasturba Medical College and Hospital, Manipal, India

Bradley S. Allen, MD

Department of Cardiothoracic and Vascular Surgery, The University of Texas Health Science Center at Houston, Memorial Hermann Children's Hospital, Houston, Texas, USA

Gianni D. Angelini, MD, FRCS

Bristol Heart Institute, University of Bristol, Bristol, UK

Tohru Asai, MD, PhD

Department of Surgery, Division of Cardiovascular Surgery, Shiga University of Medical Science, Seta Tsukinowacho, Otsu, Shiga, Japan

Hendrick B. Barner, MD

Forest Park Hospital and the Division of Cardiothoracic Surgery, Washington University School of Medicine, Saint Louis, Missouri, USA

Eric Berreklouw, MD, PhD

Catharina Hospital Eindhoven, Eindhoven, ZA, The Netherlands

Bradford Blakeman, MD

Loyola University Medical Center, Maywood, Illinois, USA

Piet W. Boonstra, MD, PhD, FECTS

Department of Cardiothoracic Surgery, University Medical Center of Groningen, Groningen, The Netherlands

Gerald D. Buckberg, MD

Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

Enio Buffolo

Department of Cardiovascular Surgery, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil

Thomas A. Burdon, MD

Department of Cardiothoracic Surgery, Stanford University School of Medicine, Stanford, California, USA
Veterans Affairs HCS, Palo Alto, California, USA

Brian F. Buxton, MBBS, FRACS

Department of Cardiac Surgery, Austin Hospital, Melbourne, Victoria, Australia

David G. Cable, MD

Cardiovascular Surgery of Alexandria, LLC, Alexandria, Louisiana, USA
Division of Cardiovascular Surgery, Mayo Clinic and Mayo Foundation, Rochester, Minnesota, USA

Antonio Maria Calafiore, MD

Division of Cardiac Surgery, European Hospital, Rome, Italy

Michel Carrier, MD

University of Montreal, Montreal Heart Institute, Montreal, Canada

Denton A. Cooley, MD

Department of Cardiovascular Surgery, Texas Heart Institute, Houston, Texas, USA
University of Texas Medical School at Houston, Houston, Texas, USA

François Dagenais, MD

University Laval, Québec Heart Institute, Québec City, Canada

Sérgio Almeida de Oliveira, MD

Division of Thoracic and Cardiovascular Surgery, Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil

Charles A. Dietl, MD

Department of Surgery, University of New Mexico, Albuquerque, New Mexico, USA

Michele Di Mauro, MD

G. D'Annunzio University, San Camillo de Lellis Hospital, Chieti, Italy

Derk J. Drenth, MD, PhD

Department of Cardiothoracic Surgery, University Medical Center of Groningen, Groningen, The Netherlands

Manoj Durairaj, MS, MCh

Department of Cardiac Surgery, Austin Hospital, Melbourne, Victoria, Australia

James I. Fann, MD

Department of Cardiothoracic Surgery, Stanford University Medical Center, Stanford, California, USA
Veterans Affairs HCS, Palo Alto, California, USA

John A. Fuller, MB, BS, FRACP, FRCP (Edin)

Department of Cardiac Surgery and Cardiology, Epworth Hospital, University of Melbourne, Melbourne, Australia

Luis R. Gerola, MD

Department of Cardiovascular Surgery, Paulista School of Medicine, University of São Paulo, São Paulo, Brazil

Guo-Wei He, MD, PhD, DSc

Department of Surgery, Oregon Health and Science University, Providence Heart and Vascular Institute, Portland, OR, USA

Department of Cardiac Surgery, Wuhan Heart Institute, The Central Hospital, Wuhan, China
Department of Surgery, The Chinese University of Hong Kong, Hong Kong

Jamie Y. Jeremy, PhD

Bristol Heart Institute, University of Bristol, Bristol, UK

Lindsay C.H. John, MBBS, MS, MD, FRCS

Kings College Hospital, Denmark Hill, London, UK

Masashi Komeda, MD, PhD

Department of Cardiovascular Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Keiichiro Kondoh, MD

Department of Thoracic Surgery, Osaka Medical College, Takatsuki, Osaka, Japan

Amir Kramer, MD

Department of Cardiothoracic Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Floyd D. Loop, MD

Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, Lyndhurst, Ohio, USA

Bruce W. Lytle, MD

Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio, USA

Michael J. Mack, MD

Cardiopulmonary Research Science and Technology Institute, Medical City Dallas Hospital, Dallas, Texas, USA

Noel L. Mills, MD

Department of Surgery, Tulane University Medical Center, New Orleans, Louisiana, USA

Seiichiro Minohara, MD

Tatsumi Clinic and Hospital, Ikeda, Osaka, Japan

Raphael Mohr, MD

Department of Cardiothoracic Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Hiroyuki Nakajima, MD

Department of Cardiovascular Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Andrew Newcomb, MD, MBBS

Department of Cardiac Surgery, Austin Hospital, Melbourne, Victoria, Australia

Masami Ochi, MD

Division of Cardiovascular Surgery, Nippon Medical School, Tokyo, Japan

Ernesto Oqueli, MD

Epworth Hospital, Melbourne, Victoria, Australia

Louis P. Perrault, MD

University of Montreal, Montreal Heart Institute, Montreal, Canada

Jack Pickleman, MD

Loyola University Medical Center, Maywood, Illinois, USA

Luiz Boro Puig, MD

Division of Thoracic and Cardiovascular Surgery, Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil

John Pym, MB, BS, FRACS, FRCSC, FACS

Lankenau and Frankford-Torresdale Hospitals and Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Joseph F. Sabik III, MD

Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio, USA

Hartzell V. Schaff, MD

Division of Cardiovascular Surgery, Mayo Clinic College of Medicine, Rochester, Minnesota, USA

Siven Seevanayagam, MBBS, MBBS, FRACS

Department of Cardiac Surgery, Austin Hospital,
Melbourne, Victoria, Australia

Pitambar Shatapathy, MS, MCh, FACS, FIACS

Department of Cardiothoracic Surgery, Kasturba
Medical College and Hospital, Manipal, India

Matthew S. Slater, MD, FACS

Department of Surgery, Division of Cardiothoracic
Surgery, Oregon Health & Science University,
Portland, Oregon, USA

Frank M.M. Smedts, MD, PhD

Department of Pathology, Canisius-Wilhelmina
Hospital, Nijmegen, The Netherlands

Hisayoshi Suma, MD

The Cardiovascular Institute, Roppongi, Minato-ku,
Tokyo, Japan

David P. Taggart, MD, PhD, FRCS

University of Oxford, Oxford, UK
Department of Cardiothoracic Surgery, John Radcliffe
Hospital, Oxford, UK

James Tatoulis, MB, BS, MS, FRACS

Private Medical Centre, The Royal Melbourne Hospi-
tal, University of Melbourne, Melbourne, Australia

Takahiko O. Tatsumi, MD

Tatsumi Clinic and Hospital, Tenjin, Ikeda, Osaka,
Japan

Alfred J. Tector, MD, MS

Midwest Heart Surgery Institute, Aurora St. Lukes
Medical Center, Milwaukee, Wisconsin, USA

Jacques A.M. van Son, MD, PhD

Department of Cardiothoracic Surgery, Catharina
Hospital, Eindhoven, The Netherlands

Song Wan, MD, PhD, FRCS(Eng)

Division of Cardiothoracic Surgery, The Chinese
University of Hong Kong, Prince of Wales Hospital,
Hong Kong, China

Cheng-Qin Yang, MD

Starr Academic Center, Providence Heart and Vascu-
lar Institute, St. Vincent Hospital, Portland, Oregon,
USA

Qin Yang, MD, PhD

Department of Maternal and Fetal Medicine, Oregon
Health and Science University, Portland, Oregon, USA
and Department of Surgery, The Chinese University
of Hong Kong, China

Anthony P.C. Yim, MD, FRCS, FACS, FCCP

Division of Cardiothoracic Surgery, The Chinese
University of Hong Kong, Prince of Wales Hospital,
Hong Kong, China

Biological Characteristics of Arterial Grafts

Histology and Comparison of Arterial Grafts Used for Coronary Surgery

J.A.M. VAN SON, F.M.M. SMEDTS, C.-Q. YANG, G.-W. HE

Expanded use of the internal mammary artery for myocardial revascularization is based on the accumulating data of superior late patency of the internal mammary artery compared with venous conduits [1–9]. The primary consideration that has led to the gradual transition of use of the internal mammary artery as the conduit of choice is its relative freedom from atherosclerosis with follow-up of up to 20 years. Since during the last decade the frequency of coronary revascularization procedures has increased considerably in patients with diseased or absent greater and lesser saphenous veins, alternatives to this arterial conduit have been sought. The right gastroepiploic artery and the inferior epigastric artery have been advocated and used selectively or when traditional conduits are unsuitable or unavailable [10–24]. Although the radial artery has been used in the past as a conduit in myocardial revascularization and has been abandoned because of its high failure rate [25–28], there has been a recent resurgence of its use [29].

During the last 8 years we have performed histologic research on the internal mammary artery, the right gastroepiploic artery, the inferior epigastric artery, and the radial artery and in this chapter we will summarize our findings.

1.1

Internal Mammary Artery

1.1.1

Anatomy

The origin of the internal mammary artery, either right or left, is on the concavity of the subclavian artery, just opposite to the thyrocervical trunk, which is the second branch on the convexity of the subclavian artery (the first branch being the vertebral artery). The internal mammary arteries line the sternum on both sides at a distance of approximately 1–2 cm from the sternal border. The internal mammary arteries are accompanied by a pair of internal mammary veins that unite to form a single vessel, which ascends medial to the artery and ends in the corresponding brachycephalic vein. The internal mammary artery lies on the chondral part of the ribs and is covered by the parietal pleura. Between the

artery and the pleura is a deep fascial plane as far as the third costal cartilage. Below this level the transversus thoracic muscle separates the vessel from the pleura.

With one exception, there is no major difference between the right and left internal mammary arteries. The proximal left internal mammary artery runs very close to the chest wall, whereas on the right side there can be up to 1 cm of connective tissue between the proximal internal mammary artery and the ribs. This may be due to the different anatomy of the subclavian arteries, the left one originating from the aorta and the right one from the innominate artery.

After the proximal medial thymic branch, the internal mammary artery anastomoses with the intercostal arteries beyond each rib until it reaches the sixth intercostal space, where it divides into two major branches. The craniocaudal branch, the superior epigastric artery, enters the sheath of the rectus abdominis muscle through the interval between the costal and sternal attachments of the diaphragm. At first the superior epigastric lies behind the rectus muscle, but then perforates and supplies the muscle and thereby generally anastomoses with the inferior epigastric artery, which originates from the external iliac artery. The musculophrenic artery is directed obliquely downward and laterally, behind the cartilages of the eighth, ninth, and tenth ribs. It perforates the diaphragm near the eighth or ninth costal cartilage, and ends, considerably reduced in size, opposite the last intercostal space. It gives off anterior intercostal branches to the seventh, eighth, and ninth intercostal spaces. Some other branches of the musculophrenic artery course to the lower part of the pericardium, dorsally to the diaphragm, and down to the abdominal muscles.

1.1.2

Histology

1.1.2.1

Morphologic Findings

The internal mammary artery was harvested in 11 individuals (aged 49–83 years; mean age, 67 years) and examined histologically at 1-cm intervals [30]. At the origin of the internal mammary artery, being a transition-

al area between the elastic subclavian artery and the internal mammary artery proper, the media invariably was elastic, containing 8–18 (mean, 10) elastic lamellae, including the internal and external elastic laminae (Fig. 1.1). In 2 individuals the media of the entire internal mammary artery was elastic along its entire length, with a number of elastic lamellae that varied from 8 to 12 (mean, 10). In the other 9 individuals an alternating histological pattern was observed: the first 20–30% of the total length of the internal mammary artery was elastomuscular. In this segment the smooth muscle content in the media prevailed over a number of five to seven (mean, six) elastic lamellae (Fig. 1.2). More downstream in these internal mammary arteries we

observed a rather abrupt transition into an elastic pattern, which continued up to 70–80% of the total length of the internal mammary artery (Fig. 1.3). This elastic segment was composed of 8 to 12 (mean, 9) elastic lamellae (Fig. 1.4). In all nine individuals we observed a second elastomuscular segment with five to seven (mean, six) elastic lamellae, analogous to the proximal one, starting at 70–80% of the total length of the internal mammary artery. In five of these nine individuals this distal elastomuscular segment extended up to the epigastric bifurcation, but in the remaining four it abruptly (at 80–90% of the total length of the internal mammary artery) converted into a muscular pattern with rare (mean, three) elastic lamellae (Fig. 1.5).

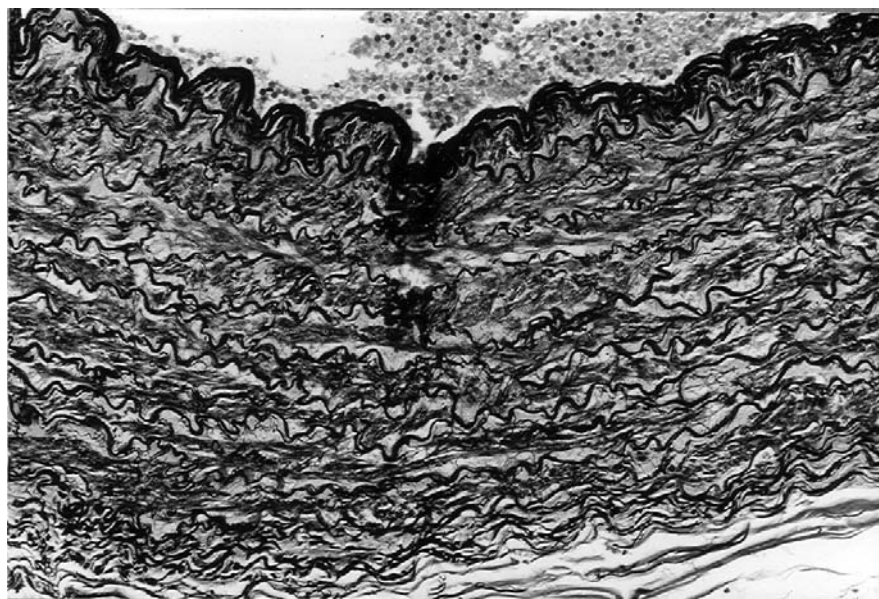


Fig. 1.1. The origin of the internal mammary artery. Note the multiple elastic lamellae

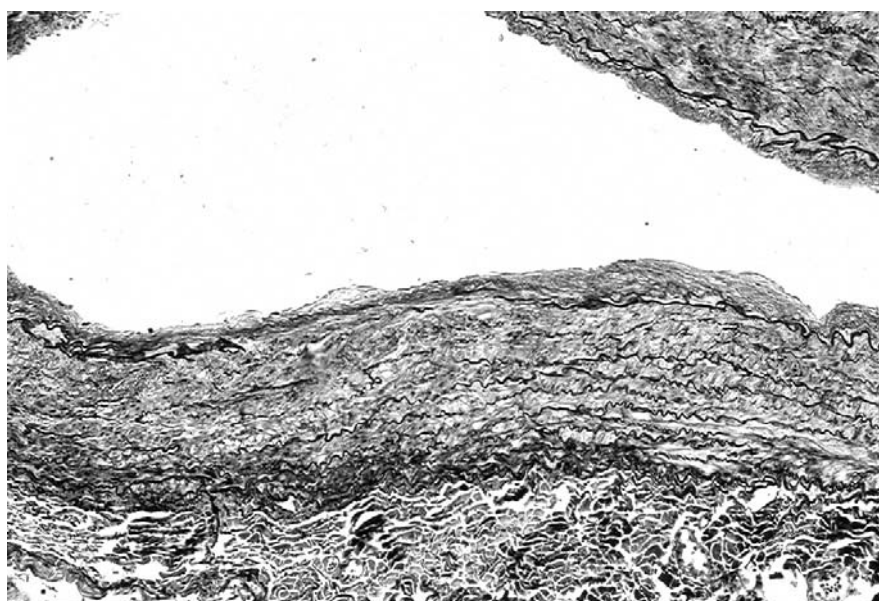


Fig. 1.2. Proximal internal mammary artery. The media is elastomuscular. There is mild intimal hyperplasia

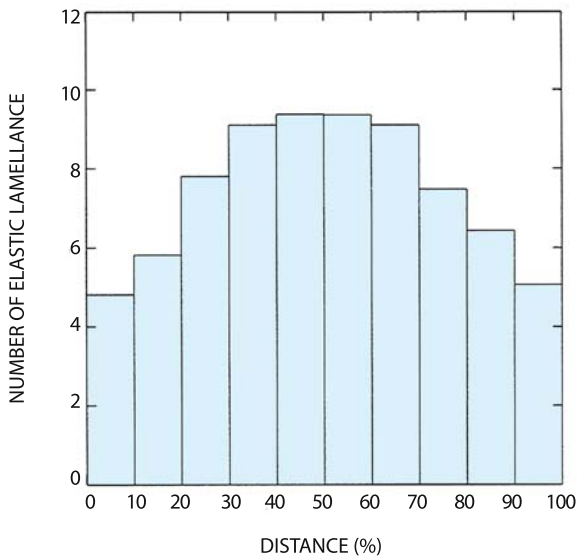


Fig. 1.3. Distribution of the mean number of elastic lamellae in the media of the internal mammary artery along its downstream course

In seven individuals the elastic or elastomuscular patterns in the distal internal mammary artery continued as an elastomuscular pattern in the proximal 1–2 cm of the musculophrenic artery, with a mean number of elastic lamellae of four; more distally the media became muscular (Fig. 1.6). In the other four individuals with a muscular pattern in the distal internal mammary artery, the latter continued into the musculophrenic artery. In all 11 individuals the media of the superior epigastric artery was predominantly muscular.

Quantitative Results. The mean cross-sectional luminal area of the proximal elastomuscular and elastic segments of the internal mammary artery (both 1.9 mm^2) was significantly greater than that of the distal elastomuscular segment of the internal mammary artery (1.2 mm^2) and that of the muscular segments of the musculophrenic artery (0.9 mm^2) and superior epigastric artery (0.7 mm^2) ($p < 0.01$). The mean cross-sectional luminal area of the distal elastomuscular segment of the internal mammary artery (1.2 mm^2) was significantly greater than that of the distal purely muscular segments of the musculophrenic artery (0.9 mm^2) and superior epigastric artery (0.7 mm^2) ($p < 0.01$), whereas that of the latter two did not differ significantly from that of the proximal segments of the musculophrenic and superior epigastric arteries with a muscular media with rare elastic lamellae (1.0 mm^2 and 0.8 mm^2 , respectively). Although the cross-sectional luminal area of the internal mammary artery along its downstream course gradually decreased, this decrease reached statistical significance only beyond the 90% segment. The small luminal diameter of the internal mammary, musculophrenic, and superior epigastric arteries in our study is mainly due to rigor mortis and cross-linking contracture of the vessel wall, caused by fixation in 4% formaldehyde solution.

In the 30–70% segment of the internal mammary artery the number of elastic lamellae (mean, nine) did not vary significantly at the various levels. Obviously, in its primarily elastic segment the number of elastic lamellae was significantly greater than that in the proximal and distal elastomuscular segments of the internal mammary artery (mean, six) ($p < 0.01$). The density of

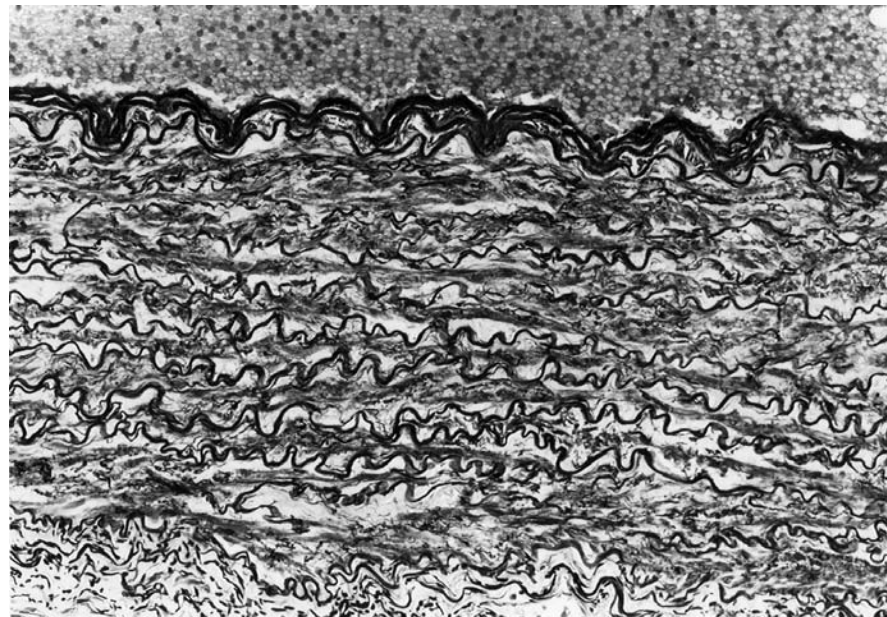


Fig. 1.4. Detail of elastic media at mid level of the internal mammary artery. Note the intact internal elastic lamina and the abundant presence of elastic lamellae. The intima consists of a thin layer of endothelial cells, which in this section, due to fixation artifact, is not attached to the internal elastic lamina

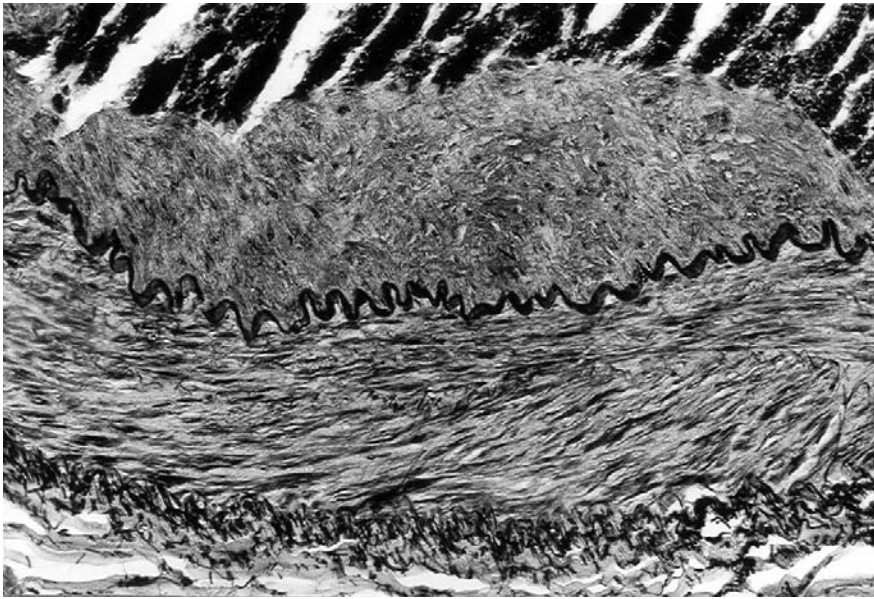


Fig. 1.5. Distal internal mammary artery with a muscular media. Note the considerable degree of intimal hyperplasia

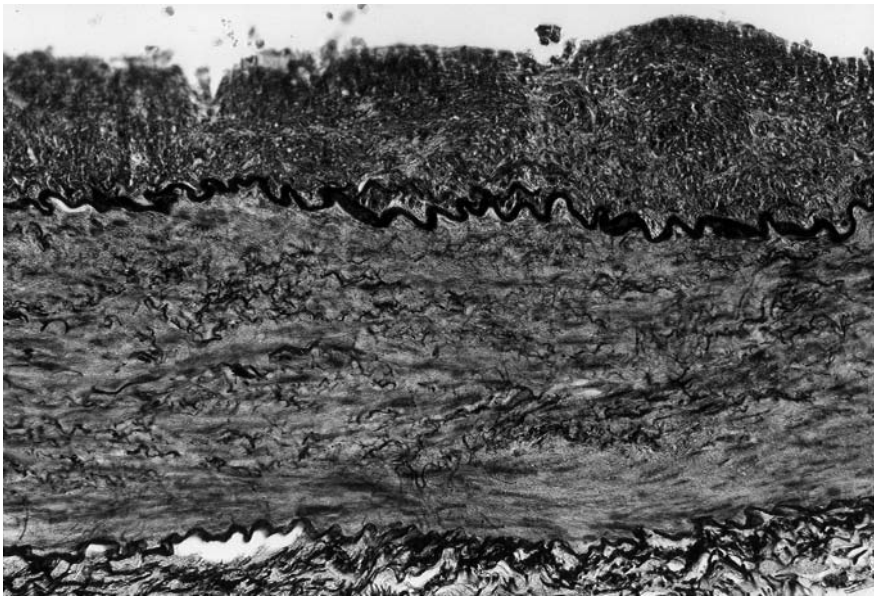


Fig. 1.6. Musculophrenic artery with a muscular media containing rare elastic fibers. There is marked intimal hyperplasia

the elastic lamellae along the downstream course of the internal mammary artery showed a similar pattern.

The absence of elastic lamellae in the media had a profound effect on the degree of intimal hyperplasia: the intima was significantly thicker in the purely muscular segment (25.6% degree of intimal hyperplasia) than in the elastic (16.7%), elastomuscular (15.3%), and muscular (with rare elastic lamellae) (17.5%) segments ($p < 0.01$). Although the degree of intimal hyperplasia varied along the downstream course of the internal mammary artery (being slightly greater in the proximal and distal elastomuscular segments than in the elastic segments), these differences were not signifi-

cant. These data are in agreement with the fact that the number of discontinuities in the circumferential internal elastic lamina increases from the elastic (median, 21; interquartile range, 7) to the elastomuscular (median, 4; interquartile range, 11) and muscular (median, 89; interquartile range, 12) segments [31].

In another morphometric analysis of the internal mammary artery and other arterial conduits we measured a mean combined width of the intima and media in the flaccid internal mammary artery of 350 ± 92 μ m (Table 1.1) [32]. In all instances the vasa vasorum were confined to the adventitia.

Table 1.1. Combined width of intima and media in various arterial conduits and left anterior descending coronary artery^a

Arteries (<i>n</i> = 17)	Width of intima and media ($\pm$ SD) (μ m)	
	Fixation in flaccid state	Fixation at pressure of 100 mmHg
LAD	320 $\pm$ 63	
IMA	350 $\pm$ 92	313 $\pm$ 209
RGEA	291 $\pm$ 109	303 $\pm$ 100
IEA	249 $\pm$ 87	284 $\pm$ 136
RA	529 $\pm$ 52	

LAD left anterior descending coronary artery, IMA internal mammary artery, RGEA right gastroepiploic artery, IEA inferior epigastric artery, RA radial artery

^a Kruskal-Wallis analysis of variance

1.2

Right Gastroepiploic Artery

1.2.1

Anatomy

The right gastroepiploic artery is the larger of the two terminal branches of the gastroduodenal artery, the other being the superior pancreaticoduodenal artery. The right gastroepiploic artery passes from right to left along the greater curvature of the stomach at a somewhat variable distance from the border of the organ. It lies between the two layers of the gastrocolic ligament or the ventral two layers of the greater omentum when these are not adherent to the colon. It gives off a large ascending pyloric branch near its origin and at its termination usually anastomoses with the left gastroepiploic branch of the splenic artery. It supplies a number of ascending gastric branches to the stomach and descending branches to the greater omentum.

1.2.2

Histology

In a histological study of the gastroduodenal and right gastroepiploic arteries, harvested in 28 patients (mean age 73.2 years), the former demonstrated mild to moderate intimal hyperplasia (Fig. 1.7) [33]. Its thickness in the immediate vicinity of the origin of the right gastroepiploic artery was highly variable: 95 $\pm$ 107 μ m. The media of the gastroduodenal artery was muscular with rare dispersed elastic fibers; its thickness was 395 $\pm$ 85 μ m.

The mean luminal diameter of the right gastroepiploic artery was 2.7 $\pm$ 0.3 mm at its origin, 2.2 $\pm$ 0.4 mm at 10 cm, and 1.8 $\pm$ 0.5 mm at 15 cm. The right gastroepiploic artery generally showed mild intimal hyperplasia at its origin (intimal thickness 50 $\pm$ 49 μ m), with a gradually decreasing degree of intimal hyperplasia along its course (distal intimal thickness, 10 $\pm$ 17 μ m) (p = 0.003). The media of the right gastroepiploic artery was muscular with rare dispersed elastic fibers (Fig. 1.8). The thickness of the media varied from 380 $\pm$ 116 μ m at the origin of the right gastroepiploic

Table 1.2. Combined width of intima and media of the right gastroepiploic artery at its proximal, mid, and distal segments

Layer	Width (μ m) ^a			<i>p</i> Value ^b
	Proximal	Mid	Distal	
Intima	58.9 $\pm$ 41	37.3 $\pm$ 22	40.8 $\pm$ 33	NS
Media	245.9 $\pm$ 107	253.7 $\pm$ 103	187.1 $\pm$ 38	NS

NS not significant

^a Data are shown as the mean $\pm$ standard deviation

^b Student's *t*-test

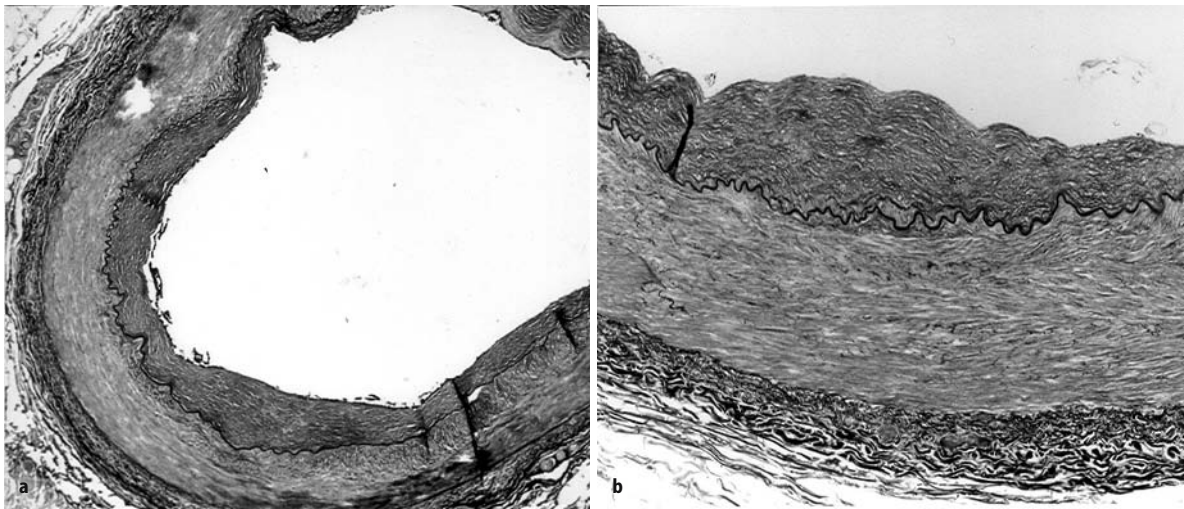


Fig. 1.7a, b. Gastroduodenal artery at origin of the right gastroepiploic artery. **a** Overview; **b** detail showing moderate intimal hyperplasia and muscular character of the media

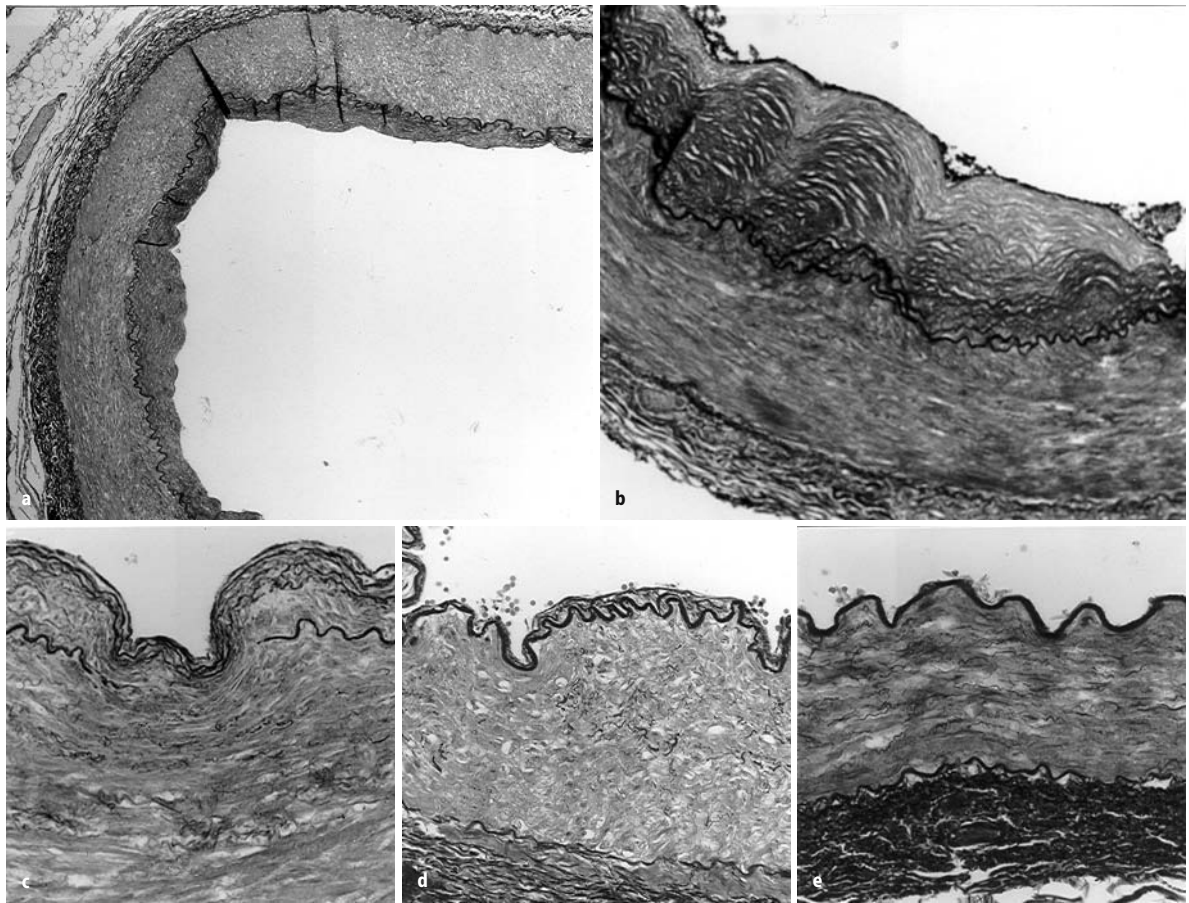


Fig. 1.8a–e. Right gastroepiploic artery. **a** Overview and **b** detail at origin from the gastroduodenal artery; **c** at 1 cm; **d** at 9 cm; and **e** at 18 cm. Note mild intimal hyperplasia **a** with focal moderate hyperplasia **b** at origin of the artery, decreasing intimal hyperplasia from proximal to distal, and muscular character of the media

artery to $155 \pm 70 \mu\text{m}$ distally ($p = 0.0001$). The number of discontinuities in the circumferential internal elastic lamina was rather constant, varying from 86 ± 30 at the origin to 93 ± 29 at 5 cm, and 58 ± 17 distally ($p = 0.79$). The vasa vasorum were confined to the adventitia.

1.3

Inferior Epigastric Artery

1.3.1

Anatomy

The inferior epigastric artery (IEA) arises from the medial side of the external iliac artery just proximal to the inguinal ligament, and at first lies in the midst of the extraperitoneal tissue at the medial side of the abdominal inguinal ring, in intimate relation with the posterior wall of the inguinal canal. The ductus deferens, as it enters the abdomen, hooks around the lateral side of the artery. Accompanied by its satellite veins, the inferior epigastric artery ascends obliquely superiorly and me-

dially toward the umbilicus; after piercing the transversalis fascia, it enters the rectus compartment by passing in front of the linea semicircularis (semilunar fold of Douglas). It then pursues a cephalad vertical course. Grossly demonstrable direct arterial communications between the superior and inferior epigastric arteries may exist in approximately 40 % of cases [34].

1.3.2

Histology

In a histological study of the inferior epigastric artery harvested in 28 individuals (mean age, 73.2 years), the mean luminal diameter of the inferior epigastric artery was $2.0 \pm 0.4 \text{ mm}$ at its origin, $1.9 \pm 0.5 \text{ mm}$ at 10 cm, and $1.1 \pm 0.5 \text{ mm}$ at 15 cm. At all three levels, the luminal diameter of the inferior epigastric artery was significantly smaller than that of the right gastroepiploic artery ($p < 0.05$). In contrast to the findings in the right gastroepiploic artery, there was substantial intimal hyperplasia in the first 1-cm segment of the inferior epigastric artery (intimal thickness, $134 \pm 131 \mu\text{m}$)

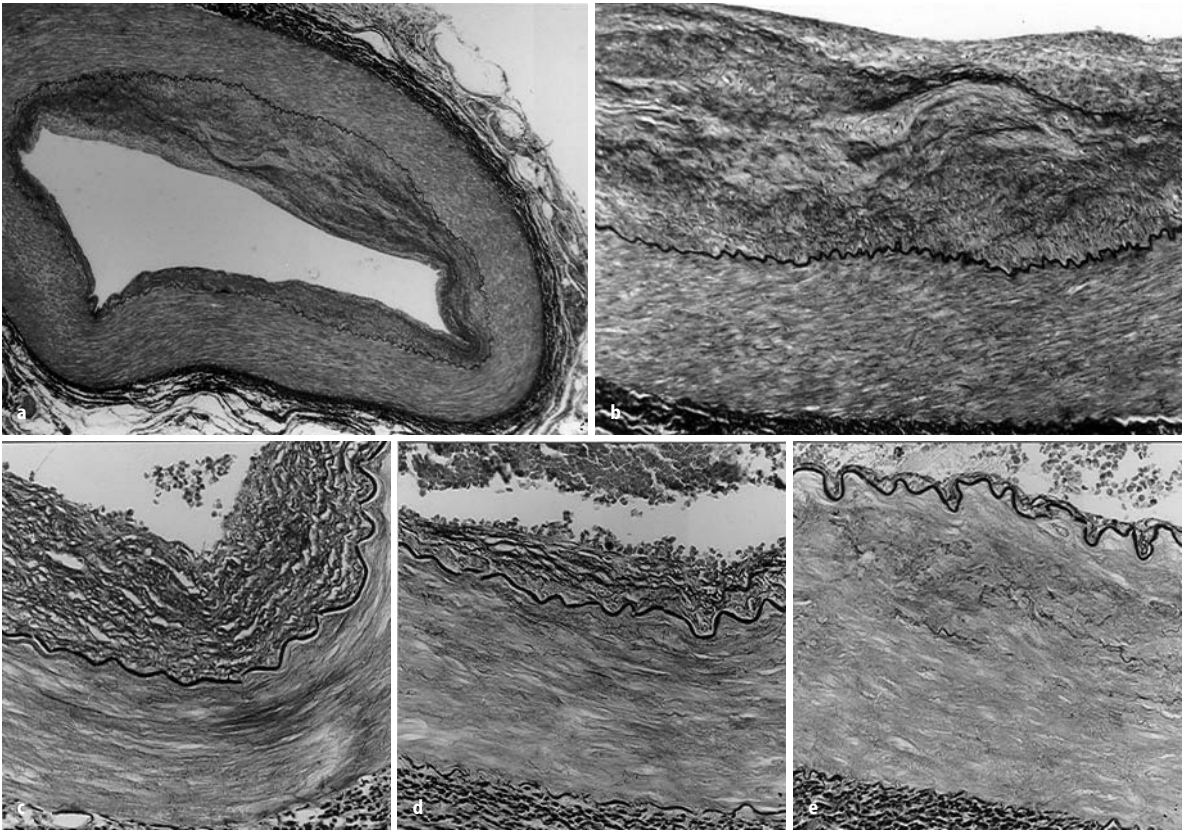


Fig. 1.9a–e. Inferior epigastric artery. **a** Overview and **b** detail at origin from the external iliac artery; **c** at 1 cm; **d** at 8 cm; and **e** at 16 cm. Note severe intimal hyperplasia in the first 1-cm segment, gradually decreasing degree of intimal hyperplasia beyond the first 1-cm segment, and muscular character of the media

($p=0.01$); the width of the intima decreased to $57 \pm 78 \mu\text{m}$ at 1 cm and then gradually decreased to trivial values distally ($p=0.01$) (Fig. 1.9). The media of the IEA was muscular with rare dispersed elastic fibers. The thickness of the media varied from $316 \pm 86 \mu\text{m}$ at 1 cm to $165 \pm 70 \mu\text{m}$ distally ($p=0.0001$). The number of discontinuities in the circumferential internal elastic lamina was rather constant and varied from 82 ± 25 at 3 cm to 35 ± 11 distally ($p=0.039$). In all instances, the vasa vasorum were confined to the adventitia.

1.4

Radial Artery

1.4.1

Anatomy

Opposite the neck of the radius, approximately 1 cm below the bend of the elbow, the brachial artery terminates in two branches, the radial and ulnar arteries. The radial artery is smaller in caliber than the ulnar artery. The radial artery passes along the radial aspect of the forearm to the wrist. The proximal part of the artery is covered by the belly of the brachioradialis muscle,

while the rest of the artery is superficial, being covered only by skin and the superficial and deep fasciae. The radial artery has numerous collateral branches, particularly in its distal segment. The vessel is accompanied by a pair of veins throughout its whole course.

1.4.2

Histology

In a histological study of the radial artery, harvested in 11 individuals (mean age 64 years), the media was purely muscular (Fig. 1.10) [32]. A mild to moderate degree of intimal hyperplasia was observed. The mean number of discontinuities in the circumferential internal elastic lamina of the radial artery (45 ± 28) was similar to that found in the elastomuscular segments of the internal mammary artery. The mean width of the intima and media of the flaccid radial artery was $529 \pm 52 \mu\text{m}$ (Table 1.1). The vasa vasorum were confined to the adventitia.

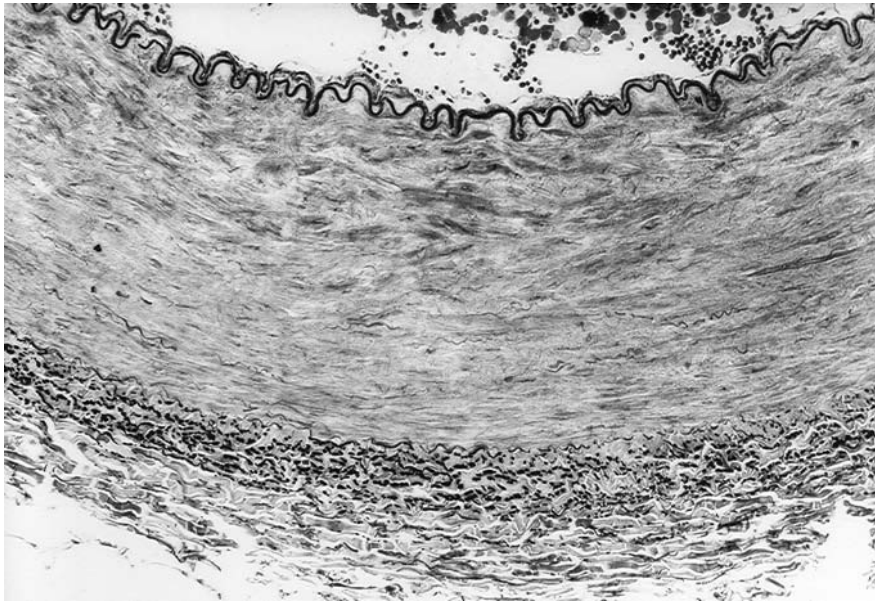


Fig. 1.10. Radial artery. Note the width of the muscular media



Fig. 1.11. Proximal intercostal artery. Note the multiple elastic lamellae in the media

1.5 Intercostal Artery

The potential suitability of the intercostal artery as a conduit in myocardial revascularization was assessed [35]. In 11 patients three combinations of histological patterns were observed along the course of the fourth to ninth intercostal arteries: a proximal elastic segment (Fig. 1.11) followed by subsequent elastomuscular (Fig. 1.12) and muscular segments ($n=3$) (Fig. 1.13), a proximal elastomuscular segment with the remainder of the artery being muscular ($n=6$), and a completely

muscular pattern ($n=2$). The mean luminal diameter of the fifth intercostal arteries varied from 1.4 ± 0.3 mm at the origin to 0.9 ± 0.2 mm at 30 cm. The mean intimal thickness at these locations was 54 ± 38 mm and 25 ± 16 mm, respectively, and the mean thickness of the media was 205 ± 38 mm and 70 ± 45 mm, respectively. The histological findings, mean luminal diameter, and mean diameter of the intima and media were similar in the intercostal arteries other than the fifth. An anatomical study concluded that it is feasible to use the intercostal artery as an in situ graft in myocardial revascularization [36].

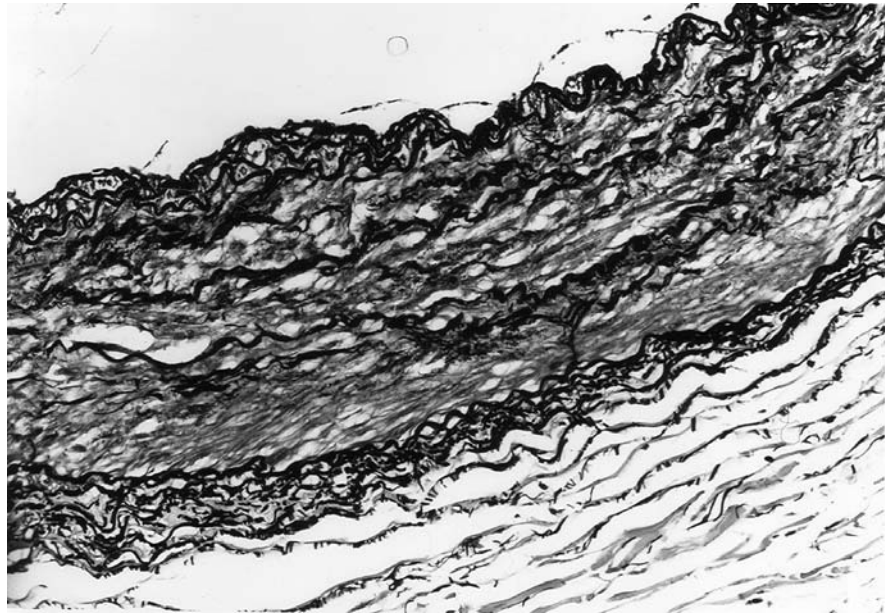


Fig. 1.12. Mid segment of intercostal artery. The media is elastomuscular

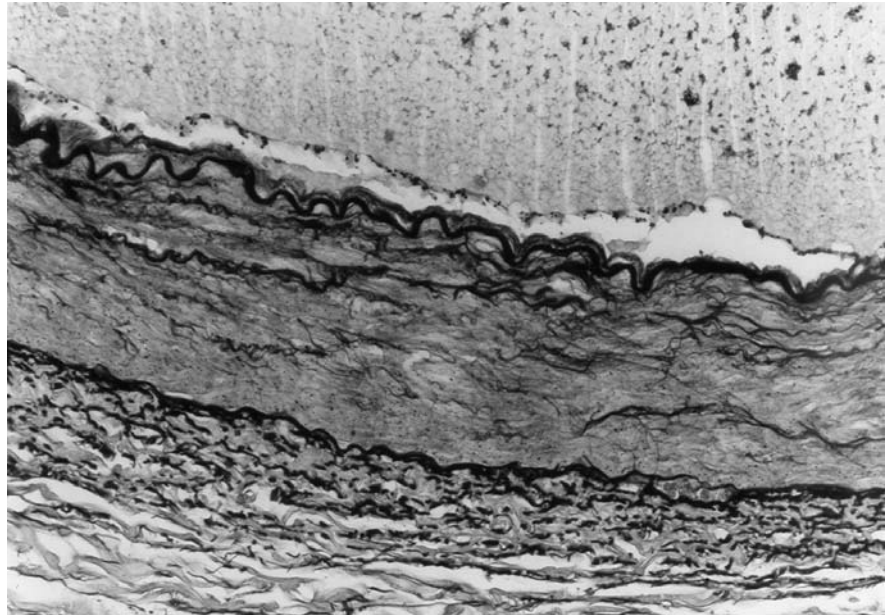


Fig. 1.13. Distal intercostal artery. The media is muscular

1.6

Comment

1.6.1

General Considerations

Over the long term, there is a striking difference in the late development of atherosclerosis in internal mammary artery bypass conduits compared with venous conduits. Comparison of internal mammary artery and vein graft patency reveals a highly significant difference at every interval [7]. Accelerated vein graft closure because of progressive intimal hyperplasia and athero-

sclerosis begins in the fifth year and approximates 5% per year, with a 10-year patency rate varying between 41% and 56% (3). In contrast, the 10-year patency rate of the internal mammary artery has been reported to be greater than 80% [3, 7]. It is intriguing that the internal mammary artery, a vessel comparable in cross-sectional diameter to the coronary artery and acclimated to the same biochemical environment, has such a low incidence of atherosclerosis. Although the cause of the apparent protection of the internal mammary artery from intimal thickening and atherosclerosis remains obscure, a few conclusions can be made on the basis of

our studies and accumulated evidence from research in vascular pathology.

Histological research has established that the first stage of intimal thickening is caused by invasion of smooth muscle cells from the media through the fenestrated internal elastic lamina [37]. In the first decade of life this intimal thickening can already be observed. Sims [38, 39] pointed out that the internal elastic lamina has a key role in arterial wall structure. His observations suggest that the occurrence of discontinuities in the internal elastic lamina provokes early and progressive intimal hyperplasia. Stimuli that trigger smooth muscle cell proliferation are most likely complex and may include leakage of blood constituents and exertion of stress forces on the smooth muscle cells [40]. Operation of these processes over a long period may contribute to progressive intimal hyperplasia. If, as the accumulated evidence suggests, damage to the internal elastic lamina in the presence of smooth muscle cells in the media has a determining role in the initiation of intimal thickening, as a result of the proliferation of smooth muscle cells from the media, it is intriguing to consider that elastic arteries may be less prone to intimal hyperplasia than muscular arteries. In the former, intimal hyperplasia develops at a considerably delayed rate because proliferative smooth muscle cells are present only to a moderate extent. In addition, the multiple elastic lamellae and the internal elastic lamina form barriers to their invasion. Moreover, elastin, the basic component of the elastic tissue of the media, is a bradytrophic, relatively inert tissue with a low metabolic rate. The media of the elastic artery therefore has a lower intrinsic demand for oxygen and substrates than the media of the muscular artery. Also, the abundant lymphatic drainage as present in the internal mammary artery may delay intimal hyperplasia [41].

In our histological studies we showed that there may be a correlation between the absence of elastic lamellae in the media and an increased number of discontinuities in the internal elastic lamina and, as a potential result of this, increased intimal thickening [30, 32]. The intima was significantly thicker in the purely muscular segments of the musculophrenic and superior epigastric arteries than in the internal mammary artery. Although one may argue that these findings may be coincidentally related but not causally, similar findings are reported by Sims and Gavin [42] in a comparative histological study between the muscular coronary artery and the primarily elastic internal mammary artery, in which the number of discontinuities in the internal elastic lamina and the degree of intimal thickening were significantly greater in the former vessel. Based on their and our observations we conclude that elastic lamellae in the media may protect against the occurrence of discontinuities in the internal elastic lamina and, secondarily, against intimal thickening, even if the

number of lamellae is small. The study by Sims and Gavin [42] also suggests that gaps in the internal elastic lamina allow smooth muscle cells of the media to proliferate into the intima and that the rate of this growth reflects the response of medial smooth muscle cells to tension on the arterial wall. Other studies by Sims [43, 44] confirm the structural importance of the internal elastic lamina and its relationship to intimal thickening. Research in vascular pathology has shown that medial smooth muscle cells are mesenchymal cells capable of changing from a contractile to a synthetic type in response to damage of the internal elastic lamina and increasing tangential tension on the vessel wall [45]. This process leads to active cell division and synthesis of collagen, elastin, and proteoglycan matrix [46, 47]. After penetration from the media into the intima, the proliferating smooth muscle cells produce elastin, often as a coherent reduplicated internal elastic lamina, which can be seen as single or multiple thin sealing layers on the luminal aspect of the defective internal elastic lamina. This phenomenon was frequently observed in our specimens, especially in arteries with a purely muscular media. Almost invariably such repair is imperfect, and with the passage of time, breakdown of the reduplicated internal elastic lamina occurs, leading to serious impairment of attachment of endothelial cells, cell loss, and the development of bare areas. Such bare areas may enhance the infiltration of macromolecules of all sizes, including lipoproteins, and cells of the circulating blood, thus accelerating the development of atherosclerotic lesions [48, 49].

Due to the effect of pulsatile stress on the proliferation of smooth muscle cells from the media into the intima, the rate of intimal thickening may be enhanced in the central aorta and its branches in comparison with the internal mammary artery, in which the hemodynamics are less vigorous [50, 51]. Such proliferative smooth muscle cell response has been observed in systemic and pulmonary hypertension and in the culture of medial cells from hypertensive animals and from experimental atherosclerosis [52–55]. We observed a considerably greater degree of intimal thickening in the subclavian artery and the first centimeter of the internal mammary artery than in the remainder of it.

The findings as presented in our studies may have implications with regard to selection of the anastomotic site in the internal mammary artery. We observed a considerable interindividual variability with regard to the extent of a primarily elastic media in the internal mammary artery. In seven patients the distal segment of the internal mammary artery was either elastic or elastomuscular, whereas in four patients the distal 10–20% segment was muscular with rare elastic lamellae. These findings suggest that, based on the assumption that use of an elastic or elastomuscular conduit is superior to use of a primarily muscular one in myocar-

dial revascularization, it may be beneficial not to use the distal 10–20% segment of the internal mammary artery. This strategy has the additional advantage that the internal mammary artery cross-sectional luminal diameter proximal to or at the 80–90% level may better match the diameter of the coronary artery than the more distal segment. Selection of the anastomotic site in the musculophrenic or superior epigastric arteries is not encouraged because of the potentially increased risk of intimal thickening and the significantly smaller luminal diameter of these vessels.

1.6.2

Internal Mammary Artery

To expand the benefits of the elastic and elastomuscular internal mammary artery, the shortest possible route to the heart should be established [56–59]. For the same reason bilateral grafting with the internal mammary artery may be beneficial [60–62]. To gain additional length of the internal mammary artery, transection of the pleura and fascia beneath it may be a valuable technique [63]. However, we do not favor its complete or partial skeletonization, as advocated by Sauvage and associates [60] and Keeley [64], respectively, because this technique has an increased risk of iatrogenic disruption of the internal elastic lamina. This may be especially deleterious in segments with a high muscular content because it may provoke enhanced intimal thickening [65].

A reported patency rate of free, pedicled internal mammary artery grafts approximating that of in situ grafts [66] is consistent with our supposition that the intima and media of the nondiseased internal mammary artery are nourished entirely from the lumen. Therefore, any discrepancy in patency rate between in situ and free internal mammary artery grafts may be attributable primarily to the proximal anastomosis.

1.6.3

Right Gastroepiploic Artery

The number of discontinuities in the internal elastic lamina in the muscular right gastroepiploic artery is greater than that in the elastic segments of the internal mammary artery [33]. This observation probably reflects the absence of a protective effect of elastic lamellae in the media against the development of discontinuities in the internal elastic lamina in the former. Therefore, we believe that some skepticism toward the long-term patency of the right gastroepiploic artery is warranted, especially if this conduit is used as a free graft. The muscular character of the media of the right gastroepiploic artery may find expression in an increased vulnerability toward intimal thickening and, ultimately, atherosclerosis of the former once its wall is exposed

to the forceful mechanical stretching of the central aortic circulation (if used as a free graft) and (to a lesser extent) the coronary circulation. Thus, although Suma and associates [67, 68] and we found only a mild to moderate degree of intimal thickening in the right gastroepiploic artery, this finding must be interpreted with caution, because it reflects the situation at the time of harvesting of the artery in its natural environment. Future clinical studies with regard to the long-term patency rate of the right gastroepiploic artery as a coronary artery bypass graft will prove whether our skepticism is justified or not.

1.6.4

Inferior Epigastric Artery

The number of discontinuities in the internal elastic lamina of the inferior epigastric artery is similar to that of the right gastroepiploic artery and elastomuscular segments of the internal mammary artery. Based on the lower elastic content of the media of the inferior epigastric artery as compared to the internal mammary artery, we hypothesize that the former may have an increased tendency toward intimal thickening. Although early patency rates of the inferior epigastric artery ranging from 88% to 97% have been reported [20, 22, 23], based on our observations, we predict less superior long-term patency rates of this arterial conduit.

A study by Perrault and coworkers [69] who performed immediate postoperative angiographic evaluation in 14 patients who had received one inferior epigastric artery graft each to the right coronary artery, a marginal circumflex coronary artery, and a diagonal coronary artery, showed that only eight grafts (57%) were patent. Although the less superior results in this report may partially have been due to the technical learning curve, a word of caution is needed against indiscriminate use of the inferior epigastric artery in myocardial revascularization until satisfactory long-term patency rates of this conduit have been established.

In a study of ours not presented above [70], we did a morphometric comparison between the right gastroepiploic and inferior epigastric arteries. We reported only mild to moderate intimal thickening in the gastroepiploic artery (GEA) its natural state. Based on our results and those of previous studies, we hypothesize that although the muscular character of the media of the GEA may increase its vulnerability to intimal thickening (as compared with the primarily elastic IMA), the development of intimal hyperplasia may be slow – following a pattern that approximates that of the GEA in its natural environment – if it is used as an in situ graft and thus is protected by retention in its usual physiologic environment. This hypothesis is corroborated by the clinical studies [15]. In this study, we observed that

at its origin, the intima of the IEA is significantly thicker ($175 \pm 131 \mu\text{m}$) than that of the GEA in the corresponding segment ($64 \pm 50 \mu\text{m}$) ($p < 0.01$). Beyond 1 cm, there was only low-grade intimal hyperplasia in the IEA. This finding leads us to conclude that it may be better not to use the origin of the IEA because of the high likelihood of substantial intimal hyperplasia in this segment.

1.6.5

Radial Artery

Reports from the 1970s have unanimously condemned further use of the radial artery as a conduit for myocardial revascularization on the basis of an alarmingly high early occlusion rate [25–28]. It may be true that the observed discrepancy in early patency between the previous and current experience with the radial artery conduit [29] may partially have been caused by accelerated intimal hyperplasia as a result of dilation of the vessel with graduated probes and by stripping of the vessel of surrounding tissue in the past. Such focal damage, which is more likely to occur in muscular conduits such as the radial artery than in elastic segments of the internal mammary artery, may trigger a cascade of events and may ultimately enhance progressive intimal thickening [31]. Vasospasm is also significantly related to the abandoned use of this conduit in 1970s (see Chapter 9 and 17).

In our studies we measured a mean width in the media of the radial artery of approximately 500 mm, as opposed to 330 mm for that of the internal mammary artery, 280 mm for that of the right gastroepiploic artery, and 240 mm for that of the inferior epigastric artery. In addition, nutrition of the thick media of the radial artery is mainly through diffusion from the lumen, as we did not observe any penetration of vasa vasorum into its media. Although the thick media of the radial artery may be advantageous with regard to ease of performance of the proximal anastomosis (as opposed to the technically more challenging proximal anastomosis when the internal mammary artery and especially the right gastroepiploic and inferior epigastric arteries are used as free grafts), it may also predispose the conduit to a potentially greater degree of ischemia (and potentially fibrosis), especially in the outer layer of its media. Because the right gastroepiploic and inferior epigastric arteries have a considerably thinner media, a less critical relationship exists between metabolic demand and supply of the media, and therefore the potential for ischemia in these vessels may be less.

In addition, we have found a considerable number of discontinuities in the internal elastic lamina of the radial artery harvested in its natural environment, with mild to moderate intimal hyperplasia. Based on these findings and the presence of a thick muscular media,

we think that the potential for intimal hyperplasia may be considerably more pronounced in the radial artery conduit than in the internal mammary artery conduit, which has the protective effect of multiple elastic lamellae in its media. This hypothesis was proven correct in the internal mammary artery, the elastic and elastomuscular segments of which had significantly less intimal thickening than the muscular superior epigastric and musculophrenic arteries.

A second major concern regarding use of the radial artery as a conduit in myocardial revascularization is the potentially deleterious effect on the vascular supply of the forearm and hand, which must not be underestimated. The occurrence of claudication in the hand and (transitory) dysesthesia of the thumb in patients in whom the radial artery was used as a conduit in myocardial revascularization has been reported [71]. In the case of thromboembolism or injury of the ulnar artery, major catastrophes may ensue. In view of these complications, the radial artery is much less dispensable an artery than are the internal mammary, right gastroepiploic artery, and inferior epigastric arteries.

In view of the potentially serious drawbacks of the radial artery as a conduit in myocardial revascularization, use of bilateral internal mammary arteries or, alternatively, the right gastroepiploic or inferior epigastric arteries should be emphasized, rather than use of the radial artery, which in our opinion should not be used as a conduit of primary choice.

In summary, arterial grafts have similarities and differences in structure and histology. The structural differences may account for the different biological behavior such as long-term patency rates. Careful choice of optimal arterial grafts is critical in the success of arterial grafting. The details of the functional assessment of arterial grafts and the clinical choice will be introduced in separate chapters.

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Endothelial Function and Interaction Between the Endothelium and Smooth Muscle in Arterial Grafts

G.-W. HE

2.1 Endothelium-Derived Relaxing Factors

The vascular endothelium was once thought to be a simple line-up for the intima in the internal lumen of the vessel. The discovery of endothelium-derived vasoactive substances [1, 2] opened a new era in the understanding of the complex function of the vascular endothelium. In general, endothelium is now known (1) to modulate vascular tone by deriving a number of vasoactive substances; (2) to play a role in antiplatelet aggregation and antithrombus formation; and (3) to have an antiatherosclerotic effect. Endothelium-dependent relaxation is particularly important in maintaining an adequate vascular tone. Endothelium-dependent relaxation is known to be the effect of a variety of different endothelium-derived relaxing factors (EDRFs). These are endothelium-derived nitric oxide (NO) [3, 4], prostacyclin (PGI_2) [1], and endothelium-derived hyperpolarizing factor (EDHF) [5–8]. These relaxing factors induce vasodilatation through different mechanisms.

PGI_2 is the first defined relaxing factor derived from endothelium. When activated by stimuli, the enzyme phospholipase A_2 in endothelial cells converts membrane phospholipids to arachidonic acid that subsequently metabolize to PGI_2 , thromboxane A_2 , and several other prostaglandins (PGE_2 , $\text{PGF}_{2\alpha}$, PGD_2) through the action of cyclooxygenase (COX). The vasorelaxation caused by PGI_2 is mediated by the rise of cyclic 3', 5'-adenosine monophosphate (cAMP) [9] that leads to the extrusion of Ca^{2+} from the cytosol [10] and the decreased sensitivity of the contractile apparatus to Ca^{2+} [11]. The relaxation may involve the Ca^{2+} -independent mechanism [12] and membrane hyperpolarization of smooth muscle cell through potassium (K^+) channels.

NO is synthesized from the amino acid L-arginine by nitric oxide synthase (NOS). There are at least two major NOS isoforms. One is expressed constitutively in neurons and vasculature, is involved in cell communication and is activated by an increase in intracellular calcium. The other isoenzyme exists in macrophages to participate in host defense and is not normally found in endothelial cells or vascular smooth muscle unless induced by cytokines [13]. NOS oxidizes L-arginine to

form NO and citrulline [14]. In the vascular system, the endothelium-derived NO diffuses from the endothelial cell and acts on the underlying smooth muscle cell layer. The subsequent upregulation of cyclic 3', 5'-guanosine monophosphate (cGMP) in smooth muscle results in the activation of cGMP-dependent protein kinase that leads to vasorelaxation [15]. Several types of K^+ channels are involved in NO-mediated hyperpolarization – ATP-sensitive K^+ (K_{ATP}) channels [16] and calcium-activated K^+ (K_{Ca}) channels [17] in a cGMP-dependent manner, K_{Ca} channels by direct activation [18], and the cGMP-independent stimulation of Na^+ - K^+ -ATPase [19].

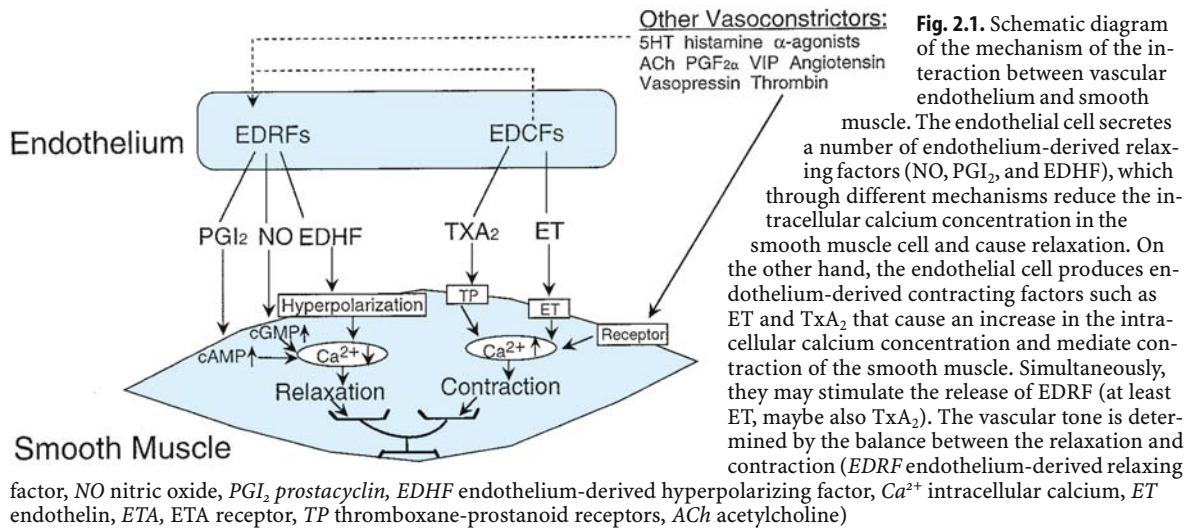
In contrast to EDNO and PGI_2 , the nature of EDHF has not been finally determined, although several substances including epoxyeicosatrienoic acids (EETs), anandamide, K^+ , H_2O_2 , citrulline, NH_3 and ATP have been suggested to be EDHF in certain vasculatures [20]. EDHF induces vascular smooth muscle relaxation via hyperpolarization of the smooth muscle cells [5–8], which involves calcium-activated K^+ channels [8]. However, all of these EDRFs are released in response to the increase of intracellular (cytosolic free) calcium concentration in the endothelial cell [7]. The actions of these EDRFs are illustrated in Fig. 2.1.

2.2 Endothelium-Derived Contracting Factors

In addition, endothelium derives a number of contracting factors (endothelium-derived contracting factor, EDCF [21]) such as TxA_2 and endothelin. These EDCFs are strong vasoconstrictors. They contract the vascular smooth muscle through the corresponding receptors.

2.3 Vasoconstrictors and Vasospasm in Arterial Grafts

There are a large amount of vasoactive substances that are related to the modulation of the vascular tone. Some of them may be more important in a particular



circulation such as the coronary circulation. It is difficult to list all the vasoconstrictor substances. However, important vasoconstrictor substances, which may be spasmogens for blood vessels, may be: (1) endothelium-derived contracting factors such as endothelin; (2) prostanoids such as thromboxane A₂ (TxA₂) and prostaglandin F_{2α} (PGF_{2α}); (3) circulating sympathomimetic substances (α-adrenoceptor agonists) such as norepinephrine and synthetic α₁-adrenoceptor agonists (methoxamine or phenylephrine); (4) platelet-derived contracting substances such as 5-hydroxytryptamine (5-HT) and TxA₂; (5) substances released from mast cells and basophils such as histamine; (6) muscarinic receptor agonists such as acetylcholine; (7) renin-angiotensin system-related substances such as angiotensin II [22]; (8) neuropeptides such as arginine vasopressin [23]; and (9) depolarizing agent potassium ion. These vasoconstrictors may be also important in the nature of vasoconstriction in arterial grafts [24]. Most of these vasoconstrictor substances contract blood vessels through receptor-mediated mechanisms. Table 2.1 lists the receptors located on the cellular membrane of vascular smooth muscle, which mediates the vasoconstriction, and of endothelium, which mediates vasodilatation.

A number of studies have been published [22, 23, 25–32] with regard to the response of the four major arterial grafts currently used for coronary artery bypass to various vasoconstrictor substances with emphasis on the most commonly used one – the internal thoracic artery (ITA). These studies may reveal the nature of the vasospasm of the grafts. In general, all vasoconstrictors tested may evoke contraction in these arterial grafts to a different extent. The extreme form of vasoconstriction is so-called “vasospasm” [33, 34].

Table 2.1. Vasoconstrictors related to vasospasm and the receptors involved (reproduced and modified from ref. [24] with permission)

Vasoconstrictors	Receptor In SMC mediating contraction	In EC mediating relaxation
Endothelium-derived contracting factors		
Endothelin	ETA, ETB	ETB
Prostanoids		
TxA ₂ ^a	TP	TP (?)
PGF _{2α}	FP	FP (?)
α-Adrenoceptor agonists		
Norepinephrine	α ₁ , α ₂	α ₂
Methoxamine	α ₁	–
Phenylephrine	α ₁	–
Platelet-derived substances		
5-HT	5-HT ₂	5-HT _{1D}
Substances released from mast cells and basophils		
Histamine	H (H ₁ , H ₂)	H ₁
Muscarinic receptor agonists		
Acetylcholine	M (non-M ₁ , non-M ₂)	M ₂
Renin-angiotensin system		
Angiotensin II	AII	AII
Arginine vasopressin		
VP1	VP1	?
depolarizing agent		
Potassium		–

TP and FP receptors in endothelial cells to be clarified SMC vascular smooth muscle cell, EC endothelial cell

^a TxA₂ is also considered as one of the endothelium-derived contracting factors; it is also derived from platelets

2.4

Vasoconstrictor-Stimulated EDRF Release in Arterial Grafts

In the last 2 decades, a large number of studies have demonstrated that many of these vasoconstrictor substances may stimulate the endothelial cell to release EDRFs. There is an obvious physiological role for this phenomenon. Since the vascular tone is determined by the balance of vasoconstriction and vasodilatation, strong vasoconstrictor substances may simultaneously stimulate the endothelial cell to release EDRFs in order to maintain an adequate vascular tone. There is even a theory, proposed by ourselves [35], that there may be no "pure" naturally secreted vasoconstrictor substances, i.e., it may be true that all naturally secreted

vasoconstrictor substances may have a vasodilator effect through the release of EDRFs stimulated by these vasoconstrictor substances. More studies, however, are needed to test this hypothesis. This concept is presented in Fig. 2.2.

In brief, the complex effects of vasoconstrictors on vascular tone and the possible receptors that mediate the action are outlined in Fig. 2.2. This diagram describes the balance between vasoconstriction and vasodilatation. In general, most pharmacological spasmogens have two opposite effects on blood vessels. On the one hand, these vasoconstrictors directly stimulate corresponding receptors located on the cellular membrane of smooth muscle and, through various mechanisms (either the opening of calcium channels or the release of intracellularly stored calcium), increase intracellular calcium concentration, which ultimately causes contraction of the smooth muscle cell. These receptors are briefly illustrated. On the other hand, simultaneously, naturally secreted vasoconstrictors stimulate receptors located on the cellular membrane of endothelium and, through receptor-effector coupling mechanisms, cause an increase in the intracellular calcium concentration that, as second messenger, mediates release of a number of endothelium-derived relaxing factors. At least three such factors have been found. These are nitric oxide (NO), prostacyclin (PGI_2), and endothelium-derived hyperpolarizing factor (EDHF). These EDRFs, through different mechanisms, reduce the intracellular calcium concentration in the smooth muscle cell and cause relaxation of the muscle. Vascular tone depends on the balance between these two actions – the direct effect of contraction of the smooth muscle cells and the indirect effect of relaxation through the release of EDRFs from the endothelial cells. Some vasoconstrictors (such as endothelin-1, U46619, $\text{PGF}_{2\alpha}$, and α -adrenoceptor agonists) predominantly contract smooth muscle and have a weak stimulating effect on the release of EDRFs whereas others such as 5-HT have a strong EDRF-stimulating effect that significantly depresses the contraction when endothelium is present. In addition, spontaneous (basal) release of EDRF (NO and EDHF) from endothelium generally depresses the vasoconstrictor-induced contraction to some extent. Apart from receptor mechanisms, shear stress is another stimulant for EDRF release.

The importance of the endothelium in arterial grafts is shown by the following fact. Some vasoconstrictors are vasoconstriction predominant (Type I). These substances contract arterial grafts even when endothelium is present because they have a weak stimulating effect on EDRF(NO) or EDRFs. In contrast, other vasoconstrictors may have balanced effects (Type II). These substances have a strong stimulating effect on the biosynthesis/release of EDRF (NO) or EDRFs. Therefore, when endothelium is present, they concomitantly stim-

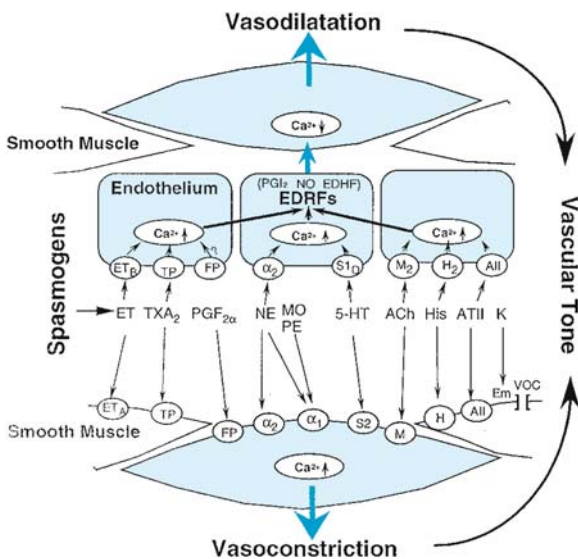


Fig. 2.2. Schematic diagram describing the balance between vasoconstriction and vasodilatation. Pharmacological spasmogens directly stimulate corresponding receptors located on the cellular membrane of smooth muscle and increase intracellular calcium concentration, which ultimately causes contraction of the smooth muscle. Simultaneously, naturally secreted vasoconstrictors stimulate receptors located on the cellular membrane of endothelium and cause an increase in the intracellular calcium concentration that, as second messenger, mediates release of a number of endothelium-derived relaxing factors (NO, PGI_2 , and EDHF), which through different mechanisms reduce the intracellular calcium concentration in the smooth muscle cell and cause relaxation. Spontaneous (basal) release of EDRF (NO) also depresses the contraction to some extent (EDRF endothelium-derived relaxing factor, NO nitric oxide, PGI_2 prostacyclin, EDHF endothelium-derived hyperpolarizing factor, Ca^{2+} intracellular calcium, ET endothelin, NE norepinephrine, MO methoxamine, PE phenylephrine, ACh acetylcholine, His histamine, ATII angiotensin II, K potassium, TP thromboxane-prostanoid receptors, FP, $\text{PGF}_{2\alpha}$ receptors, α_1 , α_1 -adrenoceptors, α_2 , α_2 -adrenoceptors, S_{1D} , 5-HT_{1D} receptors, S_2 5-HT₂ receptors, M(M_2) muscarinic receptors, H (H_2) histamine receptors, All angiotensin II receptors, VOC voltage-operated channels). (Reproduced from ref. [24] with permission)

ulate vasoconstriction through the direct contraction effect on smooth muscle and vasodilatation through the biosynthesis/release of EDRF (NO) or EDRFs. Therefore, in endothelium-intact blood vessels, these vasoconstrictors do not strongly contract the vessels. However, when endothelium is damaged or denuded, they evoke a strong contraction because of the loss of the endothelium, which leads to an imbalance between vasoconstriction, induced by its direct contraction on smooth muscle, and vasodilatation, induced by EDRF (NO) or EDRF release due to its stimulation on endothelium. Some of these vasoconstrictor substances are released from platelets. Due to the fact that EDRF (NO) also inhibits platelet aggregation, these vasoconstrictors have a particularly important pathologic significance. 5-HT is an example of this type of vasoconstrictor and directly contracts vascular smooth muscle through 5-HT₂ receptors [36] and relaxes blood vessels through the EDRF (NO) mechanism, which is mediated by 5-HT_{1D} receptors [36] located in the endothelium. When endothelium is lost, perhaps also when it is damaged, platelets aggregate in the area where endothelium is denuded and release substances such as 5-HT (also TxA₂) that strongly contract smooth muscle. We have demonstrated [24] that 5-HT plays such a role in the human IMA. 5-HT has been suggested to be an important spasmogen in coronary spasm even when endothelium is present [37]. As shown in our experiments, 5-HT does not strongly contract the IMA with intact endothelium. However, its constricting effect is unmasked when endothelium is denuded. A similar response to 5-HT has also been demonstrated in the gastroepiploic artery (GEA) [25].

2.5 Endothelium-Dependent Relaxation and Hyperpolarization in Arterial Grafts

Arterial grafts for coronary surgery are conductance arteries. The endothelium and the smooth muscle in the arterial grafts have common features with other arteries. It has been demonstrated that the release of EDRFs is an important common feature in all tested arterial grafts. For example, the endothelium-dependent relaxation exists in IMA [38], RA [29], inferior epigastric artery (IEA) [30, 31], and GEA [32]. The difference in the release of EDRFs in arterial grafts has also been noticed [31] although it is a general characteristic that all arterial grafts secrete EDRFs that induce a considerable degree of endothelium-dependent relaxation [30] in response to a number of EDRF stimuli such as acetylcholine [31], substance P [29], or calcium ionophore [29, 31]. The difference in the endothelium-dependent relaxation in the IMA and IEA may be related to the higher incidence of atherosclerosis in the latter that reduces the secretion of the EDRFs [30]. It has also been demonstrated that vascular endothelial growth factor may induce endothelium-dependent relaxation in the human IMA [39]; the relaxation has recently been demonstrated to be mediated by both NO and PGI₂ [40]. Further, physiological substances such as corticotrophin-releasing factor (CRF) induce both endothelium-dependent and -independent relaxation in the human IMA [42].

Our recent studies have shown that arterial grafts release both NO and EDHF. In general, the amount and duration of the release of NO from the IMA is more than that from the saphenous vein [43] (Fig. 2.3) Further, we have demonstrated that among the arterial grafts, the release of NO and EDHF is different. The IMA releases more NO and EDHF than the RA does (Fig. 2.4) [43].

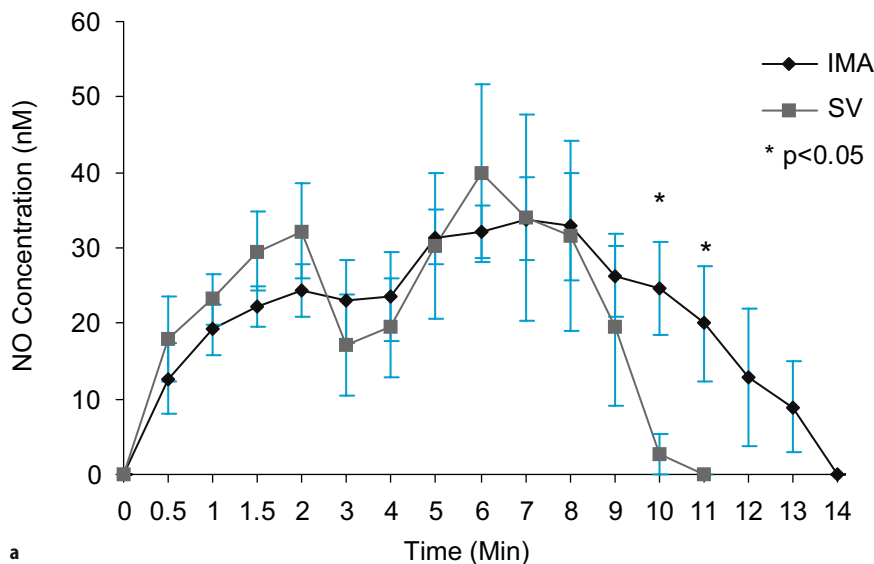


Fig. 2.3. a The time course of bradykinin ($-7.0 \log M$)-induced nitric oxide release in internal mammary artery (IMA, $n=8$) and saphenous vein (SV, $n=9$). * $p < 0.05$ compared with the saphenous vein group. (Reproduced from Liu, Ge, and He: *Circulation* 2000; 102 [Suppl III]:296–301 with permission)

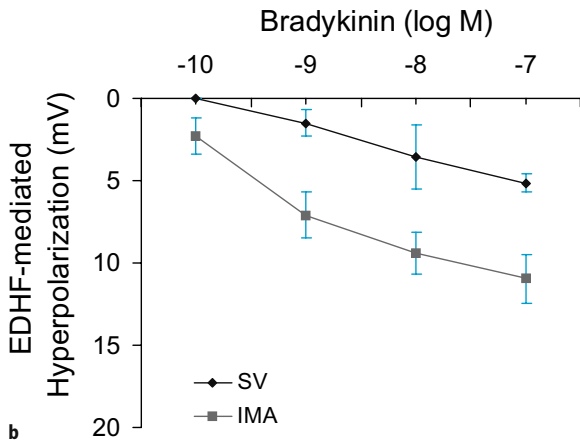


Fig. 2.3. b Bradykinin-induced hyperpolarization in internal mammary artery (IMA, $n=8$) and saphenous vein (SV, $n=8$) in the absence (a) and presence (b) of indomethacin, N^G -nitro-L-arginine, and hemoglobin. Vertical bars are 1 standard error of the mean. * $p<0.05$, ** $p<0.01$ compared with saphenous vein group (unpaired t -test). (Reproduced from Liu, Ge and He: *Circulation* 2000; 102 [Suppl III]:296–301 with permission)

2.6

The Balance Between EDRFs and EDCFs

The balance between the EDRFs and EDCFs plays a key role in maintaining an adequate vascular tone (Fig. 2.1).

The interaction between the endothelium and smooth muscle is also demonstrated by the response of the vessel to a range of vasoconstrictor substances that may be endogenous or exogenous. In general, vasospasm could be the response of a vessel to many stimulants. These stimulants may be physical (such as mechanical stimulation or temperature changes) or pharmacological (such as nerve stimulation or vasoconstrictor substances). Exogenous and endogenous vasoconstrictors are particularly important for vasoconstriction and its extreme form – vasospasm – although the exact mechanism for vasospasm is still unknown despite a large body of studies being performed on this subject over many years.

In the arterial grafts, most studies have demonstrated that the endothelium-dependent relaxation is an important part of the endothelium-smooth muscle interaction [25–28, 32]. This interaction must play an im-

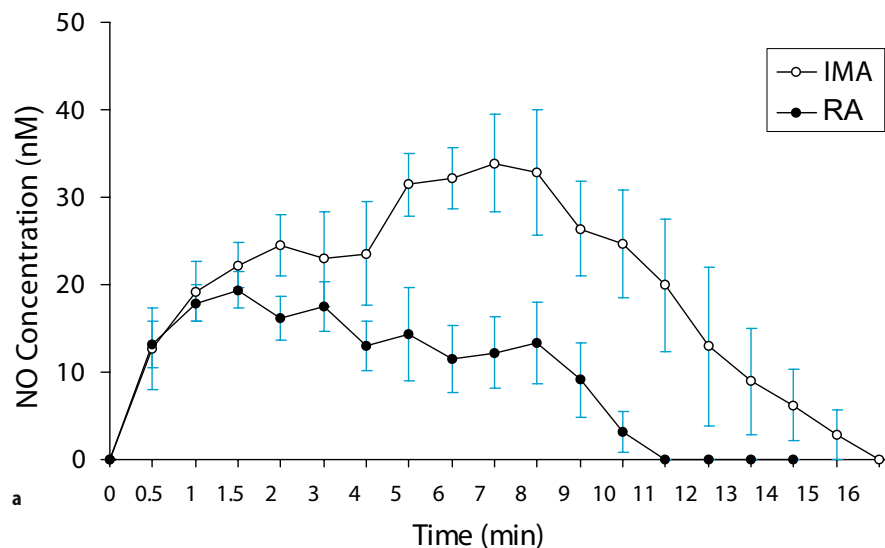
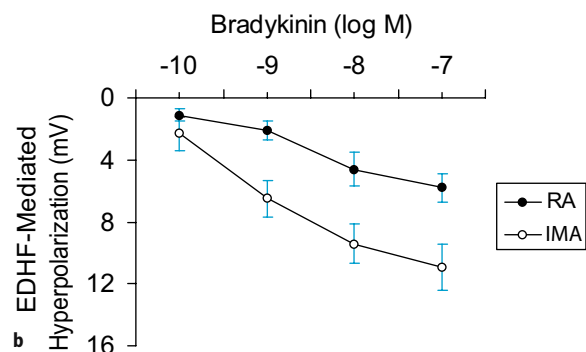


Fig. 2.4. a The time-concentration curves of NO release in IMA ($n=6$) and RA ($n=6$) where acetylcholine (ACh) $-5 \log M$ was added. The duration of NO release in the IMA was significantly longer than in RA. Five minutes after the ACh was added, the concentration of NO in the IMA was significantly higher than that in RA. * $p<0.05$, ** $p<0.01$. Data are expressed as mean $\pm$ standard error of the mean. (Reproduced from *Circulation* 2001;104[Suppl I]:344–349 with permission). **b** Bradykinin (BK)-induced endothelium-derived hyperpolarizing factor (EDHF)-mediated hyperpolarization in the internal mammary artery (IMA) and radial artery (RA) in the presence of indomethacin, N^G -nitro-L-arginine, and hemoglobin. All values are given as means and vertical error bars are 1 standard error of the mean. * $p<0.05$, ** $p<0.01$, IMA ($n=8$) vs. RA ($n=7$), unpaired t -test. (Reproduced from He and Liu: *Circulation* 2001;104 [Suppl I]:344–349 with permission)



portant role in the superior long-term patency of the arterial grafts [33]. When endothelium is impaired, the antiplatelet function of EDRFs (such as NO and PGI₂) is lost and platelets attach to the area denuded or impaired of endothelium. The coagulation cascade is activated by aggregating platelets and by thrombin. Thrombus then forms [44]. This becomes the basis for later growth and development of atherosclerotic plaque and may lead to graft occlusion. Therefore, the ideal method for the use of any arterial grafts should be able to maximally preserve the endothelial function.

In summary, arterial grafts for coronary bypass surgery are mid-sized conductance arteries. The normal endothelium-smooth muscle interaction of arterial grafts plays an extremely important role in maintaining an adequate vascular tone and producing an antispastic effect. In addition, its antiplatelet aggregation and anti-thrombotic effect are the basis for prevention of formation of atherosclerotic plaque that is directly related to the graft occlusion. Therefore, one of the key points in obtaining superior patency with arterial grafts is the maximal preservation of the endothelial function of the graft.

Acknowledgement. Supported by the Research Grants Council. Hong Kong (CUHK4127/01M&CUHK4383/03M) and St. Vincent Medical Foundation, Portland, Or. U.S.A.

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3 Clinical Physiology and Related Biological Characteristics

G.-W. HE

In comparison with standard saphenous vein grafts, use of the internal mammary artery (IMA) as a coronary artery bypass graft has produced superior long-term results [1, 2]. This is obviously related to the differences in biological characteristics between the venous and arterial grafts.

3.1 Differences in Biological Characteristics Between Venous and Arterial Grafts

Studies have demonstrated that there are differences between venous and arterial grafts. These differences are (1) that veins are more susceptible to vasoactive substances than arteries [3]; (2) that the venous wall is supplied by the vasa vasorum whereas the arterial wall may be supplied through the lumen in addition to the vasa vasorum [4]; (3) that the endothelium of arteries may secrete more endothelium-derived relaxing factor (EDRF) [5] and may release more nitric oxide (NO) [6, 7] and endothelium-derived relaxing factor (EDHF) [6, 7]; and (4) that the structure of the vein is subject to low pressure whereas the artery is subject to high pressure. Therefore, in a high pressure system after bypass surgery, venous grafts have to adapt to the high pressure whereas arterial grafts are used to it. These differences may account for the difference in the long-term patency rate.

3.2 Are There Any Differences Among Arterial Grafts?

Based on the superior long-term results in the IMA, other arteries have been used in coronary artery bypass graft (CABG) [8–14]. Such conduits include the radial artery [8], the gastroepiploic artery (GEA) [9], the inferior epigastric artery (IEA) [10, 11], the splenic artery [12], the subscapular artery [13], and the inferior mesenteric artery [14], the descending branch of the lateral femoral circumflex artery [15], and the ulnar artery [16]. In addition, the intercostal artery [17] has also

been suggested to be used as a graft. However, although long-term patency rates for IMA are well established, there are only few reports on other arterial conduits with a relatively small number of patients and shorter follow-up period involved [18–20]. It is expected that other arterial conduits will have good long-term results as the IMA does. This expectation is based on a hypothesis that all arterial conduits have similar biological characteristics such as contractility, relaxing characteristics, endothelial function, and anatomical structure. Histologic studies have also revealed that there are major differences among various grafts in terms of structure of smooth muscle such as elastic lamellae [4]. The differences observed from these studies suggest that arterial grafts, although they are arteries, are not uniform either in anatomy or in function. On the other hand, comparative functional studies [21–25] have demonstrated that there are differences in arterial grafts with regard to contractility and endothelial function. Our recent studies have demonstrated that the endothelium of the internal thoracic artery (ITA) releases more NO than the radial artery (RA) at both basal and stimulated levels. Further, the ITA has a greater hyperpolarizing effect on bradykinin-stimulated release of EDHF than the RA does [26]. These differences are the anatomical and physiological basis of the divergent clinical manifestations of the grafts and may also account for possible differences in the postoperative graft function and long-term patency rates. One of the diverse manifestations clinically observed among these arterial grafts is a different tendency to develop spasm during surgical dissection and during the perioperative period. It is the experience of many surgeons that GEA has a higher tendency to spasm than IMA [27]. Similarly, spasm of the RA is a serious problem that, together with a low patency rate which may also be related to this characteristic of the artery, led to the abandonment of this arterial graft at an early stage in the 1970s [28]. Only after the development of a method to overcome spasm of this arterial graft has it recently been reused [29].

3.3 Biological Characteristics

All arterial grafts for CABG are conductance arteries (in the opposite sense to “resistance” arteries). A common feature of arterial grafts is that removal of these arteries does not usually affect the blood supply to the organ and only in extreme situations is it a concern. The common physiological role of these conductance arteries is to carry blood flow to perfuse corresponding organs such as the heart (the coronary artery), the stomach or other visceral organs (the GEA, the splenic artery, and the inferior mesenteric artery), the hand (the RA), and the body wall (the IMA, IEA, and the subscapular artery). However, there may be differences in the function of these arteries owing to the fact that the organs they perfuse have a different physiological role so the flow required or the flow reserve for the organs may be different. To understand the differences between these arteries, studies have been conducted on the anatomy, physiology, pharmacology, and embryology at the organ, tissue, or cellular level.

3.3.1 Anatomy

The differences in gross anatomy between arterial grafts are obvious since they are at different locations of the body and supply different organs. There is evidence showing that the anatomical structure of the arteries is divergent [4]. One of the most obvious differences with regard to the structure is that some arteries contain more smooth muscle cells in their wall and therefore are less elastic, such as the GEA, IEA, and RA. In contrast, others may be more elastic, containing more elastic laminae, such as the IMA [4]. The divergence in structure may be the basis for the differences in physiological and pharmacological reactivity.

3.3.2 Contractility, Incidence of Spasm, and Comparison with Coronary Arteries

3.3.2.1 Contractility and Incidence of Spasm of Arterial Grafts

There is still a lack of knowledge as to how vasospasm develops. The correlation between the vasospasm and the reactivity of a vessel to vasoconstrictors is also unclear. However, it is presumed that vasospasm is the extreme form of vasoconstriction that may be the response of a vessel to many stimuli (spasmogens). These stimuli may be physical (such as mechanical stimulation or temperature changes) or pharmacological (such as nerve stimulation or vasoconstrictor substances).

Important vasoconstrictor substances, which may be spasmogens for blood vessels, are [24, 30] (1) endo-

thelium-derived contracting factors such as endothelin; (2) prostanoids such as thromboxane A_2 (TxA_2) and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$); (3) circulating sympathomimetic substances (α -adrenoceptor agonists) such as norepinephrine and synthetic α_1 -adrenoceptor agonists (methoxamine or phenylephrine); (4) platelet-derived contracting substances such as 5-hydroxytryptamine (5-HT) and TxA_2 ; (5) substances released from mast cells and basophils such as histamine; (6) muscarinic receptor agonists such as acetylcholine; (7) renin-angiotensin system-related substances such as angiotensin II [31]; (8) neuropeptides such as arginine vasopressin [32] or intestinal peptide [32]; and (9) depolarizing agent potassium ion. The contractility of arterial grafts to the above vasoconstrictors has been extensively studied [21–25, 30–43]. A previous study [24] revealed that there are basically two types of vasoconstrictors that are important spasmogens in arterial grafts. Type I [endothelin, prostanoids (TxA_2 and $PGF_{2\alpha}$), α_1 -adrenoceptor agonists] are the most potent vasoconstrictors and they strongly contract arterial grafts even when endothelium is intact. Type II vasoconstrictors (such as 5-HT) only induce a weak vasoconstriction when endothelium is intact. However, these vasoconstrictors probably play an important role in the spasm of arterial grafts if endothelium is lost by surgical handling.

The difference between arterial grafts with regard to the response to these vasoconstrictors is the magnitude of the response and the sensitivity to the spasmogen. Although all arterial grafts react to the above vasoconstrictors, there is a general trend that some arteries react to vasoconstrictors in a stronger manner than others do. This is best reflected by the fact that the GEA reacts more strongly to vasoconstrictors K^+ , TxA_2 , ET-1, and norepinephrine than other arteries [23]. In the comparison between the RA and IMA, the RA has a higher response to norepinephrine and 5-HT [22], angiotensin, and endothelin-1 [34]. Clinically, although all arterial grafts may develop vasospasm, it develops more frequently in the GEA [27] and RA [29] than in the IMA and IEA. Postoperative vasospasm and occlusion is the cause accounting for the early abandonment of the RA [29] and a possible cause for the abandonment of the GEA in some cardiac surgical centers.

However, there are groups of arteries that are similar in their contractility to vasoconstrictors. The IMA and IEA are in this group [23, 25]. The response of these two arteries to a number of vasoconstrictors, such as endothelin, U46619, or K^+ , is similar [23, 25].

3.3.2.2 Comparison with Coronary Arteries

In general, coronary arteries are highly reactive vessels and coronary spasm is a well-known phenomenon.

However, there is still a lack of direct comparisons between the coronary artery and coronary bypass grafts. Although previous studies have attempted to do so, the comparison was devalued when the human coronary artery was taken from the explanted heart with coronary artery disease [23]. In a normal heart, the reactivity of coronary arteries may be equal to or higher than that of arterial grafts, as demonstrated in the canine vessels [3]. However, when the large coronary artery has atherosclerotic disease it may be less reactive to vasoconstrictors compared to arterial grafts, although the reactivity of the microcoronary artery may remain high.

3.3.3 Receptors in Smooth Muscle

Most vasoconstrictors except potassium ion contract arterial grafts by activating a specific receptor. Some receptors on the smooth muscle of the arterial grafts have been characterized. For example, the IMA is an α_1 -adrenoceptor-dominant artery with little α_2 - or β -function (Fig. 3.1) [35, 44]. In contrast, the RA has both α_1 - and α_2 -function (Fig. 3.2) although its β -function is also weak (Fig. 3.3) [36].

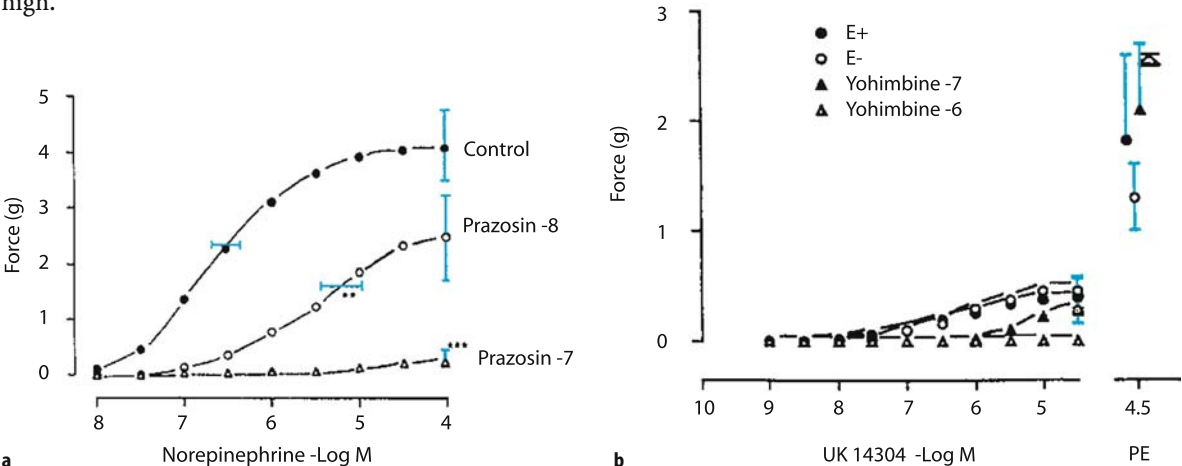


Fig. 3.1. a Mean concentration (-log M)-contraction (force, g) curves for norepinephrine (NE, an α_1 -, α_2 -agonist) in the human IMA. The NE-induced contraction is inhibited by the α_1 -agonist prazosin. This demonstrates the predominant role of the α_1 -function. **b** The α_2 -agonist UK14304 only evoked very little contraction in the human IMA and this demonstrates that there is little α_2 -function in this artery. (Reproduced from He GW et al.: *J Cardiovasc Pharmacol* 1993; 21:256–263 with permission)

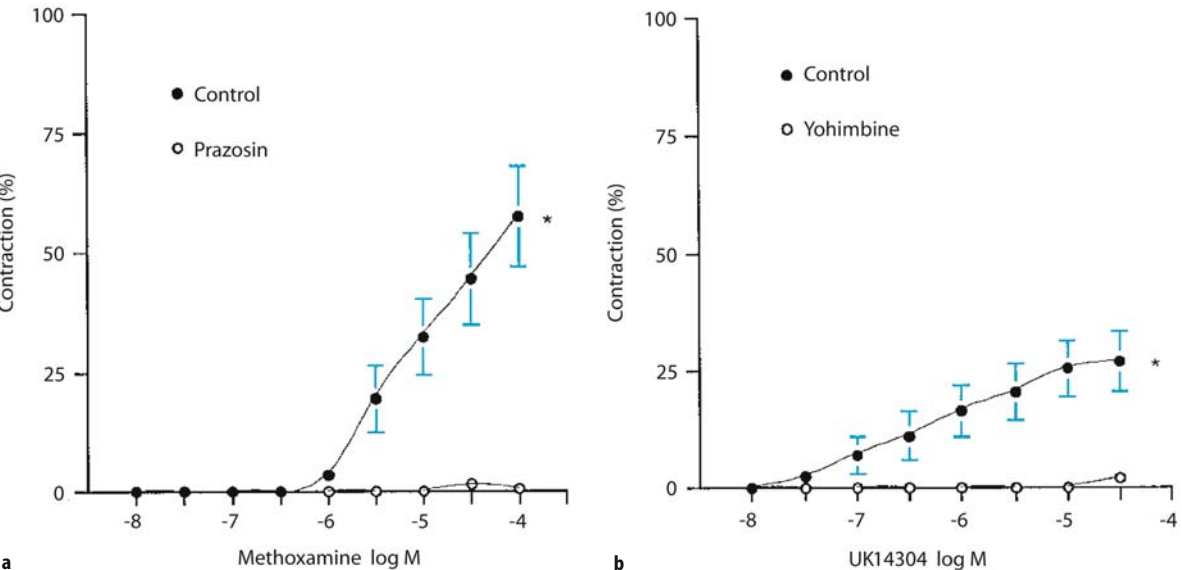


Fig. 3.2. a Mean concentration (-log M)-contraction (force, g) curves for methoxamine (MO, an α_1 -agonist) in the human radial artery (RA). The MO-induced contraction is inhibited by the α_1 -agonist prazosin. This demonstrates the predominant role of the α_1 -function. **b** The α_2 -agonist UK14304 evoked a small but substantial contraction in the human RA and this demonstrates that there is some α_2 -function in this artery. (Reproduced from He GW and Yang CQ: *J Thorac Cardiovasc Surg* 1998; 115:1136–1141 with permission)

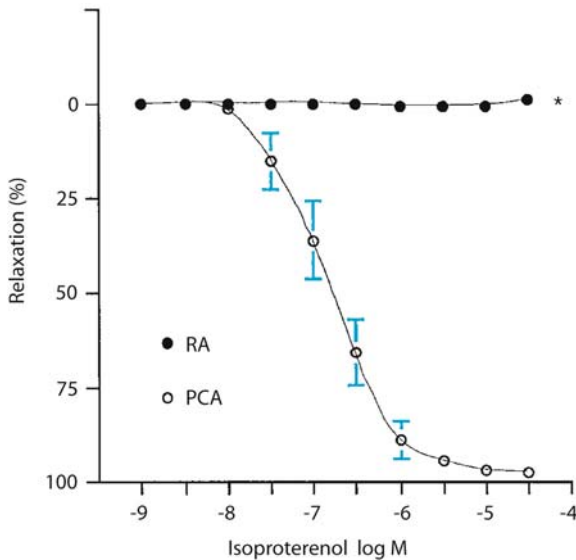


Fig. 3.3. Mean concentration ($-\log M$)-relaxation (% of the pre-contraction force) curves for isoproterenol (a full β -agonist) in the human radial artery (RA). There is very little relaxation in the RA that demonstrates little β -function. In comparison, isoproterenol induced a 100% relaxation in the porcine coronary artery that is rich in the β -function. (Reproduced from He GW and Yang CQ: *J Thorac Cardiovasc Surg* 1998; 115:1136–1141 with permission)

Other receptors functionally demonstrated in arterial grafts are ET_A , ET_B [37], 5-HT [38], angiotensin [39], TP (thromboxane-prostanoid) [40], vasopressin V1 receptors [32, 41], and vasoactive intestinal peptide [33] receptors in the IMA. There are fewer reports on the receptors in other arterial grafts [33, 34, 36].

3.3.4

Receptors in Endothelium and Endothelial Function

Receptors are also located in the cellular membrane of the endothelial cell in the arterial grafts. For example, receptors for common stimuli of EDRF such as acetylcholine, bradykinin, and substance P are present in the endothelium of arterial grafts [21, 25, 34]. The vascular endothelial growth factor (VEGF)-induced, endothelium-dependent relaxation, mediated by both NO and prostacyclin in the IMA, has been shown mainly through the KDR receptors, rather than Flt-1 receptors [45]. Most recently, corticotropin-releasing factor (CRF) receptors CRF1, CRF2 α , and CRF2 β have been shown to be present in the IMA [45]. The CRF urocortin-induced endothelium-dependent relaxation in the IMA is likely through CRF receptors allocated in the endothelium of the IMA [46].

Usually, these receptors mediate relaxation through the endothelium-dependent mechanism. However, despite the fact that the receptors in the arterial grafts have been studied for years, more studies are warranted

to understand the differences between arterial grafts regarding these receptors.

Compared to the marked difference regarding the EDRF release between the IMA and SV [5], the difference between arteries is less significant. This is partially due to the fact that the endothelial function is complex and the endothelium-dependent relaxation and hyperpolarization are composed of at least three EDRFs (see Chap. 2 for details).

We demonstrated that the IMA has more endothelium-dependent relaxation than the IEA in response to acetylcholine and calcium ionophore A23187 [25], but it was uncertain that this was due to the intrinsic physiological differences or due to the higher incidence of atherosclerosis in the IEA that would diminish such relaxation in this artery [25, 47].

Others have also found differences regarding the endothelial function between arterial grafts [42, 43].

It is most likely that in the normal arteries used as the coronary artery bypass grafts, the endothelium-dependent relaxation, as a whole, may have no major differences, i.e., the EDRF stimuli may evoke a similar level of endothelium-dependent relaxation [23, 34]. This has been demonstrated in the IMA and the RA. We have shown that the degree of endothelium-dependent relaxation induced by both substance P and calcium ionophore A23187 is similar in the RA and the IMA [34]. On the other hand, the release of each component of the EDRFs, i.e., NO, EDHF [48, 49], and prostacyclin, may be different between these arteries. With this hypothesis, we have conducted a number of studies to compare the release of these factors in arteries and vein. We have not only found that the IMA releases more NO and has more hyperpolarization to EDRF stimuli bradykinin than the saphenous vein but also than the RA ([26], see Chap. 2 for figures). These direct and quantitative studies reveal that the IMA has intrinsic characteristics regarding the endothelial function that are closely related to its superior long term patency.

These discoveries may well form the basis for clinical considerations about the choice of arterial grafts.

3.3.5

Smooth Muscle Relaxation

No major differences have been observed between arterial grafts in endothelium-independent relaxation (such as to nitroglycerin), which is often used as the index for the function of the relaxation properties in the smooth muscle [21, 25] although there may be some differences in response to vasodilator substances with regard to the sensitivity [33]. This implies that the arterial grafts may have no major difference in the relaxation property in the smooth muscle.

3.3.6

Embryological Considerations

Commonly used arterial grafts belong to different groups of arteries in various locations of the body. Basically, they can be divided into somatic arteries and splanchnic arteries [50]. Somatic arteries are those that supply the body wall. These include the IMA, IEA, the subscapular artery, and the intercostal artery. In comparison, splanchnic arteries are those that supply visceral organs. These include the GEA, the splenic artery, etc. From embryological development [50], somatic arteries are intersegmental branches to the body wall whereas splanchnic arteries are from segmental branches of primitive dorsal aorta to supply the digestive tube. There is a special type of artery that supplies the extremities – limb arteries. They are developed either from somatic arteries (upper limb arteries) or from the dorsal root of the umbilical artery (lower limb arteries).

3.3.7

Physiological Considerations

All arterial grafts for coronary artery bypass grafting are conduit arteries and their physiological function is to carry blood flow to organs. Because the organs they supply have different physiological functions, these ar-

teries are entitled to adapt to the diverse demand for blood supply to individual organs. Therefore, the structure and the reactivity of these arteries are different. This is why some of them are more spastic (more reactive to vasoconstrictors) than others.

3.3.8

Segmental Differences

All arterial grafts for CABG are *conduit arteries*. The reactivity of the grafts varies along the length. As demonstrated in the IMA, the main portion (the mid portion, composed of more than 60% of the total length of the graft) of the IMA is less reactive in comparison to the distal portion and may be also less reactive than the proximal portion (Fig. 3.4) [51, 52]. This may also be true in other arterial grafts such as in the GEA, IEA, and radial artery. Although arterial grafts at the full length are reactive [52], the major muscular components are located at the two ends of the artery (muscular regulator) (Fig. 3.5) [53]. In particular, the distal end is more efficient as the physiological regulator for the flow because this part contains relatively more smooth muscle cells and is smaller in diameter. These characteristics are physiologically important in regulating blood flow distribution. However, when such arteries are used

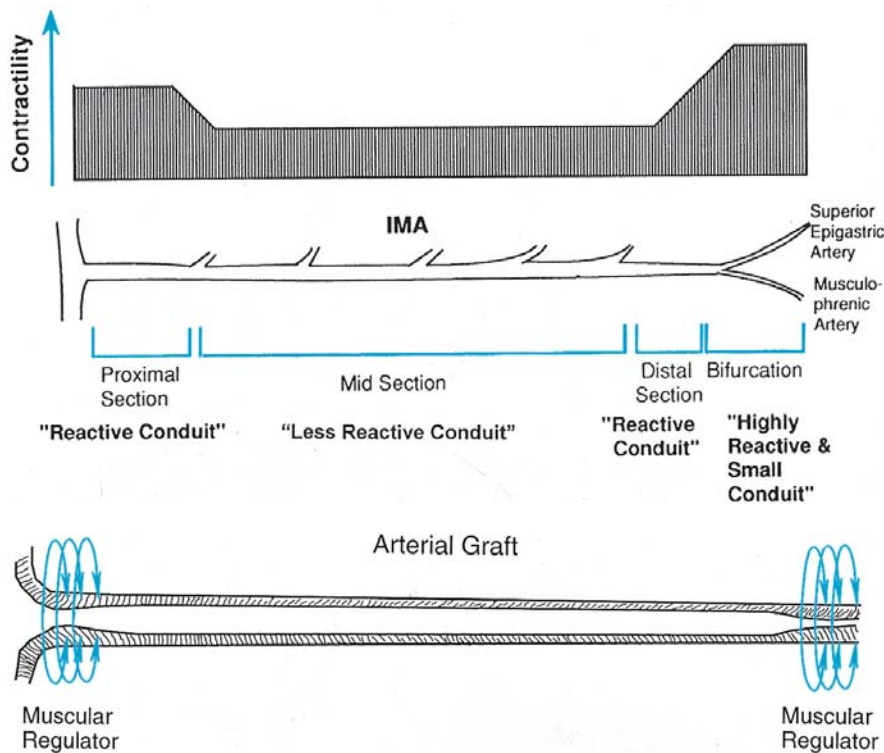


Fig. 3.4. Schema showing the different contractility in different sections of the IMA. The mid section of the IMA is a large and relatively less reactive conduit whereas the distal and the proximal sections are a pharmacologically reactive conduit. The contractility at the distal section increases towards the end and reaches its highest at the distal bifurcation. Therefore, it is advised not to use the very distal end for coronary grafting. (Reproduced from He GW: *J Thorac Cardiovasc Surg* 1993; 106: 406–411 with permission and modified with results from He GW et al.: *J Thorac Cardiovasc Surg* 1994; 108:741–746 incorporated)

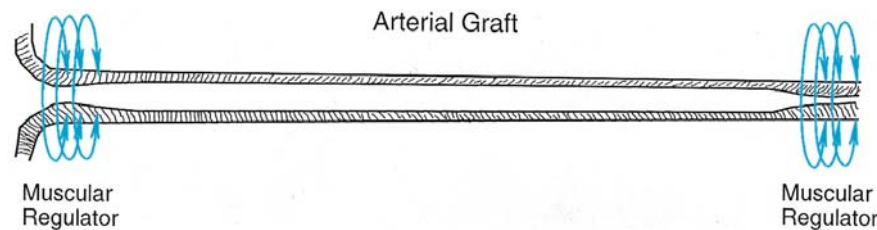


Fig. 3.5. Schema showing the concept that all arterial grafts for coronary artery bypass grafting are conduit arteries. The muscular regulators are located at both ends to regulate blood flow to the organs and to distribute blood flow according to

the need of the organ and the hemodynamic status of the whole body. In comparison, the distal end is more important in regulating the flow because this part of the artery is highly reactive and is the smallest part of the artery in diameter. (Reproduced from He GW and Yang CQ: *J Thorac Cardiovasc Surg* 1995; 110:1569–1570 with permission)

as bypass grafts, these characteristics may be detrimental. In terms of preventing vasospasm of the arterial grafts, trimming off the small and highly reactive distal end of the grafts (either IMA, GEA, IEA, or other grafts) may be important and clinically feasible.

3.3.9

Incidence of Atherosclerosis

There are two aspects with regard to the incidence of atherosclerosis in arterial grafts: (1) incidence of atherosclerosis in the in situ native position and (2) incidence of atherosclerosis after coronary grafting.

3.3.9.1

Incidence of Atherosclerosis in Native Arteries

The exact incidence of atherosclerosis in these mid-sized conduit arteries is unknown. In general, the incidence of atherosclerosis in the four major arterial grafts is low compared with the left anterior descending artery (LAD) [4]. In fact, atherosclerosis is absent or only mildly present in all four arterial grafts. Early studies demonstrated that the incidence of atherosclerosis in IMA is low [54]. It is frequently seen from angiograms that a patent IMA exists with a stenotic vertebral artery. In contrast, the incidence of atherosclerosis at the proximal end of the IEA may be high as seen in a small group of patients [25, 47]. Although the reason for this is unknown, this may be related to the fact that the incidence of atherosclerosis is higher in the lower limb arteries than the upper limb arteries and the IEA is the first branch of the external iliac artery [25]. The atherosclerosis incidence in the GEA is low as recently studied by ourselves [47] and others [55].

3.3.9.2

Incidence of Atherosclerosis in Bypass Grafts

The incidence of atherosclerosis is low in IMA grafts [1, 2], even 15–21 years later [56]. The long-term incidence in other arterial grafts remains to be studied although there is evidence showing that it could be low in the GEA [55] and RA [57].

3.3.10

Pharmacology of Vasoactive Substances in Arterial Grafts

Arterial grafts are reactive conductance arteries. Pharmacological reactivity of arterial grafts to vasoactive substances in arterial grafts includes the reactivity both to vasoconstrictor substances and to spasmolytic vasodilator substances. The former is discussed in Chap. 2, as well as above. The latter will be discussed in Chap. 4.

Acknowledgement. Supported by St. Vincent Medical Foundation, Portland, Or., U.S.A.

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Clinical Classification of Arterial Grafts

G.-W. HE, C.-Q. YANG

4.1 Introduction

Various arterial grafts have been used for coronary artery bypass grafting. However, except for the internal mammary artery (IMA), which has been regarded as the choice for left anterior descending artery (LAD) grafting, so far there is no unanimous opinion as to the best use of other grafts. Arterial grafts, on the one hand, are all conductance arteries and therefore have features in common compared with venous grafts (see Chap. 3). On the other hand, they are found in different parts of the body and have a different physiological role because the organs they perfuse have a different physiological role. To meet the physiological requirements, these arteries have a different anatomic structure (see Chap. 1) and a different physiological and pharmacological reactivity to vasoactive substances. Furthermore, they are of different embryological origin [1]. Arterial grafts are therefore not uniform in their biological characteristics.

As discussed in Chap. 3, the difference in the perioperative behavior of the grafts and in the long-term patency may be related to different characteristics. These should be taken into account in the use of arterial grafts, some of which require more active pharmacological intervention during and after operation to obtain satisfactory results. To better understand the biological behavior of the grafts, their common features and differences, a clinical classification may be useful for the practicing surgeon.

4.2 Clinical Classification

A large number of studies [2–8] have demonstrated different pharmacological reactivities of arterial grafts to vasoactive substances. For example, the gastroepiploic artery (GEA) has the highest contractility to endothelin-1, TxA₂, norepinephrine, and K⁺ [2]. Figure 4.1 shows that of the GEA, IMA, inferior epigastric artery (IEA), and coronary artery, the GEA has the highest contraction force to these four strong vasoconstrictors [3].

Based on experimental studies on the vasoreactivity, taken together with anatomical, physiological, and embryological considerations, we have proposed a functional classification for arterial grafts that may be useful clinically [2] (Fig. 4.2).

Our classification suggests that there are three types of arterial grafts as follows:

- Type I: somatic arteries
- Type II: splanchnic arteries
- Type III: limb arteries

Using anatomical considerations, somatic arteries (Type I) are located in and supply blood to the body wall. The IMA is a typical example of this type of artery. In addition, other somatic arteries such as the IEA, subscapular artery, or intercostal artery belong to this type and their contractility may be similar to that of the IMA, as already demonstrated for the IEA [4] although there are no data available yet for the others. Although the IEA was histologically demonstrated as a muscular artery [9], its pharmacological reactivity is very similar to that of the IMA [2] and their embryological origin is similar. In fact, even from histological study, the wall of the IEA is thinner than that of the GEA [10]. Therefore, it is probably reasonable to classify this artery as Type I, together with the IMA.

Splanchnic (visceral) arteries (Type II) supply blood to the visceral organs. The GEA is a typical example. Other splanchnic arteries such as the splenic artery and the inferior mesenteric artery belong to this type and their reactivity may be similar to the GEA although no data are available as yet. Type III arteries are located in the limb. The radial artery (RA) is a typical example. Other limb arteries such as the ulnar artery and the lateral femoral circumflex artery also fall into this type.

As already mentioned, the Type II artery GEA and the Type III artery RA have a higher pharmacological reactivity to vasoconstrictors. This characteristic may be extended to all Type II and Type III arteries.

Type II arteries are prone to spasm because of the higher contractility of splanchnic arteries. This characteristic of splanchnic arteries has a physiological significance in that blood flow through the splanchnic arteries is subject to tremendous changes under various cir-

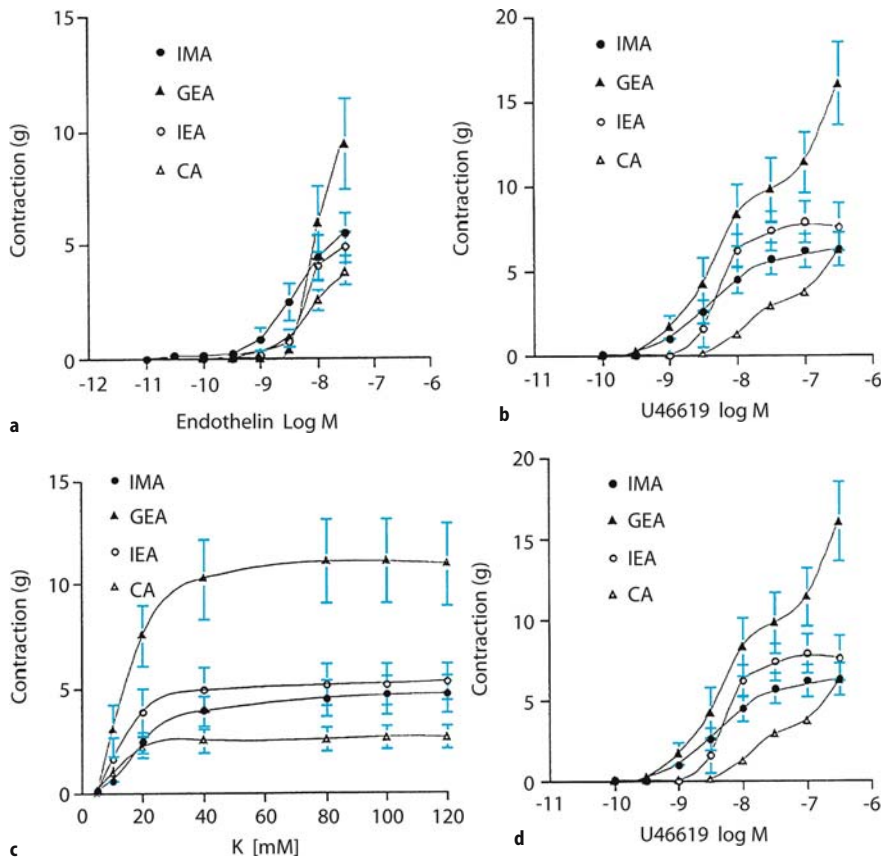


Fig. 4.1a-d. Contraction force induced by four strong vasoconstrictors (endothelin-1, TxA_2 , norepinephrine, and K^+) in three arterial grafts and the human coronary artery. The contraction force in the GEA is the highest in response to all the four vasoconstrictors among these four arteries (reproduced from He G-W, Yang C-Q: Comparison among arterial grafts and coronary artery. An attempt at functional classification. *J Thorac Cardiovasc Surg* 1995; 109: 707–715 with permission)

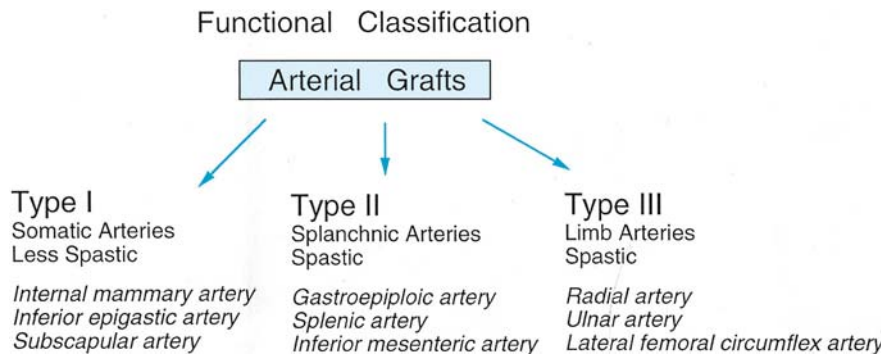


Fig. 4.2. Functional classification of arterial grafts (modified from He G-W, Yang C-Q: Comparison among arterial grafts and coronary artery. An attempt at functional classification. *J Thorac Cardiovasc Surg* 1995; 109: 707–715)

cumstances in accordance with the function of the alimentary tract. The flow increases after meals and decreases in critical situations. In contrast, Type I arterial grafts (somatic arteries) are less reactive than Type II grafts because they are mainly “less reactive” conduit arteries except at the end of the artery, which is a muscular regulator for blood flow, as demonstrated in the human IMA [11–13]. As to Type III, these arteries are located in the limbs, represented by the radial artery, and have a higher tendency for spasm compared to somatic arteries (Type I). It is a common clinical observation that arteries at the extremities are usually prone to

spasm either at physiological status or under pathological conditions (as seen in Raynaud’s disease).

The prevalence of vasospasm in arterial grafts is also correlated with their endothelial function, as mentioned in Chap. 2. We have recently demonstrated that the Type I artery IMA releases more nitric oxide (NO) and also has higher endothelium-derived relaxing factor (EDHF)-mediated relaxation and hyperpolarization than the Type III artery RA [14]. Other words, a Type I artery, particularly the IMA, may prove to have the best endothelial function among the arterial grafts and this certainly contributes to the superior patency of

this graft. Importantly, most of the studies comparing the endothelial function between arterial grafts have been performed in the vascular segments taken from the coronary artery bypass grafting patients who are old with coronary disease; the superior endothelial function of the IMA may merely reflect the fact that this artery is usually free from atherosclerosis whereas other type (Type II and III) arteries are usually more involved in atherosclerotic changes that diminish the endothelial function.

Because Type II and III arteries are prone to spasm due to a higher contractility, they require more active pharmacological intervention [2, 3, 14].

Although our classification is based on pharmacological studies and anatomical considerations, there is evidence that it is in accordance with the embryology. Taking embryological considerations into account [1], somatic arteries are intersegmental branches to the body wall. These arteries persist in the thoracic and lumbar regions as the posterior intercostal, subcostal and lumbar arteries. Near the anterior median line, intersegmental arteries are linked by a ventral somatic anastomosis. These vessels persist bilaterally as the internal mammary, the superior and inferior epigastric arteries. In our classification, these are the Type I arteries. In contrast, Type II arteries (splanchnic arteries) arise from segmental branches of the primitive dorsal aorta to supply the digestive tube. The dorsal splanchnic anastomosis persists in the GEA. The arteries of the upper limbs (Type III in our classification), such as the radial artery, also develop from intersegmental arteries as somatic arteries, although the arteries of the lower limb arise from the dorsal root of the umbilical artery. This is another reason why the limb arteries cannot be simply classified as either Type I or Type II.

The reason for classifying arterial grafts on contractility rather than relaxation is that although vascular reactivity is composed of contractility and relaxation, the latter depends on the contractility. Relaxation occurs only in an artery that is already contracted and therefore is secondary to the existing contraction. Although various vasodilators may have different relaxing effects on arterial grafts and one particular vasodilator may also have different effects on different arteries, these differences are often vasoconstrictor dependent, i.e., contraction dependent [16, 17]. Therefore, we classify the arterial grafts on the basis of reactivity to vasoconstrictors (contractility), together with considerations of endothelium-dependent relaxation, embryology, physiology, and anatomy.

There are clinical implications to this classification. First, this clinical classification may have implications with regard to the search for new arterial grafts or the prediction of the behavior of a graft. As far as vasospasm is concerned, Type I arteries may be less spastic than Type II and Type III arteries. For example, al-

though the IMA is also a reactive artery, vasospasm is encountered less in this artery than in Type II [18] or Type III [19, 20] arteries, in particular when its most reactive portion – the distal section – is trimmed off [11–13, 21]. The less spastic characteristics are obviously advantageous perioperatively. In fact, in common clinical practice since the 1980s, the IMA has been used as the first choice of arterial grafts and is always used to graft the most important coronary artery – the left anterior descending artery.

With this classification, the surgeon may predict the behavior of the arterial graft and choose an optimal pharmacological method to overcome vasospasm. For the Type II or III arteries, more active pharmacological intervention is necessary in order to prevent or treat vasospasm in these arteries.

The most important issue in coronary grafting is the long-term patency of the graft including the anastomosis. Apart from technical factors, the long-term patency is related to the endothelial function (see Chap. 2). Vasospasm is also related to the long-term patency as seen in the early use of the RA that encountered a severe spastic problem and that had reduced patency of the RA graft [19, 20]. A factor that should be taken into account in the long-term patency of the graft is the endothelial function. We have recently demonstrated that the IMA releases more NO and has higher EDHF-mediated relaxation and hyperpolarization than the Type III artery – RA [14], as mentioned above. Correspondingly, even in the largest series from Tatoulis and colleagues, who are highly experienced with arterial grafting, the patency for RA was 89% at 4 years, compared to 98% of the patency for the left IMA at 5 years [22]. Although technical factors such as targeting vessels may be involved in this difference, the aforementioned differences in the endothelial function regarding NO and EDHF between the IMA and RA may play a role.

With regard to the long-term patency, the arteries in the same type may be different due to the prevalence of the atherosclerosis either in the native artery or in the graft, or other factors. The Type I artery IMA has been well established with its superior long-term patency. Even in the Type I arteries, early reports are that the patency of the IEA is lower than expected [23, 24]. This is probably due to the following factors: (1) the IEA is used as a free graft; (2) the IEA is very small at the distal end, which increases the technical difficulties [25]; (3) the size of the proximal IEA is less than 2 mm, which makes difficulties with the aortic anastomosis [25]; and (4) the IEA, at least at the proximal part, has a higher incidence of atherosclerosis that may influence the patency [4]. The new technique for use of the IEA is, therefore, to trim off the very small part of the distal end and the atherosclerotic proximal end to be used as a part of the composite graft [25]. In this way, use of the IEA may reach a similar patency rate comparable to the IMA.

The patency rate of Type II and III arteries is not as well established as that of the IMA. Suma [26] recently reported that the cumulative patency rate estimated by the Kaplan-Meier method was 96.6% at 1 month, 91.4% at 1 year, 80.5% at 5 years, and 62.5% at 10 years. Causes of late occlusion were primary anastomotic stenosis and anastomosis to a less critically stenosed coronary artery. Voutilainen and associates [27] reported that 82.1% (23/26) of the GEA grafts were patent at 5 years. From these studies, the patency of the GEA, as a Type II artery, is acceptable but not as superior as that of the IMA, which was 95% at 10 years and 88% at 15 years [22].

The patency rate of the RA is more dramatic. There was a disappointing 35% incidence of narrowing or occlusion of the RA [28]. With modified technique, avoiding skeletonization and using calcium antagonists, the early patency increased to 93.5% at 9 months in Acar's group [19] and to 93.1–95.7% in other groups [29, 30] at 3–21 months in the early stage of the use of RA. Later, Acar and colleagues reported that the patency rate of the radial artery grafts was 83% at 5 years. In addition, Tatoulis and associates reported that the radial artery patency at 1 year was 96% and at 4 years it was 89% [22]. Interestingly, similar to the right IMA, for the radial artery there was higher patency with greater coronary stenosis.

These results may suggest that Type II and III arteries have an inferior patency to that of the IMA. However, if the vasospasm and the technical problems can be overcome and the endothelial function is well preserved, the patency of Type II and III arteries may significantly improve.

In summary, arterial grafts are biologically divergent conductance arteries. They can be functionally and clinically classified into three types. Type II (such as the GEA) and Type III (such as the RA) are more spastic than Type I (such as the IMA). In order to obtain the best results, antispastic therapy, preservation of endothelial function, and other technical modifications are essential particularly in Type II and III arteries.

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Use of Vasodilators for Arterial Grafts in Coronary Bypass Surgery



Pharmacological Studies and Guidelines for the Use of Vasodilators for Arterial Grafts

G.-W. HE, C.-Q. YANG

5.1 Pharmacological Studies

Pharmacological studies have been performed in parallel to the development of arterial grafts in coronary artery bypass grafts (CABGs) [1–15]. This is because arterial grafts are small arteries and there is a tendency to develop vasospasm in these arteries during surgery. Therefore, antispastic therapy is important in the development of arterial grafts. As discussed in the previous chapters, Type II (splanchnic arteries) and III (limb arteries, see Chaps. 1–4) arterial grafts have a higher tendency to spasm because of the spastic characteristic, and antispastic therapy in the use of Type II and III arteries is particularly important. For example, antispastic therapy using calcium antagonists is an important part of the new protocol in the revival of the radial artery (RA).

Pharmacological studies on CABGs were initially focused on the internal mammary artery (IMA). Along with the increased use of other arterial grafts, studies have also been extended to these arteries. Most studies use the *in vitro* method, studying removed segments from the grafts during surgery. The advantage of this method is that the vessel is studied in the organ bath under controlled conditions and therefore the dose and the response of pharmacological agents (vasoconstrictors and vasodilators) can be assessed highly accurately. The technique only requires the basic pharmacological equipment and is quite easy to carry out. The method has therefore gained in popularity since its early introduction [1, 2]. On the other hand, results from these *in vitro* studies need to be carefully transferred to the clinical setting, where the conditions of the arterial grafts are complicated. Nevertheless, the organ bath method can provide very useful information on the effect of vasoactive substances in the arterial grafts. Particularly, a special method that measures the individual length-tension curve of the vessel *in vitro* and sets the vessel at a pressure similar to that in the *in vivo* situation [1, 2] can provide adequate information about vasoactivity. Unfortunately, this new method we have developed [2] has only been used in our own and a few others' studies.

Surgical use of pharmacological agents such as vasodilators has a broader significance than in other medical fields because topical use of drugs is an important aspect in surgery. In CABG, use of vasodilators has two aspects: (1) systemic administration and (2) topical use of the drug intraoperatively.

Various antispastic methods have been suggested. Choice of a pharmacological agent to overcome the vasospasm encountered in the arterial grafts must be on the basis of pharmacological studies. Therefore, we have conducted a series of experiments to study the pharmacological effect of a number of vasodilator substances. The studies by ourselves and others can be outlined as follows:

5.1.1 Papaverine

The traditional topical vasodilator papaverine is a non-specific vasodilator substance, which relaxes blood vessels through multiple mechanisms. It is a phosphodiesterase inhibitor, so it may increase cGMP level in smooth muscle cells [16]. Papaverine-induced relaxation is also due to other actions such as decreased calcium influx [17, 18] or inhibition of release of intracellularly stored calcium [19]. It usually relaxes vessels (such as human IMA) at high concentrations regardless of the nature of the contraction. It has been suggested that papaverine has a satisfactory vasorelaxant effect in arterial grafts [20–22] and is still widely used. However, papaverine is not recommended for systemic use. The major concern about the topical use of papaverine is its acidic nature (pH 4.4 at $-2.6 \log M$ and pH 4.8 at $-4.5 \log M$ (as measured in our laboratory), which may damage the endothelial function. These concentrations are related to the solutions used for surgery as most recently demonstrated in the human RA [23]. Although one may argue that mixing it with blood before its use may reduce its acidity, the pharmacological action is uncertain in such a mixture. In addition, the onset of the vasodilatation effect of papaverine is slower than for other vasodilators such as nitroglycerin (NTG) and verapamil although once it reaches a plateau, the effect of papaverine is sustained [2, 21, 22]. Papaverine hy-

drochloride is relatively unstable in non-acidic solutions and a white precipitate is sometimes formed when papaverine is added to the plasmalyte solution (pH approximately 7.4) [24]. Papaverine has also been shown to be inferior to nitroglycerin in the gastroepiploic artery (GEA) [25]. In view of these points, papaverine is still an effective vasodilator for arterial grafts. Its topical spray on the adventitia of the grafts may be effective but its intraluminal injection should be avoided.

5.1.2

Nitrovasodilators

Organic nitrates (nitrovasodilators) such as NTG, glyceryl trinitrate (GTN) or sodium nitroprusside are widely used in CABG patients. The mechanism for these vasodilators is that they release nitric oxide (NO), a powerful stimulant for guanylate cyclase which increases cGMP in the smooth muscle cell. This subsequently reduces intracellular calcium concentrations and leads to relaxation of the smooth muscle cell. Nitrates are slightly more effective in blocking receptor-operated channels [1, 2] than blocking depolarizing agent-mediated contraction. Nitrovasodilators have been demonstrated to be potent vasodilators in the human IMA [15, 20, 26–31], RA [22, 29–33], GEA [25, 34], and inferior epigastric artery (IEA) [4, 34]. It has been demonstrated that NTG is effective for either topical [25], intraluminal [32], or systemic [30, 35] use. In general, nitrates are effective in treating established vascular spasm, regardless of the nature of the contraction, i.e., they are effective in reversing either receptor-mediated contraction (TxA₂ receptors, α -adrenoceptors, or ET receptors) or depolarizing agent (K⁺)-mediated contraction. However, they are less potent in the prevention of vasospasm [1, 26, 33]. This is probably related to the tolerance of a vessel to these nitrovasodilators [15, 26]. Compared with each other, NTG is more potent than sodium nitroprusside (SNP) in its vasorelaxing effect [9], but SNP is more effective in preventing ANGII and α -adrenoceptor-mediated contraction in the IMA [9].

5.1.3

Calcium Antagonists

There are three chemically divergent groups – dihydropyridine (nifedipine, etc.), phenylalkylamines (verapamil, etc.), and benzothiazepines (diltiazem, etc.). The new generation of these drugs has been developed. Of the three calcium antagonists, diltiazem is the least potent. For example, nifedipine is 15-fold more potent than diltiazem with regard to the vasorelaxant effect in the most commonly used human arterial coronary bypass graft – the IMA, as demonstrated in our previous

study [1]. However, nifedipine is not available for IV or topical use. Verapamil is more potent than diltiazem in the canine IMA (EC₅₀ –5.73 vs. –5.38 log M) and saphenous vein (–6.74 vs. –6.30 log M) [1]. We have also found that in the human saphenous vein [20] diltiazem is significantly less potent than verapamil (EC₅₀ –6.62 vs. –6.96 log mol/l). In arterial grafts the effects of vasodilators depend on the nature of the vasoconstriction. This is particularly important for calcium antagonists. When IMA contracts with depolarizing agent potassium (K⁺), nifedipine or other calcium antagonists is very effective both in preventing and reversing IMA contraction [1]. This is due to the fact that calcium antagonists relax blood vessels through a specific mechanism. Calcium antagonists reduce Ca²⁺ influx by blocking voltage-operated calcium channels, which is the major mechanism for the depolarizing agent K⁺ to contract vessels. Therefore, calcium antagonists are particularly effective in preventing or treating K⁺-induced contraction and this has been demonstrated in either IMA [37] or RA [38]. However, in contraction mediated by receptors such as TxA₂ receptors, α -adrenoceptors, ET receptors, or vasopressin (VP1 receptors), calcium antagonists such as nifedipine are less effective. In comparison to K⁺-mediated contraction, calcium antagonists are weak in either preventing or treating the contraction induced by TxA₂ mimetic U46619 [1]. In addition, we have recently reported limited effects of calcium antagonists in preventing or treating α -adrenoceptor [36], ET [15], or VP1 receptor-mediated contraction [39], which is also due to the fact that calcium antagonists are less effective in blocking receptor-operated than voltage-operated calcium channels. Others also reported [33] that diltiazem, which is used empirically to prevent RA vasospasm, had little effect on human RA contractions (receptor-independent and receptor-dependent).

5.1.4

Phosphodiesterase Inhibitors

Phosphodiesterase (PDE) inhibitors are new vasodilators. Intracellular cAMP and cGMP play a role in modulation of vascular smooth muscle tone [40]. Concentrations of cAMP and cGMP are controlled through synthesis by cyclases and through hydrolysis by PDEs. PDEs are classified into at least five types [41, 42]. PDE III inhibitors such as amrinone or milrinone are known to inhibit cGMP-inhibitable low K_m cAMP PDE [43]. The pharmacologic activities of PDE III inhibitors are increased cardiac contractility, reduction of pulmonary and systemic resistance, and inhibition of platelet aggregation [44, 45]. The cardiac and vascular smooth muscle actions are favorable in postoperative management of patients who undergo open heart surgery, particularly in patients who present ventricular dysfunc-

tion and receive arterial grafts for coronary artery bypass surgery. The effect of drugs such as milrinone on the IMA [28, 46–48] or RA [49, 50] has been studied. Although its use has been recommended in CABG, the effect of milrinone on the IMA is superior to that on the RA [50]. Particularly, it has been demonstrated that milrinone has a greater than additive vasodilatory effect when used in combination with NTG [28]. In systemic use, it was reported [35] that after cardiopulmonary bypass, milrinone and nitroglycerin dilate the IMA. On the other hand, another PDE III inhibitor enoximone is a potent *in vitro* vasodilator but exerts weak relaxant effects in IMA and GEA at concentrations in the therapeutic range [51].

5.1.5

TxA₂ Antagonists

Because of the importance of TxA₂ in vasoconstriction and thrombosis, specific TxA₂ antagonists may be useful in the antispastic therapy of arterial grafts. GR30191 has been found to be a potent vasodilator for TxA₂-mediated contraction in either IMA [46] or RA [52]. However, there are no clinical reports as yet.

5.1.6

Potassium (K⁺) Channel Openers

ATP-sensitive potassium channels (K_{ATP}) exist in a wide range of cells, particularly in endocrine cells, smooth muscle, skeletal muscle, neurons, and cardiac cells [53]. Potassium (K⁺) channel openers (KCOs) are considered to comprise a heterogeneous group of organic compounds [54]. The common features among KATP openers include a hydrophobic group, an electrodeficient aromatic ring, and a hydrogen bonding site [54]. KCOs repolarize or hyperpolarize the cell membrane. They therefore decrease the opening probability of voltage-dependent L- and T-type Ca²⁺-channels and restrain agonist-induced Ca²⁺ release from intracellular sources through inhibition of inositol trisphosphate (IP3) formation, and lower the efficiency of calcium as an activator of contractile proteins. In addition, KCOs may accelerate the clearance of intracellular free Ca²⁺ via the Na⁺/Ca²⁺ exchange pathway. The effects drive the vascular smooth muscle cells into a relaxed state and reduce membrane excitability and the reactivity of the cell [54–56]. It has been suggested that vascular smooth muscle is particularly sensitive to KCOs [53, 56–58]. Considering these characteristics, KCOs are of great value as therapeutic agents [57, 58]. Aprikalim [59, 60] and KRN4884 [61] have been studied in the human IMA and found to be potent vasodilators in a number of receptor-mediated contractions and it may, therefore, become a clinically useful antispastic drug in arterial grafts.

5.1.7

α-Adrenoceptor Antagonists

We have demonstrated that the IMA is an α₁-adrenoceptor-predominant artery with little α₂-adrenoceptor function [5] whereas the RA has significant α₂-adrenoceptor function although the RA is also α₁-adrenoceptor predominant [6]. These observations have been supported by others [62].

Therefore, the use of α-adrenoceptor antagonists such as phenoxybenzamine has a rationale and it was reported that in the RA phenoxybenzamine is an effective agent with a prolonged duration of action, specifically preventing catecholamine mediated vasospasm of radial artery conduits [63]. However, theoretically, α-adrenoceptor antagonists are effective in reversing the contraction evoked by α-adrenoceptor as reported [64] but not to other vasoconstrictors as predicted from a pharmacological viewpoint. In fact, Conant and colleagues [65] reported that phenoxybenzamine-treated radial artery failed to respond to noradrenaline but did respond to vasopressin, angiotensin II, endothelin-1, and KCl. The nature of vasoconstriction is complex and may involve many other vasoconstrictors (see Chaps. 1–3). Theoretical considerations and experimental studies have indicated that use of phenoxybenzamine as the sole agent to release spasm in the arterial grafts is inappropriate.

Further, a novel calcium antagonist with α₁-adren-ergic receptor blocking activity, AJ-2615, has been studied by ourselves with regard to inhibition of vasoconstriction in the IMA [66], and this may open up a new method for antispastic protocols.

5.1.8

Beta-Receptor Agonists and Dopamine Receptor Agonists

We have demonstrated that the β-adrenoceptor function is weak in both IMA [67] and RA [6], despite the coexistence of at least three distinct beta-adrenoceptors in human internal mammary artery [68]. Therefore, use of β-adrenoceptor agonists is unlikely relax the IMA and RA to a significant degree and this has been demonstrated to be true [51]. This study showed that although dobutamine (a beta-receptor agonist) is a potent *in vitro* vasodilator, it exerts weak relaxant effects in IMA and GEA at concentrations in the therapeutic range.

Due to the complexity of the interaction between dopamine and dopamine receptors as well as α₁-adrenoceptors, dopamine-induced responses are complex and dose-dependent [69]. In RA, dopamine enhanced the norepinephrine-induced contraction. In GEA, small concentrations (<10⁻⁷ mol/l) of dopamine attenuated the norepinephrine-induced contraction but larger concentrations did not. In IMA, dopamine induced a

vasorelaxation on the norepinephrine contraction only at higher concentrations (10^{-6} – 10^{-5} mol/l) [69]. Most likely, dopamine is not suitable to be used primarily for the vasorelaxant effect in the arterial grafts but one should be aware of its effect on the graft when it is used primarily for its inotropic effect.

5.1.9

Vascular Endothelial Growth Factor

Similar to dopamine and β -adrenoceptor agonists, the use of vascular endothelial growth factor (VEGF) may not be the primary consideration for antispastic therapy in arterial grafts. However, the potent hypotensive effect of VEGF due to its systemic vasorelaxation is demonstrated in the IMA through the endothelium-dependent mechanism [70] and, most likely, the NO and PGI₂ mechanisms through KDR receptors [71].

5.1.10

Commonly Used Antihypertensive Drugs

The above vasodilators already include some commonly used antihypertensive drugs. The relaxation responses in IMA to adenosine (a nucleoside), enalaprilat (a competitive inhibitor of angiotensin-converting enzyme), fenoldopam (a D1-dopamine receptor agonist), hydralazine, labetalol (an α - and β -adrenergic blocker), nicardipine (a calcium channel blocker), nicorandil (K_{ATP} channel opener), nitroglycerin (NTG, a nitrovasodilator), and sodium nitroprusside (SNP, a nitrovasodilator) were compared [72]. The order of efficacy of the *in vitro* relaxation was as follows: SNP, NTG, nicardipine, nicorandil, fenoldopam, hydralazine, adenosine (a nucleoside), and labetalol. The potency was in the order of NTG, SNP, fenoldopam, nicorandil, hydralazine, adenosine, and nicardipine. In addition, angiotensin receptor antagonist GR117289C was studied in the IMA [73].

5.1.11

Combination of Vasodilators

All vasodilators have their own limitations in some respect because each of them has a specific mechanism to relax the vessel. A combination of these vasodilators may overcome these disadvantages and therefore produce a better effect. Some of the combinations have been studied in the IMA and RA. For example, calcium antagonists and NTG may have a synergistic effect in IMA [20, 21, 63, 74, 75], as in RA [22, 23], as a topical solution for the preparation of the grafts. The combination of NTG and verapamil has been reported by ourselves to successfully release the spasm in arterial grafts through intraluminal injection [76]. The method is used successfully by others to relieve the coronary

spasm [77] and is now even used in the catheterization laboratory for preventing RA spasm with success [78].

A combination of other vasodilators has also been reported. The more than additive effect of milrinone on NTG has also been demonstrated by ourselves [28] although such an *in vivo* effect has not yet been demonstrated [35]. The combined use of enoximone (a PDE III inhibitor) and dobutamine (a β -receptor agonist) exerts a greater than additive vasorelaxant effect on IMA and GEA [51].

5.2

Factors Determining the Effects of Vasodilator Substances

An adequate understanding of the mechanism of vasoconstriction and the effect of vasodilators is essential before any proposal is made to use vasodilators. We will review these aspects in addition to those already discussed above.

5.2.1

The Nature of Vasoconstriction and the Mechanism of the Vasodilators

It is well known that vasoconstriction may be evoked by various stimulants. Mechanical stimulation, nerve stimulation, as well as vasoconstrictor substances are the common stimulants of vasoconstriction. Details of the nature of vasoconstriction in the four major arterial grafts (IMA, GEA, IEA, and RA) have been published [4–12, 15, 26–39, 46–52] and further reviewed [79, 80, see also Chaps. 1–3].

5.2.2

The State of the Contraction

In general, there are critical differences in the state of the vascular smooth muscle before and after induction of contraction that affect the responses to vasodilator substances. In other words, the effect may be different when a vasodilator is used before or after the contraction. This is especially important for GTN. We have reported this phenomenon in the human IMA [1, 4–6]. In this artery, although GTN may effectively reverse the already established contraction, it has little efficacy in preventing contraction when mediated by potassium ion or TxA₂. More recently, we have observed this phenomenon in other vasoconstrictor-mediated contractions (α -adrenoceptor agonists or ET) in the human IMA [5, 6, 15]. The cause of this difference is still unclear, although the cGMP mechanism, as previously proposed [1], or rapid tolerance [15] may be a possible explanation. It may also be related to the hypothesis that relaxation of smooth muscle that involves reversal

of a latch state is less dependent on the inhibition of Ca^{2+} mobilization or on dephosphorylation of myosin [81, 82].

5.2.3

Duration of the Use

When repeatedly used, tolerance to some vasodilators may develop. Tolerance is a well-recognized phenomenon for nitrates [83, 84], which is a disadvantage in clinical use.

5.2.4

The Concentration of Vasodilator

The plasma concentration of a vasodilator agent is also a key point in its use. Vasodilators may have a complete reversing effect on vasoconstriction in vitro at high concentrations but these concentrations may never be reached in vivo by systemic administration of the vasodilator. An example of this is that nifedipine, at a non-clinically relevant concentration ($>10 \mu\text{M}$), depresses the contraction induced by ET in the human IMA, but this concentration is far higher than the plasma concentration achievable after normal therapeutic doses of this drug.

5.2.5

Rate of Onset of Effect

The rate of onset is another factor to be considered in evaluating vasodilators. This is particularly important during surgery, in which a rapid onset is always desirable. In regard to the onset of the effect for each vasodilator, nitrates are the fastest, papaverine the slowest, and calcium antagonists are intermediate [20, 21].

The above discussion is focused on the IMA. Although the effect of vasodilators on other arterial conduits (inferior epigastric artery, gastroepiploic artery, and radial artery) has been studied less, the results from the limited studies so far are in accordance with these observations [4, 6, 22, 23, 34, 50, 63, 64, 85–89].

Taken together, we may conclude that there is no “perfect” vasodilator for dilating the IMA or other arterial grafts. Under some circumstances, a combination of vasodilators may be preferable. Table 5.1 outlines the effects of each vasodilator with regard to the type of vasoconstrictor, rapidity of onset, duration of action, tolerance, pH, and availability for systemic use. This information may also be useful for other arterial grafts such as RA and GEA, in which spasm is more frequently encountered and therefore use of vasodilators is even more important.

Table 5.1. Summary of the effects of vasodilators on contractions mediated by various vasoconstrictors in the human IMA at clinically relevant concentrations

Vasodilators	Nature of contraction					Vasodilatation					
	Depolarizing agent mediated	Receptor-mediated TxA_2	α	ET	Angiotensin II	Onset	Duration	Tolerance	Acidity	Systemic use	Inotropic effect
Organic nitrates											
NTG [1, 9, 13–15, 21, 26]	+++	++++	++++	++++		Fast	Short	Yes	No	Yes	No
SNP [9, 13, 14, 27, 29]	++		++			Fast	Short	Weak	No	Yes	No
Calcium antagonists											
Nifedipine [1, 15, 27, 36, 38, 47]	++++	+ / ++	+ / ++	++		Fairly fast	Long	No	No	No	-
Verapamil [1, 20–23, 38]	++++					Fairly fast	Long	No	No	Yes	-
Diltiazem [1, 38]	++++					Fairly fast	Long	No	No	Yes	-
Papaverine [1, 2, 13, 21, 22, 27]	+++	+++	+++			Slow	Long	No	Yes	No	No
PDE inhibitors											
Milrinone [28, 46–50]	+++	+++	+++	+++				No	Yes	Yes	+
TxA_2 antagonists											
GR30191 [52]	++	++++	++	++				No		N/A	No
Potassium channel openers											
Aprikalim [59, 60]	++	++	+++	+++				No		N/A	No
KRN4884 [61]	++		+++	+++	+++			No		N/A	No
α-Adrenoceptor antagonist											
Phenoxybenzamine [63–65]	+	+	++++	+				No			No
Calcium antagonist with α-adrenoceptor antagonism											
AJ-2615 [66]	++++	++	++++	++				No		N/A	No
Angiotensin antagonist											
GR117289C [73]	+	+++	++	++	++++			No		N/A	No

TxA_2 thromboxane A_2 , α α -adrenoceptor, ET endothelin-1, Angiotensin II

5.3

Guidelines for the Use of Vasodilators for Arterial Grafts in CABG

Based on the above discussion, we propose the following guidelines for the use of vasodilators for arterial grafts in coronary artery bypass surgery [37, 90].

1. Judicious use of vasodilators must be based on the understanding that there is no "perfect" vasodilator which is effective for *every* situation. Vasoconstriction (or spasm) may be caused by multiple mechanisms. Vasodilators relax vascular smooth muscle through a specific mechanism or mechanisms. Selective vasodilators such as calcium antagonists are more potent when the vessel is constricted by vasoconstrictors through voltage-operated calcium channels but are less effective when the vessel is constricted through receptor-operated channels. On the other hand, less selective (or non-selective) vasodilators (such as nitrates or papaverine) also have their limit for clinical use.
2. Perioperative administration of vasodilators *does not* necessarily need to be focused only on arterial grafts. Vasodilators (GTN, sodium nitroprusside, calcium antagonists, or phosphodiesterase inhibitors) are frequently used for coronary bypass surgery for dilating peripheral vasculature or coronary vessels. Vasodilators used for these purposes are usually also effective in dilating arterial grafts.
3. For more spastic Type II and III arterial grafts (see Chaps. 1–4), systemic use of vasodilators such as calcium antagonists may be necessary to avoid spasm of these grafts.
4. Careful and correct surgical dissection during harvesting of the arterial grafts is important in prevention of spasm of the grafts during surgery.
5. If clinical signs of "hypoperfusion syndrome" (low cardiac output, left ventricular failure, rising pulmonary wedge pressure, hypotension) or ischemia should appear in a patient already receiving vasodilator treatment for any reason and these manifestations are suspected to be due to arterial graft spasm, change of vasodilators may be wise.
6. When the patient is on sympathomimetic agents for hypotension or inotropic support, it should be kept in mind that those agents may evoke arterial graft contraction.
7. If one vasodilator is not effective in treating graft spasm, a combination such as GTN with calcium antagonists may be effective.
8. Although during surgery, papaverine may be satisfactory for topical use, it may be wise to avoid its use for intraluminal injection. For intraluminal use, other vasodilators such as nitrates or calcium antagonists, or a combination of these vasodilators,

may give fast onset, full vasodilatation without concerns about endothelial damage. An example of such a combination is GTN plus verapamil cocktail [20–23, 76–78].

9. The role of some commonly used vasodilators such as PDE inhibitors, angiotensin antagonists, KCOs, α -adrenoceptor antagonists, β - and adrenoceptor agonists has yet to be determined in arterial grafts. The role of the new generation of vasodilators such as new calcium antagonists, new PDE inhibitors, TxA₂ antagonists, and KCOs needs to be studied. These drugs may prove to be useful under certain circumstances.
10. The endothelium of the grafts plays a key role [91, 92] in both antispastic and long-term patency [93] and, therefore, it is particularly important to protect the endothelium in the grafts when any vasodilator solution is used. This includes normal pH of the solution, avoiding high pressure in the lumen, and no mechanical damage during harvesting [94], etc.

In summary, the use of vasodilators for arterial grafts is a complex issue. Although enormous progress has been made, the continuing search for the best solution for preventing and treating vasospasm is warranted.

Acknowledgement. Supported by St. Vincent Medical Foundation, Portland, Or., U.S.A.

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Myocardial Protection During Coronary Bypass Surgery Using Arterial Grafts



Myocardial Management in Arterial Revascularization

B.S. ALLEN, G.D. BUCKBERG

The objectives of every cardiac operation must be a technically perfect anatomic result and avoidance of intraoperative damage in pursuit of this goal. Nevertheless, perioperative myocardial damage remains the most common cause of morbidity and death following technically successful coronary bypass operation. This occurs whether the conduits are arterial or venous. Cardiac damage from inadequate myocardial protection leading to low output syndrome can prolong hospital stay, and may also result in delayed myocardial fibrosis leading to cardiac dysfunction months to years later [1, 2]. Cardioprotective strategies, like cardiac operations, have evolved to the point that it is essential to understand various techniques in order to limit intraoperative damage during a complicated operation. Surgeons must refrain from using simplistic cardioplegic protection strategies for the very reason that simplicity and safety are not synonymous. As with technical aspects of the surgical repair, the primary object of protection techniques is the use of the best strategy. Integration of surgical techniques is usually required to perform the best technical operation. Similarly, optimal myocardial protection also requires integration of various techniques to achieve the best results. Most surgeons would not abandon a complex surgical procedure (like all arterial revascularization) that was proved superior solely because of its lack of simplicity. Likewise, we should not choose a protection strategy for simplicity, unless it provides optimal and complete myocardial protection. Optimal myocardial protection is as important as an excellent technical repair in achieving the best long-term outcome with surgical correction. Although, the surgeon might desire *simplicity*, the patient is only concerned with *success*.

This chapter describes how oxygenated cardioplegia solutions can be delivered warm to allow their use for active resuscitation before ischemia is imposed, cold to limit damage, and again warm to avoid and reverse ischemic and reperfusion damage before and after aortic unclamping [1, 2]. It focuses primarily on the principles that form the basis for clinical strategies for cardioplegic delivery that can ensure that the selected cardioplegic solution can exert its desired effect, and it describes how these can be implemented. The described

Table 6.1. Myocardial supply/demand balance during aortic cross-clamping

Supply	Demand
Noncoronary collaterals	Electromechanical activity
Intrinsic substrate stores	Wall tension (glycogen) Temperature (metabolic rate)

principles are directly applicable to use of all arterial conduits during coronary revascularization. Issues of protection are important here, due to potential conduit discrepancy between arterial grafts and the coronary artery. Clearly, the long-term patency of arterial grafts must be matched by absence of intraoperative damage while they are constructed.

Table 6.1 lists the factors affecting the myocardial energy supply/demand balance during aortic clamping. The two factors affecting supply include oxygenated blood coming from noncoronary collateral blood flow, and intrinsic or extrinsic substrate stores. All surgeons have noted noncoronary collateral flow during aortic clamping, as blood appears in the coronary arteriotomy site during coronary revascularization despite a flaccid aorta. The second determinant of supply is myocardial glycogen or exogenous glucose to provide anaerobic metabolism to generate some energy during ischemia to maintain cell membrane viability. Anaerobic glycolysis requires the presence of substrate (i.e., glucose or glycogen), and a metabolic environment (i.e., buffering) to allow anaerobic energy production. Myocardial oxygen demands are determined principally by electromechanical activity. Cardiac arrest is used because the fibrillating or beating ischemic heart has a much higher energy requirement. The second determinant of demand is the wall tension within the myocardium, that is minimized by asystole, and the third the myocardial temperature that governs metabolic rate directly.

6.1 Cardioplegic Prerequisites

Essential clinical prerequisites for cardioplegia include (1) a solution that is shown to be safe through testing

under experimental conditions, in ischemic models, (2) the distribution of flow to all cardiac regions, (3) periodic replenishment to counteract noncoronary collateral washout, and (4) strategies for protection in various clinical conditions.

6.2

Cardioplegic Composition

The cardioplegic objectives are to stop the heart safely, allow continued energy production, and counteract deleterious effects of ischemia. The principles which underlie the composition of any cardioplegic solution are enumerated in Table 6.2. First, immediate arrest lowers energy demands to avoid depletion by ischemic electromechanical work, and high-energy stores are enhanced with oxygenated solutions compared to crystalloid solutions, that deplete adenosine triphosphate (ATP) before arrest [1, 2]. Second, reducing myocardial temperature during perfusion lowers metabolic rate during ischemia. Third, substrate (i.e., glucose or glycogen) and Krebs cycle intermediates (i.e., glutamate or aspartate) [3] enhance anaerobic or aerobic energy production (or both) during aortic clamping. Fourth a buffer such as TRIS (hydroxymethyl) aminoethane (THAM), bicarbonate, phosphate, or perhaps some other buffer optimizes the small energy output of anaerobic glycolysis during ischemia [1, 4]. Fifth, there must be some degree of membrane stabilization with exogenous additives or hypocalcemia [1, 5, 6]. Magnesium enrichment improves protection by preventing calcium influx, even in the presence of hypocalcemia. The role of steroids, calcium channel blockers, and procaine is uncertain at this time. Oxygen radical scavengers (i.e., superoxide dismutase [5], catalase, allopurinol, coenzyme Q₁₀ [CoQ₁₀], [6]) may counteract the cytotoxic oxygen metabolites during ischemia and reperfusion [7]. Sixth, myocardial edema is limited by altering the osmolarity and colloid osmotic pressure of the cardioplegic solution during infusions [7].

It is essential that only cardioplegic solutions designed and tested for a specific purpose be utilized.

Table 6.2. Pharmacologic cardioplegia

Principle	Method
Immediate arrest	K ⁺ , Mg ²⁺ , procaine
Hypothermia	10°–20°C
Substrate	Oxygen, glucose, glutamate, aspartate
Appropriate pH (buffer)	THAM, bicarb., phosphate
Membrane stabilization	Ca ²⁺ , steroids, procaine Ca ²⁺ antagonist, magnesium O ₂ radical scavenger

These solutions should be delivered according to established experimental protocols, and, most importantly, the aim must be *complete* preservation of metabolic and functional parameters. A failure to reconstitute creatine phosphate or other metabolic levels following aortic unclamping should be looked at as a protection failure, in the same way that a residual ventricular septal defect (VSD) or AV valve regurgitation is a technical failure. Optimal protection is as important as the technical aspects of the repair in achieving the best long-term outcome for the patient. Using arterial grafts will not improve long-term survival if the patient is left with myocardial dysfunction as a result of poor protection.

6.3

Blood Cardioplegia (Table 6.3)

We have selected blood as the cardioplegic vehicle, since this physiologic source of oxygen is available readily in the extracorporeal circuit, and its use limits hemodilution when large volumes of cardioplegia are needed. An additional advantage of a blood cardioplegic vehicle is to ensure the buffering capacity of blood proteins, especially histidine imidazole groups [8]. Furthermore, the rheologic benefits on the microvasculature afforded by erythrocytes enhance papillary muscle perfusion compared with oxygenated crystalloid cardioplegia and reduce coronary vascular resistance and edema formation [9]. The erythrocytes of blood cardioplegia also contain abundant endogenous oxygen free radical scavengers (i.e., superoxide dismutase, catalase, and glutathione) [10], which may reduce oxygen-mediated injury during reperfusion. Their benefits enumerate only the known benefits of using blood as the vehicle for delivering oxygenated cardioplegia. We are confident that further studies will reveal other naturally occurring blood components (i.e., enzymes, cofactors, substrates, and electrolytes) that are important and would otherwise need to be added to any artificially constructed solution.

Blood cardioplegia is *not* just any crystalloid solution added to blood. Solutions like Plegisol (St. Thomas solution) were specifically developed to work best as a crystalloid solution, with the constituents adjusted to

Table 6.3. Blood cardioplegia

Oxygenation during arrest
Reoxygenation during replenishment
Avoids reperfusion injury
Avoids hemodilution
Endogenous
Oxygen radical scavengers
Buffers
Oncoconicity

provide optimal protection at these levels [11, 12]. Mixing Plegisol (or other crystalloid cardioplegia solutions) with blood alters the final (delivered) composition, and, as such, may not provide the same level of protection. These solutions must be tested and compared to blood cardioplegic solutions that convey established benefits. Conversely, blood cardioplegic solutions were developed to provide the ideal levels of the various components only after they are mixed with blood [1, 3, 12, 13]. Therefore, it is important that the surgeon recognize the limitations of crystalloid solutions, and employ blood cardioplegic solutions that have been specifically formulated for that purpose.

The versatility of blood cardioplegia provides the cardiac surgeon with an extremely powerful tool to actively treat the jeopardized myocardium as well as to prevent ischemic damage, provided attention is directed toward ensuring adequate delivery of the cardioplegic solutions. Tables 6.4 and 6.5 enumerate the principles that underlie our experimentally and clinically tested blood cardioplegic solutions [1, 2, 13, 14]. The cold cardioplegic solution contains 500–600 $\mu\text{M/l}$ calcium without glutamate or aspartate, but the cardioplegic solution used for warm cardioplegic induction and warm reperfusion contains glutamate and aspartate and a lower ionic calcium achieved by adding more citrate phosphate dextrose (CPD).

Table 6.4. Warm blood cardioplegia solution

Cardioplegia additive	Volume added (ml)	Component modified	Concentration delivered ^a
KCl (2 mEq/ml)	10	K ⁺	8–10 mEq/l
THAM (0.3 mol/l)	225	pH	pH 7.5–7.7
CPD	225	Ca ²⁺	0.2–0.3 mM/l
MgCl ₂ (2 mEq/ml)	9	Mg ²⁺	4–6 mEq/l
Aspartate/glutamate	250	Substrate	13 mmol/l each
D50 W	40	Glucose	<400 mg/dl
D5 W	200	Osmolarity	380–400 mOsm

THAM tromethamine, CPD citrate-phosphate-dextrose; D50 W 50% dextrose in water

^a When mixed in a 4:1 ratio with blood

Table 6.5. Cold blood cardioplegia solution

Cardioplegia additive	Volume added (ml)	Component modified	Concentration delivered ^a
KCl (2 mEq/ml)	5	K ⁺	8–10 mEq/l
THAM (0.3 mol/l)	200	pH	pH 7.6–7.8
CPD	50	Ca ²⁺	0.5–0.6 mM/l
MgCl ₂ (2 mEq/ml)	9	Mg ²⁺	4–6 mEq/l
D5 W	550	Osmolarity	340–360 mOsm

THAM tromethamine, CPD citrate-phosphate-dextrose, D50 W 50% dextrose in water

^a When mixed in a 4:1 ratio with blood

6.4

Operative Strategy

The strategies for clinical cardioplegia may be separated into the phases of (1) induction, (2) maintenance and distribution, and (3) reperfusion.

6.4.1

Cardioplegic Induction

Cardioplegia may be given immediately after extracorporeal circulation has begun, provided that the pulmonary artery is collapsed to attest to the adequacy of venous return. Starting the infusion shortly before aortic clamping ensures aortic valve competence. We always deliver cardioplegia over time instead of by dose, as the heart takes up nutrients and is cooled over time. We do not aim for a specific flow, but deliver the cardioplegia at a continuously measured aortic root or coronary sinus pressure of 30–50 mm Hg.

6.4.2

Cold Induction

Cardioplegic induction in operations on hearts with reasonably normal energy reserves is intended to (1) stop the heart promptly to lower oxygen demands, (2) produce hypothermia to reduce O₂ demands further, and (3) create an environment which allows continuous anaerobic energy production during intervals between cardioplegic replenishments in order to prevent ischemic damage (Table 6.6). An initial cold (4°–8°C) infusion containing a high concentration of potassium (i.e., 20–25 mEq/l, KCl) will produce asystole promptly. Measurement of the aortic infusion pressure will allow detection of aortic incompetence if it is caused inadvertently. Cold induction is usually given from 4–5 months to allow for uniform cooling throughout the myocardium. Cardioplegic solutions stop the heart by depolarizing the cell membrane. Higher cardioplegic potassium concentrations (i.e., 15–30 mEq/l) are usually necessary to produce then to maintain asystole, but raising K⁺ > 30 mEq/l is unnecessary during cardioplegic induction, and only increases the potential for systemic hyperkalemia. Combining hypocalcemic and magnesium enrichment with potassium will also quicken arrest with blood or crystalloid cardioplegia [11, 15]. Cardioplegic K⁺ can be reduced to 8–10 mEq/l during subsequent cold cardioplegic infusions (i.e., multidose cardioplegia; see “Cardioplegic Maintenance” below) since perfusion or topical hypothermia potentiates the effectiveness of any cardioplegic potassium concentration.

Failure to produce arrest within 1–2 min may be due to (1) incomplete aortic clamping, (2) aortic insufficiency produced by distortion of the noncoronary cusp

Table 6.6. Blood cardioplegic induction

Cold	Warm
Global hypothermia	"Active resuscitation"
Prompt asystole	

by a large right atrial cannula, (3) incomplete decompression by the venous cannula resulting in admixture of venous blood returning to the left heart and diluting of the cardioplegic solution, and (4) inadvertent failure to add sufficient potassium to the cardioplegic solution. Palpation of the left ventricle during cardioplegic induction allows detection of left ventricular distention that occurs if venous drainage is inadequate or aortic insufficiency has been produced. Corrective measures include readjusting the position of the venous cannula within the right atrium and/or moving it away from the coronary cusp. Discontinuation of the cardioplegic infusion and immediate ventricular venting are necessary if these maneuvers fail to produce decompression. Undue concern should not be directed toward reducing the temperature of the cardioplegic solution much below 10°C since minor differences in solution temperature (i.e., between 5° and 10°C) will not produce major differences in myocardial temperature or oxygen demands during the brief interval of cardioplegic infusion, especially after the heart is arrested.

Cardioplegic infusions may cause myocardial edema (especially if the myocardial cells are ischemic), if perfusion pressure is allowed to become excessive (i.e., > 80 mm Hg) since the myocardial contractile force and muscle tone which limit fluid flux mechanically are overcome by pharmacologic asystole, and hypothermia interferes with normal cell volume regulation by decreasing the effectiveness of the Na⁺/K⁺ pump [2, 7, 16]. Clinical cardioplegic perfusion pressures of 80–100 mm Hg are probably safe during cardioplegic induction since myocardial electromechanical activity persists during part of the infusion, the full extent of perfusion hypothermia is not instantaneous, and the integrity of the capillary bed has not yet been altered by ischemic damage. Conversely, once the heart is arrested, keeping perfusion pressure at or below 50 mm Hg during reinfusions and reperfusion will limit edema when cardioplegic replenishments are delivered to myocardial regions containing capillary endothelial cells that may have been damaged because they did not receive adequate cardioplegic protection during previous infusions.

6.4.3

Warm Induction

Cardiac operations upon ischemic hearts (i.e., cardiogenic shock, extending myocardial infarction, hemodynamic instability) or in patients with left or right

ventricular hypertrophy or dysfunction pose more difficult problems in myocardial protection. Depletion of energy reserves and glycogen stores is common in such hearts; they (1) are less tolerant to ischemia during aortic clamping, (2) cannot sustain cell metabolism when blood supply is interrupted, and (3) use oxygen inefficiently. The induction of warm blood cardioplegia in the energy depleted heart is, in a sense, the first phase of reperfusion.

A brief (i.e., 5-min) infusion of warm oxygenated cardioplegic solution can be used as a form of active resuscitation in energy-depleted hearts [3, 17] which must undergo prolonged (i.e., 2 h) subsequent aortic clamping. Normothermia optimizes the rate of cellular repair, and enrichment of the oxygenated cardioplegic solution with amino acid precursors of Krebs cycle intermediates (aspartate and glutamate) improves oxygen utilization capacity. Substrate enriched warm (37°C) blood cardioplegic induction results in myocardial oxygen uptake in energy depleted hearts (subjected to 45 min of normothermic global ischemia) which exceeds basal requirements markedly (Fig. 6.1) and results in improved recovery despite two additional hours of aortic clamping with multidose blood cardioplegia (to simulate the time needed for operative repair) [18, 19] (Fig. 6.2). The extra oxygen may be used to repair cell damage and to replace the energy stores (creatine phosphate) which can be used to sustain anaerobic metabolism during the ischemic intervals until the next cardioplegic replenishment. Left ventricular venting during warm induction lowers wall tension maximally [20].

In contrast to cold cardioplegic induction, the *duration* of cardioplegic delivery during normothermic in-

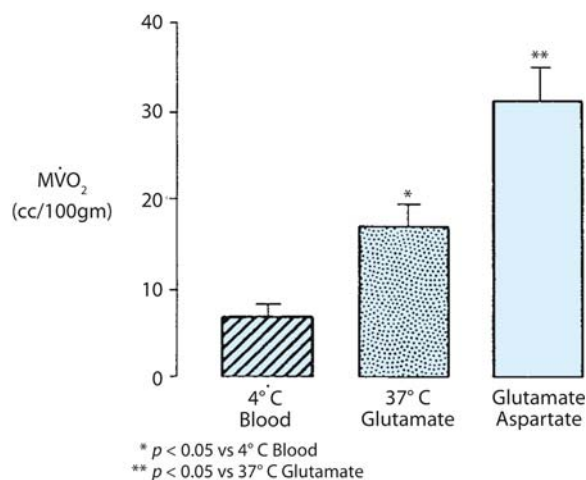


Fig. 6.1. Oxygen consumption during induction of blood cardioplegia. Note: (1) twice as much oxygen consumed by hearts given warm (37°C) glutamate blood cardioplegia compared to cold (4°C) blood cardioplegia, (2) > threefold increase in oxygen consumption by aspartate enrichment of warm glutamate blood cardioplegia (MVO₂, myocardial oxygen consumption)

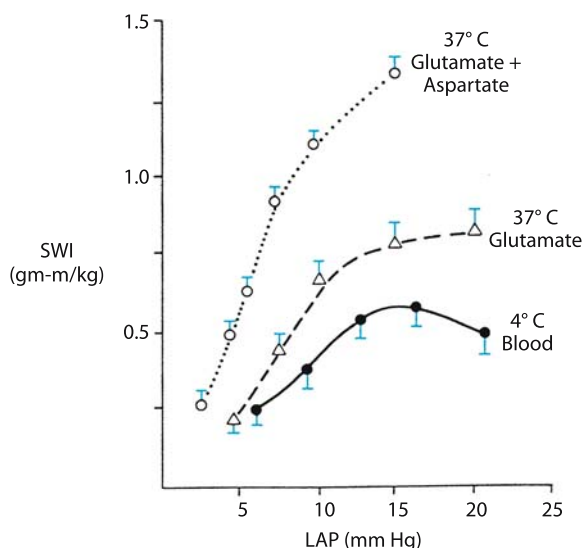


Fig. 6.2. Left ventricular performance 30 min after blood reperfusion. Note: (1) normal ventricular performance after warm (37°C) induction of aspartate enriched glutamate blood cardioplegia; (2) moderate depression in ventricular performance after warm induction with glutamate blood cardioplegia; (3) severe depression in ventricular failure after cold (4°C) blood cardioplegia (LAP left atrial pressure, SWI stroke work index)

duction is more important than the volume of cardioplegia given because the heart takes up oxygen over time and not by dose. Whereas the basal myocardial oxygen requirements of the healthy heart subjected to normothermic arrest are only 1 ml/100 g per minute or 5 ml/100 g during 5 min, the energy-depleted heart consumes approximately 25–30 ml O₂ over a 5-min induction interval under experimental conditions [3, 21]. Administration of this same cardioplegic volume for 1 min would allow only 20% of the oxygen to be used compared to the fivefold greater O₂ uptake which can occur when the same volume of cardioplegia is given over 5 min.

The operation does not need to be prolonged during warm induction of oxygenated cardioplegia. Distal anastomoses into occluded left anterior descending or right coronary arteries can be constructed in coronary operations provided aortic insufficiency is not produced by distorting the heart. More immediate arrest during warm induction of blood cardioplegia occurs when the concentration of the cardioplegic agent is transiently increased (i.e., to 25 mEq/l K⁺). The arrested heart then tends to stay that way with a lower potassium concentration (8–10 mEq/l) especially in the presence of hypocalcemia and elevated magnesium levels. Primarily using a warm cardioplegic solution with a potassium concentration of 8–10 mEq/l helps (1) prevent hyperkalemia in longer operations requiring longer volumes of cardioplegia, (2) prevents the ischemic cell from being left in a high (20–30 mEq/l) hyperkalemic

environment, which can promote calcium influx leading to cell damage and (3) allows the same cardioplegic solution to be used during warm reperfusion (hot shot).

Warm cardioplegic induction must be followed by the administration of cold cardioplegia to provide perfusion hypothermia to prevent ischemic damage during the subsequent period of aortic clamping. The prolonged aortic clamping during cardioplegic induction (5 min of warm and 3–5 min of cold blood cardioplegia) does not add ischemia when the cardioplegic ingredients are mixed with blood or some other form of oxygen (i.e., fluorocarbons, bubbled oxygen, or stroma-free hemoglobin). A 5-min interval of warm blood cardioplegic induction has previously been used in hemodynamically unstable patients, particularly those in cardiogenic shock [22–24]. It is now apparent that many hearts not exhibiting cardiogenic shock may also be energy depleted, as decreased levels of ATP are reported in hypertrophied hearts with pressure or volume overload and those with coronary artery disease [25, 26]. In addition, the risk profile of patients requiring operation is increasing and recent studies show that there is increased uptake of oxygen and glucose during warm substrate-enriched blood cardioplegic induction in noncardiogenic shock patients; this (1) is most pronounced in patients who were unstable preoperatively (CHF, left main disease, unstable angina) or who are hypertensive with or without left ventricular hypertrophy, (2) persists throughout normothermic induction, and (3) correlates directly with the preoperative score described by Parsonnet that predicts higher perioperative mortality [27, 28]. The normothermic infusion is delivered both antegrade and retrograde to ensure cardioplegic distribution as in cardiogenic shock patients (to be described subsequently).

6.4.4

Cardioplegic Maintenance

All hearts receive some noncoronary collateral blood flow via pericardial connections. The volume of this flow is variable [29], but is sufficient to wash away all cardioplegic solutions with the exception of those given to donor hearts excised for subsequent transplantation. Myocardial temperature increases after the cardioplegic solution is discontinued, as the heart is rewarmed by the noncoronary collateral blood flow that has the same temperature as the systemic perfusate. Efforts at controlling noncoronary collateral flow by reducing either systemic flow rate or systemic perfusion pressure, or by using profound levels of systemic hypothermia (<25°C), must be tempered by the recognition of the possible hematologic consequences of deep hypothermia, and the potential deleterious effects of hypoperfusion of other vital organs (brain and kidney) at low systemic flow rates.

Periodic replenishment of the cardioplegic solution at approximately 20-min intervals counteracts noncoronary collateral washout. Multidose cardioplegia is necessary even if electromechanical activity does not return since low-level electrical activity may precede recurrence of visible mechanical activity, and can lead to delayed recovery if cardioplegic replenishment is not provided [10]. Periodic replenishment (1) maintains arrest, (2) restores desired levels of hypothermia, (3) buffers acidosis, (4) washes acid metabolites away which inhibit continued anaerobiosis, (5) replenishes high-energy phosphates if the cardioplegic solution is oxygenated, (6) restores substrates depleted during ischemia [30] and (7) counteracts edema with hyperosmolarity.

Cardioplegic replenishment with low-potassium (8–10 mg/l) solutions limits systemic hyperkalemia. Replenishment of oxygenated cardioplegic solutions at 200–250 mL/min over 2 min ensures a gentle perfusion pressure (less than 50 mm Hg) to avoid edema, and allows enough time for the heart to use the delivered oxygen. Myocardial oxygen uptake may exceed basal demands by as much as tenfold during each 2-min replenishment [31]. Asanguineous cardioplegic solutions without oxygen should be reinfused after similar intervals, but anoxic solutions should be given as a fixed volume and as rapidly as possible to limit the duration of anoxia, provided perfusion pressure does not exceed 50 mm Hg. High perfusion pressure during cardioplegic reinfusions should direct suspicion toward the possibility of (1) obstruction of the infusion cannula or (2) kinking or twisting of one of the grafts.

6.4.5

Cardioplegic Distribution

To ensure an adequate cardioplegic solution distribution is especially important in coronary patients where maldistribution of flow is the reason for operation. Our studies show that it is safer to clamp the aorta for 2–4 h with good cardioplegic distribution than for as little as 30 min when the same cold cardioplegic solution is given without attempts to deliver it beyond coronary stenosis [32, 33] (Fig. 6.3). Homogeneous hypothermia is not a necessary immediate goal provided the heart remains arrested. The myocardial oxygen requirements of asystole are so low at 22°C (0.3 ml/100 g per minute) that they cannot be reduced substantially by reducing temperature further. A prompt fall in myocardial temperature will be achieved by perfusion of cardioplegia through the grafts after distal anastomoses are constructed. However, this is only accomplished with arterial grafts if they are connected to the aorta. Because distribution of cardioplegia through grafts may not always be possible with arterial revascularization, the order of grafting is less important; but we would still rec-

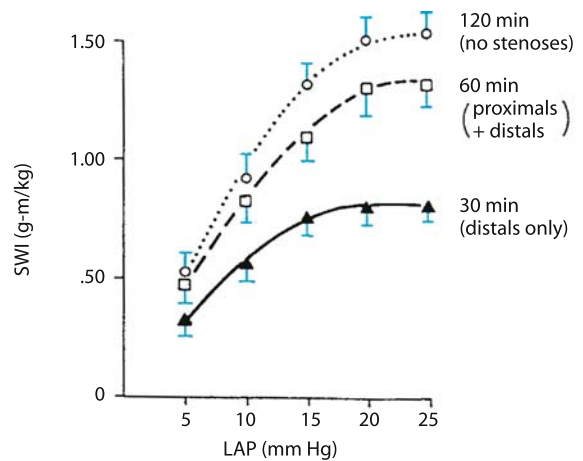


Fig. 6.3. Left ventricular performance after blood cardioplegic infusion in dogs with no stenosis, and those where attempts were made to distribute the cardioplegic solution beyond stenosis. Note the partial recovery following 30 min of aortic clamping when no attempt was made to distribute the cardioplegic solution, and the normal performance following 120 min of aortic clamping when cardioplegic distribution was unimpeded

ommend grafting any free grafts which will be anastomosed to the aorta first to allow for improved cardioplegic delivery. Conversely, with vein grafts we usually graft the largest area of remote myocardium first.

Possible strategies to ensure cardioplegic distribution with arterial grafting include constructing both proximal anastomoses during a single period of aortic clamping, or delivering retrograde cardioplegia. Most operations will require both routes of delivery because many arterial grafts are left in situ (i.e., internal mammary artery, IMA), which prevents distribution of cardioplegia via the newly constructed grafts.

All Anastomoses During Aortic Clamping. This prolongs the duration of aortic clamping but ensures cardioplegic delivery provided each proximal anastomosis is accomplished immediately after each anastomosis. The obligatory prolongation of aortic clamping is counterbalanced by the improved cardioplegic distribution as shown in a recent report by Weisel et al. [34]. Prolongation of aortic clamping may be problematic if complete revascularization is not possible, or many in situ arterial grafts are utilized, as no protection can be offered to these areas of contracting muscle that cannot be revascularized due to unsuitable distal vessels. Retrograde cardioplegic administration circumvents this problem by ensuring distribution to areas supplied by obstructed vessels as well as those receiving in situ arterial grafts [19, 35, 36], and can be delivered during construction of proximal anastomoses to further limit the ischemic duration while the aorta is clamped. The construction of all anastomoses during a single period of aortic clamping also circumvents possible dislodge-

ment of atheromatous intra-aortic debris during application of a tangential aortic clamp.

6.5

Cardioplegia Pressure

Antegrade cardioplegia is often delivered without directly monitoring the infusion pressure. The surgeon or perfusionist can therefore only estimate the actual perfusion pressure [2, 16, 37]. This may result in cardioplegia being delivered at a pressure, which is higher or lower than desired. Furthermore, even if the pressure is monitored, the optimal cardioplegia infusion pressure remains essentially unknown. Although a high cardioplegic perfusion pressure is thought to be deleterious, especially to ischemic tissue, the definition of high remains undefined. What pressure is required to insure distribution to all areas of the myocardium, and the consequences of even moderate elevation of cardioplegic infusion pressure, must be understood.

To investigate this question, we protected hearts with blood cardioplegia delivered either at high (80–100 mm Hg) or low (30–50 mm Hg) pressure [16]. In unstressed (nonischemic) hearts, there was complete preservation of myocardial and vascular function using either low or high cardioplegia infusion pressure. However, even in normal hearts there was still an increase in myocardial edema when an infusion pressure of 80–100 mmHg was used. In contrast, the effect of cardioplegia infusion pressure was quite different if the heart was first stressed. In stressed hearts low cardioplegia infusion pressure protected the heart from further damage, and resulted in complete preservation of myocardial and vascular endothelial cell function. This implies that a cardioplegic infusion pressure of 30–50 mm Hg is high enough to ensure adequate myocardial distribution, since without adequate distribution, myocardial protection is poor. Conversely, when cardioplegic infusions were delivered at a slightly higher (80–100 mmHg) pressure, there was post bypass myocardial and vascular endothelial cell dysfunction, increased edema, and decreased ATP levels. We therefore always deliver cardioplegia at a measured pressure of 30–50 mm Hg in arrested hearts.

Direct intravascular pressure measurement is the only reliable method for determining either aortic or coronary sinus pressure during cardioplegic delivery [2, 16, 37]. This conclusion was reached by obtaining simultaneous measurement of intravascular pressure in either the aorta or coronary sinus during cardioplegic infusions and comparing it to calculated pressure from the known pressure drop in the tubing system at various flow rates [2, 16, 37]. This demonstrated that: (1) calculated pressure does not accurately reflect the measured intravascular pressure during either antegrade or

retrograde delivery, (2) the variability between calculated and measured intravascular pressure increases as either antegrade or retrograde cardioplegic flow rate is raised, and (3) a precise measurement is essential, since fingertip estimation is inaccurate. This discrepancy between the calculated and measured intravascular pressure probably results from differences related to calibration with roller pumps, and wide fluctuations in cardioplegic delivery system pressure which can develop when temperature, flow, and viscosity are varied in systems containing rigid and compliant components. Direct intravascular measurement circumvents this problem and provides the surgeon with a more reliable pressure measurement. Direct aortic monitoring should, therefore, be used to prevent inadvertent elevations in pressure, since even small changes may significantly affect myocardial protection [16].

6.6

Retrograde Cardioplegia

This method has the theoretical advantages of (1) distribution of cardioplegia in diffuse coronary disease, especially when all areas cannot be revascularized, and (2) the ability to distribute cardioplegia to areas receiving in situ arterial grafts since with all arterial grafting, techniques for perfusion of cardioplegia down vein grafts are abandoned. One exception is with a long ra-

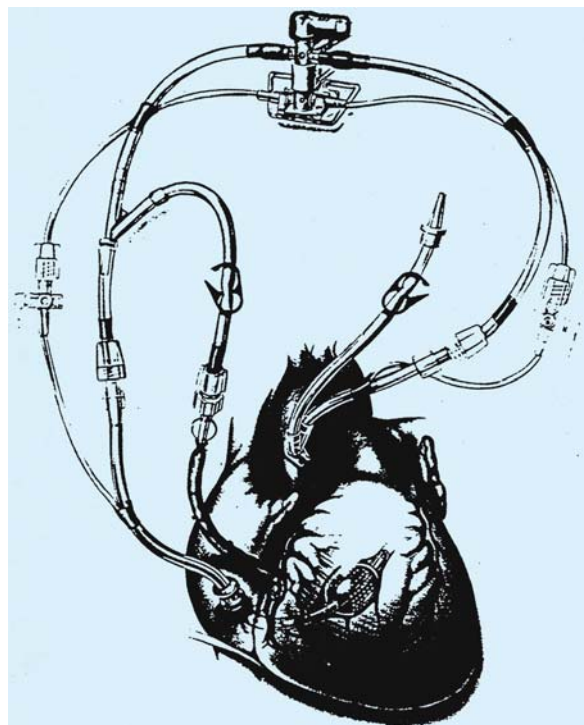


Fig. 6.4. Cardioplegic delivery system in current clinical use

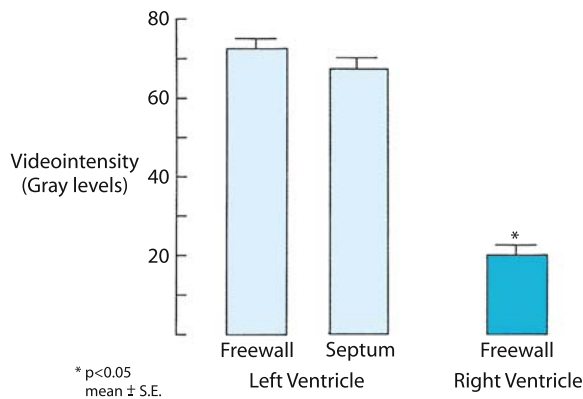


Fig. 6.5. Myocardial perfusion assessed by contrast echocardiography of the right and left ventricular (freewall and septum) during retrograde cardioplegic delivery in 12 patients. Note the decreased right ventricular perfusion compared to the septum and left ventricular freewall

dial artery graft that can be perfused directly. The need for using both antegrade and retrograde cardioplegic delivery in coronary operations is emphasized by experimental and clinical data [35, 38]. Figure 6.4 depicts our current clinical method for antegrade and retrograde delivery. We have shown poor cardioplegic distribution to jeopardized myocardium with antegrade infusions under conditions of experimentally simulated coronary stenosis [35, 36], as well as redistribution of cardioplegic flow away from vulnerable subendocardial muscle. Conversely, retrograde cardioplegia is directed preferentially toward subendocardial muscle despite occlusion of the coronary artery supplying the jeopardized region. The right ventricle is not protected consistently by retrograde cardioplegia, as right ventricular cooling and post-bypass functional recovery are somewhat variable in experimental studies of isolated cold retrograde cardioplegia. These experimental findings have recently been confirmed clinically by contrast echocardiography that demonstrated poor right ventricular myocardial perfusion with retrograde delivery [39] (Fig. 6.5). Preliminary clinical observations suggest also that antegrade and retrograde cardioplegia supply different vascular beds, because glucose and O_2 uptake increase, and lactate washout occurs when switching from antegrade to retrograde cardioplegia, or from retrograde to antegrade cardioplegia [40] (Fig. 6.6). Therefore in patients with complete occlusion of the RCA and right ventricular dysfunction we believe an arterial graft (RIMA, or radial artery) directly anastomosed to the aorta should be utilized to allow antegrade distribution of cardioplegia.

We now routinely use both antegrade and retrograde cardioplegia in all patients undergoing coronary artery bypass grafting as well as other procedures. Overall mortality in a recent series was 2.8% (Table 6.7) and the majority of patients were in the high risk cate-

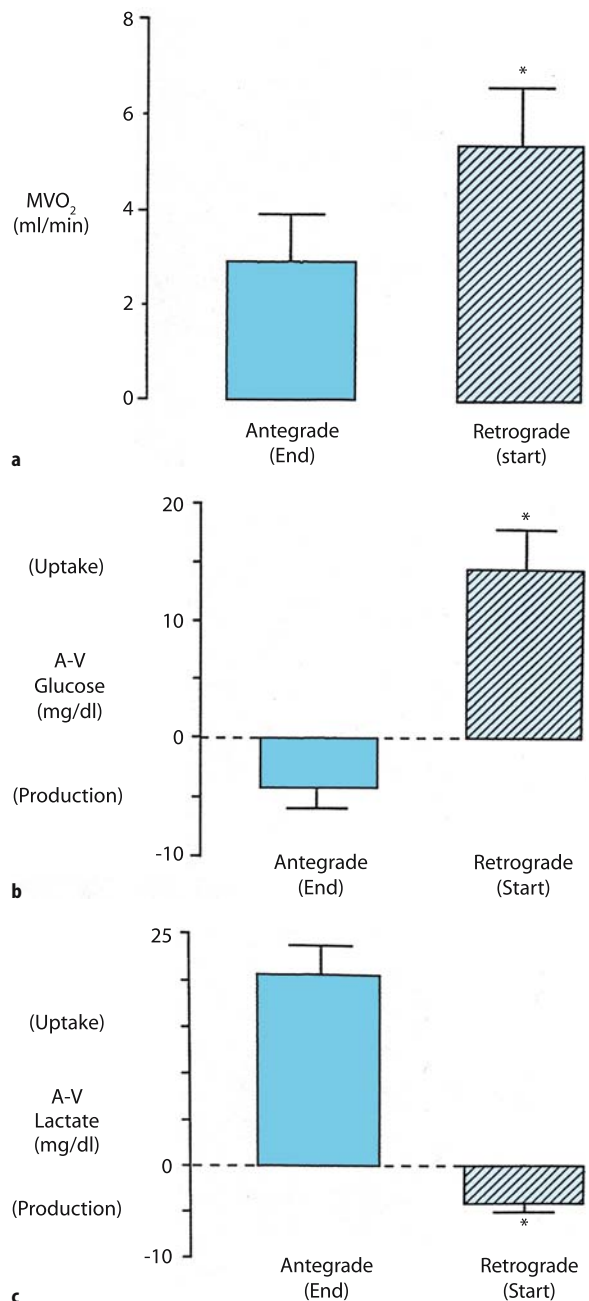


Fig. 6.6a-c. Metabolic measurements during warm cardioplegic induction at the end of antegrade (solid bar) and at beginning of retrograde (hatched bar) administration in 26 patients. Note: **a** myocardial O_2 uptake increase when switching from antegrade to retrograde delivery; **b** glucose consumption increases; and **c** lactate consumption switches to production when changing from antegrade to retrograde delivery. A similar pattern was observed when switching from retrograde to antegrade delivery in separate studies

gory. This combined antegrade/retrograde approach has increased the safety of using IMA or other arterial grafts in high risk patients who otherwise would have received vein grafts because of previous inability to provide ade-

Table 6.7. Antegrade/retrograde blood cardioplegia

CABG	261
Shock or EF, 0.2 or AMI	49
Reops.	48
AVR and/or MVR	103
Dissecting aortic aneurysm	3
Pediatric CHD	123
	490 patients
Mortality	2.8 %

Types of operation where combined antegrade/retrograde blood cardioplegia was used

CABG coronary artery bypass grafting, AVR aortic valve replacement, MVR mitral valve replacement, CHD congenital heart disease

quate cardioplegic distribution to large myocardial segments. Normally we divide the blood cardioplegic volume delivered equally between antegrade and retrograde cardioplegia during all phases of cardioplegic administration (i.e., warm induction, multidose cold blood cardioplegic replenishments, and warm reperfusion). Even with all arterial grafts, antegrade infusions are still delivered to ensure distribution to areas (i.e., right ventricle) not perfused by retrograde delivery.

6.7

Specific Issues with all Arterial Conduits

Proponents of different techniques of intraoperative myocardial protection have traditionally, and for uncertain reasons, taken adversarial positions (i.e., ischemic arrest versus ventricular fibrillation, blood versus crystalloid cardioplegia, antegrade versus retrograde cardioplegia). The fundamental issue is the development of a thoughtful strategy for cardioplegic distribution, and this can be achieved by combining the benefits of both antegrade and retrograde cardioplegic techniques (Table 6.8). We suspect that application of this combined strategy will allow more critically ill patients to undergo safe internal mammary artery grafting and to experience the same complete immediate recovery of regional and global function shown in patients who receive vein grafts. A critical factor, if grafting large arterial segments, supplying large myocardial regions is to be sure of adequate flow via the arterial conduit before

Table 6.8. Advantages of combined antegrade/retrograde cardioplegic techniques

Prompt arrest
Ensure distribution (IMA, AI, coronary occlusion)
Limit CP volume
Uninterrupted valve procedures
Avoid ostial cannulation
Flush coronary debris/air

IMA internal mammary artery, AI aortic insufficiency, CP cardioplegia

anastomosis. This includes (a) opening the radial artery (to observe a large flow), while the proximal end is intact, (b) the same maneuver with the gastroepiploic artery with papavarine, and (c) adding papavarine or a Fogerty dilator to the IMA if there is not abundant flow to supply a large vascular bed.

Failure to ensure adequate antegrade flow due to the caliber of the prevailing arterial conduit may lead to ventricular failure caused by inadequate graft perfusion, rather than inadequate myocardial protection. Under these circumstances, an added vein graft may be very useful (i.e., flow is enhanced by augmenting distal flow when a small IMA graft supplies large LAD vessels.)

6.8

Reperfusion

Reperfusion injury is defined as the functional, metabolic, and structural alterations caused by reperfusion after a period of temporary ischemia (i.e., aortic clamping) [19]. The potential for this damage exists during all cardiac operations because the aorta must be clamped to produce a quiet bloodless field. Reperfusion damage is characterized by (1) intracellular calcium accumulation [41], (2) explosive cell swelling with reduction of postischemic blood flow and reduced ventricular compliance [41, 42], and (3) inability to utilize delivered oxygen, even when coronary flow and oxygen content are ample [13, 43]. Our studies show that the fate of myocardium jeopardized by global and regional ischemia is determined more by the careful control of the conditions of reperfusion and composition of the perfusate than by the duration of ischemia itself [44]. The cardiac surgeon is in the unique position to counteract the potential of reperfusion damage since the conditions of reperfusion and the composition of the perfusate are under the surgeon's immediate control.

Postischemic reperfusion damage after global ischemia can be avoided or minimized by substituting a brief (i.e., 3- to 5-min) warm (37°C) blood cardioplegic infusion during the initial phase of reoxygenation for the normal blood reperfusion which would be provided by aortic unclamping [13] (Fig. 6.7). The principles (Table 6.9) that are addressed during controlled reperfusion include (1) reoxygenation with blood to start aerobic metabolism for energy production to repair cellular injury, (2) delivery of the reperfusion over time rather than by dose to maximize O₂ utilization [45], (3) lowering energy demands by maintaining temporary cardioplegia to allow the limited O₂ ability to be channeled toward reparative processes [46], (4) replenishing substrate (i.e., glutamate) which allows optimal aerobic energy production to occur [18], (5) making the perfusate pH alkalotic to counteract tissue acidosis

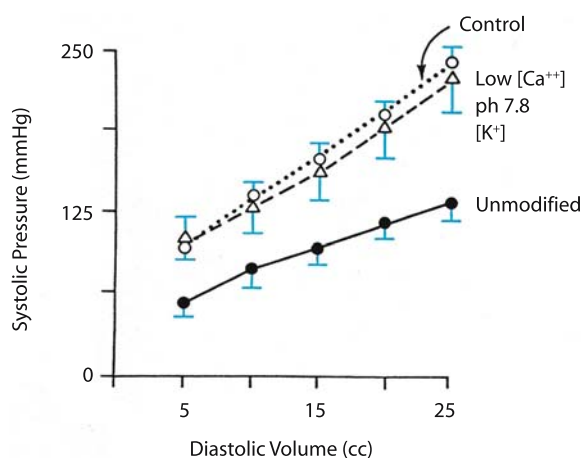


Fig. 6.7. Left ventricular performance 30 min after 1 h of topical hypothermic ischemic arrest. Note the normal postischemic performance when a blood cardioplegic perfusate containing low calcium, high pH, was given just prior to removal of the aortic clamp, and the depressed myocardial performance when the perfusate was unmodified

Table 6.9. Warm cardioplegic reperfusion

Principle	Method
Provide O ₂	Blood
Optimize metabolism	Normothermia
Duration	5–10 min
Maintain asystole	KCl
Replenish substrate	Glutamate/aspartate
Reverse acidosis	Buffer
Limit Ca ²⁺	CPD
Counteract edema	Hyperosmolarity Gentle pressure

CPD citrate phosphate dextrose

and optimize enzymatic and metabolic function during recovery [47], (6) temporarily reducing ionic calcium available to enter the cell (i.e., chelation with citrate phosphate dextrose) [48], (7) inducing hyperosmolarity and decreasing perfusion pressure (i.e., 50 mm Hg to reduce and minimize reperfusion edema) [49, 50], and (8) warming the perfusate to 37°C to optimize the rate of metabolic recovery [19, 51]. Hypothermic reperfusion is not used because it retards metabolic rate and slows repair [52, 53].

Clinical studies by Teoh et al. [54] document the metabolic and functional value of using a warm blood cardioplegic perfusate strategy in elective coronary operations, and we use a warm blood perfusate before aortic unclamping in all operations. The capacity to avoid or minimize reperfusion damage by reperfusion cardioplegia makes this technique a valuable adjunct to the cardiac surgeon's armamentarium, especially if cardioplegic distribution has been problematic, or if aortic clamping has been prolonged. We have used reperfusion cardioplegia as the primary form of cardiac protection (to avoid reperfusion injury) when ho-

mogeneous cardioplegic delivery was questionable. Starting systemic and cardioplegic rewarming about 5 min before unclamping the aorta ensures normothermia. Delivery of this warm cardioplegic reperfusate at 150 ml/min for 3–5 min avoids high reperfusion pressure (i.e., 50 mm Hg). Longer infusions (i.e., 5–10 min) may be useful if there has been poor cardioplegic distribution during aortic clamping or if the cross-clamp interval has been prolonged, especially in the setting of preoperative myocardial dysfunction. Recurrence of cardiac electromechanical activity during reperfusion cardioplegia is rare despite the low potassium concentration. Return of ventricular activity is not problematic as oxygenated blood is being delivered and the rate is usually slow, limiting metabolic demands.

With all arterial grafting, increasing reliance is placed on retrograde delivery. Antegrade reperfusion is also provided, especially if a large right coronary artery is grafted with the proximal anastomosis attached to the aorta attached to the aorta. However, if distribution is suboptimal, then rearrest is easily accomplished by starting a high K⁺ cardioplegic infusion to ensure arrest. Electromechanical activity resumes usually 1–2 min after aortic unclamping unless there is systemic hyperkalemia. Failure to recover contractility requires temporary ventricular pacing to avoid the myocardial edema that may follow prolonged perfusion of the flaccid heart. Palpation of the left ventricle detects distention so that a vent can be inserted if necessary.

6.9

Topical Hypothermia

Topical cooling is a useful adjunct when problems in cardioplegic distribution are anticipated especially if there is right ventricular hypertrophy or pulmonary hypertension. Topical cooling retards the recurrence of electromechanical activity by keeping myocardial temperature low and counteracts the effects of coronary collateral washout of the cardioplegic solution. Surface cooling may not be essential with multidose cardioplegia since the oxygen requirements of the arrested heart below 20°C are extremely low. The value of topical hypothermia is limited most in coronary patients because (1) the heart must be removed from the pericardial well for all but very proximal left anterior descending and right coronary anastomoses, and (2) injury to the phrenic nerve (especially with ice slush) may cause unavoidable respiratory complications [55–57], which may be problematic in elderly patients. We reviewed 150 consecutive coronary patients undergoing coronary artery bypass grafting (50 with topical ice slush, 50 with 4°C saline, and 50 without topical cooling) [58]. Patients that received ice slush topical hypothermia had a higher incidence of phrenic nerve palsy (9/50 vs

3/50 vs 0/50, $p < 0.05$), pleural effusion (25/50 vs 7/50 vs 9/50, $p < 0.05$), and atelectasis (33/50 vs 34/50 vs 18/50, $p < 0.05$). Conversely, there was no improved protection afforded by the use of topical cooling as measured by postoperative cardiac outputs, ECG changes, postoperative enzymes, inotropic requirements or deaths. We therefore do not use topical hypothermia during coronary operations if complete revascularization is possible unless cardioplegic distribution to the right ventricle is suboptimal, as retrograde cardioplegia should always provide protection of the left ventricular myocardium.

6.10

Conclusions

In conclusion, significant advances have been made in protecting the heart against perioperative myocardial damage. These principles are readily applicable to all arterial grafting. The role of cardioplegic myocardial protection has expanded to allow cardioplegic solutions to be used for active resuscitation, to prevent ischemic injury, to avoid reperfusion damage and to reverse ischemic and reperfusion damage. The persistent evidence of some enzymatic signs of myocardial necrosis in patients who do not need postoperative circulatory assistance [59] suggests a more subtle form of intraoperative damage may still be occurring.

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Cardiac Protection from the Viewpoint of Coronary Endothelial Function

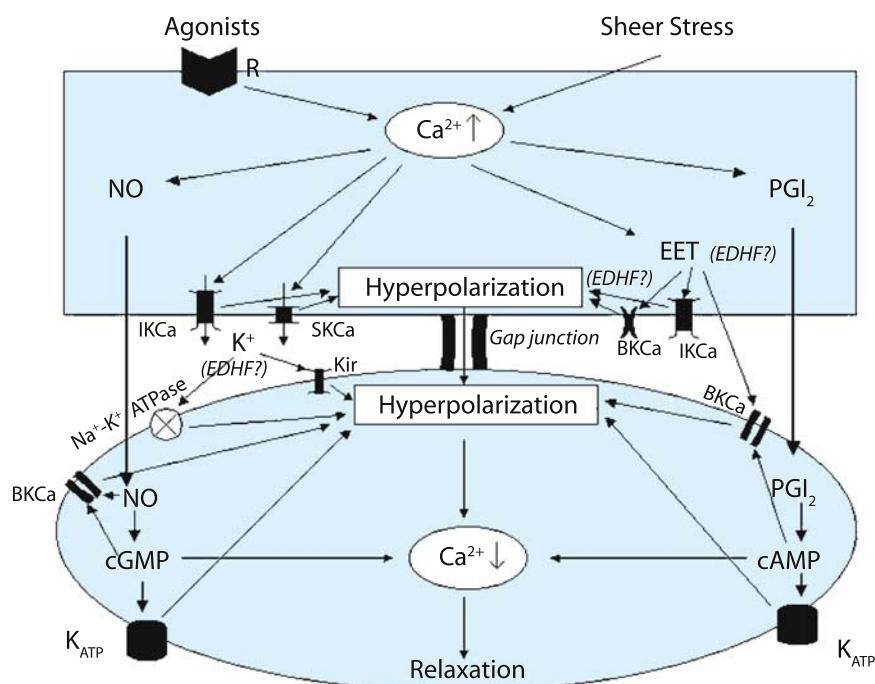
Q. YANG, A.P.C. YIM, G.-W. HE

During open heart surgery including coronary artery bypass grafting (CABG) using cardiopulmonary bypass, the heart is usually arrested for precise intracardiac repair or coronary grafting. Ischemia-reperfusion injury is the major problem in open heart surgery; cardioplegia was initially designed to protect the myocardium from this injury. It is now well known that coronary circulation plays a key role in myocardial perfusion. Injury to the coronary circulation may change the coronary resistance and therefore affect the coronary flow. The reduction of coronary flow may damage the myocardium perfusion that, in addition to the ischemia-reperfusion injury to the myocardium, may further damage the myocardial function. Due to the differences between the cardiac myocytes and vascular (endothelial and smooth muscle) cells in structure and function, cardioplegia may have an adverse effect on

coronary circulation; this has drawn the attention of many researchers in the past few decades. In addition to the usual cardioplegic solutions, for organ transplantation, cardioplegic or organ preservation solutions are used to preserve the heart or other organs. The endothelium-smooth muscle interaction may also be changed during the preservation. This chapter will discuss myocardial protection from the point of view of the protection of the coronary endothelial function.

Endothelium is critical in regulating vascular tone, and the endothelium-dependent relaxation is mediated by three different endothelium-derived relaxing factors (EDRFs) – nitric oxide (NO), prostacyclin (PGI₂), and endothelium-derived hyperpolarizing factor (EDHF) (Fig. 7.1) [1–3]. There is a considerable body of research on the endothelial function during cardioplegic arrest in cardiac surgery. Although some studies have

Fig. 7.1. Schematic diagram describing the pathways of endothelium-dependent vasorelaxation. Under shear stress or the stimulation of agonists, $[Ca^{2+}]_i$ increases in endothelial cells that leads to the release of prostacyclin (PGI₂), nitric oxide (NO), and endothelium-derived hyperpolarizing factor (EDHF). These three endothelium-derived relaxing factors decrease the $[Ca^{2+}]_i$ in smooth muscle cells through different mechanisms and ultimately relax the smooth muscle (BKCa large conductance calcium-activated potassium channel, IKCa intermediate conductance calcium-activated potassium channel, SKCa small conductance calcium-activated potassium channel, Kir inward rectifier potassium channel, KATP ATP-sensitive potassium channel, cAMP cyclic 3', 5'-adenosine monophosphate, cGMP cyclic 3', 5'-guanosine monophosphate, EET epoxyeicosatrienoic acid). (Reproduced from Yang Q, He GW: Effect of cardioplegic and organ preservation solutions and their components on coronary endothelium-derived relaxing factors. *Ann Thorac Surg* 2005; 80:757–767)



suggested the preservative effect of crystalloid cardioplegic or organ preservation solutions on the endothelial function [4–6], numerous studies have provided evidence for endothelial damage after exposure to these solutions. Histological examination and cell culture approach also revealed that crystalloid hyperkalemic cardioplegic solutions impair the vascular endothelium and reduce the ability of coronary endothelial cells to replicate [7, 8].

7.1

Possible Mechanisms Underlying the Damage of Cardioplegia and Organ Preservation on Endothelial Function

The “so-called” effect of solutions on coronary endothelium is often mixed with the effects due to other factors combined with cardioplegia procedure. Damage (or protection) to the endothelium may result from not only the solution per se, but also from the other components of the procedure. Theoretically, these may include:

1. Direct action of the solutions due to their intrinsic characteristics (the components of the solution, such as hyperkalemia). This has been discussed in our recent review [9] and will be presented in the next section.
2. Adjuncts to the cardioplegic procedure such as hypothermia or the infusion pressure or duration acting both as independent factors and through their interaction with cardioplegic solutions [10];
3. The effect of ischemia-reperfusion injury.
During cardiac surgery, the heart is arrested and subjected to ischemia-reperfusion injury. To protect the heart, cardioplegia is usually used to initially stop and then to maintain the still condition of the heart that not only facilitates the precise operation but more importantly minimizes the energy consumption of the heart during this period. In the case of heart transplantation, cardioplegia or organ preservation solutions are used to preserve the donor heart or other organs. During the preservation and the transplantation, the donor heart is subjected to ischemia injury. When the heart starts to beat, it is subjected to reperfusion injury and therefore the ischemia/reperfusion injury is a key point in heart transplantation.
The ischemia-reperfusion injury may involve both myocytes and coronary endothelium-smooth muscle. Therefore, the protection of the heart should also involve these two aspects. The injury to the heart involves (1) the ischemia-reperfusion injury to the myocytes and coronary circulation and (2) possible injury to the coronary circulation by the cardioplegia due to its hyperkalemic components.

The injury to the coronary circulation may involve both NO and EDHF mechanisms. The NO mechanism is susceptible to ischemia-reperfusion whereas the EDHF mechanism may be altered by the hyperkalemic cardioplegia. To further protect the heart, supplemental therapy for NO and optimizing the components of cardioplegia to restore the EDHF mechanism may be important.

The oxidative stress-induced endothelial cell activation is the key component of the detrimental effect of ischemia-reperfusion. With expression of a set of proinflammatory, procoagulant, and vasoactive genes, a series of protein production steps in endothelial cells is promoted that causes intravascular microthrombosis, reduced blood flow and activation of inflammatory cells. Among these proteins, the production of E-selectin, P-selectin, and intercellular adhesion molecules (ICAMs) leads to neutrophil recruitment, and neutrophils have been recognized as the principal effector cells of ischemia-reperfusion injury [11]. The leukocyte-endothelium adherence was indeed observed following cardioplegic arrest and reperfusion [12]. Recently, the cellular mechanism underlying the endothelial activation has been revealed with the study of nuclear factor kappa-B (NF- κ B). Oxidative stress activates the tyrosine phosphorylation of I κ B α , an inhibitor of NF- κ B that binds to NF- κ B in the cytoplasm; such phosphorylation dissociates I κ B α from NF- κ B. The translocation of functional NF- κ B to the nucleus with binding to the target genes results in transcriptional activation of these genes [13]. In patients undergoing cardiopulmonary bypass with cardioplegic arrest, NF- κ B increased dramatically after reperfusion compared with before cardioplegia [14]. Therefore, targeting of the signaling pathway of endothelial cell activation may ameliorate cardioplegic arrest and reperfusion-induced endothelium impairment. Better recovery of coronary vascular response to serotonin and bradykinin in porcine coronary vessels [15], and to acetylcholine in the neonatal lamb heart [16] was obtained by adding deferoxamine or manganese superoxide dismutase to the cardioplegic solution to reduce the oxygen-derived free radicals [15] or with leukocyte molecule CD18 (ligand for ICAM-1) antibody prior to cardioplegic arrest [16]. Moreover, transfection of NF- κ B decoy oligonucleotides into isolated heart blocked ICAM-1 upregulation and inhibited increase in neutrophil adhesion [17].

4. Other factors involved in isolated working heart models or in vivo models when these models are used to study endothelial function.

Taken together, the “true” effect of the solutions on the endothelium should be carefully distinguished from

other factors in order to identify the possible damaging effect due to the intrinsic characteristics of the solutions. The solution-related impact on the endothelial function, particularly on individual EDRFs, is addressed in this chapter.

7.2

Influence of Cardioplegic and Organ Preservation Solutions on Individual EDRFs

7.2.1

Influence of the Solutions on PGI₂

The increase of release of PGI₂ during myocardial ischemia with/without cardioplegic arrest has been demonstrated [18, 19]. Gene expression of COX-1 and PGI₂ synthase was not altered after cardioplegia but COX-1 protein level was significantly reduced accompanied by increased expression of COX-2 [20]. However, the combined effect of ischemia-reperfusion was not excluded. It is also unknown how long this increase would be maintained for under hypoxic conditions.

7.2.2

Influence of the Solutions on NO

Studies have suggested impaired NO-related endothelial function during cardiopulmonary surgery. By measuring the end-products of NO – nitrite and nitrate, Gohra and coworkers demonstrated that NO release decreased significantly at approximately 70 min of crystalloid cardioplegic arrest in human coronary vasculature and it was further reduced after reperfusion [21]. Similarly, the inability of the endothelium to release nitric oxide associated with reduced endothelium-dependent vasodilatation after infusion with University of Wisconsin (UW) solution [22] or loss of NO production after cardioplegia-reperfusion associated with decreased protein level of constitutive NO synthase [20] was demonstrated. The NO loss after cold (4°C) ischemic storage with crystalloid cardioplegia was recovered by chronic oral administration of L-arginine, the physiological substrate of NO [23]. However, the combined ischemia-reperfusion injury was probably the main cause of the NO-related endothelial dysfunction in these and other studies [24, 25].

We have demonstrated when the effect of ischemia-reperfusion is excluded, the NO-related, endothelium-dependent vasorelaxation after exposure to oxygenated crystalloid hyperkalemic cardioplegia to acetylcholine or substance P is well preserved in either porcine epicardial coronary arteries [26] or neonatal rabbit aorta [27]. Although in these studies the indomethacin-resistant relaxation is actually mediated by both NO and EDHF, the unchanged endothelium-dependent response and the susceptibility of EDHF to cardioplegic

solution [28–30] provide convincing evidence for the minimal impact of hyperkalemic cardioplegic solution on the NO-related function after exposure for a certain period (1 or 2 h).

7.2.3

Influence of Cardioplegic or Organ Preservation Solutions on EDHF

We have conducted a series of experiments to investigate the effect of cardioplegic solution and organ preservation solutions on EDHF-mediated function. With exclusion of the effect of ischemia/reperfusion and elimination of the effect of PGI₂ and NO, we have demonstrated that hyperkalemia [28, 29], St. Thomas' Hospital cardioplegia (ST) [30] and UW solution [31] impair EDHF-related function either in porcine or human coronary arteries [28, 29]. The mechanism is due to the opposite effect of EDHF and hyperkalemia. Hyperkalemia depolarizes whereas EDHF hyperpolarizes the smooth muscle membrane. The persistent depolarizing effect of hyperkalemia even after wash-out of cardioplegic solution restricts the hyperpolarizing effect of EDHF [29, 31, 32]. Use of potassium channel openers as hyperpolarizing cardioplegia may overcome this shortage of hyperkalemic cardioplegia [33].

7.3

Influence of Different Components in Cardioplegic and Organ Preservation Solutions on Endothelial Function

7.3.1

Effect of K⁺ on Endothelial Function

K⁺ is the key component in cardioplegic/organ preservation solutions. The concentration of K⁺ varies in different solutions. In UW solution, it is as high as 125 mM whereas it is only 20 mM in ST and 10 mM in histidine-tryptophan-ketoglutarate (HTK) solution, respectively. The importance of K⁺ concentration with regard to coronary endothelial impairment was revealed. K⁺ at 30 mmol/l but not at 20 mmol/l abolished the endothelial-dependent, 5-hydroxytryptamine-induced vasodilatation [34].

In contrast, studies by others [35] and ourselves have demonstrated that hyperkalemia per se does not significantly alter the endothelium-dependent relaxation as a whole to acetylcholine or substance P in porcine coronary arteries (to K⁺ 50 mmol/l) [26] and neonatal rabbit aorta (to K⁺ 100 mmol/l) [27]. These contradictory results stimulate further investigations as to the effect of hyperkalemia on individual relaxing factors derived from endothelial cells. Up to date, there is a little evidence showing that the reduction of the production of NO is due to hyperkalemia. Rather, it is most

likely due to the combined ischemia-reperfusion injury. When the capability of the endothelium to release NO is preserved or there is no presence of specific NO inhibitors, the endothelium is tolerant to hyperkalemia as far as the endothelium-dependent relaxation is concerned as shown above [26, 27, 35]. Most recently, with measurement of NO by a NO-specific electrode, we provided direct evidence for the first time that NO release is not affected by 1-h exposure to 20 mM K^+ [36].

On the other hand, in contrast to NO, susceptibility of EDHF to a high concentration of K^+ has been demonstrated in accumulating studies. When the effect of PGI_2 and NO is inhibited by indomethacin and N^G -nitro-L-arginine (L-NNA), the endothelium-dependent relaxation/hyperpolarization (mediated by EDHF) to a number of EDRF stimuli is impaired by incubation with K^+ , ranging from 20 to 125 mM in porcine and human coronary arteries [28, 29, 32]. Realizing that L-NNA cannot abolish the production of NO, we further added oxyhemoglobin, a scavenger of NO, to abolish the effect of residual NO and demonstrated again the detrimental effect of hyperkalemia on the EDHF-mediated relaxation and hyperpolarization in porcine coronary micro-arteries [37].

The mechanism of the reduced EDHF-mediated relaxation in hyperkalemic solutions is twofold. First, hyperkalemia depolarizes the coronary smooth muscle membrane and the prolonged depolarization increases the difficulty for subsequent hyperpolarization. Second, EDHF hyperpolarizes the vascular smooth muscle cell through opening K^+ channels, the function of which may be blocked by K^+ that is a natural K^+ channel blocker [29, 32].

7.3.2

Effect of Mg^{2+} on Endothelial Function

The introduction of Mg^{2+} into cardioplegia helps to achieve immediate heart arrest during cardiac surgery, and the enrichment of Mg^{2+} may counteract the unfavorable effect of hypocalcemia on sarcolemmal membrane by preventing calcium influx and thus obtain a better membrane stabilization [38]. In addition to the protective effect on myocardium [39, 40], Mg^{2+} has been proven to be a potent vasodilator through both endothelium-dependent and -independent mechanisms [41, 42]. The fact that Mg^{2+} infusion improves methacholine-induced vasorelaxation demonstrated the importance of endothelium in the effect of Mg^{2+} in the human forearm vessels [43]. Pretreatment with NOS inhibitor L-NAME/L-NMMA reduces Mg^{2+} -mediated vasodilatation and NO donor sodium nitroprusside or a cGMP analogue, 3-guanosine monophosphate, restores the response to Mg^{2+} , indicating the role of the NO-cGMP pathway in the action of Mg^{2+} [41, 42]. Moreover, the involvement of the COX system marked with

the production of PGI_2 has also been suggested in Mg^{2+} -induced relaxation [42, 44]. Tofukuji and associates reported that hyper- Mg^{2+} cardioplegia (25 mM Mg^{2+}) is superior to hyper- K^+ cardioplegia in terms of preserving beta-adrenoceptor-mediated and endothelium-dependent regulation of the coronary microcirculation in pigs undergoing cardiopulmonary bypass [45]. Further, Pearson and colleagues observed the inhibitory effect of hypomagnesemia on endothelium-dependent vasodilatation induced by acetylcholine or adenosine diphosphate and they proposed that such impairment of endothelial function is due to the decreased release of NO [46].

In addition, a recent study by our laboratory demonstrated that in porcine coronary arteries, Mg^{2+} preserves the EDHF-mediated relaxation and hyperpolarization and restores the EDHF function impaired by hyperkalemia [37].

7.3.3

Effect of Procaine on Endothelial Function

Similar to Mg^{2+} , the local anesthetic procaine is added to cardioplegia to induce asystole and obtain membrane stabilization [38]. Procaine is recognized as a vasodilator [47, 48]. At 1 mM, procaine relaxes vascular smooth muscle not only in an endothelium-independent but also in an endothelium-dependent manner that is closely related to NO but not PGI_2 [48]. We further showed that procaine does not affect EDHF function in the coronary circulation [49] despite the fact that it depolarizes the membrane of vascular smooth muscle cells by reducing K^+ conductance [50].

7.4

Effect of Different Additives to Cardioplegic or Organ Preservation Solutions on Endothelial Function

The additives that are aimed at protecting endothelial function may be categorized as follows.

1. *NO substrates or donors.* The benefit of the supplementation of NO precursor L-arginine or NO donors such as nitroglycerin in cardioplegia on post-ischemic ventricular performance and endothelial function has been well established, and thus it is considered as an effective replacement therapy in cardiac surgery [51–53].
2. *PGI_2 analogues.* PGI_2 analogues such as iloprost and OP-41483, added to crystalloid cardioplegia, provide better preservation on cardiac function after ischemic arrest [54, 55].
3. *EDHF analogues.* Addition of epoxyeicosatrienoic acid_{11,12} (EET_{11,12}), the possible analogue of EDHF,

- to hyperkalemic solution may partially restore the bradykinin-induced, EDHF-mediated endothelial function in porcine coronary arteries [56]. Further, the benefit of EET_{11,12} supplementation in ST solution was shown under moderate hypothermia [57].
4. *K⁺ channel openers (KCOs)*. When added to hyperkalemic cardioplegia, aprikalim reduces the Na⁺-Ca²⁺ exchange outward current elevated by hyperkalemia and thus may attenuate the [Ca²⁺]_i elevation, leading to improved contractile function after cardioplegia in the ventricular myocyte [58]. In addition, supplementation with aprikalim in traditional hyperkalemic solutions preserves EDHF-mediated coronary relaxation, indicating its protective effect on endothelial function [59]. Other KCOs such as KRN4884 have been demonstrated to have a preconditioning effect on the EDHF-mediated relaxation and may be beneficial if added to cardioplegic solutions [60].
 5. *Scavengers of oxygen-derived free radicals*. Supplementation of crystalloid cardioplegic solution with free radical scavengers, such as ascorbate and deferoxamine, reduces postreperfusion myocardial injury [61] and preserves the endothelium-dependent vasodilatation in coronary microvessels [15].
 6. *Sodium-hydrogen ion exchange (NHE) inhibitors*. The cardioprotective effect of NHE inhibitors is not only observed with perioperative administration to patients undergoing bypass surgery [62], but is also demonstrated when added to blood cardioplegia [63]. The decreased accumulation of intracellular Na⁺ and subsequently decreased Ca²⁺ overload contribute to the reduced postischemic infarct size and tissue edema due to the supplementation of selective NHE type 1 isoform inhibitor cariporide. In isolated postischemic left anterior descending coronary artery rings, maximum relaxation in response to acetylcholine was significantly greater in the cariporide group than in the vehicle group, indicating the preservation effect of cariporide on endothelium [63].
 7. *Other substances*. Adenosine has been shown to partially attenuate the microcirculatory injury by cardioplegia [64], but the effect is controversial [65]. Adding phosphodiesterase III inhibitor (E-1020) to Bretschneider's HTK cardioplegic solution has been shown to improve myocardial functional recovery [66]. The finding that 17 β -estradiol prevented intracellular Ca²⁺ loading or hypercontracture of ventricular cardiomyocytes in high K⁺ exposure [67], together with its direct favorable effects on vascular endothelial function [68], raises the possibility of 17 β -estradiol as a cardioprotective adjunct in hyperkalemic cardioplegia. The effect of prevention of Ca²⁺ overloading by Ca²⁺ antagonists highlights the cardiovascular protective effect

of Ca²⁺ antagonist-supplemented cardioplegic solutions [69, 70]. In addition to these strategies, metabolic substrate (i.e., glutamate, aspartate, fumarate, etc.)-enriched solutions have been clinically used for a long time for better myocardial protection [71]. However, little is known regarding the consequence of such enrichment on endothelial performance.

In summary, due to the differences between the cardiac myocytes and vascular (endothelial and smooth muscle) cells in structure and function, the cardioplegic or organ preservation solutions primarily designed to protect the myocardium may have a detrimental effect on coronary vascular endothelial cells, as demonstrated in the past few decades. One must be aware that under either experimental or clinical settings, the reported effect of the solutions on coronary endothelium is often mixed, with many other factors such as ischemia-reperfusion injury, temperature, and perfusion pressure and duration, not only the components of the solutions per se. In evaluation of a clinically used solution and in the development of a new solution, these factors should be carefully distinguished from the effect of the solution. The key component of the cardioplegic and heart preservation solutions that causes cardiac arrest – high concentrations of potassium ion (hyperkalemia) – is the major component that has been studied regarding the endothelial function. The primary contributor of the endothelium-dependent relaxation, the NO pathway, is mainly impaired due to ischemia-reperfusion injury. Its resistance to the moderately increased potassium concentrations used for cardioplegia (~20 mEq/l) explains the excellent clinical results by using either crystalloid or blood cardioplegia. On the other hand, the second endothelium-dependent relaxation pathway – the EDHF pathway that is usually a “backup” of the NO pathway – is significantly altered (damaged) by hyperkalemia even at the moderately high concentration of potassium. This is because hyperkalemia inhibits potassium channels in the endothelium and smooth muscle that are related to either the release of EDHF from the endothelium or the target of the action of EDHF. Magnesium has a protective effect on this pathway because it hyperpolarizes the coronary smooth muscle membrane and therefore has a “synergetic” effect with EDHF. When combined with ischemia-reperfusion and other factors that significantly impair the NO pathway, the effect of hyperkalemia on the EDHF pathway becomes an important issue in the protection of coronary endothelium. A variety of new additives aimed at protecting these two major endothelium-dependent pathways may further improve the protection of the coronary endothelium from other factors such as ischemia-reperfusion injury. All these issues should be taken into account in the development

of new cardioplegic and heart preservation solutions in the future in order to provide the "perfect" cardiac protection.

Acknowledgement. Supported by the Research Grants Council, Hong Kong (CUHK4127/01M and 4383/03M) and St. Vincent Medical Foundation, Portland, Or., U.S.A.

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Percutaneous Coronary Interventions Versus Coronary Artery Bypass Surgery

Needle or Knife? A Comparison Between Percutaneous Coronary Interventions (Including Plain Balloon Angioplasty and Coronary Stenting) and Coronary Artery Bypass Surgery

D.J. DRENTH, P.W. BOONSTRA

8.1 Introduction

In 1977 Andreas Gruntzig introduced plain balloon angioplasty into the treatment options of coronary artery stenosis in order to revascularize ischemic myocardium [1]. This new treatment option was complicated often by dissections of the coronary artery in short term and the long term by high stenosis rate. So-called acute procedure related complications were frequently leading to urgent coronary artery bypass grafting in those days. Moreover, restenosis rate after plain balloon angioplasty was relatively high. The introduction of bare metal stents reduced the dissection rate substantially as well as the restenosis rate. These rapid technological advances in percutaneous coronary interventions (PCI), its relative ease of use and its lower level of discomfort for the patient, have made PCI a very attractive alternative for surgery in many patient subsets nowadays. These developments allow cardiologists to revascularize ischemic myocardium in a rapidly increasing number of patients. In this chapter we will deal with the latest prospective randomized studies comparing PCI and coronary bypass grafting (CABG).

8.2 Percutaneous Coronary Interventions

The success of interventional procedures is strongly affected by anatomical lesion characteristics [2]. One can distinguish relative simple lesions that are easy to treat percutaneously, meaning a low risk for periprocedural complications and morbidity and more difficult lesions, resembling a higher risk for periprocedural complications and morbidity. Based on these lesion characteristics, the American College of Cardiology and American Heart Association have provided a risk classification for stent implantation (Table 8.1). Additional factors influencing clinical outcome after PCI are increasing age, unstable angina pectoris, decreased left

Table 8.1. Lesion classification system for the anatomic risk groups PCI (stent) era and AHA/ACC [2]

Low risk
Discrete (length < 10 mm)
Concentric
Readily accessible
Non-angulated segment (< 45°)
Smooth contour
Little or no calcification
Less than totally occlusive
Not ostial in location
No major side branch involvement
Absence of thrombus
Moderate risk
Tubular (length 10–20 mm)
Eccentric
Moderate tortuosity of proximal segment (> 45°, < 90°)
Irregular contour
Moderate or heavy calcification
Total occlusions < 3 months old
Ostial in location
Bifurcation lesions requiring double guide wires
Some thrombus present
High risk
Diffuse (length > 20 mm)
Excessive tortuosity of proximal segment
Extremely angulated segments > 90°
Total occlusions > 3 months old and/or bridging collaterals
Inability to protect major side branches
Degenerated vein grafts with friable lesions

ventricular function, previous myocardial infarction, diabetes mellitus, renal failure, large area of myocardium at risk and multivessel disease [2].

Although stenting prevents restenosis from vascular recoil and remodeling compared to balloon angioplasty, in-stent restenosis caused by neointimal proliferation is still a major problem after stenting [2, 3].

8.3 Coronary Artery Bypass Grafting

Sabiston was the first surgeon who used the saphenous vein bypassing an obstruction in the right coronary ar-

tery in 1962 [4]. This technique was followed rapidly by the introduction of the left internal thoracic artery as an arterial conduit for CABG. Accumulating evidence demonstrated a significant survival benefit when this arterial graft was used instead of the venous graft for bypassing a stenosis in the left anterior descending artery [5]. The success of coronary bypass grafting has increased substantially with the improvement of anesthesiological techniques, cardiopulmonary bypass systems, cardiac protection techniques, postoperative care, etc. In addition, the introduction of preoperative risk stratification tools has improved the results of coronary artery bypass grafting further [6].

8.4

PCI Versus CABG

Compared to PCI, CABG is not hampered by lesion characteristics [7]. Outcome after CABG is merely affected by patient age, sex, left ventricular function and co-morbidity like peripheral vascular disease, renal dysfunction, diabetes mellitus and of course surgical skills [7].

Hoffman et al. performed a meta-analysis of 13 randomized trials on 7,964 patients comparing PCI with CABG [8]. This meta-analysis contained also data from the pre-stent era. Neither plain balloon angioplasty, coronary stenting nor CABG provided a statistically significant survival advantage at 1, 3 or 8 years. A statistically significant 1.9% risk difference advantage favoring CABG over percutaneous transluminal coronary angioplasty (PTCA) for all trials at 5 years ($p < 0.02$) was found, but no significant advantage at 1, 3 or 8 years. Patients randomized to plain balloon angioplasty had more repeat revascularizations at all time points (risk difference 24–38%, $p < 0.001$); with stents, this risk difference was reduced to 15% at 1 and 3 years. Stents also resulted in a significant decrease in non-fatal myocardial infarction at 3 years when compared with CABG. For diabetic patients, CABG provided a significant survival advantage over plain balloon angioplasty at 4 years but not at 6.5 years.

Table 8.2 depicts the most recent prospective randomized trials comparing PCI with CABG patients with single vessel left anterior descending (LAD) disease and in patients with multivessel disease.

Table 8.2. Results of randomized studies comparing PCI and CABG

Study (year)	MVD/SVD	Modality	N	Follow-up (years)	Follow-up D/MI/TLR (%)	Endpoint	Endpoint (%)	p value
SIMA [11] (2000)	SVD (LAD)	Stenting CABG (IMA)	62 59	2.4	2/5/24 2/4/0	D, MI, TLR	31 7	<0.004
Diegeler [12] (2002)	SVD (LAD)	Stenting MIDCAB	110 110	0.5	0/3/29 2/5/8	D, MI, TLR	31 15	0.003
Drenth [14] (2004)	SVD (LAD)	Stenting MIDCAB	51 51	4	0/9.8/15.6 3.9/1.9/3.9	D, MI, CVA, TLR	27.5 9.8	0.02
ERACI II [24] (2001)	MVD	Stenting CABG	225 225	1.6	3.1/2.3/16.8 7.5/6.6/4.8	D, MI, CVA, TLR	23 19	ns
AWESOME [25] (2001)	MVD	PTCA ± stent CABG	222 232	3	20/na/na 21/na/na	D	20 21	ns
ARTS [26] (2001)	MVD	Stenting CABG	600 605	1	2.5/6/22.4 2.8/4.7/4	D, MI, CVA, TLR	26.5 12	<0.05
ARTS [17] (2004)	MVD	Stenting CABG	600 605	3	3.7/7.3/29.2 4.6/5.7/7.3	D, MI, CVA, TLR	34.2 16.7	<0.001
SoS [3] (2002)	MVD	Stenting CABG	408 500	1	5/4/21 2/7/6	TLR	21 6	<0.05
MASS II [15] (2004)	MVD	Stenting CABG Medicine	205 203 203	1	4.4/8/13.3 4/2/0.5 1.5/3/8.3	D	4.4 4.0 1.5	ns

SVD single vessel disease, LAD left anterior descending coronary artery, MVD multivessel disease, D death, MI myocardial infarction, TLR target lesion revascularization, na not assessable, ns not significant

8.4.1

Left Main Stem Disease

Until now, patients with a diameter stenosis of 50 % or more in the left main stem have not been enrolled in prospective randomized trials comparing PCI and CABG. Only data from non-randomized studies are available, which are mainly focused on highly selected patients having contraindications for CABG [9, 10].

PCI seems to be a valuable treatment option in patients having left main coronary disease in particular in the setting of acute myocardial infarction, and it might save lives especially in those patients with good preintervention TIMI flow (grade >2). In addition, long-term clinical outcome of patients surviving to hospital discharge is favorable.

On the evidence from level I/a to date, surgical revascularization should be considered for patients with left main stenosis greater than 50 % [7].

8.4.2

Single Vessel Disease (Proximal LAD)

Table 8.2 shows the three randomized studies comparing PCI with CABG in patients with proximal LAD disease (more than 50 % diameter stenosis in the proximal LAD) with a few differences in their study design. In the SIMA trial, results of PCI were compared with those of *on-pump* LIMA-LAD, where Diegeler and Drenth studied results of *off-pump* LIMA-LAD via an anterolateral thoracotomy [11–14]. Furthermore, in the SIMA trial and in the study performed by Diegeler et al., patients with a proximal stenosis of the LAD (type A, B and C) were included, whereas high-risk lesions (type B2/C) were included in the study performed by Drenth et al. These studies were only designed for a comparison of their combined primary endpoint (death, myocardial infarction, target vessel revascularization with or without stroke). The combined primary endpoint of each study was significantly more often reached in the PCI group due to target vessel revascularization at 0.5, 2.4 and 4-year follow-up respectively. Diegeler and Drenth additionally reported a better anginal status after CABG where the SIMA group did not find a difference in anginal status between the two treatments.

It can be concluded from these studies that in patients with single vessel disease of the proximal LAD, CABG is associated with a statistically significant event free survival, less angina, and fewer target lesion revascularizations when compared with coronary stenting. However, functional health status does not differ between the two treatments.

8.4.3

Multivessel Disease

Table 8.2 shows the major randomized studies comparing PCI with CABG in multivessel disease (diameter stenosis more than 50 % in at least two major epicardial vessels). However, the extrapolation of these results to the “real world” is limited due to differences in study designs. The ARTS, ERACI and SOS trials included patients in whom the cardiac surgeon and the cardiologist expected to obtain a similar extent of revascularization, while primary endpoints differed. The AWESOME study randomized patients with refractory angina who had an extremely serious operative mortality risk and only had mortality as the primary endpoint. MASS also included a medical treatment group.

All these randomized controlled trials have a relative short-term follow-up (1 year), except the 3-year follow-up of the ARTS trial. Like studies focused on single vessel disease, almost all studies focused on multivessel disease show that the primary combined endpoint (death, myocardial infarction and revascularization) is reached statistically significantly more often after PCI than after CABG as a result of more target vessel revascularization after PCI. As a consequence of the cumulative effect of three consecutive PCIs of three targets in one patient, primary endpoints were reached even more frequently than in single vessel disease trials [3, 15–17]. In addition, CABG demonstrated significantly better relief of anginal complaints than PCI. At 3-year follow-up the ARTS trial identified arterial LAD grafting to be the best predictor of event free survival after CABG and DM and high pressure stent deployment as the strongest predictor of events after stenting [17].

In conclusion, these prospective randomized trials in single vessel and multivessel disease have relatively short follow-up. Included patients had predominantly relatively low-moderate risk lesion subsets for PCI. Trials that last longer tend to show a better outcome in surgically treated patients in relieving angina pectoris and providing a better event-free survival as a result of reduced target vessel revascularization rates compared to stenting.

8.5

Drug Eluting Stents

Restenosis after stent deployment in coronary vessels is mainly caused by neointimal proliferation of vascular smooth-muscle cells after migration from the media of the vessel wall into the lumen of the stent. In order to prevent such proliferation, drug eluting stents (DES), containing coatings with antiproliferative drugs, e.g., sirolimus or paclitaxel, were introduced recently. In-

deed less intima proliferation in-stent-restenosis was found after deployment of these DES in mild-moderate risk lesions compared to non-coated or “bare metal” stents [18–20].

A non-randomized study reported a 9.7% major adverse cardiac event rate at 1 year if DES were applied in consecutive de novo lesions (“the real world”) [21]. Additionally, an angiographic 6-month follow-up study evaluating restenosis after DES deployment identified in-stent restenosis, ostial location, diabetes mellitus, total stent length (per 10 mm increasing), reference diameter (per 1.0 mm increasing) and LAD location as independent multivariate predictors for restenosis [22].

Another non-randomized study performed in a consecutive series of DES deployment in 155 patients having multivessel coronary disease (diameter stenosis more than 50% in at least two major epicardial vessels) showed a 22.3% cumulative major adverse cardiac or cerebrovascular event rate (death, myocardial infarction and repeat target vessel revascularization) at 6 months follow-up [23]. Target vessel revascularization was required in 6.7% of lesions in 14.3% of patients as a result of restenosis or progression of disease [23]. Predictors of major adverse cardiac events were diabetes, total stent length per patient and maximum stent length per vessel.

In conclusion, follow-up of DES is relatively short (up to 2 years) and mainly studied in relatively low-risk patient subsets. Prospective randomized controlled trials have shown that DES have better short-term results over bare metal stents. Predictors of restenosis like lesion length, vessel diameter, bifurcation lesions and diabetes mellitus remain, although with less impact than in bare metal stents. Surgical revascularization has a significantly better symptomatic benefit than PCI with DES. However, differences in survival are not significant. Prospective randomized trials comparing DES and CABG with long follow-up are needed to assess the efficacy of these stents, especially in high-risk lesions and patients with diabetes mellitus and/or multivessel disease.

8.6

Revascularization Strategy

Since the introduction of coronary stenting, treatment strategies have developed favoring PCI over surgery in single vessel disease and even in multivessel disease. This development is mainly driven by the existing knowledge that survival after CABG is no longer significantly different from survival after coronary stenting. From this point of view other parameters like quality of life, cost and cost-effectiveness have been introduced to identify the most favorable treatment. Further studies

are needed to prove which treatment strategies are best tailored to the patient. But on evidence to date, surgical revascularization results in significantly better symptomatic benefit, better than PCI without DES. Therefore, it can be suggested that in patients in whom the success of coronary stenting is difficult to guarantee, based on their angiographic findings (Table 8.1), surgery remains the best first choice of treatment.

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Clinical Choice of Arterial Grafts

Considerations in the Choice of Arterial Grafts

G.-W. HE

Various arterial grafts have been used for coronary artery bypass grafting (CABG), but a unanimous opinion as to the best use of these grafts has not yet been formed, except for the internal mammary artery (IMA), which has been accepted as the first choice, usually for the left anterior descending artery (LAD) if the artery needs to be grafted [1, 2].

As to the patency of the right internal mammary artery (RIMA), early reports gave conflicting results: the angiographic patency was 98% for the RIMA and 93% for the LIMA in 50 patients [3], pedicled RIMA patency rates equaled those of pedicled LIMA (95.1 vs 96.7, NS) and the grafted vessel did not alter the patency rates of IMA [4]. Dietl [5] reported that the prevalence of perioperative myocardial infarction in the right coronary artery distribution was significantly higher, and the reoperation rate for graft failure and the prevalence of deep sternal wound infection in diabetics was significantly higher for RIMA than for the right gastroepiploic artery (GEA). However, the most recent reports from large series in Melbourne in 2,127 arterial to coronary conduits over 15 years clearly showed [6] that the LIMA patency at 5 years was 98%, at 10 years it was 95%, and at 15 years it was 88%. The right internal thoracic artery (RITA) patency at 5 years was 96%, at 10 years it was 81%, and at 15 years it was 65%, and the interval from operation to angiogram was not associated with IMA patency (96% patency for LITA and 88% patency for RITA, remaining stable when studied at <1, 1–4, 5–9, 10–14 and >15 years) [7].

Based on the superior long-term results of the IMA [1, 2], other arteries have been used in CABG [8–14]. Such conduits include the radial artery [8], the GEA [9], the inferior epigastric artery (IEA) [10, 11], the splenic artery [12], the subscapular artery [13], and the inferior mesenteric artery [14], the descending branch of the lateral femoral circumflex artery [15], and the ulnar artery [16]. In addition, the intercostal artery [17] has also been suggested to be used as a graft. The long-term patency rates for IMA are well established as mentioned above. Although there are few reports on other arterial conduits with a relatively small number of patients, the long-term patencies for GEA and radial artery (RA) have recently been established. Suma [18, 19]

recently reported that the cumulative patency rate estimated by the Kaplan-Meier method for GEA was 96.6% at 1 month, 91.4% at 1 year, 80.5% at 5 years, and 62.5% at 10 years. Causes of late occlusion were primary anastomotic stenosis and anastomosis to a less critically stenosed coronary artery. Voutilainen and associates [20] reported that 82.1% (23/26) of the GEA grafts were patent at 5 years. From these studies, the patency of the GEA, as a Type II artery, is acceptable but not as superior as the IMA, the patency of which was 95% at 10 years and 88% at 15 years [21].

The patency rate of the RA is more dramatic. There was a disappointing 35% incidence of narrowing or occlusion of the RA [22]. With modified technique, avoiding skeletonization and using calcium antagonists, the early patency increased to 93.5% at 9 months in Acar's group [23] and to 93.1–95.7% in other groups [24, 25] at 3–21 months in the early stage of the use of RA. Later, Acar and colleagues reported that the patency rate of the radial artery grafts was 83% at 5 years [26]. In addition, Tatoulis and associates reported that the radial artery patency at 1 year was 96% and at 4 years it was 89% [6]. Interestingly, similar to the right IMA, for the radial artery there was a higher patency with greater coronary stenosis.

Arterial grafts are not uniform in their biological characteristics (see Chaps. 3, 4). The difference in the perioperative behavior of the grafts and in the long-term patency may be related to different characteristics. These should be taken into account in the use of arterial grafts, some of which are subjected to more active pharmacological intervention during and after operation to obtain satisfactory results. Clinical choice of grafts must be based on the general condition of the patient, the biological characteristics of the graft, the anatomy of the coronary artery, the match between the coronary artery and the graft, and the technical considerations including antispastic management.

9.1 General Condition of the Patient

9.1.1 Non-technical Factors Related to the Graft Failure

Cholesterol level, particularly a high level of low-density lipoprotein (LDL) and triglycerides, may affect the patency of the graft. In addition, other factors such as high level of Lp(a), a thrombogenic molecule, which is related to hypercoagulable state may also influence the long-term patency [27]. Other risk factors for the coronary artery disease such as smoking, hypertension, and, in particular, diabetes may also affect the fate of the graft. In addition, diabetes has been thought to be a contraindication for bilateral IMA grafting due to possible increase of sternal wound infection [28] although this has not been proved in other studies [29]. However, these factors do not account for the difference between the venous and arterial grafts.

9.1.2 Age

It is obvious that the age of the patient is one of the important factors. The main advantage of arterial grafts is the superior patency compared with the venous graft. Young patients benefit more from this advantage. For a single IMA, there is almost no contraindication [30]. However, although there are no uniform criteria with regard to the age for complex arterial grafting such as bilateral IMA grafting, 65 years of age has been suggested to be the upper limit [30]. This, however, may largely depend on the surgeon's experience and preference. Essentially, there is no age limit for taking the RA although in general the RA is taken from those less than 70 years of age [31]. In general, arterial grafts are more indicated in patients who are expected to live for more than 10 years, which is beyond the benefit of the vein graft.

9.1.3 Urgency of the Operation

In catastrophic emergencies it may be wise not to perform relatively time-consuming arterial grafts.

9.1.4 Other Situations

Extreme chest deformities, significant disease of the subclavian arteries, or of the IMAs are probably contraindications for the use of IMA [30].

9.2 Biological Characteristics

9.2.1 Adequate Size

The size of a vessel depends on the transluminal pressure. In the collapsed status, the size of the vessel is obviously not the size in vivo under the physiological pressure. In general, all major arterial grafts have an adequate size for coronary grafting, as measured at a pressure of 100 mmHg, which is between 2.0 and 2.5 mm [11]. However, there are some specific concerns. The adequacy of the size of the IMA has been discussed although it is generally agreed that the size of the LIMA is usually adequate for LAD. The RA is larger than other arterial conduits, being larger than the coronary artery, and therefore this is not a concern [31]. In contrast, the IEA is normally small and the distal size of the IEA is often very small (1–1.2 mm), so the adequacy of its size is questionable unless it is used as a composite graft to the LIMA [32]. Fewer questions about the size of the GEA have been raised although it may look quite small during harvesting due to the frequent spasm of this spastic artery. The intercostal artery may have a small size under most situations so it has not been developed as a graft. Recent studies particularly addressed the adequate perfusion of the arterial graft and found that the myocardium may be hypoperfused by arterial grafts [33]. During exercise, the flow reserve of the arterial graft may not be adequate. Therefore, it is probably necessary to consider the size of the graft to match a particular coronary branch.

9.2.2 Thickness of the Wall and the Intimal Hyperplasia

The combined width of intima and media is in the following order: IEA < GEA < IMA < RA [34]. The correlation between the thickness of the vascular wall and the development of atherosclerosis or graft occlusion is still unknown. Intimal hyperplasia has been suggested to be an adverse effect in the long-term patency [34], but this is still speculative and there are no clinical data to support this hypothesis.

9.2.3 Anatomic Structure of the Graft

The IMA is an elastic artery with well-formed internal elastic laminae while the IEA, GEA, and particularly the RA are muscular [34]. It has been speculated that a more elastic structure is favorable in a higher long-term patency [34], but this hypothesis needs to be supported by more clinical data.

9.2.4

Adequate Length

As far as the usable length is concerned, the LIMA has an adequate length to the LAD system. The RA has an adequate length to graft to any coronary artery branches, with an average length of 20.5 (15.2~23.5) cm [35]. In contrast, the maximal length of the IEA is 17 (15~22) cm, measured from autopsy [36]. Due to its very small diameter at the distal end, the available length is sometimes limited [32, 37]. In a study by Buche [37], the average length of the right IEA was 13.1 ± 1.3 cm although on extensive dissection the length of the IEA could be up to 19 cm. Buche also suggests that the IEA is harvested only when the length and size are adequate by routine preoperative angiography [37]. Together with other considerations, the IEA has been used as a part of a composite graft with the LIMA [32]. The pedicle GEA has an adequate length to the posterior descending artery (PDA), as this is the most common target vessel for the GEA [19, 27], and to the obtuse marginal arteries [27].

9.2.5

Pedicle Versus Free Graft

Although in a recent report, free grafts of IMA reached similar patency rates compared to the pedicle IMA [38], studies by others [30] have disagreed with this. Dion and associates reported a 80 % patency rate for free IMA graft vs. 96 % for the in situ graft [30]. A pedicle graft may be more physiological than the free graft. This is also true for the GEA. Further, a pedicle graft would have an intact vasa vasorum supply to the wall of the graft whereas the free graft can only be nourished from the intraluminal blood supply, which may not be adequate. Finally, although the role of nerve supply to the arterial graft is not well established, physiologically it may play a role in the integrity of the graft as an organ and therefore may play a role in the superior long-term patency. For these reasons, if it is possible to use a pedicle graft, then it is always the preferred choice.

9.2.6

Incidence of Spasm

As mentioned above, it is obvious that if a graft is less spastic, it would have fewer postoperative ischemic problems or even better long-term patency [39, 23, 40]. Type I arteries (IMA, IEA) fall into this category. However, as long as the spastic characteristic is recognized, as for the GEA and RA, adequate pharmacological therapy may produce similar results to those for the Type I arteries [19, 23, 41]. The revival of the RA is a typical example. Incidence of spasm during harvesting may also be related to the technique. Gentle manipulation may reduce the incidence but there is no evidence showing that spasm can be totally avoided by gentle harvesting without pharmacological intervention.

9.2.7

Incidence of Atherosclerosis and Occlusion Rate

Arteries with a low incidence of atherosclerosis provide favorable grafts. The IMA is a typical example. The GEA also has a low incidence of atherosclerosis [34, 36, 42] and it is a favorable graft from this point of view. In contrast, the IEA, at least in the proximal portion, has a high incidence of atherosclerosis [36, 44] and therefore is not as good as the IMA [58] unless used as part of a "Y" graft, as suggested by Calafiore [32], in which the required length of the IEA is short so the atherosclerotic proximal part can be resected [32]. Medial calcifications (Monckeberg's disease) are also seen in the IEA [45].

The incidence of atherosclerosis in the RA is unknown, but it has been observed that the RA has a higher degree of atherosclerosis than the IMA [46]. Further, the RA atherosclerosis is correlated to the presence of diabetes, aortofemoral disease, femoral-popliteal disease, age, and male gender [46].

The biological characteristics of the major arterial grafts are summarized in Table 9.1.

Table 9.1. Summary of the biological characteristics of the major arterial grafts. (Reproduced with permission from He GW. *Ann Thorac Surg* 1999; 67:277–284)

Artery	Type ^a	Size	Wall ^b thickness and hyperplasia	Structure	Length	Possible pedicle graft	Incidence of spasm ^a	Incidence of atherosclerosis
IMA	I	Adequate	+++	Elastic	Adequate	Yes	Low	Low
IEA	I	Small at distal	+	Muscular/elastic	Limited	No	Low	May be higher
GEA	II	Adequate	++	Muscular	Adequate	Yes	High	Low
RA	III	Adequate	++++	Muscular	Adequate	No	High	Unknown

^a According to the functional classification in ref. [39]

^b According to ref. [34]

9.3

Anatomy of the Coronary Artery

9.3.1

Anatomic Location of the Coronary Artery Branch

Many surgeons choose the target vessel for arterial grafts with consideration of the anatomy of the coronary artery. For example, the anatomy of the RCA is variable so the anatomic correlation between the RIMA and RCA is not as consistent as that between the LIMA and the LAD [27]. The classic pattern of coronary anatomy exists in only 50–60% of patients [27]. When the dominant left coronary artery configuration is associated with a right coronary artery that contributes only varying amounts of perfusion to the right ventricle and zero to the left ventricle, use of the RIMA may be contraindicated [27]. Further, the GEA is preferred for a graft to the PDA [9, 19, 27].

9.3.2

Status of the Native Coronary Artery

The severity of the native coronary artery disease is also a factor to determine the target vessel for arterial grafts. For example, it has been suggested that the target vessels for the IEA must be those that are completely occluded or severely stenotic with low coronary resistance and in territories not totally infarcted in order to avoid the “string sign” [32].

9.4

Vessel Match Between the Graft and the Coronary Artery

The match between the arterial graft and the native coronary artery includes the size match and length match that are discussed above.

9.5

Technical Considerations

9.5.1

Personal Experience

It is obvious that the use of arterial grafts at large depends on the surgeon's preference except for the use of the left IMA, which has been unanimously accepted as the choice for LAD unless there is a contraindication. The technique of arterial grafting is more difficult and time-consuming than for venous grafts particularly when multiple arterial grafts are used.

9.5.2

Antispastic Protocol

As mentioned above, antispastic therapy is an important procedure under some circumstances such as in RA grafting, in which such a protocol is a key step for the revival of the RA. Various antispastic methods have been suggested. Papaverine despite its acidic nature is still widely used. Nitrovasodilators are also recommended [49, 47–49]. Use of the calcium antagonist diltiazem is a key point in the revival of the RA [23] and recently other calcium antagonists such as verapamil have also been used [41]. The combination of vasodilators may achieve an even better antispastic effect. For example, nitroglycerin and verapamil can be used effectively [41] and this mixture of pharmacological agents, but not papaverine, has been demonstrated to be effective [50] and maximally preserve the endothelium in the RA [51]. The use of new vasodilators in arterial grafts such as PDE inhibitor milrinone [52, 53], potassium channel openers [54–56], TxA_2 antagonists [57], angiotensin receptor antagonists [58], new calcium antagonists with α_1 -adrenergic receptor blocking activity [59], and vascular endothelial growth factor [60, 61] opens up a new era in the antispastic therapy of arterial grafts.

9.6

Conclusion

Arterial grafts are biologically divergent conductance arteries. Although it has been shown that use of arterial grafts may achieve superior long-term patency, the choice of the grafts with regard to the target vessel, patency rate, and vasospasm [62, 63] and the combination of the grafts is continuously evolving. Clinical choice of grafts must be based on the general condition of the patient, the biological characteristics of the graft, the anatomy of the coronary artery, the match between the coronary artery and the graft, and the technical considerations including antispastic management.

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Internal Thoracic Artery Grafting

History of Internal Thoracic Artery Grafting and Alternative Arterial Grafts

M. DURAIRAJ, B. BUXTON

The early successful treatment of injuries to the heart at the end of last century provided evidence beyond doubt that it was possible to operate successfully on the heart. Dr. Ludwig Rehn of Frankfurt is generally accredited with performing the first successful heart operation in August 1897 on a 22-year-old gardener who was stabbed in the heart and collapsed. He entered the chest through the left fourth intercostal space to find a massive collection of blood in the pleural cavity and continuous bleeding from a hole in the pericardium. Rehn enlarged this hole to expose the heart and a gaping 1.5-cm right ventricular wound. Using a small intestinal needle and silk he sutured the wound during diastole managing to control all bleeding. He went on prophetically to state: "This proves the feasibility of cardiac suture repair without a doubt! I hope this will lead to more investigation regarding surgery of the heart. This may save many lives." [1].

Rudolph Matas [2], who successfully repaired arterial aneurysms, was first to prove that it was possible to repair a diseased segment of an artery. Subsequent surgical therapies mostly developed incrementally by new generations of surgeons building on the knowledge and experience of their predecessors. The progress of open-heart surgery and arterial grafting is a story of delay, frustration and perseverance marked by flashes of brilliance from the visionaries and innovators. Carrel [3] and Gibbon [4] were such men pioneering the development of coronary artery grafting techniques and techniques involving slowing or arresting the heart respectively.

Early attempts to improve the coronary artery circulation to boost the supply of blood to the myocardium were indirect. Cervical sympathectomy was championed by Charles Emile Francois-Frank [5] and performed by Charles Mayo and his father to denervate the heart and therefore reduce the rate of contractility. In 1901 Kocher [6] observed that a patient with angina became asymptomatic after a total thyroidectomy. While improving anginal symptoms thyroidectomy left patients hypothyroid. It was Elliott Cutler who performed the first subtotal thyroidectomy with the specific objective of relieving angina [7]. Although his patient was improved symptomatically, the widespread use of this

operation was not popular because of the risk of recurrent laryngeal nerve injury and airway obstruction.

Beck [8] and O'Shaughnessy [9] promoted the collateral circulation to the myocardium from the epicardium by a number of procedures, including artificial pericarditis, and muscle or omental flaps. Obstruction of coronary venous drainage was shown to relieve symptoms and was associated with a reduction of angina clinically and also experimentally in dogs [10]. Beck went on to develop two operations combining the development of collateral circulation with techniques of coronary venous ligation (Beck I Procedure). Subsequently, he added a brachial arterial graft between the descending thoracic aorta and the coronary sinus, followed by partial ligation of the coronary sinus at a later date. This procedure was known as the Beck II Procedure [11] and was designed to increase the supply of arterial blood to the coronary sinus, a procedure which fell into disrepute because of the high perioperative mortality.

Vineberg postulated that anastomoses could develop between the coronary arteries and the transplanted internal thoracic artery (ITA) as early as 1941 at McGill University [12]. He mobilized the left ITA, leaving the side branches, and ligated the vessel distally. The ITA was subsequently implanted into a tunnel in the left ventricular muscle alongside the left anterior descending coronary artery (LAD) (Fig. 10.1). By 1962, Vineberg [13] had reported 140 operations with an initial mortality of 33%, which subsequently fell to 2% in the decade between 1954 and 1963. These patients had no, or only slight, angina and showed marked clinical improvement. When coronary angiography was developed at the Cleveland Clinic, significant anastomoses were demonstrated in approximately 80% of these patients. This operation continued to be used until about 1970, when direct aortocoronary bypass techniques were introduced.

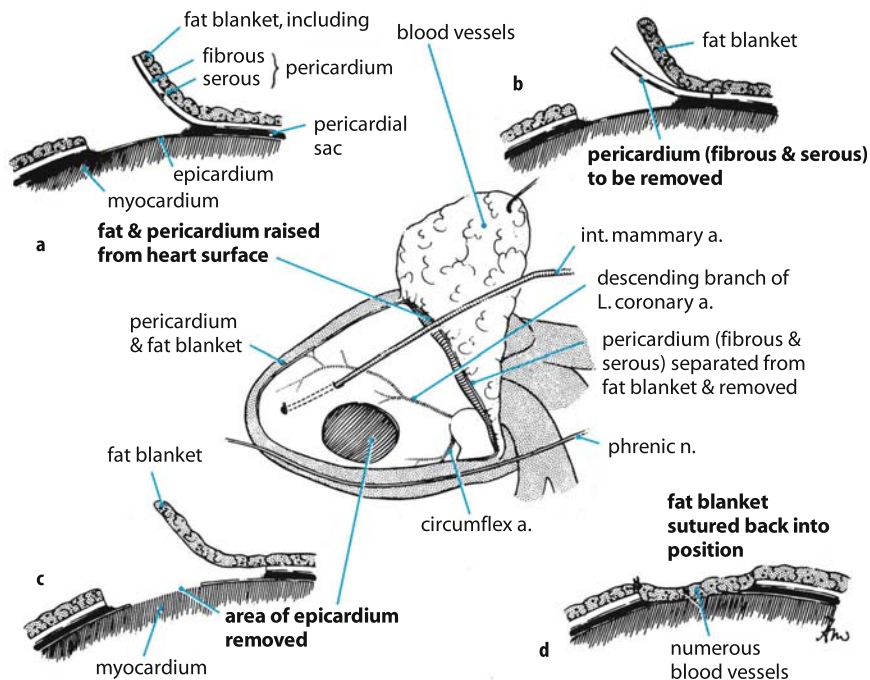


Fig. 10.1a–d. The Vineberg procedure. (Reproduced with permission from [98])

10.1 Early Direct Arterial Revascularization Techniques

The period from the 1950s to the 1960s saw the introduction of most of the surgical techniques used today. Gordon Murray, a Canadian surgeon, used heparin to prevent experimental graft thrombosis in 1940 [14]. Later, he interposed a segment of vein to repair a coronary artery in an animal model, which he reported in a paper he presented at the Graduate Fortnight of the New York Academy of Medicine in October, 1951 [15]. Murray also reported the first arterial autograft inter-

position in a coronary artery following excision of a lesion (paper read at the Congress of the International Society of Angiology, Lisbon, September, 1953) [16]. The following year, Murray succeeded experimentally in performing direct coronary artery bypass grafting using carotid, axillary and ITAs [17].

The direct approach to removing an obstructing atheromatous plaque by endarterectomy appealed to surgeons because of its simplicity. Charles Bailey reported the first closed coronary endarterectomy of the right coronary artery in 1957 [18]. Bailey performed seven of these procedures without mortality. The efficacy of a coronary artery endarterectomy

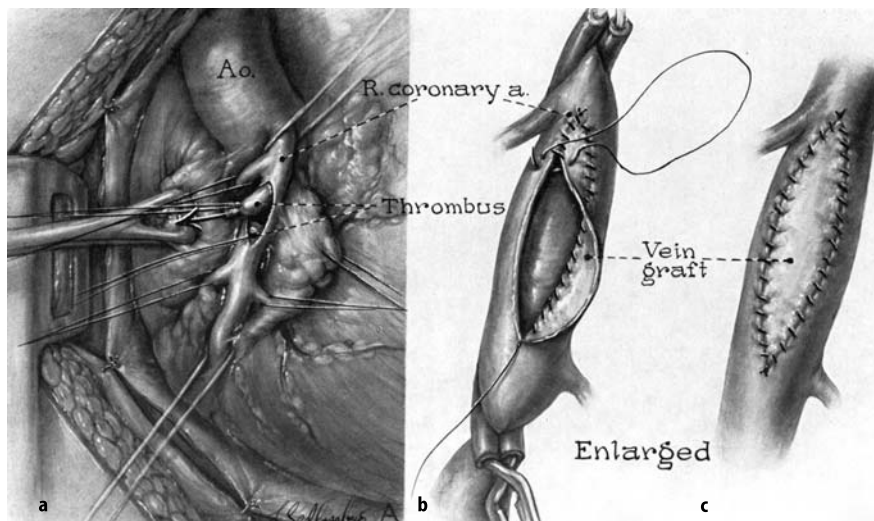


Fig. 10.2a–c. Sabiston's saphenous vein patch graft technique. (Reprinted with permission from [99])

was improved by the use of patch techniques [19] (Fig. 10.2).

It may have been Longmire who first used the ITA to bypass a lesion in the right coronary artery. During an endarterectomy, he found that it was not possible to repair the coronary artery. In desperation, he anastomosed the ITA to the right coronary artery beyond the endarterectomized segment [20]. A few years later in 1961 [21], Robert Goetz anastomosed the right internal thoracic artery to the right coronary artery using a sutureless method and he is generally regarded as having performed one of the earliest arterial reconstructions for coronary artery disease.

In 1964 Spencer et al. [22] demonstrated the value of laboratory research when he performed 16 ITA anastomoses to the circumflex coronary artery in dogs. Building upon this research, George Green [23] began a program of ITA anastomoses to distal LAD segments. This work was conducted in a surgical laboratory at the New York University in 1965 and established the feasibility and potential long-term patency of this type of anastomosis in humans. A number of other arterial conduits were introduced in the United States to supplement and extend the application of ITA grafting. The use of the

intercostal artery was suggested by Pearce et al. [24] in 1966, the gastroepiploic artery by Bailey in 1967 [25] and the splenic artery by Bloomer in 1968 [26].

Unknown to surgeons in the West, Kolesov performed six operations between 1964 and 1967 [27] in Leningrad, using a combination of the Vineberg technique and direct arterial anastomoses between the ITA and the LAD, an operation he performed without coronary angiography or cardiopulmonary bypass (CPB) through a small left anterior thoracotomy (Fig. 10.3). In 1991 he reported 33 cases using these techniques [28].

10.2

Coronary Arteriography

The introduction of coronary arteriography was to have a profound impact on the development of coronary artery surgery. Forssman [29], in 1929, performed self-catheterization of the right heart by advancing a catheter proximally through a vein in his left cubital fossa using fluoroscopic guidance. He repeated the procedure on several occasions. After severe criticism, he abandoned the procedure and turned to urology. Zimmerman [30] catheterized the left heart, which later became standard practice following the introduction of the Seldinger technique.

The introduction by Sones and colleagues [31] of selective coronary arteriography was a monumental contribution to the advancement of coronary artery surgery. Diagnostic coronary arteriography allowed a precise diagnosis and assessment of the quality of the arteries, and paved the way for coronary artery bypass surgery and percutaneous revascularization. In the late 1950s, Sones and colleagues were using an image intensifier and fluoroscopy to record photographic images of injections into the aortic root on 35-mm cinefilm. In 1958, when the first Phillips 11-inch amplifier was installed [32], the equipment was so large and cumbersome that it was necessary to dig a pit beneath the table, so that Sones could crouch to observe the field. On 24 October 1958, a routine procedure was being done, with Sones in the pit and Dr. Royston Lewis as his assistant. Dr. Lewis recalls that he prepared 40 cc of contrast medium for injection into the aortic root, a common practice that flooded the aortic root and permitted some visualization of both coronary arteries. This procedure was state-of-the-art for that time. Because of some transient distraction, Dr. Sones took his eye off the screen; at this precise moment, the catheter drifted into the ostium of the right coronary artery and descended for several centimetres, a fact that was not appreciated immediately. When Dr. Lewis received his instructions to inject 40 cc of contrast medium into the aortic root, the entire dose was injected into the right

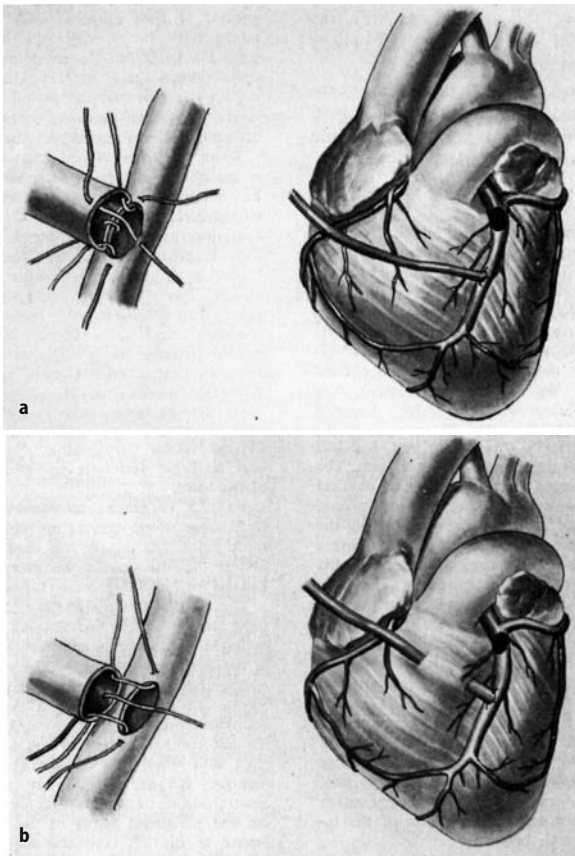


Fig. 10.3a, b. Kolesov's anastomotic technique. (Reprinted with permission from [27])

coronary artery, well under the ostium and under very high pressure. Apart from a very short period of asystole lasting 6.5 s, the procedure was well tolerated and when the film was reviewed, the first right selective coronary arteriogram had been performed and the value of the procedure was recognized.

10.3

Saphenous Vein Coronary Artery Bypass

The development of coronary artery bypass surgery at the Cleveland Clinic followed rapidly and saphenous vein became widely used as a coronary artery bypass graft. Effler and Favaloro [33] initially interposed saphenous vein grafts into the right coronary artery after excision of a segment. Subsequently, the upper end of the vein graft was attached to the aorta and an end-to-side anastomosis constructed in much the same way it is performed today.

Other teams, including Dudley Johnson of Milwaukee [34], Urschell and Mitchell in Dallas, and Spencer and Green in New York [35], reported results of early saphenous vein grafting between 1968 and 1970. Green [23] and Favaloro [36, 37] employed a combination of single and bilateral ITA grafting, alone and in combination with saphenous vein grafting. These operations were later extended to include patients who required valve replacement or aneurysmectomy. It was Johnson who was credited with extending the application of saphenous vein bypass grafting by performing sequential and multiple vein grafts to the LAD [34].

10.4

Internal Thoracic Artery Grafting

In 1968, the ITA became more widely applied as new surgical techniques evolved. Bailey and Hirose [38] attached the right ITA to the right coronary artery. After being denied the opportunity of performing the first procedure in his own hospital, Green accepted the invitation of Dr. David Tice to perform the first elective ITA to LAD anastomosis in the United States at the New York Veterans' Hospital in February 1968. In the same year, Green went on to operate on 18 patients, placing the ITA graft to the distal one-third of LAD segments that measured about 1.5 mm in diameter. While there were no early operative deaths, one-third of the patients died prior to leaving hospital. At postmortem examination they were found to have severe triple vessel disease. Green went on to use the saphenous vein, as described by Favaloro, to graft the right coronary artery because he thought that it was a better size match than the ITA. In 1969 he began performing grafts to the circumflex coronary artery branches to supplement the

ITA graft, thus resolving the problem of postoperative mortality from uncorrected coronary stenoses. By 1974, both Barner et al. [39] and Kay et al. [40] reported a large series of bilateral ITA grafts.

So enthusiastic was Sterling Edwards [41] from the University of New Mexico, that he used both ITAs and in 1973 reported the technique of adding a pedicled splenic artery to produce a complete arterial reconstruction. He had performed 15 splenic artery anastomoses by 1975. When he was unable to use the splenic artery because it contained an aneurysm, he substituted the right gastroepiploic artery to complete the coronary artery reconstruction using arterial grafts. This was not reported.

10.5

Expanded Use of the ITA Graft

A number of innovative techniques have been used to extend the application of the ITA. While bilateral ITA grafting was a logical development, its introduction was slow. Although first reported in 1965, the next 30 years saw only sporadic publications of the results of bilateral ITA grafting [39, 42–53]. Attachment of the ITA under tension to the right side or to vessels of small diameter, for example, a diagonal branch, may have obscured any benefit from bilateral over single ITA grafting. In the past, differences in patient selection and insufficient follow-up have resulted in difficulties assessing the results of single compared with bilateral ITA grafting [54, 55]. Recent studies by Buxton [56], Stevens [57] and Lytle [58] have shown that bilateral ITA grafting definitely improved 15- to 20-year survival compared with single ITA grafting for multivessel coronary artery bypass grafting. However, these are retrospective studies and future randomized controlled trials (RCT) like the ART trial [59] will prove or disprove these findings. Recent studies involving bilateral ITA grafts have also indicated that the potential sternal wound infections in diabetic patients can be avoided by routinely skeletonizing the ITA grafts [60].

Detachment of the ITA pedicle from the subclavian vessels for use as a free graft [61–63] has greatly expanded the use of the right ITA by extending its use to distal branches of the right and left systems. Early results show that the patency is similar to, but perhaps not quite as good as, the results of pedicled ITA grafting [64]. Some of the graft failures were attributed to difficulty with the anastomosis between the free ITA and the aorta. Alternative techniques using a vein patch on the aorta for the proximal anastomosis were described by Kanter and Barner in 1987 [65].

ITA grafts were used more efficiently by constructing multiple distal anastomoses using a single conduit [66, 67]. Sequential distal anastomoses not only in-

creased the range of ITA grafting but also limited the need for saphenous vein grafting. The early results of sequential ITA grafting, published by Rankin [68], Dion [69] and Palatinos [70], confirmed the efficacy of these grafts. Innovative techniques of attaching other arterial grafts to the side of the left ITA have extended the use of ITA grafting to all areas of the heart and avoided an anastomosis between the ITA and the aorta [71, 72].

10.6 Alternative Arterial Grafts

In 1983, Singh and Sosa [73] presented the preliminary angiographic results of ITA grafts showing excellent patency compared with that of the saphenous vein. In a landmark paper, Loop et al. [74] presented a large series of patients who had reangiography, confirming that the in-situ left ITA artery anastomosed to the LAD was an excellent graft and far superior to the saphenous vein. These observations triggered the search for alternative arterial grafts that could be used to supplement either one or both internal thoracic arteries.

John Pym [75] published his early series of gastroepiploic artery to coronary anastomoses in 1987, at about the same time as Suma [76] and Carter [77]. The efficacy of this procedure was confirmed by Suma [78]; his large series of patients showed excellent patency on angiographic follow-up. The inferior epigastric artery was introduced by Puig in 1990 [79]. The publication of early results by Buche [80] suggested that this might be a useful conduit. However, the inconsistency of the length and diameter of this conduit, together with disease at the lower end adjacent to its origin from the external iliac artery, have limited the usefulness of this graft.

Acar [81], when reviewing some of Carpentier's early radial artery grafts [82], found to his surprise that many of these grafts remained patent and had an excellent appearance 10 years after the initial surgical procedure. Acar went on to reevaluate the use of the radial artery as a graft using careful harvesting techniques and vasodilators. A 5-year graft patency study by Acar suggests that this arterial conduit is probably superior to the saphenous vein [83]. A randomized trial by Fremes [84] comparing saphenous veins and radial artery patencies found that the radial artery grafts are associated with a lower rate of graft occlusion at 1 year than saphenous vein grafts. However, the 5-year interim results of the Radial Artery Patency and Clinical Outcome (RAPCO) trial by our group [85] do not support the hypothesis that the radial artery has superior patency to or is associated with fewer clinical events than free right ITA or saphenous vein grafts. In about 5% of patients, the radial artery cannot be harvested without compromising the blood flow to the hand, and in this situation the

ulnar artery may be assessed for use as a bypass graft [54].

There have been reports of other arterial grafts, such as the subscapular artery. In desperate circumstances, Mills and colleagues [86] grafted the subscapular artery between the circumflex marginal branches and the aorta and reported good short-term results.

10.7 ITA Grafts and Minimally Invasive Coronary Artery Bypass Grafting

The LITA graft has been at the centre of evolving techniques in cardiac surgery. Buffolo [87], Benneti [88] and Subramanian [89] repopularized the concept of 'off pump' surgery for coronary revascularization. This procedure combined with the introduction of the LAST (left anterior small thoracotomy) approach by Calafiore [90] in 1996 led to the increasing use of the MIDCAB (minimally invasive direct coronary bypass) technique. Of all the MIDCAB procedures, LITA to LAD MIDCAB has been the most standardized procedure with proven clinical results [91]. It is debatable whether off pump revascularization is better than on pump. A recent RCT by Puskas [92] has shown that off pump CABG has benefits over on pump CABG in terms of decreased cost. Mortality rates, stroke and graft patency were similar in both the groups at 1 year.

The development of the Heartport Port-Access System (Cardioversions, Division of Ethicon, Johnson and Johnson Co., Somerville, NJ) in 1996 [93] was an important milestone in the evolution of endoscopic cardiac surgery. The advancements in three-dimensional visualization systems and robotically assisted endoscopic instruments led to the concept of totally endoscopic coronary artery bypass (TECAB). In 1998, Loulmet [94] was the first to successfully perform totally endoscopic CABG without opening the chest. The technique of revascularization of the LAD with the LITA has been safely reproduced using TECAB on the arrested heart (Mohr [95] and Dogan [96]) and in 2001 TECAB on the beating heart was reported for the first time with grafting of the LAD with the LITA [97].

10.8 The Future

Most of the techniques used today for coronary artery bypass grafting were developed in the latter half of the 20th century. Improving percutaneous techniques and graft durability, and limiting the progress of native coronary artery disease, will remain the greatest challenges for cardiologists and cardiac surgeons treating patients with ischemic heart disease in this century.

Understanding the aetiology and prevention of intimal hyperplasia and atherosclerosis will come from molecular biological research and decoding of the base sequences of the human genome. In the future, new molecular biological techniques are likely to replace many of the currently used invasive procedures.

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Surgical Techniques for Internal Thoracic Artery Grafting

S. SEEVANAYAGAM, B. BUXTON

11.1 Introduction

The left internal thoracic artery (LITA) is used in nearly every coronary artery reconstruction, either alone or in conjunction with the right internal thoracic artery (RITA) or other arterial or venous grafts. Bilateral ITA grafting is believed to confer survival benefit [1]. Bilateral internal thoracic artery usage in everyday practice is increasing. The anatomy, physiology, harvesting and grafting techniques therefore assume enormous relevance to the surgeon.

11.2 Anatomy

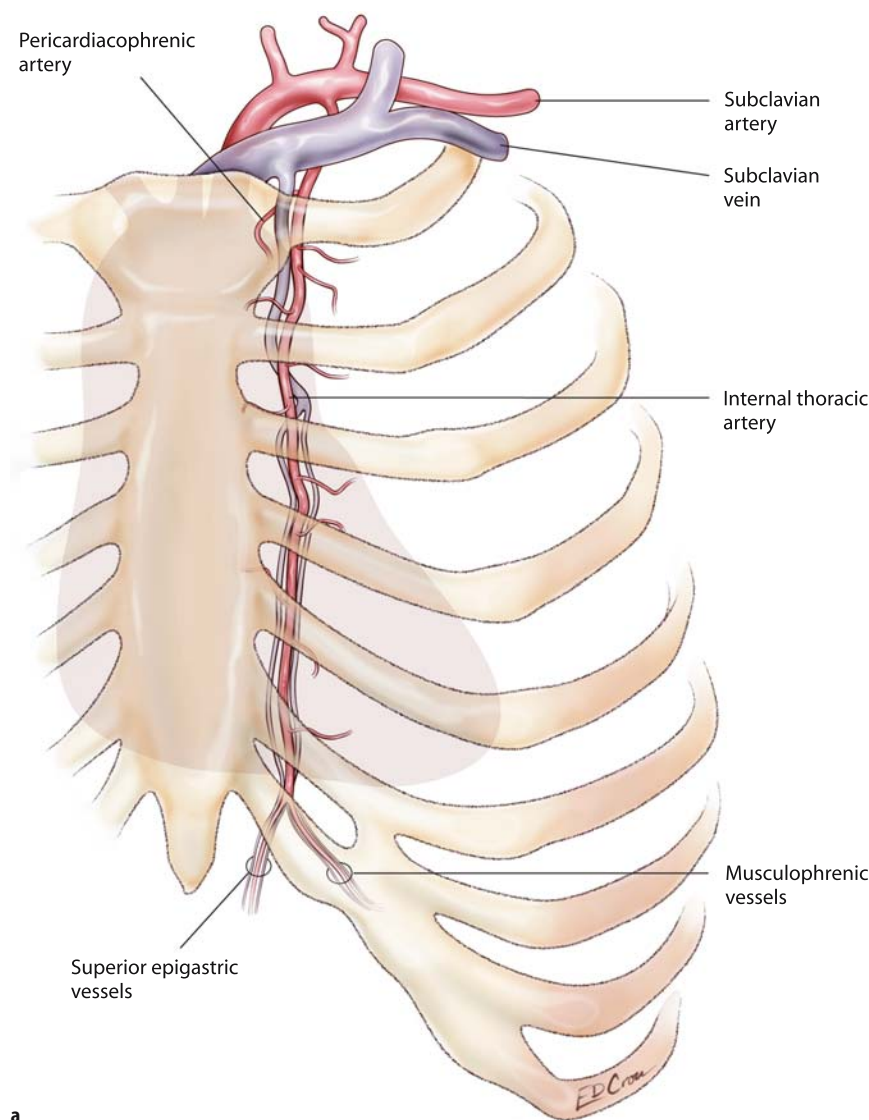
The internal thoracic artery (ITA) arises from the first part of the subclavian artery behind the head of the clavicle. It passes medially and anteriorly to descend behind the first six intercostal cartilages and the intercostal spaces approximately 1 cm lateral to the border of the sternum (Fig. 11.1a). The ITA and veins lie in the plane between the internal intercostal and transverse thoracic muscle layers (Fig. 11.1b). The ITA divides into the musculophrenic and superior epigastric arteries usually at the level of the sixth intercostal space (Fig. 11.1a). Variations of the terminal branches and the level of termination are common [2]. There are variable numbers of perforating sternal and anterior intercostal branches; they normally arise singly but can arise as common trunks (sternal/perforating and sternal/intercostal). In some patients, a persisting posterior intercostal artery does not connect with the ITA and may represent an important collateral blood supply to the sternum [3] (Fig. 11.2).

11.3 Harvesting

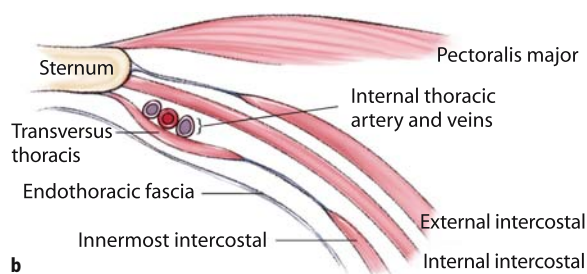
The in-situ ITA conduit may be harvested as a pedicle with its adjacent veins and pleura attached, or it may be skeletonized. The ITA should be mobilized fully, espe-

cially at the superior aspect, to prevent any tethering of the conduit to the chest wall and consequent angulation or tension from the medial part of the inflating lung. During harvest, the pleura may be opened widely, allowing the fully mobilized ITA pedicle to lie near the phrenic nerve, anterior to the hilum of the lung. Alternatively, an extra pleural technique can be employed; however, in this case the ITA conduit needs to be routed in a plane posterior to the thymic fat pad to prevent the pedicle lying in the retrosternal space with consequent risk of injury during later re-sternotomy.

The sternum is opened and the appropriate side elevated by a retractor. The endothoracic fascia is divided to expose the pleura and extrapleural fat. The pleura is then entered medial to the ITA pedicle (Fig. 11.3a). The pleural incision extends from the first to the sixth intercostal space. Alternatively, in the extrapleural technique aimed to preserve the pleura, it may be carefully peeled back far enough laterally to expose the internal thoracic vessels. It is important to enter the correct plane by reflecting the transversus thoracis muscle behind the sternum, commencing in one of the lower intercostal spaces (Fig. 11.3b). Retraction of the pedicle displays the venae comitantes and the internal thoracic artery itself. The perforating and anterior intercostal branches are clipped near the ITA and divided with electrocautery close to the chest wall to avoid damaging the ITA. The first and second perforating branches are particularly large and often require division by scissors between metal clips. Mobilization is continued proximally to the inferior border of the subclavian vein. Complete mobilization of the ITA allows it to lie free, medial to the lung, thus avoiding tension on the conduit by the medial edge of the lung during ventilation. Dissection is continued beyond the bifurcation of the ITA into the superior epigastric and musculophrenic branches.



a



b

Fig. 11.1. **a** Anatomy of the internal thoracic artery; **b** transverse section of the anterior aspect of a typical interspace. The internal thoracic artery and veins lie between the transversus thoracis and intercostalis intimis muscles about 1 cm lateral to the sternal edge. (© 1998 Cardiac Surgery Publishing Office, Melbourne, Australia)

Skeletonization of the ITA is achieved by carefully clipping the branches close to the ITA and involves the additional step of separating the ITA from the underlying transversus thoracis muscle and the venae comitantes. This allows the artery to be free of any other attachments resulting in extra available length. It preserves sternal vascularity better than the standard pedicle technique and may reduce the incidence of

sternal wound complications [3, 4]. A variation of this technique is semi-skeletonization, where the venae comitantes are harvested along with the ITA leaving behind the attachment to the transversus thoracis muscle. In the full pedicle form of harvesting, the transversus thoracis muscle, endothoracic fascia and pleura are divided lateral to the internal thoracic vessels, leaving a pedicle approximately 1.5 cm in width (Fig. 11.3c).

The terminal branches of the ITA are double clipped beyond the bifurcation and the conduit sprayed with papaverine hydrochloride solution 80 mg/100 ml (2 mmol/l). The papaverine solution is mixed with an equal volume of blood [final concentration 40 mg/100 ml (1 mmol/l)] and injected into the lumen of the ITA, which is clipped and allowed to dilate passively.

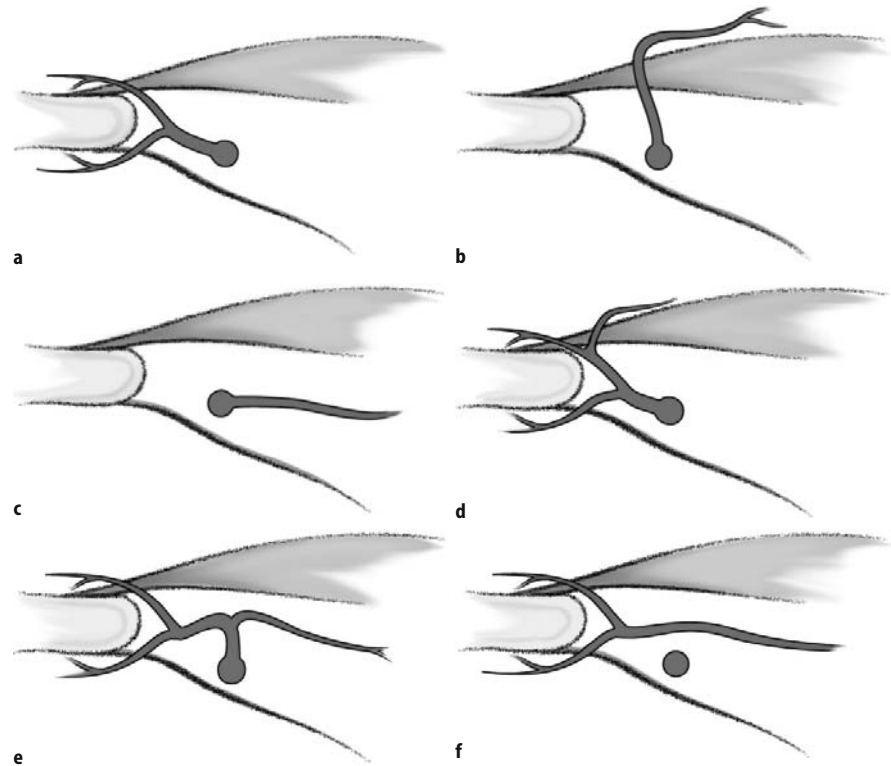


Fig. 11.2a–f. Arterial branches of the internal thoracic artery in the anterior intercostal space. **a** Sternal; **b** perforating; **c** intercostal; **d** sternal/perforating; **e** sternal/intercostal; **f** persisting posterior intercostal. (Modified from de Jesus RA, Acland RD. Anatomic study of the collateral blood supply of the sternum. *Ann Thorac Surg* 1995;59(1):163–168)

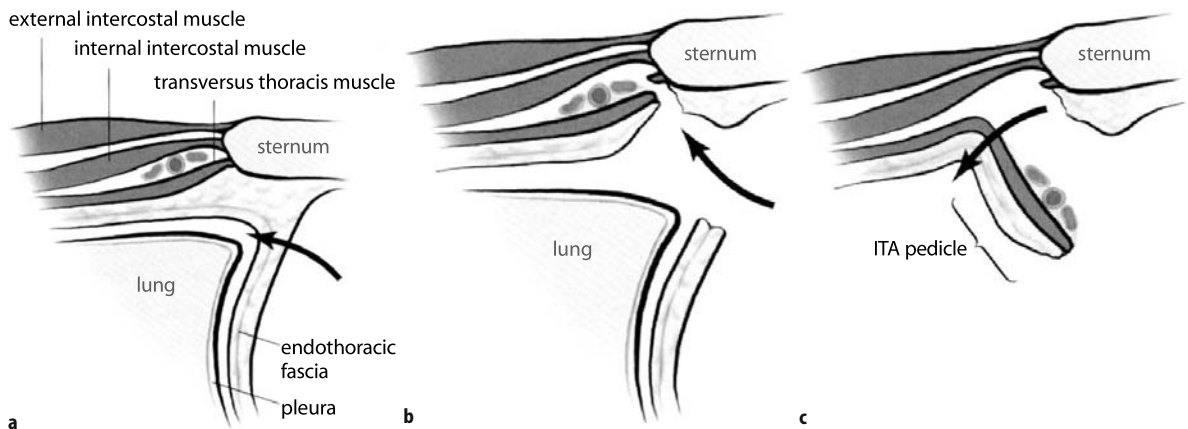


Fig. 11.3. **a** Horizontal/coronal section of the anterior chest wall. Line of incision into the pleural cavity. **b** Detachment of the transversus thoracis muscle, the extrapleural fat, and parietal pleura to display the internal thoracic vessels. **c** The pleura is reentered laterally to fashion the internal thoracic artery pedicle when skeletonization is not employed. (© 1998 Cardiac Surgery Publishing Office, Melbourne, Australia)

11.3.1

The Left Internal Thoracic Artery

The in-situ LITA conduit may be anastomosed to any of the branches of the left coronary system. In the most common scenario, when anastomosed to the left anterior descending artery or the diagonal branches, the LITA is passed through a window in the pericardium anterior to the left phrenic nerve. Alternatively, if the LITA is to be anastomosed to intermediate or circumflex marginal branches the pedicle is passed behind the left phrenic nerve [5].

11.3.2

The Right Internal Thoracic Artery

11.3.3.1

In-Situ RITA Conduit

The RITA may be used as an in-situ graft to bypass proximal lesions on the right side. More recently, however, improved results have followed the use of in-situ RITA to graft vessels on the left side [6–8]. The pedicle enters the pericardium from the right through a slit or window anterior to the right phrenic nerve. If the LAD or diagonal branches are to be grafted, the RITA is

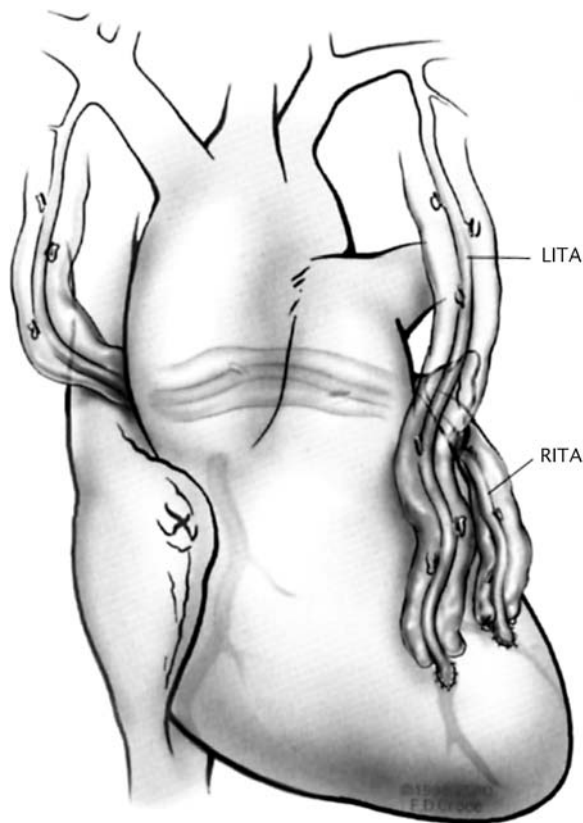


Fig. 11.4. Use of in situ right internal thoracic artery conduit to reach the left side via the transverse sinus. (© 1998 Cardiac Surgery Publishing Office, Melbourne, Australia)

passed anterior to the aorta behind the thymus, the normal plane for grafts anastomosed with the aorta. The RITA is angled inferiorly to reach the upper or middle third of the LAD or a high diagonal branch. Alternatively, the in-situ RITA conduit, after entering the pericardium, can be passed through the transverse sinus to emerge near the left atrial appendage, lateral to the pulmonary artery (Fig. 11.4). It is then anastomosed to the diagonal, intermediate or anterior marginal branch of the circumflex coronary artery.

11.3.3.2 Free RITA Conduit

The RITA is commonly used as a free graft because when in situ, its length is usually insufficient to reach the distal branches of the right coronary artery, LAD or circumflex system [9, 10]. In addition the free RITA can be used in a T- or Y-graft configuration along with the LITA, allowing complete ITA revascularization of the left coronary system. Mobilization of the pedicle, ligation of branches and transection of the distal end are identical to the procedures used for the in-situ technique. The internal thoracic vein is divided between clips before it reaches

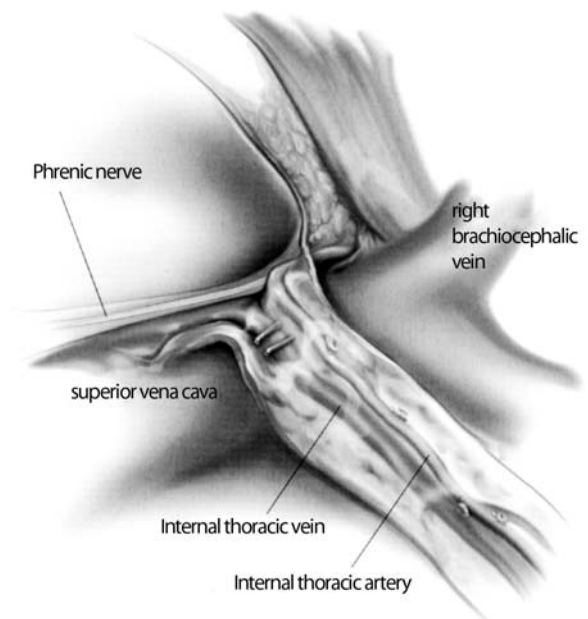


Fig. 11.5. Superior end of the right internal thoracic artery pedicle illustrating the close proximity of the right phrenic nerve, requiring care during transection of the right internal thoracic artery for use as a free graft. (© 1998 Cardiac Surgery Publishing Office, Melbourne, Australia)

the brachiocephalic vein (Fig. 11.5). The artery is then followed to the inferior border of the right subclavian vein and divided. The pericardiophrenic artery is seen near the level of the inferior border of the subclavian vein, close to where the ITA is transected. It usually requires division. At this level, the phrenic nerve has a variable relationship with the ITA and care must be taken to avoid damaging the nerve. The phrenic nerve is normally located anteromedial to the ITA, but may enter the thorax posterior to the ITA.

11.4 Histology

The ITA is an elastic artery with a thin intima and a well-formed internal elastic membrane. The media is formed by a combination of elastic lamellae and smooth muscle cells. Smooth muscle cells interspersed with elastic fibers increase toward the distal end, where the media is predominately muscular [11]. Vasa vasorum are seen in the adventitia but sparse in the media.

11.5 Goals of Arterial Grafting

The goals of coronary artery bypass grafting are to revascularize vessels with a lumen greater than 1 mm,

and have a stenosis greater than 50%. Other objectives are to provide symptomatic relief with low operative morbidity and mortality, to provide a durable reconstruction, to prolong survival and to reduce the incidence of late complications.

11.6

Grafting Strategy

The choice of grafts and their deployment are of major importance in determining the outcome of the coronary artery bypass procedure. A single ITA supplemented by saphenous vein grafts is probably the most common surgical reconstruction performed for correcting coronary artery disease. The LITA is normally grafted to the LAD. In an unusual circumstance, for example when the LAD is free from disease or of poor quality, the LITA is anastomosed to a diagonal or circumflex marginal branch. Where possible, saphenous vein grafts are attached to a small or an infarct-related artery to minimize the myocardial damage should the graft fail. In patients who present with cardiogenic shock or those who have severe pulmonary disease, morbid obesity, or when the ITA has been injured during removal, saphenous vein grafts are used occasionally as the sole bypass conduits.

Bilateral ITA grafting has been used for several decades but has not been universally popular because of the increased time required for harvesting and the potential for chest wall complications, which occur more frequently in obese or diabetic patients. No agreement has been reached about the late benefits of bilateral ITA grafting. More recently, bypassing the left, compared with the right, coronary system with bilateral in-situ ITA grafts has been associated with improved survival [7, 8]. Our policy is to routinely use bilateral in-situ ITA grafts in younger patients who have no contraindications (such as diabetes, severe pulmonary disease or obesity). In approximately one-third of the patients, however, the RITA will not reach an appropriate position on the diseased coronary artery and is used as a free graft that is anastomosed proximally to the aorta, or to the side of the LITA as a T- or Y-graft. More recently, another segment of an arterial graft (commonly a segment of radial artery) has been added to the distal RITA (graft extension) so that it will reach the desired location.

Complete arterial grafting has been adopted by some units and is increasing in popularity. Complete arterial grafting can be achieved by using combinations of the ITA, radial artery, gastroepiploic artery and inferior epigastric artery grafts. Most patients require three conduits but if additional grafts are necessary, sequential distal anastomoses, T- or Y-grafting, graft extension or a combination of these techniques is employed.

11.7

Grafting Techniques

Coronary artery bypass graft surgery (CABG) does not require the opening of a cardiac chamber and is therefore not technically open-heart surgery. Conventional CABG is performed using cardiopulmonary bypass (CPB), which provides the excellent operating conditions required for the precise anastomosis of a small graft to a small coronary artery. Bypass grafting is conducted under conditions of mild hypothermic CPB (32–34°C) and the anastomoses are performed under a single aortic cross clamp using antegrade and retrograde cardioplegia for myocardial protection. Normally, distal anastomoses are performed first and a proximal anastomosis is constructed after each distal end, or all distal ends are anastomosed prior to removal of the aortic cross clamp and the proximal ends attached to the aorta using a partial occlusion clamp.

11.7.1

The Distal Anastomosis

All anastomotic techniques require precise apposition of the endothelium of the graft to that of the native coronary artery to produce a reconstruction without a stenosis. The length of the arteriotomy is normally two to three times the diameter of the native coronary artery to avoid narrowing at either end of the anastomoses. It is important to open the coronary artery in the midline and to prevent any atheroma from being dissected from the overlying adventitia. The graft is fashioned at an angle of 45° to the long axis and carefully trimmed to remove any corners, which may impede suturing. Forehand or backhand suturing techniques are popular and use continuous monofilament suture.

11.7.2

Sequential Distal Anastomoses

Sequential anastomoses allow the most efficient use of precious arterial conduits by maximizing the number of distal anastomoses [12]. Sequential anastomoses can be performed readily with vein grafts; sequential grafting using arterial conduits is more difficult because of their small size and their vasoreactivity [13]. Sequential anastomoses are commonly performed between branches of the same major coronary arteries. Common combinations are: (1) the LAD and an adjacent diagonal branch; (2) two circumflex marginal branches; (3) the posterolateral and posterior descending branches of the right coronary artery; and (4) the posterior descending branch and the right coronary trunk.

The position of the side-to-side and the end-to-side anastomoses depends on the location of the atherosclerotic plaques and the lie of the coronary arteries. In

most circumstances it is easier to perform the terminal end-to-side anastomosis first and preference is given for this anastomosis to be located on a vessel of large diameter to facilitate flow through the graft. The end-to-side anastomosis is identical to the technique described above for a single graft; once completed, the side-to-side anastomosis is constructed. Side-to-side anastomoses between a graft and a coronary artery can be performed using a parallel method when the graft and the coronary artery lie in the same direction, or using a diamond method when they cross at a right angle. Mastering the technique of sequential anastomoses requires practice. Judgment is required to assess the direction of the sequential graft so it can be attached to the most suitable segments of the native artery. A little extra length between sequential anastomoses is preferable to allow for distension of the graft when the aortic cross clamp is released and the heart commences to beat. Insufficient length may cause tension, angulation and even dehiscence of the anastomosis.

11.7.3

The Proximal Anastomosis

The free ITA is usually sutured to a small aortotomy (3 mm) using monofilament suture. If the aorta is atherosclerotic or calcified, the ITA may be sutured to a vein patch in the aorta [6] or anastomosed to the left ITA as a T- or Y-graft [14].

11.7.4

ITA T- or Y-Grafting

The development of strategies to perform complete arterial grafting using both ITAs was developed by Tector et al. [14], who attached the free RITA to the side of the

in-situ LITA (Fig. 11.6). Using this technique, he was able to graft the LAD and/or the diagonal with the LITA. The RITA, used as a side arm graft, was anastomosed to the intermediate or circumflex marginal branches. The T-graft can be performed with the anterior (chest wall) surface of the LITA or with its posterior wall. The anastomosis is performed either at a right angle (T-graft) or obliquely (Y-graft). This end-to-side anastomosis is sited at the level of the second or third perforating branch on the LITA if the intermediate or a high diagonal branch is to be grafted, or below the third intercostal perforating branch on the LITA if the more lateral circumflex marginal branches are to be grafted [15]. This anastomosis is normally performed prior to cardiopulmonary bypass to minimize the cross clamp time (Fig. 11.7).

11.7.5

ITA Graft Extension

In some patients, the in-situ ITAs are too short to reach the desired position on the diseased coronary artery. This is a particular problem on the right side, where the posterior descending and in particular the posterolateral branches require a long length of conduit. Stretching the ITA or using fasciotomies [16] may account for many early graft failures using the in-situ RITA [6]. The use of a second arterial conduit, commonly radial, or rarely inferior epigastric or ulnar, artery as an extension of the RITA is a simple alternative, which maximizes the use of the in-situ and free arterial conduits [17, 18]. The end-to-end anastomosis between the ITA and the second arterial conduit is performed obliquely using a 7/0 or 8/0 monofilament suture. The proximal clamp is removed from the ITA before the suture is tied to judge the correct tension so that the diameter of the

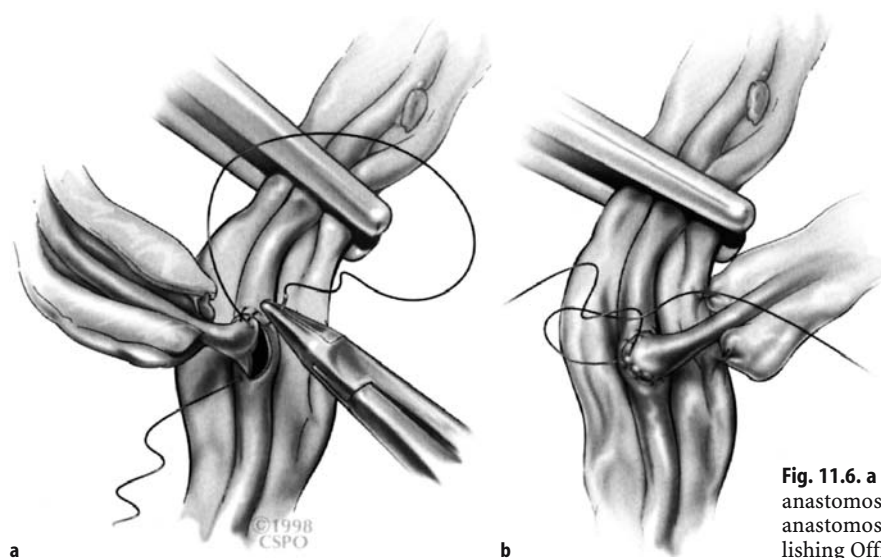


Fig. 11.6. **a** Posterior suture line in a T-graft anastomosis. **b** Completed end-to-side anastomosis. (© 1998 Cardiac Surgery Publishing Office, Melbourne, Australia)

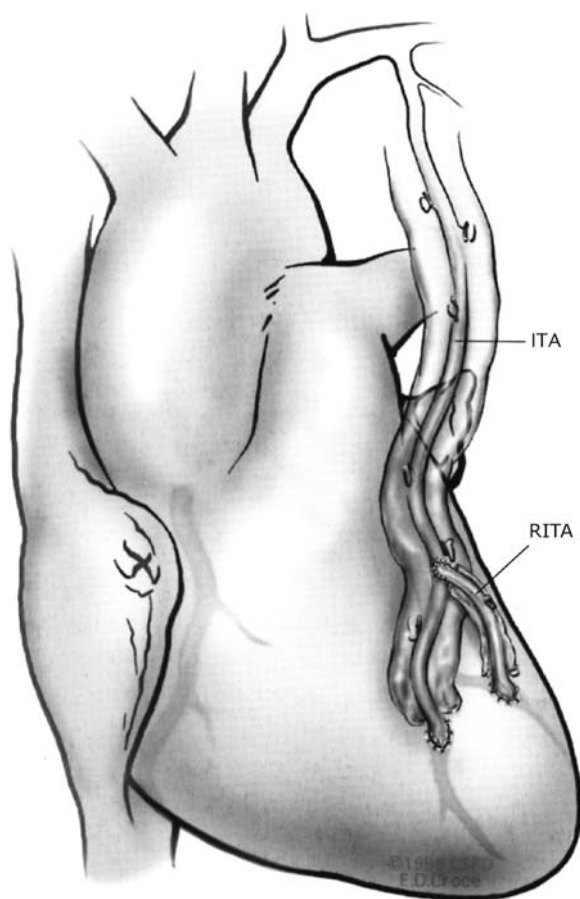


Fig. 11.7. The left internal thoracic artery is anastomosed to the left anterior descending coronary artery and the radial artery is attached to a diagonal, intermediate or circumflex marginal branch. (© 1998 Cardiac Surgery Publishing Office, Melbourne, Australia)

anastomosis is maximized. This type of 'composite in-situ' graft will reach any part of the coronary artery architecture without tension. The extension graft can be used in a single or sequential manner using the techniques described above.

11.8

Beating Heart Bypass Surgery

Coronary artery bypass graft surgery without the use of cardiopulmonary bypass is increasing. The off pump coronary bypass surgery (OPCAB) uses conventional patient preparation, anaesthetic techniques and conduit harvesting methods. Cardiopulmonary bypass is not employed. Careful haemodynamic monitoring, pharmacologic manipulation and judicious positioning and retraction of the heart enable the coronary artery targets to be visualized [19]. Specially designed positioning and suction devices such as Octopus 4/

Starfish/Urchin (Medtronic Inc., Minneapolis, MN, USA) have greatly facilitated the positioning of the heart for OPCAB surgery.

The target coronary artery is mobilized from the epicardial fat and encircled with a silastic sling (Quest Medical Inc., Allen, TX, USA). The ITA pedicle is clamped with a spring bulldog clamp and the distal end prepared for anastomosis. The silastic sling or Deithrich bulldog clamp (Johnson & Johnson Inc., Raynham, MA, USA) is used to occlude the target vessel. An arteriotomy 4–5 mm in length is made in the coronary vessel and the ITA is anastomosed in a standard fashion using a continuous 7/0 or 8/0 polypropylene suture. An intracoronary shunt can be used during the construction of the anastomosis to maintain coronary flow and removed just prior to the conclusion of the anastomosis. The stabilizer/positioning device is then repositioned to expose the next target vessel and so on to complete the revascularization.

In patients with cardiogenic shock, unstable haemodynamics or dilated ventricles beating heart surgery may be carried out with the assistance of cardiopulmonary bypass for haemodynamic support. This pump assisted beating heart surgical technique prevents any myocardial injury associated with the aortic cross clamping and cardioplegic arrest associated with conventional coronary bypass graft surgery.

Over the last decade, several prospective randomized studies on OPCAB surgery have been published in the cardiac surgical literature. Some of these have shown OPCAB surgery to be safe and comparable to conventional coronary bypass surgery using cardiopulmonary bypass with respect to completeness of revascularization, short term patency, and event free outcomes. They have also shown OPCAB to be better with respect to lowering of costs, better neurocognitive outcomes and preservation of renal function [20, 21]. However, some questions remain before OPCAB surgery becomes the norm in clinical practice [22].

11.9

Less Invasive Surgical Techniques

Many of the less invasive surgical techniques discussed in the previous edition of this book (MIDCAB, Port Access CABG, etc.) have been shown to have limited applicability and are not in widespread use. Robotics assisted cardiac surgery is continuing to evolve and is limited to centres with the facility at this stage. The exact role of these surgical methods has yet to be defined.

11.10

Conclusions

The use of one or both ITAs as in-situ grafts is now recognized as the cornerstone of coronary artery bypass grafting. Complex techniques using a combination of ITAs and other arterial conduits have evolved to provide complete arterial grafting for most patients. Less invasive techniques are being developed to reduce the cosmetic deformity and the physiological impact of bypass surgery. The durability and clinical outcomes of these newer procedures require further evaluation before they can be recommended for general use.

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Long-Term Results of Internal Thoracic Artery Grafting

J.F. SABIK III, F.D. LOOP

12.1 Introduction

The long-term success of coronary artery bypass surgery is directly related to graft patency. Internal thoracic artery grafts, because of their resistance to arteriosclerosis, have stable and excellent late patency, and their use in myocardial revascularization has resulted in better survival and freedom from recurrent ischemia and reintervention compared with revascularization with saphenous vein grafts alone. In this chapter, the long-term patency and clinical benefits of internal thoracic artery grafting will be reviewed.

12.2 History

Prior to development of cardiopulmonary bypass and coronary artery bypass grafting, Vineberg implanted internal thoracic arteries into the left ventricular muscle to improve myocardial blood flow and treat ischemia [1–3]. The first direct left internal thoracic artery to left anterior coronary artery bypass revascularization was performed by Demikov in 1953, and in 1967, Kolessov reported performing the same procedure [4, 5]. Green and colleagues were early proponents of using internal thoracic arteries as bypass grafts and in the 1970s popularized its use [6]. However, it was not until the mid-1980s, when several landmark papers described the clinical benefits of internal thoracic artery grafting, that this procedure became an important and widely adopted part of coronary surgery [7–13].

12.3 Patency

The clinical benefits of internal thoracic artery bypass grafts are directly related to the fact that they have better long-term patency than saphenous vein grafts. Internal thoracic artery graft patency remains stable over long periods, whereas saphenous vein graft patency declines over time (Fig. 12.1). The 10-year patency of in-

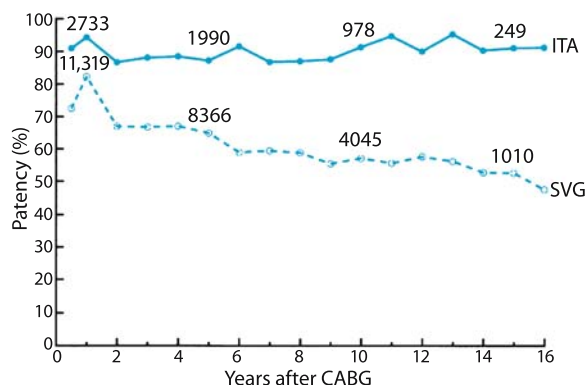


Fig. 12.1. Unadjusted internal thoracic artery and saphenous vein graft patency by year after coronary artery bypass surgery (CABG). Numbers represent number of grafts studied at corresponding year after CABG. (Reprinted with permission [19])

ternal thoracic artery grafts is 90–95%, versus only 50–60% for saphenous vein grafts [4, 9–11, 16–24]. One year after surgery, only 80–90% of saphenous vein grafts are patent. This is due to technical errors, intimal hyperplasia, and thrombosis. From 1 to 5 years after surgery, 1–2% of patent saphenous vein grafts occlude per year, and from 6 to 10 years after surgery, 4–5% occlude per year. The increase is due to development of arteriosclerosis. By 10 years, only 50–60% of saphenous vein grafts are patent, and only half of those are free of angiographic arteriosclerosis [10, 12, 14, 15, 20, 21, 23, 24].

Unlike saphenous vein grafts, internal thoracic artery grafts rarely develop arteriosclerosis [10–13, 22, 25, 26], explaining why their patency is stable over time. Less than 4% of internal thoracic arteries have clinical evidence of arteriosclerosis, and less than 1% have important luminal narrowing [25, 27, 28]. This resistance to arteriosclerosis is believed to be due to the vessels' histologic structure [28]. Their nearly continuous internal elastic lamina is thought to inhibit smooth muscle cell migration and thereby prevent arteriosclerosis.

Another important reason why internal thoracic arteries have excellent long-term patency is their functioning endothelium, which produces both prostacy-

clin and endothelium-derived relaxing factor [30–32]. Both are potent vasodilators and inhibitors of platelet function, and thus they would be expected to enhance graft patency [31, 32].

A weakness of internal thoracic artery grafts is their susceptibility to spasm and occlusion when used to graft coronary arteries with only moderate stenosis and important native coronary artery competitive blood flow [15, 18, 19, 33–43]. This observation was first made by Barner in 1974 [34]. He reported that 11% of internal thoracic artery grafts failed because of native coronary artery competitive flow, a phenomenon he termed “disuse atrophy.” Similar findings were reported by Geha and Baue [35], who observed that internal thoracic artery grafts often fail when used to bypass coronary arteries that are not severely stenotic. They concluded that a marginal lesion in a coronary artery should be a contraindication to using an internal thoracic artery. These findings are consistent with the physiology of arterial grafts [36–41]. Unlike saphenous veins, arteries are muscular and can autoregulate their size in response to blood flow demand. When internal thoracic arteries are used to bypass coronary arteries with only moderate stenosis, demand for internal thoracic artery blood flow is low, and the graft constricts and with time may atrophy and fail.

To determine if there is a degree of coronary artery stenosis below which internal thoracic artery grafts should not be used, my colleagues and I at The Cleveland Clinic Foundation reviewed and analyzed 2,999 postoperative angiograms of 2,121 internal thoracic artery bypass grafts [18]. Degree of proximal coronary artery stenosis was used as a surrogate for competitive flow. As expected, internal thoracic artery graft patency

decreased as proximal coronary artery stenosis decreased; however, there was no degree of proximal coronary artery stenosis below which internal thoracic artery patency declined markedly (Fig. 12.2).

We then investigated whether there is a level of coronary artery stenosis below which saphenous vein grafts may have better patency than internal thoracic artery grafts [19]. To do this, we reviewed and analyzed 6,193 postoperative angiograms of 8,733 saphenous vein grafts and 2,121 internal thoracic artery grafts. At all times after surgery and at all levels of clinically important coronary artery stenosis ($\geq 50\%$), internal thoracic artery graft patency was better than saphenous vein graft patency when the left anterior descending, diagonal, circumflex, and posterior descending arteries were bypassed. However, internal thoracic artery graft patency was not always superior to saphenous vein graft patency when grafting the main right coronary artery. In moderately stenosed vessels ($< 70\%$), saphenous vein graft patency was better than internal thoracic artery graft patency at 1 year after surgery and equivalent at 10 years. We therefore recommend that internal thoracic arteries be used to bypass left-sided coronary arteries. When grafting the right coronary artery system with an internal thoracic artery, the posterior descending should be grafted when possible, and internal thoracic arteries should not be used to bypass main right coronary arteries with stenosis of less than 70%.

Other risk factors associated with internal thoracic artery graft patency include (1) coronary artery grafted, (2) younger age, (3) diabetes, (4) female gender, (5) quality and run-off of the target coronary artery [48], and (6) laterality of the graft [18, 19, 44–48]. Internal thoracic artery grafts to the left anterior descending have better patency than grafts to other coronary arteries [18, 19]. This may be due to the technical ease of grafting anterior coronary arteries and the greater run-off of the left anterior descending as compared with the other coronary arteries. Internal thoracic arteries with greater blood flow demand are less likely to fail.

The risk factors of younger age, diabetes, and female gender may be surrogates for diffuse, aggressive coronary arteriosclerosis. Patients with these characteristics often have small, diffusely diseased coronary arteries, and bypass grafts to them are more likely to fail because of poor outflow and the technical difficulties of grafting small arteries.

Some studies have suggested that right internal thoracic arteries have a lower long-term patency than left internal thoracic artery grafts [18, 22, 47]. However, intraoperative measurements have demonstrated that pedicled left and right internal thoracic arteries have similar blood flows, and early (< 1 year) postoperative patencies of right and left internal thoracic artery bypass grafts are similar [44–46]. Therefore, the reason that right internal thoracic artery grafts may have lower

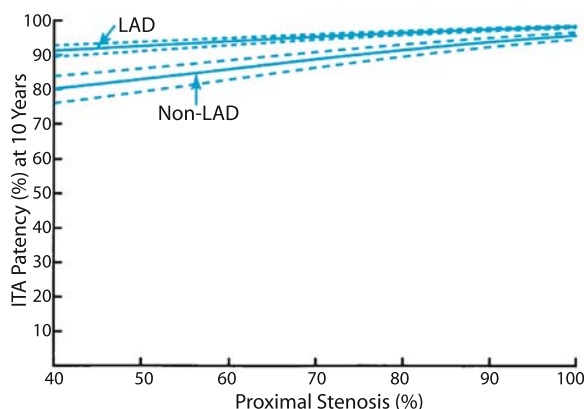


Fig. 12.2. Estimates of ITA patency to the LAD and non-LAD coronary arteries 10 years after CABG, according to degree of proximal coronary artery stenosis. Solid lines are point estimates enclosed within dashed 70% confidence limits. Graph depicts male nonsmokers with a left internal thoracic artery graft; date of operation = 1974 (CABG coronary artery bypass grafting, ITA internal thoracic artery, LAD left anterior descending coronary artery). (Reprinted with permission [18])

long-term patency than left internal thoracic artery grafts could be related not to the *characteristics* of right internal thoracic arteries but instead to *how they are used*. Possible explanations for their lower patency include the following:

1. The course an in situ right internal thoracic artery graft takes in the mediastinum to reach its target coronary artery.
2. The more muscular (and therefore more prone to spasm) distal segment of the right internal thoracic artery is often included, so that the in situ right coronary artery is long enough to reach its target coronary artery.
3. Right internal thoracic arteries are less likely to be used to bypass the left anterior descending [45, 47–50].

12.4

Survival

12.4.1

Single Internal Thoracic Artery Grafting

Although no randomized trial has compared survival of patients who have internal thoracic artery grafting rather than saphenous vein grafting to the left anterior descending, there have been many observational studies showing a survival advantage of internal thoracic artery grafting at 10, 15, and 20 years after surgery [7–9, 16, 17, 51–58]. Loop and colleagues compared 10-year survival of patients who received an internal thoracic artery graft to the left anterior descending with or without additional saphenous vein grafts to that of patients who received only saphenous vein grafts [9]. Survival was significantly better in patients who received internal thoracic artery grafts (86.6% vs. 75.9%, $P < .001$). This beneficial effect was observed in patients with single vessel disease (93.4% vs. 88.0%, $P = .05$), double vessel disease (90.0% vs. 79.5%, $P < .0001$), triple vessel disease (82.6% vs. 75.9%, $P < .0001$), normal left ventricular function (87.6% vs. 78.5%, $P < .0001$), and left ventricular dysfunction (76.5% vs. 60.4%, $P < .002$).

Cameron and colleagues reviewed the survival of patients in the Coronary Artery Surgery Study (CASS) and found that those who received internal thoracic artery grafts had significantly better 15-year survival than those who received only saphenous vein grafts ($P < .001$) [51]. Internal thoracic artery grafting was beneficial in multiple subgroups of patients, including men, woman, patients with normal and decreased left ventricular function, and younger as well as older (>65 years) patients. An interesting observation in this study was that the survival benefit of internal thoracic artery grafting increased with time, suggesting that the

initial choice of bypass conduit had a greater influence on survival than any postoperative factor, including arteriosclerosis progression. The authors recommended that internal thoracic artery grafting should not be withheld from any subgroup of patients undergoing coronary artery bypass surgery.

Eighteen-year survival after internal thoracic artery grafting versus saphenous vein grafting to the left anterior descending was reported by Boylan and colleagues from The Cleveland Clinic Foundation [54]. Survival of 100 patients who had each type of graft was compared, and at 18 years survival was better in those who received an internal thoracic artery graft (80% vs. 65%, $P = .0006$). Similar to the study of CASS patients by Cameron et al., Boylan and colleagues demonstrated that the survival advantage of internal thoracic artery grafting not only persisted in the second decade after surgery, but also increased.

Most patient subgroups, including men, women, the elderly, those with extensive coronary artery disease, and those with decreased left ventricular function, have been shown to derive long-term survival advantage from internal thoracic artery grafting to the left anterior descending [9, 51, 57–61]. Therefore, with the exception of emergency surgery or poor internal thoracic artery blood flow due to conduit damage, subclavian stenosis, radiation injury, or arteriosclerosis, left internal thoracic artery grafting to the left anterior descending is indicated in most patients undergoing coronary artery bypass surgery.

12.4.2

Bilateral Internal Thoracic Artery Grafting

Because of its beneficial clinical effects, left internal thoracic artery grafting to the left anterior descending is an integral part of surgical coronary revascularization. Although logic suggests that using a second internal thoracic artery graft would further improve long-term outcomes of revascularization, bilateral internal thoracic artery revascularization has not been widely adopted. The Society of Thoracic Surgeons' Adult Cardiac National Database (Fall 2003) shows that bilateral internal thoracic artery utilization in the United States is only 3–4%. There are several possible reasons for this. First, bilateral internal thoracic artery grafting is technically more difficult and time consuming than single internal thoracic artery grafting. Second, it may be associated with increased risk of sternal wound infection in some patients. Third, there is a general lack of conviction among surgeons that it confers any long-term benefit over single internal thoracic artery grafting.

There are no randomized studies comparing single to bilateral internal thoracic artery grafting. However, in the last 10 years there have been many observational

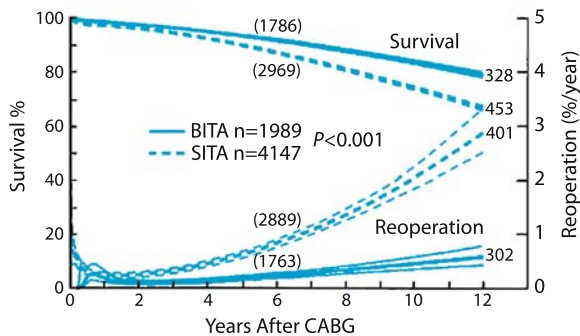


Fig. 12.3. Comparison of survival and reoperation hazard function curves in propensity-matched patients (BITA bilateral internal thoracic artery grafting, CABG coronary artery bypass grafting, SITA single internal thoracic artery grafting). (Reprinted with permission [62])

studies that have used sophisticated statistical techniques to demonstrate the long-term benefits of bilateral internal thoracic artery grafting [62–65]. In 1999, Lytle and colleagues compared the outcome of 8,123 patients who received single internal thoracic artery grafts to that of 2,001 patients who received bilateral internal thoracic artery grafts [62]. Patients were followed for a mean of 10 years after surgery, and to adjust for bias in patient selection, multiple statistical methods, including multivariable analysis, bootstrap bagging, and propensity matching, were used. Five-, 10-, and 15-year survival for the bilateral internal thoracic artery group was 94%, 84%, and 67%, compared with 92%, 79%, and 64% for the single internal thoracic artery group ($P < .001$; Fig. 12.3). In all subgroups, even those at high risk from comorbidity (age, diabetes, left ventricular dysfunction), bilateral internal thoracic artery grafting was associated with enhanced long-term survival.

To determine whether this benefit persisted in the second decade after surgery, Lytle and colleagues in 2004 again reviewed survival of their cohorts of single and bilateral internal thoracic artery patients [63]. Survival of 1,152 propensity-matched single and bilateral internal thoracic artery patients was compared. Mean follow-up was 16.5 years, and many patients were followed for more than 20 years. Seven-, 10-, 15-, and 20-year survival of the bilateral versus single internal thoracic artery patients was 89% vs. 87%, 81% vs. 78%, 67% vs. 58%, and 50% vs. 37%, respectively ($P < .0001$). The improved survival of the bilateral internal thoracic artery group not only persisted, but continued to increase during the second decade after surgery. Improvement in survival at 20 postoperative years with bilateral internal thoracic artery grafting was 10% or greater in the majority of patients. However, the incremental survival benefit of bilateral grafting was not equal and did not occur at the same time in all subgroups. Young patients with few or no comorbidities

were at low risk of death with either type of grafting, and their benefit occurred late in the follow-up period; by contrast, patients with comorbidities derived their survival benefit early in the follow-up period. The only subgroup reported to have worse survival with bilateral internal thoracic artery grafting was elderly patients (>80 years) with small body surface area, and this decrement in survival occurred early after revascularization.

In another large study of patients undergoing multivessel revascularization, Stevens and colleagues from the Montreal Heart Institute compared the long-term outcome of 1,835 patients who received bilateral internal thoracic artery and saphenous vein grafting with that of 2,547 patients who received single internal thoracic artery and saphenous vein grafting [64]. Survival at 5, 10, and 15 years for patients who received bilateral internal thoracic artery grafting was 97%, 93%, and 89%, compared with 95%, 88%, and 79% for those who received single internal thoracic artery grafting ($P < .001$). Multivariable analysis with propensity score adjustment to adjust for selection bias demonstrated that bilateral internal thoracic artery grafting reduced late mortality [hazard ratio (HR) 0.74, 95% confidence limits 0.60–0.90].

Similarly, Buxton and colleagues compared survival of 1,269 patients who received bilateral internal thoracic artery grafts to 1,557 who received single internal thoracic artery grafts [65]. At a mean follow-up of 52 postoperative months, multivariable analysis showed that single internal thoracic artery grafting was a risk factor for late death (HR=1.4).

Not all studies comparing single versus bilateral internal thoracic artery revascularization have found improved survival with the bilateral strategy [66, 67]. There are several possible explanations for this. First, single internal thoracic artery grafting to the left anterior descending results in good outcomes during the first postoperative decade, making it necessary to follow patients into the second postoperative decade to identify a benefit of bilateral internal thoracic artery grafting. Few institutions have a sufficient number of patients, long-term follow-up, and the predilection for bilateral internal thoracic artery grafting necessary to do this. Second, patient variability is an important determinant. If patient subgroups that benefit only slightly from bilateral internal thoracic artery grafting are compared, it will be difficult to identify an improvement in survival unless large numbers of patients are followed for long periods. Third, it might be important which coronary artery is grafted with the second internal thoracic artery. Some bilateral internal thoracic artery revascularization strategies might not improve outcomes.

To determine whether a bilateral internal thoracic artery revascularization strategy influences outcomes,

Schmidt and colleagues divided their bilateral internal thoracic artery patients into two groups and compared survival [68]. Group 1 had the left internal thoracic artery grafted to left anterior descending and the right internal thoracic artery grafted to the right coronary artery, and Group 2 had the right internal thoracic artery grafted to the left anterior descending and the left internal thoracic artery grafted to the circumflex. Hospital mortality was similar for both groups, but long-term survival was better when both internal thoracic arteries were used to bypass left-sided coronary arteries. Survival curves diverged at 6 years. At 9.6 postoperative years, survival in group 1 was 70.1 % and in Group 2, 93.1 % ($P=.02$). Similarly, Naunheim and colleagues have reported that using the second internal thoracic artery to graft the right coronary artery offers no survival advantage over single internal thoracic artery grafting [67], and Carrel and colleagues and Pick and colleagues have separately found that using both internal thoracic arteries to graft left-sided coronaries may increase survival over single internal thoracic artery revascularization [69, 70].

In summary, bilateral internal thoracic artery grafting improves long-term survival after coronary revascularization. However, not all patients benefit equally and not all revascularization strategies are equally effective.

12.5

Freedom from Recurrent Ischemic Events

12.5.1

Single Internal Thoracic Artery Grafting

The excellent and stable long-term patency of internal thoracic artery grafts improves freedom from recurrent ischemic events after coronary artery bypass surgery compared with a revascularization strategy of saphenous vein grafts alone. Loop and colleagues found lower event-free survival in patients receiving a left internal thoracic artery graft to the left anterior descending [9]. At 10-year follow-up, they reported that patients with saphenous vein grafts alone had a 1.4 increase in late myocardial infarction ($P<.0001$), 1.3 increase in hospitalization for cardiac events ($P<.0001$), 2.0 increase in reoperation ($P<.0001$), 1.2 increase in angina ($P<.004$), and 1.3 increase in all cardiac events ($P<.0001$) when compared with patients receiving an internal thoracic artery graft to the left anterior descending.

Cameron and colleagues also reported greater freedom from angina, myocardial infarction, and reoperation in patients with internal thoracic artery grafts to their left anterior descending as compared to those with only saphenous vein grafts [7]. Freedom from angina at 5, 10, and 15 years for patients with left internal

thoracic artery bypass grafts to the left anterior descending was 68 %, 55 %, and 24 %, respectively, vs. 59 %, 49 %, and 27 % for patients with saphenous vein grafts alone. Patients with internal thoracic artery grafts had improved freedom from angina early after surgery; however, by 10 years, return of angina was similar for those with and without an internal thoracic artery graft to the left anterior descending. Others have reported similar findings [8, 9, 16, 17, 52, 53].

Freedom from myocardial infarction at 5, 10, and 15 years for patients with left internal thoracic artery bypass grafts to the left anterior descending was 94 %, 84 %, and 73 %, respectively, vs. 91 %, 77 %, and 54 % for patients with only saphenous vein grafts [7]. Cameron and colleagues also found that myocardial infarctions were less likely to be fatal in patients with internal thoracic artery grafts as compared with those receiving only saphenous vein grafts (17 % vs. 30 %) [7]. This was because fewer infarctions in the distribution of the left anterior descending occurred in patients with internal thoracic artery grafts.

Unlike survival and myocardial infarction, reoperation is a “soft” end point. Its occurrence depends on a decision made by both patient and surgeon, and many biases enter into this decision. Internal thoracic artery grafting to the left anterior descending decreased the need or bias for reoperation. Cameron and colleagues reported that freedom from reoperation at 5, 10, and 15 years for patients with left internal thoracic artery bypass grafts to the left anterior descending was 98 %, 96 %, and 94 %, respectively, vs. 94 %, 85 %, and 78 % for patients receiving only saphenous vein grafts [7].

12.5.2

Bilateral Internal Thoracic Artery Grafting

Bilateral internal thoracic artery grafting decreases recurrence of late ischemic events after coronary artery bypass surgery compared with a revascularization strategy of single internal thoracic artery grafting. Lytle and colleagues found an increase in reoperation (HR 4.91, 95 % CL 3.30–7.55) and percutaneous coronary intervention (HR 1.84, 95 % CL 1.46–2.30) in patients who received single versus bilateral internal thoracic artery grafting [62] (Fig. 12.3). Stevens and colleagues reported that bilateral internal thoracic artery grafting reduced the risk of myocardial infarction (HR 0.79, 95 % CL 0.67–0.93) and coronary reoperation (HR 0.41, 95 % CL 0.21–0.80) compared with single internal thoracic artery grafting [64]. They did not find a difference in freedom from percutaneous intervention in patients with single versus bilateral internal thoracic artery grafting.

12.6

Conclusions

After nearly four decades of coronary artery bypass surgery, internal thoracic artery grafts have proven to be the best conduit for revascularization. They are resistant to arteriosclerosis and have excellent and stable long-term patency. Use of the left internal thoracic artery to revascularize the left anterior descending improves both long-term survival and freedom from cardiac events. The survival benefit of internal thoracic artery grafting increases with time, and patient-related factors, such as age, gender, and left ventricular dysfunction, do not decrease this benefit. Internal thoracic artery grafting of the left anterior descending should be an integral part of nearly all surgical coronary revascularizations.

Use of two internal thoracic artery grafts in myocardial revascularization further improves long-term outcomes of coronary artery bypass surgery. All patients do not benefit equally or at the same postoperative time, however. The survival benefit in high-risk patients appears sooner after surgery than in low-risk patients. Studies show that not all bilateral internal thoracic artery revascularization strategies are equally effective in improving the long-term outcomes of coronary revascularization, and using the internal thoracic arteries to graft the two most important left-sided coronary arteries may be preferable.

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Bilateral Versus Unilateral Internal Thoracic Artery 13 in Coronary Bypass Grafting

E. BERREKLOUW, G.-W. HE

13.1 Introduction

The long-term event-free survival after coronary bypass surgery is related to the preoperative status of the patient, progression of atherosclerotic disease in the native coronary arteries and patency of the conduits used [1]. In comparison to the saphenous vein, it has been shown that the left internal thoracic artery (LITA) has a superior patency and leads to a better (event-free) survival after 10 years [2]. The LITA is now widely accepted as the standard conduit for making an anastomosis with the left anterior descending artery (LAD) [2]. Use of the right internal thoracic artery (RITA) so far has been less widespread. Although it took a longer time to prove, the additional benefit of using bilateral internal thoracic arteries (BITA) is now more evident. In this chapter, we will focus on the differences in in-hospital and late outcome between the BITA and LITA in coronary artery bypass grafting (CABG).

13.2 History

As surgical treatment of myocardial ischemia, the pedicled LITA and RITA were used for implantation into the myocardial muscle, first experimentally by Vineberg and Kato [3] in 1965, and later clinically by Bloomer and coworkers [4] and Favaloro [5] in 1967. On 8 February 1968, Bailey and Hirose [6] anastomosed the RITA to the right coronary artery through a right thoracotomy on a beating heart. The use of both pedicled ITAs for making direct anastomoses with coronary arteries was first reported by Suzuki and colleagues [7] in 1972, although his coauthor Kay had started such operations as early as 1968. Kolesov from Russia used both pedicled ITAs also at that time [8, 9].

13.3 Indications for Use of Bilateral ITAs

The common indications for the use of both ITAs are patients with multivessel disease [10] and young age [11]. A calcified aorta, shortage of veins or reoperations, because of failure of vein grafts, are other frequent indications [12–14]. Patients with a high risk for vein graft failure, as in hypercholesterolemia, hyperlipidemia, nicotine abuse or small vessel disease, are considered good candidates for the use of both ITAs. Bilateral ITAs can be used in women [15], patients with advanced age [16], unstable angina [10, 17, 18], mainstem disease [10, 19, 20], left ventricular hypertrophy, previous myocardial infarction [10], poor left ventricular function [15], hypertension [21], hyperlipidemia [21] or renal failure. Some consider diabetes [10] and adipositas [22] not to be contraindications. Both ITAs have been used also in congenital disorders and Kawasaki disease [23–25]. Combinations with other surgical techniques such as left ventricular aneurysmectomy [22], coronary thrombectomy [22], or minimal invasive surgery [26] have been reported. If complete revascularization with only arterial grafts is indicated in two-vessel or mainstem disease, one can use both ITAs as pedicled grafts in most of these cases [27]. If one wants to perform complete arterial revascularization in three vessel disease, with the ITAs as the only arterial conduits, one pedicled LITA and a free RITA can be utilized as a Y-graft [28, 29]. Another option in three vessel disease is to use both pedicled ITAs in combination with other arterial conduits such as the right gastroepiploic artery [30, 31], an inferior epigastric artery [32, 33] or one or two radial arteries [33–35].

The use of bilateral ITAs is recommended in patients under 60 years of age because the major benefit of bilateral ITA is expected better long-term survival. However, it may be desirable to use them in older patients as well, provided that the estimated surgical risk is low.

13.4

Relative Contraindications

Significant proximal stenoses of one or both subclavian arteries can prohibit the use of the ITA at the involved side, although in some cases these stenoses can be corrected preoperatively by a vascular operation or percutaneous balloon dilatation [36]. Damage of an ITA during takedown can be another reason to refrain from its use. If the obstruction or damage is proximal and localized and cannot be repaired, the ITA can still be used as a free graft. Diabetes [37–40] and/or adipositas with a Quetelet index >30 [38, 39, 41, 42] are considered by some as relative contraindications because of an increased risk of compromised chest wound healing. The proponents of skeletonized ITA techniques, however, claim no wound complications in diabetic patients [43]

and this is supported by a recent study [44]. Severe pulmonary emphysema can put a strain on the length of usable ITA, while lung function can be compromised further [38, 39, 45, 46]. Others consider as relative contraindications a poor left ventricular function, advanced age [40], poor general condition or other serious co-morbidity, impending infarction or failed percutaneous transluminal coronary angioplasty (PTCA).

13.5

Early Mortality

The operative or hospital mortality as reported in major series in the literature is shown in Table 13.1 [10–96]. In a study of 231 patients, Ramström and co-workers found that small vessel disease, insufficient

Table 13.1. Operative or hospital mortality, myocardial infarction, IABP

Author	Year	# Vein patients	Mortality (%)	Infarction (%)	IABP (%)	# SITA patients	Mortality (%)	Infarction (%)	IABP (%)	# BITA patients	Mortality (%)	Infarction (%)	IABP (%)
Galbut [77] ^a	1985									227	4.0	7.5	
Tector [78]	1986									215	0.9	1.4	0.9
Cameron [79]	1986	216	4.1	9.7		532	1.9	5.5		38	0	0 ^d	
Lytle [52]	1986									500	1.4	3.8	
Jones [80]	1987	81	7.4			437	0.9			117	0.9		
Buxton [81]	1988	1681	0.8			726	1.2			377	1.1		
Cosgrove [40]	1988	338	1.8	0.6	0.6	338	0.3	0.9	0.3	338	0.9	2.1	0.6
Henze [82]	1989									100	0		
Fiore [83]	1990					100	2.0			100	9.0		
Galbut [17] ^a	1990									1087	2.7	2.0	
Kouchoukos [39]	1990	633	7.9	0.8	12.2 ^d	687	2.8	2.0	3.2	246	3.7 ^d	2.0	4.5
Yakirevich [84]	1990									60	0		
Fiore [10]	1991									586	3.6	2.6	
Barner [19]	1992									45	0	2.2	
Bical [53]	1992									100	1.0		
Galbut [21] ^{a,b}	1993					736	6.4	1.4	18.6 ^d	731	3.1 ^d	2.1	11.1
Ramström [49]	1993									231	3.5	9.6 ^f	
Accola [48]	1993									674	1.9	3.4	2.8
Dion [85]	1993									400	2.0	4.0	
Galbut [20]	1993									280	1.4	5.0	
Ozaki [86]	1993									68	0		
Ashraf [87]	1994					150	2.0	1.3		150 ^e	1.3	2.0	
Paolini [65] ^c	1994					38	0	5.2	7.1	42	0	7.1	9.5
Berrekouw [42]	1994					100	0	1.0	2.0	100	1.0	5.0	0
He [50]	1994	1664	8.5		19.6 ^d	3359	2.7			199	3.5 ^d		6.0
Dewar [88]	1995					765	3.0			377	2.1		
Buche [89]	1995									256	1.2		
Dietl [60]	1995									114	2.6	5.3	
Carrel [90]	1996					80	1.2	3.6	2.4	80	2.4	4.8	2.4
Bical [43] ^a	1996									560	1.6		
Gerola [91]	1996									201	2.9	2.4	
Jones [92]	1997									500	1.8	0.6	2.2
Pick [93]	1997					161	0.6	5.0		160	0	3.0	
Schmidt [94]	1997									498	1.8	2.6	1.8
Buxton [95]	1998					1557	1.7	1.5		1269	0.9	1.2	
Lytle [51]	1999					8123	0.7			2001	0.7		
Stevens [96]	2004					2547	2.3			1853	1.2		

^a Skeletonized ITAs only, ^b ≥ 65 years old, ^c Left main disease only, ^d P value <0.05, ^e RITA as free graft only

^f Significant enzyme release

grafting, age ≥ 60 years, history of smoking, diabetes, family history of coronary artery disease and repeated CABG were independent risk-factors for early mortality [49]. We found in an analysis of 199 BITA, 3,359 SITA and 1,664 vein-graft patients that old age (≥ 70 years), long perfusion time, and emergency operation were risk factors for operative mortality [50]. Recently, Lytle and associates demonstrated in a study of 8,123 SITA and 2,001 BITA patients that age > 60 years, peripheral vascular disease and female gender were associated with in-hospital death, and not the number of ITAs used [51].

13.6

Myocardial Infarction

The perioperative myocardial infarction rate as reported in major series in the literature is shown in Table 13.1. Interpreting the data, one should keep in mind that there are substantial differences in the definition of perioperative myocardial infarction. From these studies it appears that there is no difference in infarction rate between the use of one or two ITAs. Comparing two different time-frames, also Lytle and colleagues showed that with increasing experience the incidence of myocardial infarction becomes significantly less [52].

13.6.1

Use of Intra-aortic Balloon Pump

The rate of use of the intra-aortic balloon pump (IABP) as reported in major series in the literature is also shown in Table 13.1. In general, no distinction is made between low cardiac output and myocardial ischemia as indications for the use of IABP, nor is it mentioned if the IABP was introduced pre-, intra- or postoperatively. By logistic regression analysis in a relatively small series of 200 BITAs and SITAs, we found that perioperative myocardial infarction and female gender were predictive for inotropic support and/or use of IABP, rather than the use of one or two ITAs [42].

13.6.2

Rethoracotomy for Bleeding

The incidence of rethoracotomy for bleeding has been reported in major series in the literature as shown in Table 13.2. Seven of the nine studies showed a significant difference between the BITA and SITA. Cosgrove and coworkers, in a study of 1,014 all-vein SITA and BITA patients, found no difference in the rate of reoperation for bleeding or patients receiving blood transfusions. However, there was a marginal increase in the volume of blood transfused in BITA patients [40].

Schönberger and associates found in a study of 200 BITA and SITA patients that none of the patients who received low dose aprotinin (2 million KIU in the pump prime) underwent repeat thoracotomy for excessive bleeding, while this was the case in 8 % of BITA patients without aprotinin treatment. Postoperative bloodloss and use of homologous blood products after ITA surgery was significantly diminished with aprotinin [54].

13.6.3

Sternal Wound Complications

Mediastinitis is a serious complication, which can be lethal. Its occurrence prolongs hospitalization and increases costs substantially. The definition of a sternal wound infection may, however, differ substantially between various reports. The incidence of sternal wound infection as reported in major series in the literature is also shown in Table 13.2. The predictive factors for sternal wound complications, as found by several authors by multivariate logistic regression analysis, are shown in Table 13.3. In summary, it is likely that BITA grafting, among other factors, is an independent risk factor for sternal wound complications. Specifically, BITA grafting in association with one or more other risk factors will increase the likelihood of such complications. In high risk patients, it may be wise to use skeletonized ITAs or to perform unilateral ITA grafting in combination with one or two radial arteries and/or the right GEA to achieve complete arterial revascularization.

On the other hand, recent studies suggested that skeletonized BITA significantly reduces the sternal infection [44, 97].

13.6.4

Pulmonary Complications

The incidence of pulmonary complications, defined as acute respiratory failure or prolonged (more than 48 h) mechanical ventilation, as reported in major series in the literature is shown in Table 13.2. In seven studies pulmonary complications were compared between SITA and BITA. Hauters and coworkers compared 30 BITA with 123 SITA patients, in whom the ipsilateral pleural space was systematically opened [63]. Acute respiratory failure was significantly more frequent and mechanical ventilation significantly longer in BITA, than in SITA patients. On the 9th postoperative day, forced vital capacity was significantly reduced to 59.6 % of the preoperative value in patients with SITA and to 47.1 % in patients with BITA grafts. Late results were obtained in 111 patients. After a mean follow-up of 7 months, forced vital capacity was still significantly reduced to 86.8 % of the preoperative value in patients with SITA and to 78.1 % in patients with BITA. On the other hand, Aarnio and colleagues compared 100 BITA

Table 13.2. Rethoracotomy for bleeding, sternal wound and pulmonary complications

Author	Year	# Vein patients	Rethoracotomy (%)	Sternal wound (%)	Pulmonary (%)	# SITA patients	Rethoracotomy (%)	Sternal wound (%)	Pulmonary (%)	# BITA patients	Rethoracotomy (%)	Sternal wound (%)	Pulmonary (%)
Galbut [77] ^a	1985									227	2.2	1.8	
Lytle [52]	1986	338								500	6.2		5.2
Cameron [79]	1986	216		3.2		532		2.8		38		2.6	
Cosgrove [40]	1988	338	3.8	0	3.6	338	2.7	0.3	1.8		5.3	2.4 ^d	3.2
Hazelrigg [38]	1989	230		0.4		1626		0.5		726		1.7 ^d	
Loop [37]	1990	1085		1.0		4073		0.9		1346		1.7	
Kouchoukos [39]	1990	633	3.6	1.3	14.2 ^d	687	4.7	1.9	5.2	246	5.3	6.9 ^d	8.5
Galbut [17] ^a	1990									1087	1.7	1.5	3.2
Grossi [99]	1990	962		0.8		1263		2.1		131		3.8	
Hauters [63]	1991					123			3.0	33			13.0 ^d
Fiore [10]	1991									586	3.1	2.7	5.1
Aarnio [64]	1991					100	10.0			100	20.0 ^d		
Bical [53, 66]	1992									100		0	
Barner [19]	1992									45		0	
Ramström [49]	1993									258			5.0
Accola [48]	1993									674	2.1	3.6	
Galbut [21] ^{ab}	1993					736	3.5	1.2	5.2	731	2.1	1.4	5.1
Dion [85]	1993									400	5.8	4.1	7.2
Galbut [20]	1993									280	2.5		7.5
Berrekouw [42]	1994					100	0	2.0	3.0	100	2.0	0	3.0
He [50]	1994	1664	5.6	1.3		3359		1.2		199	2.5	2.5	
Ashraf [87] ^c	1994					150	6.0	2.0		150	4.6	1.3	
Dewar [88]	1995					765	5.1	1.0		377	8.2 ^d	0.8	
Buche [89]	1995									256	2.3		
Zacharias [100]	1996	366		1.6		1583		1.9		46		4.3	
Carrel [90]	1996					80	3.6	1.2	2.4		2.4	4.8 ^d	3.6
Bical [43] ^a	1996									560	3.0	1.1	1.6
Gerola [91]	1996									201	1.9	0.9	3.9
Parisian Study [41]	1996	157		1.9		677		2.7		126		8.7 ^d	
Jones [92]	1997									500	1.8	1.0	4.6
Pick [93]	1997					161	5.0	2.5	2.0	160	2.5	2.0	1.0
Stähle [101]	1997	2666		1.7		7323		1.7		155		3.6	
Schmidt [94]	1997					1557				498	1.8	1.0	
Buxton [95]	1998					8123		1.7		1269			2.0
Lytle [51]	1999								1.4	2001		2.5 ^d	
Peterson [97]	2003									79			1.3
Lev-Ran [44]	2004							1.1		515			1.9
Paulis [98]										450			4.7

^a Skeletonized ITAs only, ^b ≥ 65 years old, ^c RITA as free graft only, ^d P < 0.05

Table 13.3. Predictors for sternal wound complications (multivariate logistic regression analysis) (see text for references)

Obesity
Diabetes (insulin dependent)
Age (> 75 years)
Female gender
Congestive heart failure
Hospital environment
Interval between admission and surgery
Year of surgery
BITA grafting
Cross clamp/cardiopulmonary bypass/operating times
Reoperation
SITA grafting
Coronary bypass grafting
BITA grafting in presence of diabetes
Blood transfusions (number of)
Reexploration
Pneumonia/ventilation > 48 h
Postoperative renal failure
IABP
Inotropic agents > 24 h
Sternal rewiring

with 100 SITA patients and showed that BITA grafting did not cause excessive pulmonary complications, pleural effusion at discharge, pain in the sternotomy wound, or pain on breathing [64]. In a series of 100 BITAs and 100 SITAs, we showed that postoperative low cardiac output and age 60 years, rather than the use of one or two ITAs, were predictors of pulmonary complications [42]. In summary, if a patient has a compromised lung function, as can be the case in pulmonary emphysema, it is likely that the lung function will be worsened by BITA grafting and that such patients will need mechanical ventilation for more than 48 h. This can be a risk factor for sternal wound complications as well. In such patients with compromised lung function preoperatively, it may be wise to use skeletonized ITAs and leave the pleural spaces closed, or to perform unilateral ITA grafting in combination with one or two radial arteries and/or right GEA to achieve complete arterial revascularization.

13.6.5

Stroke

The incidence of stroke as reported in major series in the literature is shown in Table 13.4. In six studies the incidence of stroke was compared between SITA and BITA patients. In two of these studies a comparison was made also with a vein-graft-only group. There does not seem to be an increased incidence of stroke after BITA grafting.

13.6.6

Phrenic Nerve Lesions

The incidence of phrenic nerve lesions, also characterized as diaphragmatic dysfunction or phrenic nerve paralysis, as reported in major series in the literature, is shown in Table 13.4. Two studies compared the incidence of phrenic nerve lesions after SITA or BITA grafting and both studies showed that there does not seem to be a difference [42, 65]. Bical and coworkers showed that the incidence of phrenic nerve palsy after BITA grafting diminished with increased surgical experience [53, 66]. Abd and colleagues studied nine patients with diaphragmatic dysfunction due to phrenic nerve injury after ITA grafting, of which seven were bilateral and two unilateral. Topical cardiac hypothermia was the prevailing mechanism, but dissection of the ITA with electrocautery, traction or vascular compromise to the phrenic nerve, or a combination of these factors, could be additionally involved. Phrenic nerve recovery occurred from 4 to 27 months after surgery with a rocking bed ventilation treatment. Unilateral diaphragmatic recovery was sufficient for restoration of symptom-free supine ventilation [67]. O'Brien and associates showed in a swine model that, compared with complete dissection of the LITA, sparing the pericardiophrenic artery during LITA dissection significantly improved left phrenic nerve perfusion and function [46].

13.6.7

Internal Thoracic Artery Malfunction

The diagnosis of ITA malfunction is difficult, and is probably underreported by most investigators. ITA malfunction can be defined as a situation wherein one or more ITAs deliver insufficient blood flow to the myocardium resulting in ischemia, which can lead to myocardial infarction, ventricular fibrillation, shock or death. It is likely that some of the hospital deaths, perioperative myocardial infarctions or incidences of low cardiac output should be attributed to hypoperfusion of one or more ITAs. In large series of patients with an ITA to the LAD, ITA hypoperfusion was identified in 0.3–1.9% [68, 69]. It appears that the female gender carries an increased risk of ITA hypoperfusion [68]. In a series of 712 patients, in whom 'complex' ITA grafting was performed, Jones and coworkers reported five patients with ITA hypoperfusion, in four of whom BITA grafting was performed. As possible causes for a discrepancy in ITA flow and myocardial demand the authors suggested: cardiac hypertrophy, large LAD supplied by a small ITA and sequentially grafted arteries [70]. There might also be a higher chance for ITA malfunction when the ITAs are used as Y-grafts only [29, 71]. The ITA can be patent, but a subclavian stenosis

Table 13.4. Stroke, phrenic nerve lesions, and ITA malfunction

Author	Year	# Vein patients	Stroke (%)	Phrenic nerve (%)	ITA mal-function	# SITA patients	Stroke (%)	Phrenic nerve (%)	ITA mal-function	# BITA patients	Stroke (%)	Phrenic nerve (%)	ITA mal-function
Galbut [77] ^a	1985									227		4.4	
Lytle [52]	1986									500	2.6		
Cosgrove [40]	1988	338	2.1			338	1.2			338	2.4		
Jones [70] ^b	1989									712			0.7
Kouchoukos [39]	1990	633	4.6			687	2.0			246	0.8		
Galbut [17] ^a	1990									1087	1.8		
Vájtai [68]	1992					3076			0.3				
Bical [53, 66]	1992									50		6.0	
Barner [19] ^c	1992									45	2.2		
Galbut [20] ^c	1993									280	1.4		
Galbut [21] ^{a,d}	1993					736	4.1			731	2.7		
Accola [48]	1993									674	1.6		
Dion [85]	1993									400	0.5	1.5	1.5
Paolini [65] ^c	1994					42		0		38		0	
Berrekouw [42]	1994					100	0	0		100	1.0	1.0	
Tector [29] ^e	1994									287			2.1
Carrel [69]	1996					2125			1.9				
Bical [43] ^a	1996									560	1.1		0.4
Gerola [91]	1996									201	0.4		
Jones [92]	1997									500	1.2		
Pick [93]	1997					161	1.5			160	1.0		
Nicholson [71] ^e	1997									75			
Buxton [95]	1998					1557	1.3			1269	1.2		2.7

^a Skeletonized ITAs only, ^b Complex ITA grafting, ^c Left main disease only, ^d ≥65 years old, ^e ITA Y-grafts only

can be present or there may be traction on the ITA by the sternal retractor. The ITAs can be of small caliber anatomically, or they can be diffusely or localized atherosclerotic. During takedown, the ITAs can be surgically traumatized by direct mechanical damage, electrocautery, hemathoma or dissection by external or internal manipulation. The anastomoses may not be patent or there may be insufficient length of the pedicle or traction by hyperinsufflated lungs. Inadequate routing through the pericardium, twisting the pedicles around their longitudinal axis or kinking at the anastomoses may be other causes. Competition between ITA and coronary artery flow or other conduits can lead to a (reversible) 'string sign' of an ITA [72–74]. Hypovolemia, specifically when sudden and severe [75], or low perfusion pressure will lead to an inadequate ITA flow. Spasms, localized or diffuse, or a high peripheral resistance will diminish ITA flow as well. Severe anemia will augment the deleterious effects of reduced ITA flow. Because initial blood flow through ITAs is less compared to comparable vein grafts, the safety margin will be smaller after extensive ITA grafting than after grafting with saphenous veins only. For that reason, all mentioned causes of malfunction should be treated aggressively. If substantial ischemia persists, one or more vein grafts should be added to the areas that have been grafted with the arterial conduits, and can be a life saving procedure [47].

13.6.8

Hospital Stay

Reported mean length of hospital stay (LOS) after BITA grafting is between 8 and 20 days [13, 21, 42, 48, 62, 76]. In three studies LOS was compared between SITA and BITA surgery. In two studies no significant difference was demonstrated [42, 62], while in one study, in patients of 65 years of age and older, a slightly longer LOS after SITA grafting was found [21].

13.7

Late Results

13.7.1

Late Survival

The cumulative actuarial survival, as reported in the literature, is shown in Table 13.5. Dewar and colleagues found no statistical difference in overall 5- and 7-year survival rates after SITA or BITA grafting, even when the data were stratified in patients 60 years and patients >60 years of age [76]. For patients of 65 years of age and older, Galbut and associates found a significantly better 8-year survival after BITA than after SITA grafting [21]. After 15 years follow-up of 5,880 primary CABG patients, of whom only 276 were BITA patients,

Sergeant and colleagues found, in a quite complicated statistical model, no additional benefit or risk of death after surgery with the use of sequential or double ITA grafts.

In a recent report on a large retrospective study of 8,123 SITA and 2,001 BITA patients, Lytle and associates [51] found that survival for the bilateral ITA group was 94%, 84%, and 67%, and for the single ITA group 92%, 79%, and 64% at 5, 10, and 15 postoperative years, respectively ($P < .001$). In other studies, at 12 years of follow-up, there was a mean 6.3% difference in freedom from death between BITA and SITA grafting. After stratification for different age cohorts this advantage could be demonstrated for all age groups, with the exception of patients younger than 50 years [11, 14]. The latter can be explained by the fact that young SITA patients had an excellent survival as well, be it with a higher number of reoperations compared to patients that underwent BITA grafting (personal communication with Lytle). Predictors for mortality, as analyzed with multivariate regression techniques, were female gender, incomplete revascularization, left main disease, number of grafts, not using the microscope and not using an ITA graft [15]. In comparing the results of BITA with SITA grafting we should also consider the vessel on which the second ITA is placed. Fiore and coworkers [10] and Carrel and colleagues [47] always placed the RITA on the right coronary artery (RCA), while Pick and associates [93] and Gerola and coworkers [17] always anastomosed the RITA to the left coronary system. Buxton and colleagues [95], Lytle and associates [51] and Farinas and coworkers [102] placed the RITA on the RCA in 20%, 27% and 47% respectively. Sergeant and colleagues [103] placed most RITAs on a diagonal artery. Schmidt and associates demonstrated a significantly better overall 9.5-year survival when the RITA was placed on left-sided coronary arteries, rather than on the right coronary artery. The survival curves began to diverge at 6 years and became significantly different at 8 years [94]. Also, Farinas and coworkers found a better, although not significant, 10-year survival after BITA grafting, using both ITA to the left coronary system, rather than to the left and right coronary vessels [102]. On the other hand, Lytle and coworkers found that neither total arterial revascularization nor the specific vessels grafted with BITA improved results (late death, reoperation or PTCA) compared to the general strategy of BITA grafting [51].

Figure 13.1 shows the 20-year survival curves after veins-only, and SITA and BITA grafting are presented after pooling the available data from the literature with the same follow-up period with the weighted average method. For pooling data, one has to keep in mind the limitations of comparing late follow-up data from different reports, as stated above.

Table 13.5. Late survival, angina-free rate, and myocardial infarction rate

Author	Year	Follow-up	Follow-up mean/median	# Vein patients	Survival (%)	Angina-free (%)	Infarction (%)	# SITA patients	Survival (%)	Angina-free (%)	Infarction (%)	# BITA patients	Survival (%)	Angina-free (%)	Infarction (%)
Cameron [79]	1986	5	10.3	216	85.9	59.1	9.2	532	91.2	67.5	5.7	38	100	79.0	7.8
Dewar [88]	1995	5						765	92.1			377	89.5		
Dewar [88] ^d	1995	5						280		77.8	98.2	160		88.1	96.2 ^k
Dewar [88] ^e	1995	5						486		81.8	98.8	216		83.0	96.8 ^k
Accola [48]	1993	5										674	90.0		
Pick [93]	1997	5	9.8					161	90.0			160	96.0 ^a		
Lytle [51]	1999	5						8123	92.0			2001	94.0 ^a		
Galbut [17] ^a	1990	4–7	3.3									1058	89.8		
Berrekouw [27]	1994	8	5					143	92.0	35.1	77.8	143	96.0	51.4	95.1 ^k
Carrel [90]	1996	8	?					80	94.0	73.7		80	92.0	80.0	
Galbut [20] ^{c,i}	1993	8	3.6					689	60.7	96.7 ^j	2.0	708	67.9 ^a	96.6 ^j	2.4
Schmidt [94] ^b	1997	9.5	7.1									311	70.1 ^{a,i}	91.6 ^j	
Schmidt [94]	1997	9.5	7.1									187	93.1 ^{a,i}	94.6 ^j	
Galbut [17]	1990	10	3.3									1058 ^c	80.0	96.0	
Galbut [77] ⁱ	1985	10	4									207 ^c	83.0	69.0	5.3
Buxton [95]	1999	10	4.3									1269	86.3 ^a		
Fiore [104] ⁱ	1991	10	4.5									518	81.0	40.0	81.0 ^k
Pick [93] ⁱ	1997	10	9.8									160	84.0 ^a	67.0 ^a	2.1 ^a
Cameron [79]	1986	10	10.3	216	72.0	48.6	23.3	161	74.0	37.0	19.0	38	88.9	70.0	14.0
Lytle [51]	1999	10						8123	79.0	55.3	15.6	2001	84.0 ^a		
Fiore [83] ⁱ	1990	10						100	82.0			100	84.0		
Gerola [91]	1996	10	5.9									201	88.3	81.9	3.5
Farinas [102]	1999	10	8.0	200	83.0			200	90.0			200	87.0 ^a		
Jones [92]	1997	11	7.1									500	87.9	93.2 ^j	
Cameron [79]	1986	14	10.3	216	57.0	27.3	46.4	532	72.0	23.5	27.2	38	86.0	67.0	14.0
Lytle [51]	1999	15	10.3					8123	64.0			2001	67.0 ^a		
Fiore [83] ⁱ	1990	15	14.4					100	59.0	27.0	59.0	100	74.0 ^a	36.0 ^a	75.0 ^{a,k}
Galbut [17] ^{c,i}	1990	15	3.3									1058 [*]	60.0		
Fiore [104] ⁱ	1991	15	4.5									518	72.0	20.0	77.0 ^{a,k}
Galbut [17] ^{c,i}	1990	14–17	3.3									1058 [*]	56.2	75.0	19.6
Cameron [106]	1995	19	17.2	214	38.0			409	50.0			39	63.5 ^a		

^a P < 0.05, ^b LITA-LAD and RITA-RCA, ^c Skeletonized ITAs only, ^d Patients ≤ 60 years, ^e Patients > 60 years, ^f ≥ 65 years, ^g Significant for the survival curve during 15 years
^h RITA-LAD and LITA-CX, ⁱ Between two groups RITA-RCA and RITA-LAD, ^j Class I and II CCSC, ^k Infarction-free survival, ^l Hospital survivors
^m Equivalent non-cardiac mortality, but significantly fewer late cardiac-related deaths

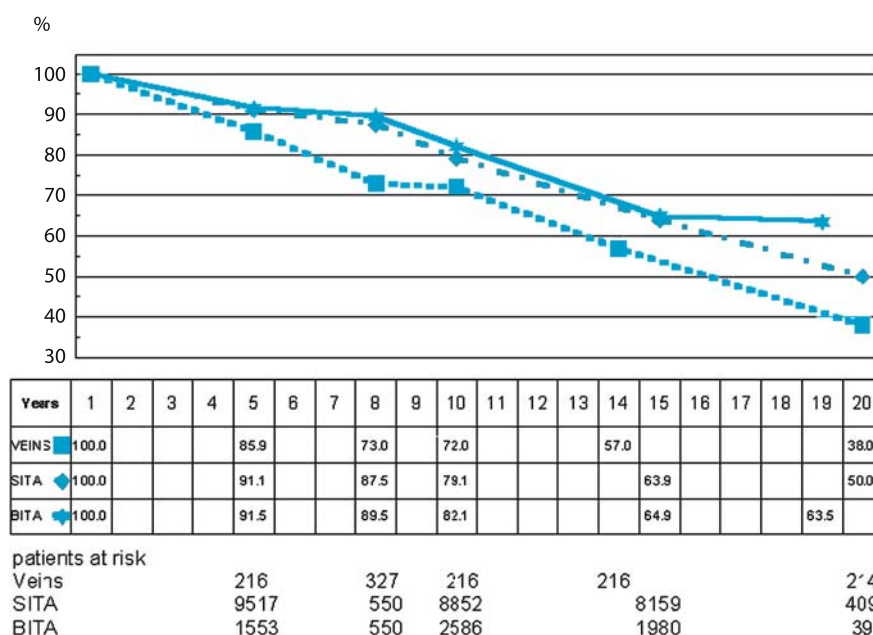


Fig. 13.1. Survival

13.7.2

Recurrent Angina Pectoris

Angina is considered a “soft” end-point as it is a subjective variable. In comparing studies in respect to angina free (Class I CCSC) survival, rarely is information available if recurrent angina (Class II or more CCSC) has been noted somewhere during the follow-up or if the angina has been noted only at the end of the follow-up. This last method can imply that patients received anti-anginal medication somewhere during follow-up, but do not show angina at the end of the follow-up. It would be better to note angina at any moment it reappears and report the use of anti-anginal medication and outcome of exercise ECG tests as well, in a time-related fashion. At the end of follow-up often the results of patients that fulfill the complete follow-up period are mixed with the results of patients with a shorter follow-up period. The angina-free rates and angina-free survival rates as reported in major series in the literature are shown in Table 13.1. In seven studies postoperative angina was compared between SITA and BITA grafting; in one study a comparison was made with a vein-graft-only group. At 5 years of follow-up, Dewar and coworkers did not find a significantly different angina-free survival after BITA or SITA grafting, also not after stratification for patients of 60 years or less or patients older than 60 years of age [88]. Eight years after BITA or SITA grafting, Carrel and colleagues [90] and our group [42] were not able to demonstrate a significant difference in the angina-free rate or angina-free survival. Predictors of angina recurrence were female gender, diabetes and left ventricular dysfunction (ejection fraction <0.45) [90]. At the same follow-up, we found female gender

and a higher left ventricular diastolic pressure, rather than the use of one or two ITAs as predictors of angina-free survival [42]. At 10 years, Pick and associates showed a significantly improved angina-free survival after BITA (67%) compared to SITA (37%) grafting. On the basis of multivariate analysis they found the use of a single ITA, obesity, female gender, and preoperative hypertension to be predictors of recurrent angina [93]. Cameron and coworkers reported a substantial difference in angina free survival after 13 years of follow-up in a relatively small group of BITA patients (67.0%) versus a larger group of SITA (23.5%) and vein (27.3%) patients [79]. After 15 years of follow-up, Fiore and coworkers also demonstrated a significantly greater freedom from recurrent angina pectoris after BITA (36%) than after SITA (27%) grafting [83].

13.7.3

Late Myocardial Infarction

Reports of early or late myocardial infarctions differ in the definition of an infarction between institutions. Late infarction rates as reported in major series in the literature are shown in Table 13.5. Six studies compared the late myocardial infarction rate after SITA versus BITA grafting. In one of these studies the results were compared with a vein-graft-only group. At 5 and 8 years of follow-up, Dewar [88] and our group [42] could not show a significant difference in the incidence of myocardial infarction after BITA or SITA grafting. At 10 years of follow-up, however, Pick and associates found a significantly diminished risk of late myocardial infarction after BITA (2.1%) versus SITA (19.0%) graf-

ting. Multivariate analysis showed that diabetes and single ITA grafting were predictors for late myocardial infarction [93]. After 15 years of follow-up, Fiore and coworkers also demonstrated a significant difference in actuarial freedom from myocardial infarction between BITA (75%) and SITA (59%) grafting [104]. Recently, Sergeant and associates [105] found no additional benefit of the use of both ITAs on the freedom from myocardial infarction over a period of 15 years. However, in only a minority of their patients was the RITA placed on another vessel than the diagonal branch of the LAD and the mean number of grafts per patients was only 2.4 [103]. Cameron and coworkers demonstrated that the mortality rates associated with late myocardial infarction were significantly different between those with vein grafts only (32.8%) and those with SITA (19.1%) or BITA (7.7%) grafts [106].

13.7.4

Reintervention Free Survival

Reintervention may relate to reoperation or PTCA. A common indication for reinterventions is the progression of disease in the native circulation or failure of saphenous vein grafts. The rate of late reinterventions as reported in major series in the literature is shown in Table 13.6.

There was no significant difference in coronary reintervention rate after BITA or SITA grafting after 5 [88], 8 [42], and 10 [93] years of follow-up. However, Carrel and colleagues [90], at 8 years of follow-up, demonstrated a significantly better reintervention-free survival after BITA (95%) than after SITA (84%) grafting, mainly due to the lower number of PTCAs. Lytle and

colleagues recently demonstrated in a large number of studied patients that, at 12 years of follow-up, the reoperation-free survival after BITA grafting (76.8%) was significantly better than after SITA grafting (62.4%), and that this applied to all age cohorts [51]. The use of a SITA was, among other factors, an important risk factor for reoperation or PTCA. Cameron and coworkers reported significantly fewer reoperations after SITA grafting compared to vein grafting, at 14 years of follow-up. In a small group of 38 BITA patients no reoperation was necessary [79]. At 15 years follow-up, Fiore and associates did not find a significant difference in actuarial freedom from intervention (PTCA and reoperation together) or reoperations alone, but a significantly lower PTCA rate after BITA (3.3%) than after SITA (11.3%) surgery [107].

13.7.5

Event Free Survival

Event-free survival is the most important study endpoint for evaluating the outcome of coronary interventional therapy. Although different definitions are used, event-free survival should include all relevant cardiac-related events. The event-free survival, as reported in the major publications in the literature, is shown in Fig. 13.2. There was no significant difference in freedom from all ischemic- and interventional-related events between SITA and BITA patients at 5 [88] and 8 [42, 90] years of follow-up. However, at 10 years of follow-up, Pick and colleagues found a significantly better freedom from occurrence of any cardiac event for patients receiving BITA grafts. They found SITA grafting as the best single predictor for the occurrence of any

Table 13.6. Repeat CABG and PTCA rates

Author	Year	Follow-up	Follow-up mean/median	# Vein patients	Reoperation (%)	# SITA patients	Reoperation (%)	PTCA (%)	# BITA patients	Reoperation (%)	PTCA (%)
Cameron [79]	1986	5	10.3	216	6.1	532	2.2		38	0	
Dewar [88] ^c	1995	5				280	1.8	9.0	160	0.6	4.5
Dewar [88] ^d	1995	5				486	2.0	3.7	216	0.6	1.6
Berrekouw [27] ^a	1995	8	5			143	0	4.4	143	0	5.0
Galbut [20] ^{a,e,f}	1993	8	3.6			689	0.6	1.3	708	0.4	1.8
Carrel [90]	1996	8	?			80	1.2	11.4 ⁱ	80	6.4	
Schmidt [94] ^g	1997	9.5	7.1						311	0.6	
Schmidt [94] ^h	1997	9.5	7.1						187	0	
Gerola [91]	1996	10	5.9						201	0.5	3.0
Cameron [79]	1986	10	10.3	216	14.6	532	3.7		38	0	
Galbut [77] ^a	1985	10	4						207	1.0	
Pick [93]	1997	10	9.8			161	2.0	14.0	160	3.0	8.0
Jones [92]	1997	11	7.1						500		
Lytle [51]	1999	15	10.3			8123	62.4 ^j		2001	76.8 ^{i,j}	
Fiore [83] ^{a,b}	1990	15	14.4			100	26.0		100	21.0	
Fiore [104] ^a	1991	15	4.5						518	1.9	1.5
Galbut [42] ^{a,b,e}	1990	17	3.3						1058	5.2	

Follow-up in years: ^a hospital survivors, ^b reoperation or PTCA, ^c patients ≤60 years, ^d patients >60 years, ^e Skeletonized ITAs only ^f ≥65 years, ^g LITA-LAD and RITA-RCA, ^h RITA-LAD and LITA-CX, ⁱ P < 0.05, ^j Reoperation-free survival

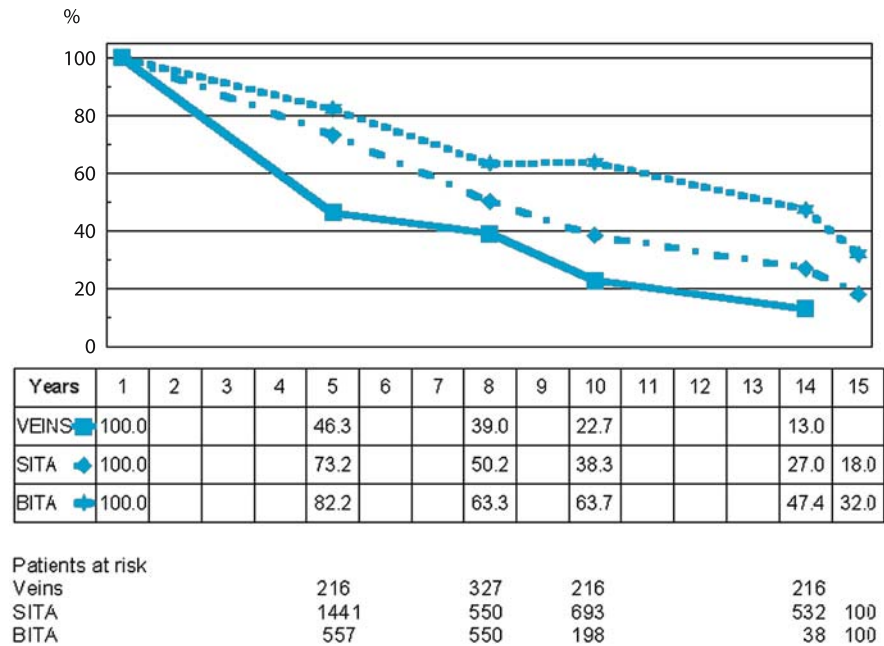


Fig. 13.2. Event-free survival

cardiac event, with a risk ratio of 2.9 [93]. At 15 years follow-up, Fiore and coworkers also demonstrated a significantly greater freedom from all ischemic events after BITA grafting [104].

Predictors for late cardiac events were female gender [42, 90], left ventricular end-diastolic pressure [42], left ventricular dysfunction (ejection fraction <0.45) [90], and diabetes [90]. These risk factors were almost the same risk factors as for recurrent angina, which is the main component in late cardiac events.

In Fig. 13.2 the 15-year event-free survival curves after veins-only, SITA and BITA grafting are presented after pooling the available data from the literature with the same follow-up period as the weighted average method. For pooling data, one has to keep in mind the limitations of comparing late follow-up data from different reports, as stated earlier.

13.8

Postoperative Flow Measurements

Flow rates through the ITA, as through saphenous veins, depend more on the coronary run-off than on the conduit flow capacity. Adequate flow regulation according to myocardial demands of the area supplied can be expected, even early postoperatively, provided that distal anastomoses are created which do not restrict the blood flow [108]. Nishida and coworkers investigated graft flow in 48 patients who received a RITA to the LAD. The flow of the RITA-LAD graft (42.3–21.1 ml/min) was the same as the flow of the LITA to the LAD (42.1–19.6 ml/min) [109].

13.9

Late ECG-Stress Testing

Results of electrocardiographic (ECG) stress testing have been reported after a mean follow-up of 0.3–7.1 years after BITA grafting [42, 110, 111]. In these reports, the percentage of patients with negative stress tests varied from 81.0% to 96.6%. After a mean follow-up of 5 years, we could not demonstrate a significant difference in the percentage of negative ECG-stress tests in 115 patients after SITA (88.7%) compared to 118 patients after BITA grafting (82.6%) [42]. Finci and coworkers demonstrated a significant increase in workload and double product (maximal blood pressure × maximal heart rate) in 31 patients 4 months after BITA grafting [110].

13.10

Late Blood Flow Studies

Morita and coworkers studied the coronary sinus bloodflow reserve in 20 BITA, 30 LITA plus vein grafts, and nine vein graft patients, 1 month after the operation. The postoperative coronary sinus bloodflow per 100 g of left ventricular mass at rest was similar among the three groups and increased significantly during exercise, in all three groups [112]. Also, Kitamura and colleagues demonstrated, on the basis of coronary sinus flow measurements, that bloodflow reserve provided by bilateral ITAs was equivalent to that of saphenous veins alone or of saphenous veins plus LITA [113].

13.11 Late Patency Rates

Patency of conduits used for grafting, preoperative status of the patient, and progression of coronary artery sclerosis in the native system determine the late results after coronary bypass surgery [1]. Most patients are restudied in response to recurrent chest pain suggestive of angina. Recatheterization studies that include almost all of the available patients are obviously of most value in this regard. Some studies report the number of patients, while others report the number of grafts or anastomoses studied. Often, it is unclear how patency was defined, and in particular that of sequential grafts. Also the patency of pedicled grafts can be mixed with those of free ITA grafts. Vein graft patency in patients where both ITAs were used is likely biased by the fact that these vein grafts probably have been placed on the least attractive coronary vessels. At the end of a relatively long follow-up no reliable information about patency is available, because the number of patients at risk at that time is very small. The late patency rates of vein grafts, LITA and RITA, as reported in the major publications, are shown in Table 13.7. Thirteen studies compared the patency of LITA versus RITA grafts. In seven of these the results were compared with the patency of vein grafts as well. Only in the study of Fiore and coworkers [83] does the re-catheterization rate approach 100%. It has been shown that bilateral ITAs implanted in the myocardial muscle (Vineberg procedure) can remain patent for more than 20 years [114, 115]. After a very short follow-up (1–32 weeks postoperatively), Rankin and coworkers restudied 207 patients in whom complex ITA grafting was performed and demonstrated the following patency rates: RITA to LAD 100%, RITA to RCA 95%, and RITA to CX 90%. However, the number of RITAs was small, never ex-

ceeding 20 per group [116]. After a relatively short follow-up of 6 months, Dion and colleagues investigated 175 patients in whom sequential ITA grafting was performed. They showed a patency rate of 94.3% of anastomoses of the RITA routed through the transverse sinus [117]. In another study with a maximum follow-up of 4 years (average 13 months), Dion and colleagues found a small but significantly better patency for LITA (96.2%) versus RITA (92.0%) *anastomoses*, but no difference between pedicled LITA (96.7%) versus pedicled RITA (95.1%) *grafts*. Pedicled ITAs showed a significantly better patency (96.1%) than free ITAs (79.6%), the patency of which did not differ significantly from vein graft patency (84.7%). The authors also demonstrated that the grafted vessel did not influence the patency rate of ITA anastomoses (LAD versus CX versus RCA) [85]. After 4.8 years of follow-up (mean 13.2 months), Buche and associates demonstrated a 98.6% patency rate of 74 RITAs that were directed to the circumflex artery through the transverse sinus [89]. After 9 years of follow-up, Schmidt and coworkers did not find a significant difference in ITA patency if the LITA was placed on the LAD and the RITA on the RCA or if the RITA was placed on the LAD and the LITA was placed on the CX [94]. In a recatheterization study at 10 years of follow-up in 814 patients, in whom 103 RITAs were used, Huddleston and associates found a significantly better actuarial patency of LITA (52.9%) compared to RITA grafts (31.2%) [118]. The authors proposed two explanations for their findings: firstly, a more distal segment of the RITA was used for the anastomosis, and secondly the majority (69%) of the RITAs were used for the diagonal, compared to only 11.3% of the LITAs. The 10 years patency of LITA grafts of 52.9%, as reported by the authors, is substantially lower than the 69% [119], 76% [120], 87% [121], 93% [2], 95% [122] patency rate for LITA-LAD grafts after about

Table 13.7. Late patency rates overall

Author	Year	Follow-up (mean)	% of total patients	# Vein patients (grafts)	Patency (%)	# LITA patients (grafts)	Patency (%)	# RITA patients (grafts)	Patency (%)	P value
Bical [111]	1996	4 (1.8)	18.6			104 ^a	93.9	104 ^a	97.5	NS
Dion [85]	1993	3.9 (1.1)	47.0			(170) ^c	97.1	(168) ^c	92.8	
Barner [123]	1985	5	51.9			(108)	88.1	(21)	84.6	NS
Pick [93]	1997	(6.9)	26.3	84 ^a	54.0	84 ^a	88.0	84 ^a	75.0	
Galbut [20] ^{b,d}	1993	8 (3.6)	6.9			48	94.7	49	79.6	
Schmidt [94]	1997	8.6 (4.1)	17.9	89 ^a	83.3	89 ^a	89.3	89 ^a	93.7	NS
Barner [124]	1982	8.8 (5.3)	19.7					(23)	95.7	
Jones [92]	1997	8.8 (4.1)	17.8			89 ^a	89.2	89 ^a	92.6	NS
Lytte [125]	1983	9 (2.2)	36.8			28 (26) ^a	92.9	28 (27) ^a	85.2	
Huddleston [118]	1986	10 (4.2)	19.7	(1376)	20.0	(837)	52.9	(103)	31.2	<0.005
Gerola [91]	1996	10 (4.3)	41.0	(28)	35.4	(34)	93.8	(33)	84.1	NS
Galbut [77] ^b	1985	11.5 (4.5)	13.2	(26)	50.0	(37) ^b	92.0	(30) ^b	87.0	
Fiore [83]	1990	13 (4.2)	96.3	(166)	30.0	(98)	82.0	(91)	85.0	NS
Galbut [17] ^b	1990	15 (4.4)	5.1	53 ^a	65.3	53 ^{a,b}	92.1	53 ^{a,b}	84.9	

Follow-up in years: ^a all patients combined, ^b skeletonized ITAs only, ^c free and pedicled grafts, ^d patients ≥65 years

10 years, as reported by others. This can be explained by the fact that the vast majority of Huddleston's patients undergoing postoperative coronary arteriography did so because of recurrent symptoms [118]. Other interesting findings in this study were that there was no significant difference in patency of the ITA grafts for skeletonized, narrow or broad pedicled harvesting techniques, and patency of ITA-LAD grafts (54.0%) was significantly better than in ITA grafts to other coronary arteries (diagonal 41% and others combined 20.5% at 10 years). Gerola and associates [91] performed recatheterizations after 10 years in 40% of their SITA and BITA patients and showed no significant difference in actuarial graft patency for LITA and RITA grafts, but the patency of both of these grafts was independently significantly better than saphenous vein graft patency. Also, the RITA placed through the pericardial transverse sinus showed a good (93.7%) patency after 10 years of follow-up. After 13 years of follow-up, Fiore and colleagues found by re-catheterization of 96% of their studied patients that there was no significant difference in actuarial patency between SITA (82%) and BITA (85%) grafts, while the attrition rate of saphenous vein grafts approached 70% by the 12th postoperative year [83]. One can conclude that the pedicled RITAs show a similar long-term patency to that observed with the pedicled LITAs and that their patency is superior to that of the saphenous vein in all coronary locations.

13.12

Conclusions

Comparisons of single pedicled ITA grafting and bilateral pedicled ITA grafting can be performed at similar operative mortality, incidence of myocardial infarction, use of IABP, rethoracotomy for bleeding, pulmonary complications, strokes, phrenic nerve lesions, ITA malfunction, and duration of stay in the hospital. However, it is likely that sternal wound infections are more common, specifically if other risk factors are involved that predispose to this complication. It seems that the late survival, recurrent angina-free, reintervention-free, and event-free survival, especially at 10 years or more of follow-up, are better after BITA than after SITA grafting. Also the late incidence of myocardial infarction, especially after 10–15 years of follow-up, is likely to be less after BITA grafting. Pedicled RITAs show a similar long-term patency to that observed with pedicled LITAs and their patency is superior to that of the saphenous vein in all coronary locations. Although the current information is still limited, it is our opinion that the use of both pedicled ITAs is indicated for patients of 60 years and younger, favorably to revascularize the most important left-sided vessels. But it may be

advisable to use these conduits in older patients up to 75 years of age, or maybe even older, depending on the coronary anatomy, left ventricular function, general condition and co-morbidity of the patient, and providing that the surgical team has the ability to perform the operation with low morbidity and mortality. To obtain better long-term results than with saphenous vein grafts, the goal in coronary bypass surgery should be to perform a complete revascularization with arterial conduits only. In two-vessel or main-stem disease, this goal can often be achieved by using two pedicled ITAs. In three-vessel disease, it is necessary to use one pedicled LITA and a free RITA as a Y-graft, or to use both pedicled ITAs in combination with other arterial conduits as the right gastroepiploic artery, inferior epigastric artery, or one or two radial arteries. Combinations of arterial conduits can also be indicated in patients with predisposing factors for complications of BITA grafting. Further, the role of BIMA in the minimally invasive approach still has to be determined. Based on their superior histological and physiological properties as the best arterial conduits, it is recommended that we should continue to use both ITAs as much as possible, knowing that two ITAs are better than one.

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14 Left-Sided Myocardial Revascularization with Bilateral Skeletonized Internal Thoracic Artery

R. MOHR, A. KRAMER

14.1 Introduction

The current conventional and most commonly used operative procedure for myocardial revascularization includes one internal thoracic artery (ITA) together with one or more saphenous vein grafts (SVG) [1, 2]. The major surgical objective is to supply the left anterior descending coronary artery with an ITA in order to improve patient survival [3, 4].

ITA patency rate exceeds that of SVG and long-term patency remains high, in contrast to vein grafts which are subject to late closure as a result of progressive atherosclerosis [3]. Besides better survival, the superior patency rate is associated with better angina-free survival and decreased rates of reoperations and reinterventions [5].

Since SVG failure is a major drawback of coronary artery bypass grafting (CABG), surgical techniques of arterial myocardial revascularization with minimal use of SVG were attempted. Two popular techniques for achieving this goal are bilateral and sequential ITA grafting [6–8]. In most centers, the ITA is isolated from the chest wall as a pedicle, together with the vein, muscle, fat and accompanying endothoracic fascia [3, 4, 9]. Harvesting is relatively quick due to the fact that cautery is used to separate the pedicle from the chest wall. However, cauterization damages the blood supply to the sternum, which in turn impedes sternal healing and exposes the sternum to the risks of early dehiscence and infection, particularly in operations in which both ITAs are used [10–13].

A surgical technique was recently developed wherein the ITA is dissected as a skeletonized vessel [14, 15]. The skeletonized artery is isolated gently with scissors and silver clips, without the use of cauterization. Skeletonized ITA dissection leaves the vein, muscle and accompanying tissue in place (Fig. 14.1). The advantage is that the dissected artery is longer [16] and its spontaneous blood flow is greater than that of the pedicled ITA [17], allowing the use of both ITAs as grafts to all necessary coronary vessels [9]. In many cases, no additional vein grafts are required [9]. Another advantage of using ITA as a skeletonized artery is the preservation of col-

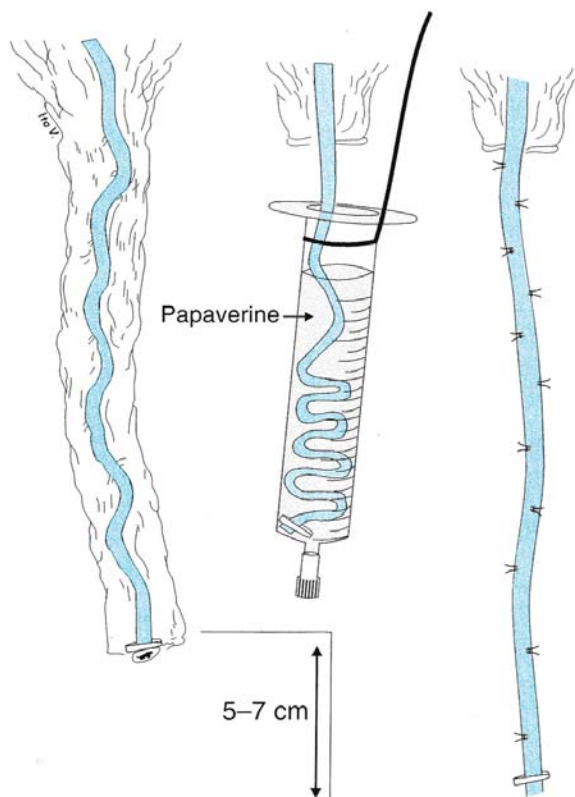


Fig. 14.1. Pedicled internal thoracic artery (*left*), the “Jacuzzi”: skeletonized ITA inside a syringe filled with papaverine solution (*middle*) and skeletonized ITA (*right*)

lateral blood supply to the sternum, enabling more rapid healing and decreasing the risk of infection [18].

The use of left ITA as a bypass graft has been shown to result in better early patency rate and improved survival in all patients, including elderly patients [13, 19], but most published series have failed to show additional survival benefit with the use of bilateral ITA [1, 2].

The lack of survival benefits and the technical complexity of performing complete arterial revascularization with bilateral ITAs are the probable causes of the relative lack of popularity of this technique. The Society of Thoracic Surgeons (STS) database includes 153,000 CABG operations performed in the United

States and Canada, only 4% of which involved the use of bilateral ITAs [20].

In contrast to most previously published reports, three important large-scale studies have shown that long-term survival with bilateral ITA is better than that with single ITA. Lytle et al. reported that the 10- and 15-year survival rates of bilateral ITA patients were 84% and 67%, compared to 79% and 64%, respectively, for patients with single ITA ($p < 0.001$). Reoperative and angina-free survival, as well as freedom from additional revascularization procedures, was significantly higher in the bilateral ITA subset [21]. In another study performed by Buxton et al. [22], the 10-year actuarial survival of bilateral ITA patients was $86 \pm 3\%$ compared to $71 \pm 5\%$ for a single ITA ($p < 0.001$). In that report, the use of bilateral ITAs improved the rate of freedom from late myocardial infarction and reoperations. The third report by Schmidt et al. demonstrated that survival benefit with bilateral ITA operations is achieved by grafting the ITA conduits to coronary arteries supplying the left ventricle (left-sided revascularization) rather than to the right coronary system [8].

Studies reporting results of bilateral ITA grafting contain preselected patients operated upon over a relatively long period [8, 9, 21, 22]. Most were non-obese and non-diabetic patients and were preselected for this procedure according to their life expectancy. Most of them were young and only a few of them were older than 70 years.

The bilateral skeletonized ITA technique was adopted in the Tel Aviv Sourasky Medical Center in April 1996 as the preferred method for myocardial revascularization. Routine use of this ITA-harvesting technique enabled the surgeons to acquire the dexterity necessary for dissecting the skeletonized ITA and to minimize the time required for a learning curve. The routine use of SVG was stopped and since then vein grafts have been used as a third optional graft, in emergency CABG operations, or in cases with contraindications for the use of two ITAs.

From April 1996 to July 1999, 1,000 consecutive patients underwent bilateral skeletonized ITA grafting. They comprised 71% of the 1,408 patients who underwent CABG during this time period in the Tel Aviv Sourasky Medical Center. This was a non-selected group of patients: there were 770 males and 230 females; 420 patients were older than 70 years and 312 were diabetic. Myocardial preservation technique was intermittent warm cardioplegia.

The average number of grafts was 3.1 per patient [2–6]. The gastroepiploic artery was used in 231 patients and 158 saphenous vein grafts were implanted in 142 patients.

14.2

Harvesting and Preparation of the Skeletonized ITA [16]

In our harvesting technique, we follow instructions and recommendations given by Cunningham et al. [15]. The ITAs are dissected as skeletonized arteries [14] before heparin administration to decrease the risk of damage and hematoma formation in the region of the side branches during dissection. A standard median sternotomy incision is used with only rare application of bone wax. Later dissection of the ITA is easier if meticulous hemostasis is obtained on the sternal edges to avoid bleeding into the surgical field. We favor the use of the special ITA retractor for ITA take-down because of the good exposure of both left and right ITAs obtained with minimal trauma to ribs and chest wall.

We favor elective opening of pleura before ITA dissection in order to facilitate exposure. Though it is possible to completely skeletonize the ITA from its origin to its distal bifurcation without opening the pleura, dissection of proximal ITA with its anterior and pericardial branches is easier and safer when the pleura is open.

To avoid thermal injury to the ITA, it is extremely important to keep the cautery setting on low throughout the dissection. Cautery may be used to cut the endothoracic fascia and expose the underlying ITA. Using the tip of the *cold* cautery as a dissector, the artery can be gently separated from the chest wall leaving the accompanying veins, fascia and adipose tissue in place. Forceps rarely touch the artery itself but may grasp the small remnants of soft tissue that cling to the adventitia of the ITA. The initial cut in the endothoracic fascia is extended inferiorly until the terminal bifurcation of the ITA into its lateral musculophrenic and medial superior epigastric branches is visualized. Terminal bifurcation usually occurs at the sixth intercostal space. These terminal branches are left intact to allow blood flow through the ITA until it is ready for use. Branches are divided between clips using scissors. Care is taken not to place the clip flush with the ITA. Once branches are controlled, scissors or low cautery are used to divide the remaining medial and lateral soft tissue attachments. After the distal portion of the artery is freed, an additional cautery cut in the endothoracic fascia is made to allow dissection superiorly.

The proximal third of the ITA occasionally has large anterior perforating branches that may initially seem too short to allow satisfactory clip application. With careful dissection proximally and distally to the branch, suitable length can usually be obtained. One must not apply excessive traction on the ITA as these branches can tear easily, causing serious bleeding. If insufficient branch length precludes safe application of two clips, it is best to apply a clip to the ITA side of the branch. The branch is then separated and the cautery is used to ob-

tain hemostasis on the chest wall. Meticulous technique is necessary to avoid tearing these branches or, worse, avulsing them from the ITA itself. Should a tear or avulsion occur, small atraumatic vascular clamps are applied proximally and distally, thus allowing adequate visualization. Precise sutures of 8-0 polypropylene can then be placed without compromising the ITA lumen.

Throughout the dissection, the ITA is intermittently sprayed with dilute papaverine solution to minimize spasm and to prevent dissection. Care is taken to keep well away from the ITA when using the cautery even in the low setting. As the origin of the ITA is approached, pericardial branches are identified and divided. Lowering the operating table facilitates exposure of collaterals in this portion of the ITA. To obtain maximum ITA length, diameter and flow, it may be necessary to divide the internal thoracic vein to obtain satisfactory exposure of these most proximal collateral branches. While the retractor is still in place and exposure is good, the superomedial pleural reflection is divided with cautery. This maneuver increases the usable length of the artery as it allows the ITA to drop into a "groove" between the pleura and pericardium. A vertical incision is made in the lateral pericardium from its free edge to the phrenic nerve. The left ITA is mobilized through this incision and penetrates the pericardial cavity anterior to the phrenic nerve. This maneuver also allows the ITA to lie medially and posteriorly to the lung; thus ventilation does not produce any notable stretch or distortion of the artery. Additionally, the artery is somewhat protected from injury should resternotomy be required. The vessel is then carefully inspected for any signs of inadequate hemostasis or wall trauma. Bleeding points are controlled with a clip or fine suture. It is not unusual to notice small areas of adventitial blood staining at clip application points. A clip can occasionally partially cut through a branch, causing bleeding and localized staining. It is extremely important to minimize adventitial blood staining by applying another clip if possible. When necessary, one can momentarily occlude the ITA to allow placement of a suture. These small, well-localized areas of staining do not preclude use of the ITA. However, longer areas of wall hematoma or wall discoloration are worrisome as they can be associated with intimal tears and dissection. Should distal dissection be suspected, this portion of the ITA is discarded.

Heparin is administered before distal ITA division. Medium-sized hemoclips are used to secure the distal stumps of both ITAs and the proximal stump of the right ITA when this conduit is used as a free graft. Hemoclips are used to block the distal ITA, enabling hydraulic distention of the skeletonized artery by pulsations of arterial pressure wave against the walls of the blocked artery.

The skeletonized artery is put in a small syringe filled with 1:30 papaverine saline solution ("Jacuzzi";

Fig. 14.1). This bath of papaverine is sufficient to relax any spasm produced during dissection without the risk of endothelial damage caused by other antispastic maneuvers such as intraluminal papaverine injection or mechanical dilatation [16].

14.3

Strategies of Left-Sided Arterial Revascularization

14.3.1

The Ante-aortic Cross Arrangement [23]

We prefer to use bilateral ITAs as in situ grafts for myocardial revascularization. The two ITAs in combination with the right gastroepiploic artery provide three sources of blood supply [23]. We believe that more blood sources are associated with better, long-term outcome. The cross arrangement (Fig. 14.2) is based on two assumptions: the first is that patency rate of the right ITA on the left anterior descending artery (LAD) is similar to that of the left ITA on the LAD [24–26]. The second is that in order to improve late survival every effort should be made to use both ITA grafts for bypass of the left system [6]. We do not use the cross technique in cases with short right ITA, very long ascending aorta, enlarged right ventricle too distal or calcified, or unpredictable LAD anastomotic site and in cases with high probability of repeat surgery such as valve operations [27, 28]. We always try to avoid the use of the ITA distally to its bifurcation. This is especially important with right ITA to LAD. This portion of the ITA is very delicate and prone to spasm, dissection and intimal disruption [29]. We feel it is dangerous to rely on the extra length obtained by using this distal portion for LAD anastomosis. A major concern of surgeons using bilateral ITA is the risk of damage to an artery crossing the midline (right ITA) in case of future repeat operation. The extra length obtained by skeletonizing dissection very often enables the surgeon to move the right ITA superiorly above the origin of the innominate artery and secure it under the pericardial fat and thymic remnants before chest closure [23, 30]. This maneuver decreases the risk of damage to the artery during potential resternotomy and avoids kinking of the right ITA when this artery is too long. In relatively rare situations when both ITAs are very long, it is possible to use the left ITA as a sequential graft to circumflex marginal and posterior descending artery (PDA) or sequential graft to circumflex marginal and posterolateral branch of right coronary artery (RCA) (Fig. 14.2a: two sources of myocardial arterial blood supply). In these cases using T-shaped terminal anastomosis is recommended (Fig. 14.2a). Together with the diamond-shaped anastomosis of sequential grafting it results in shorter segments of ITA between anastomoses, thus avoiding po-

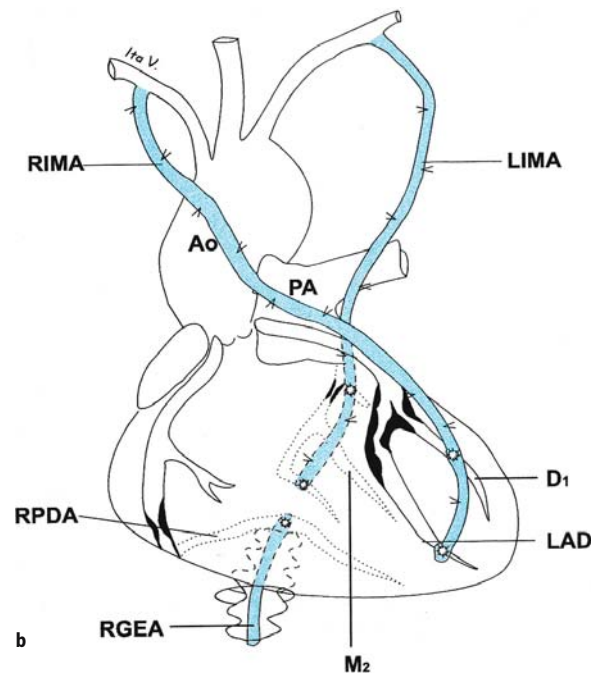
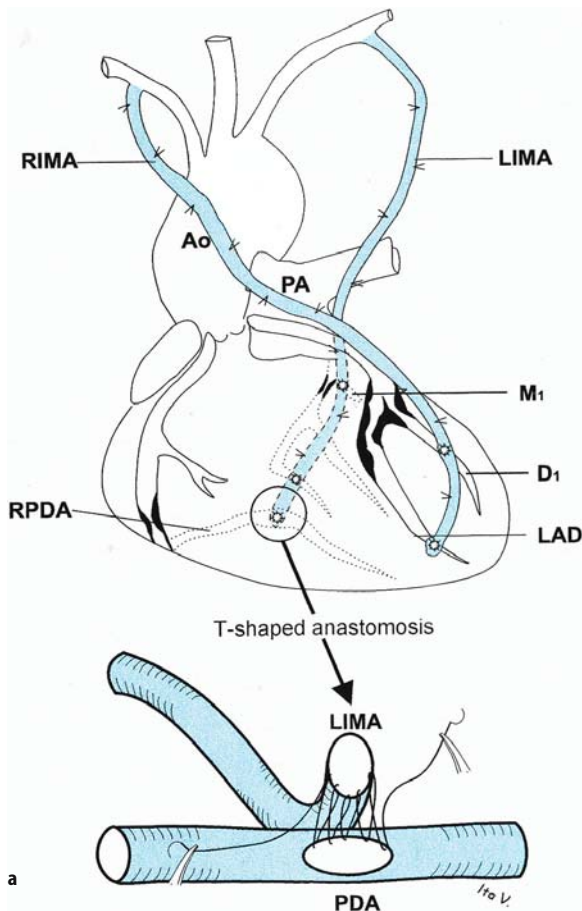


Fig. 14.2. The cross arrangement **a** with two ITAs; and **b** with two ITAs and gastroepiploic artery (*RIMA* right internal mammary artery, *LIMA* left internal mammary artery, *RPDA* right posterior descending artery, *RGEA* right gastroepiploic artery)

tential tension of the left ITA along its course between the subclavian and the PDA.

14.3.2

The Composite Arrangement [27, 28, 30]

When the in situ right ITA cannot reach the LAD anastomotic site, especially in situations where we have to construct the LAD anastomosis more distally, we use the right ITA as a free graft and a composite arterial graft is prepared before connection to cardiopulmonary bypass (Fig. 14.3a). Most of the composite grafts include end-to-side anastomosis of a free right ITA on an in-situ left ITA. However, when the proximal part of the left ITA is damaged or when its spontaneous free flow is not sufficient (subclavian stenosis), a left ITA can be anastomosed end-to-side to an in-situ right ITA (Fig. 14.3b) [28]. A third variation of the composite graft is the small y-graft (mini-composite), wherein a small distal section of an ITA is anastomosed end-to-side to a more proximal part of the same artery (Fig. 14.4). This arrangement is preferred by some surgeons for LAD-diagonal or LAD-intermediate branch anastomosis.

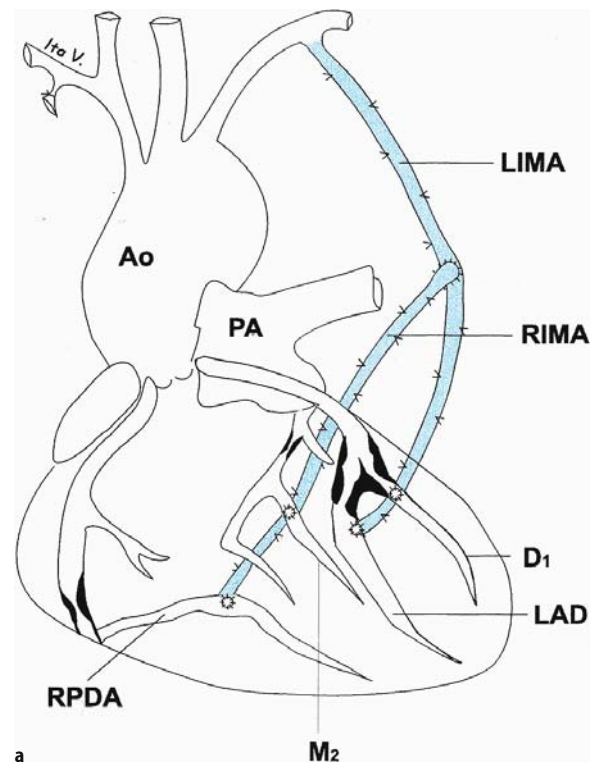


Fig. 14.3. Composite arrangements for bilateral ITA grafting: **a** free right ITA (to circumflex marginals and PDA) is anastomosed end-to-side to in situ left ITA (to LAD).

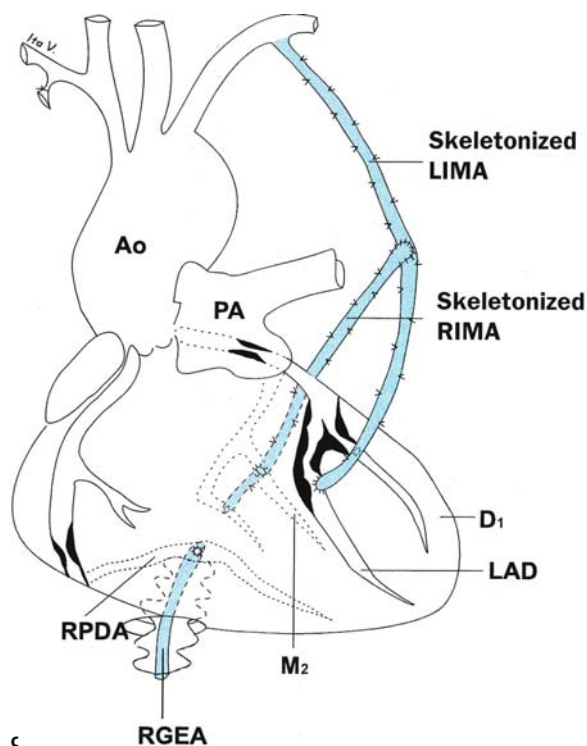
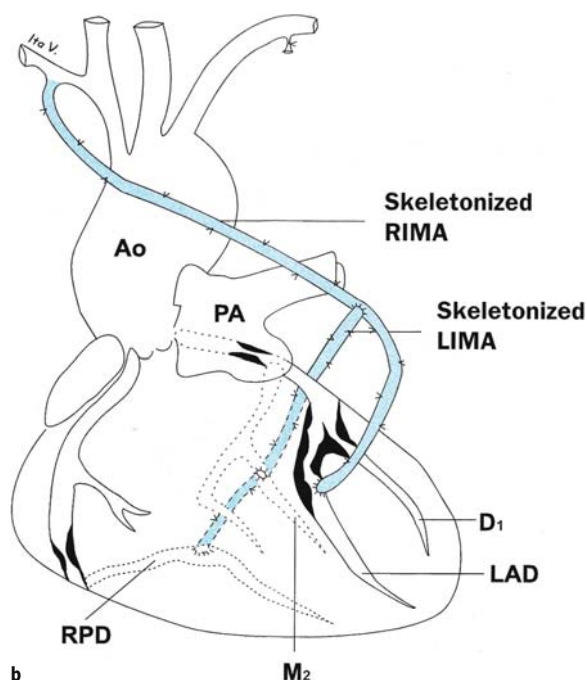


Fig. 14.3. **b** end-to-side anastomosis of free left ITA to in situ right ITA; **c** composite graft to LAD and circumflex, and gastroepiploic artery to PDA; **d** reverse-composite graft: free right ITA to LAD and left in situ ITA to circumflex marginals (abbreviations as in Fig. 14.2)

Both ITA grafts are palpated after 5–10 min in the papaverine solution. The pulse should be strong and spontaneous free flow is almost always greater than

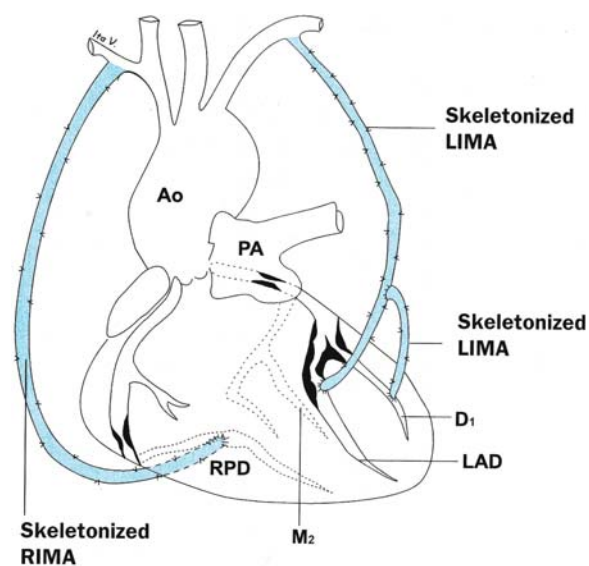
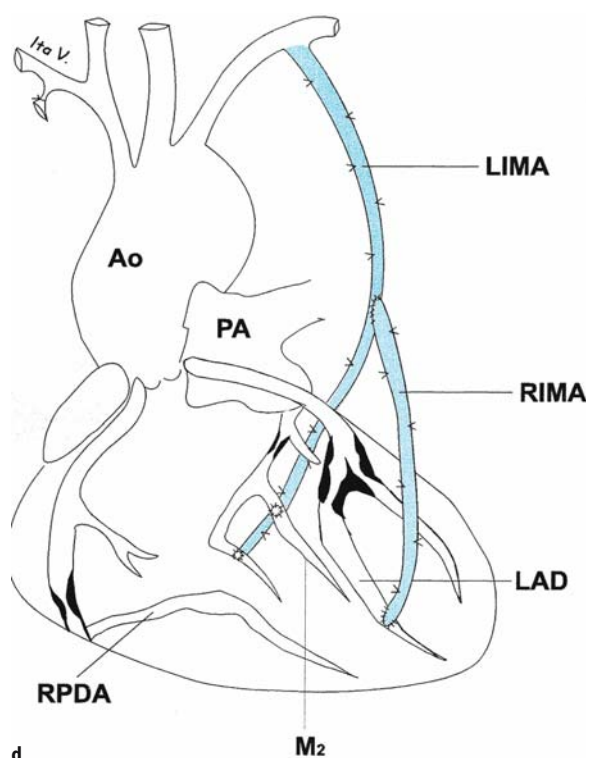


Fig. 14.4. In situ right ITA to RCA and left ITA to LAD with mini-composite graft (abbreviations as in Fig. 14.2)

150 ml/min. The composite anastomosis is usually constructed as a T anastomosis [9], at the level of the mid-pulmonary artery. However, y-shaped or even inverted y-shaped anastomoses may be constructed when they seem to us more suitable for the specific pathology or anatomy of the patient's coronary circulation [31]. The proximal composite anastomosis of free right ITA on

the left ITA may sometimes be performed during cardiopulmonary bypass after constructing all distal and sequential right ITA anastomoses. This is the safest way to precisely determine the best location of the proximal composite anastomosis without any compromise of left ITA flow to the LAD [28].

Preventing compromise of left ITA flow to the LAD may also be achieved by constructing the most proximal sequential anastomosis (diagonal) of the right ITA before constructing the more distal anastomosis (circumflex marginals and RCA) [27].

If the free right ITA is too short to reach the PDA or posterolateral branch of the RCA, we very often use the right gastroepiploic artery (RGEA) or even a vein graft to bypass these branches of the RCA (Fig. 14.3c). We prefer vein grafts when the PDA is not suitable for RGEA grafting, such as in cases with non-critical RCA stenosis and potential for high competitive flow in the PDA [28].

Despite the extra length obtained with skeletonization, in some cases the left ITA is not long enough to reach a very distally located anastomotic site on the LAD. In this situation, extra length may be obtained with the composite arrangement by anastomosing the free right ITA to the LAD and the left ITA to the marginal branches of the circumflex (reverse composite graft; Fig. 14.3d) [32].

14.3.3

The In-Situ Arrangement

When no graft to the posterior wall of the heart is necessary (the circumflex region), the left ITA is grafted to the left anterior descending and the right ITA to the RCA or its posterior descending branch. The right ITA grafted on the RCA has a relatively low patency rate [3, 26]. In fact, the RCA is often calcified or severely fibrotic; therefore, the edges of the arteriotomy are unable to remain separated from each other after the incision. We therefore prefer the right ITA to PDA anastomosis.

It should be noted that, in most cases, it is impossible to reach the PDA with the ITA graft when employing the regular technique of isolating the pedicled ITA. A skeletonized right ITA, however, is longer and can usually easily reach the better quality distal posterior descending artery (Fig. 14.4). This in-situ arrangement is not included in the cohort of 1,000 patients evaluated in the current report as it does not comprise grafting of the circumflex, and therefore cannot be regarded as left-sided arterial grafting.

14.3.4

Consideration of Sequential Grafting with Skeletonized ITA [7, 9, 33, 34]

Sequential grafting is essential if only ITAs are used for complete myocardial arterial revascularization. The

economic approach of sequential grafting using diamond-shaped side-to-side anastomosis and terminal T-shaped perpendicular anastomosis for branches of the circumflex and RAC is our preferred approach. It carries the advantage of sparing ITA length using the shortest possible ITA segments between anastomoses. Potential pitfalls of kinking of the graft in the anastomotic region are prevented by using very short arteriotomies (2–3 mm) [16].

To prevent tension between anastomoses after filling the ventricle, the length of the ITA segment between anastomoses is usually 5–10 mm longer than the actual distance between anastomotic sites on the coronaries [27].

Side-to-side parallel anastomosis is often used for sequential LAD diagonal grafting with the left ITA. The proximal diagonal anastomosis is performed first. The length of left ITA distal to the diagonal anastomosis should be exactly equal to the distance between LAD and diagonal arteriotomies as this distance will not increase with filling of the heart. The skeletonized ITA length usually increases after initiation of blood flow through the artery [28].

A common pitfall in this LAD diagonal arrangement is kinking of ITA when the segment between anastomoses is too long. This problem, which is not observed when using the pedicled ITA, can be solved by using diamond-shaped side-to-side anastomosis for the diagonal, by using the y-graft (mini-composite) technique or by using the right ITA for the diagonal anastomosis in cases with right ITA on left ITA composite graft. The parallel side-to-side anastomosis is also preferred for bypass of the intramyocardial coronary artery or for vessels buried inside a deep layer of epicardial fat. Constructing a diamond-shaped anastomosis exposes the ITA to the risk of seagull-wing kinking [25] (Fig. 14.5).

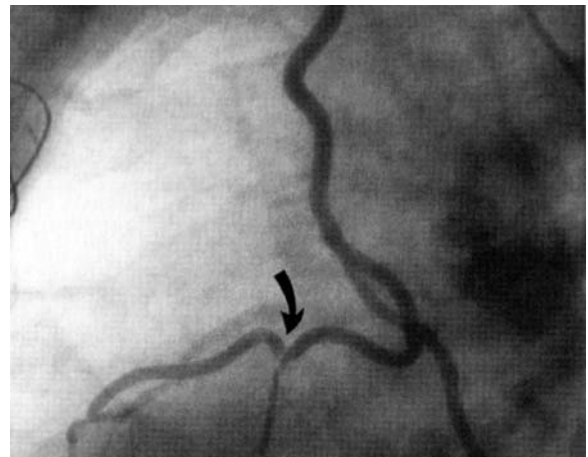


Fig. 14.5. Seagull-wing kinking (arrow) of left ITA in the site of a diamond-shaped anastomosis to intramyocardial diagonal artery

This pitfall can easily be overcome by the parallel side-to-side anastomosis accommodated by positioning the ITA graft in a gentle curved course. The skeletonized ITA graft should not be too long. Excessive length can create sharp-angled curves or twists, especially in the most proximal segment of the artery between its origin and the first coronary anastomosis or near the composite anastomosis (Fig. 14.6). This may be pre-

vented by accurate measurement and by aligning the artery medially in a gentle curve before sternal closure. The composite technique should not be used in cases with non-critical left main or LAD anastomoses because of concern regarding string sign or even occlusion of one of the composite limbs in the presence of high competitive flow in the native coronary artery (Fig. 14.7).

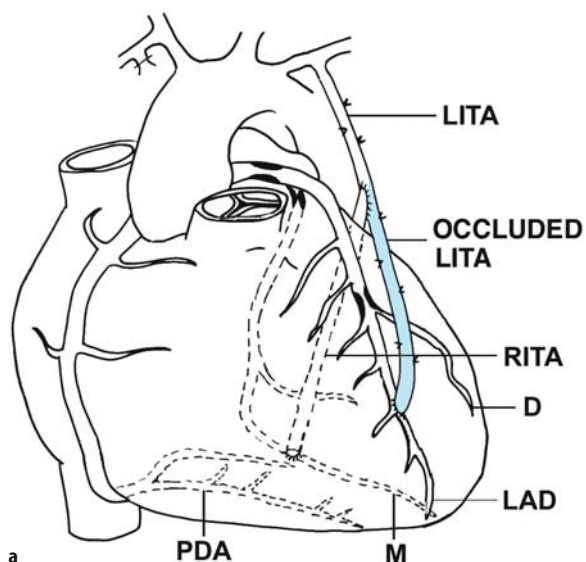
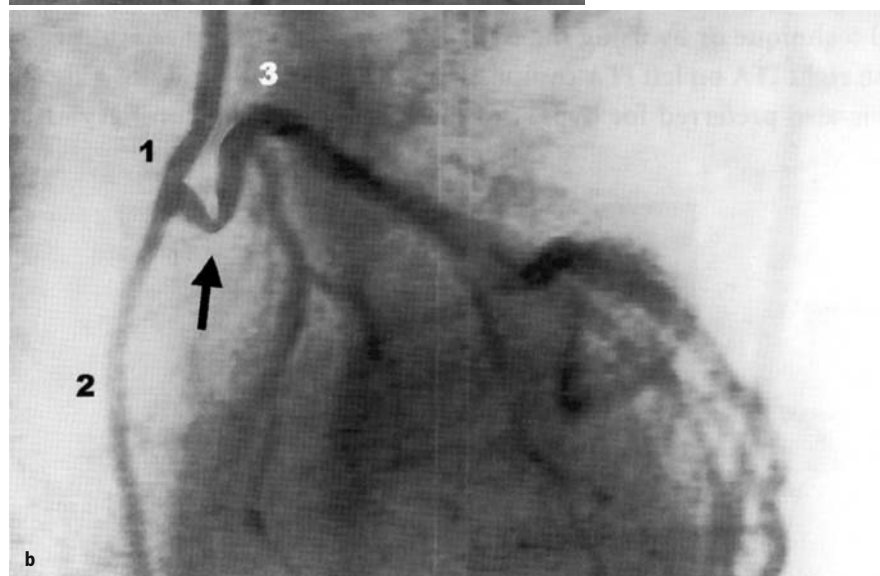
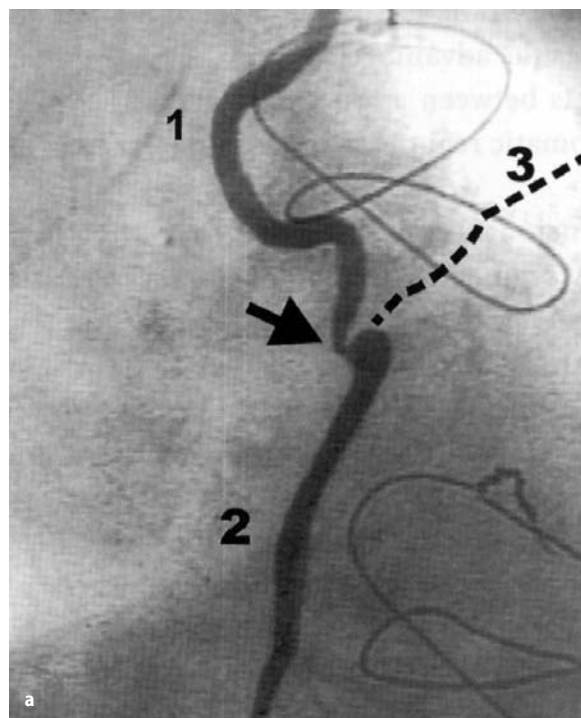


Fig. 14.7. Competitive flow in a patient with composite T-graft (LITA to LAD and free RITA attached to LITA is connected distally to marginal branch of circumflex): **a** Schema of postoperative angiogram.

Fig. 14.6. a Short right ITA: stretch causing deformation and narrowing of left ITA (arrow) (1 proximal left ITA, 2 right ITA, 3 occluded left ITA distal to composite anastomosis). **b** Excessive length of right ITA (3), causing twisting and narrowing (arrow) near proximal composite anastomosis (1) to left ITA (2)

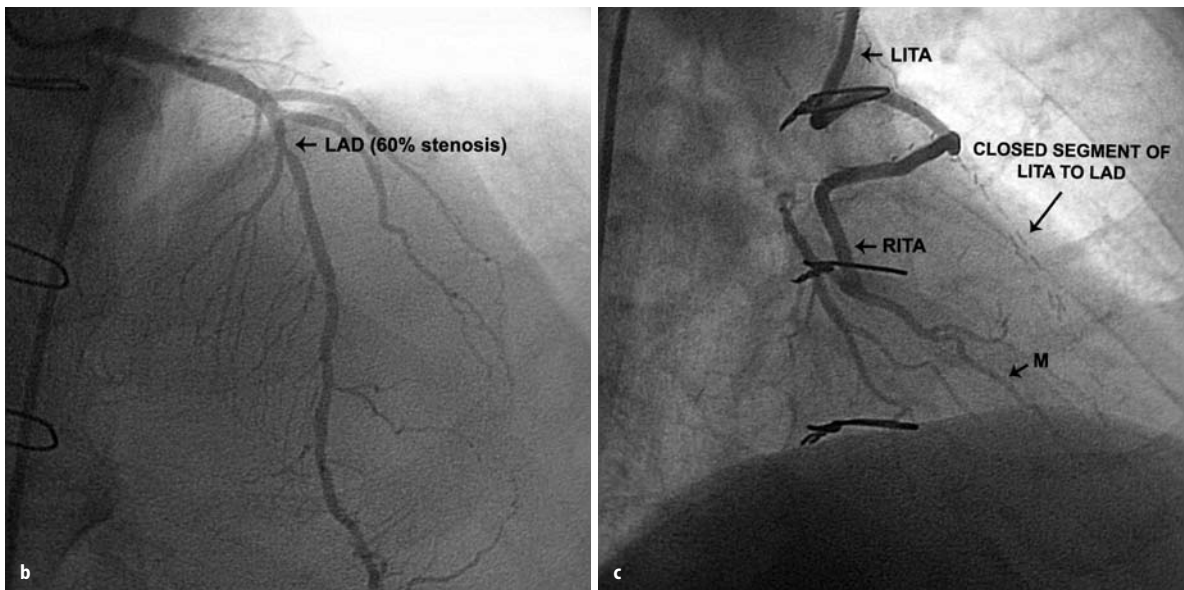


Fig. 14.7. **b** injection to left system; **c** injection to ITA (*RITA* right thoracic artery, *LITA* left internal thoracic artery, *PDA* posterior descending artery)

14.4 Clinical Results [35, 36]

The operative mortality in the cohort of 1,000 patients undergoing left-sided arterial grafting between April 1996 and July 1999 was 3.3%. The mortality of urgent and elective cases was 2.8%, and that of IABP supported patients was 13.8% (5 of 36, $p=0.001$). Independent predictors of 30-day mortality were peripheral vascular disease (PVD) (OR 2.9, 95% CI 1.06–7.95) and CHF (OR 3.3, 95% CI 1.4–7.7). There were 10 perioperative infarcts and 16 patients sustained strokes. Sternal wound infection occurred in 22 patients, and mortality rate for patients with mediastinitis was 32% (7 of 22) [37]. Increased risk of sternal infection was found among patients with COPD (9 of 83, 10.8%) and diabetes mellitus (13 of 296, 4.4%). COPD (OR 5.7, 95% CI 2.1–15.74) and diabetes (OR 2.72, 95% CI 1.04–7.1) were also found to be independent predictors for deep sternal infection using multivariable logistic regression analysis [36].

Follow-up between 40 and 78 months postoperatively was available in 938 of the 967 surviving patients (97%). There were 79 late deaths and 6-year actuarial survival (Kaplan-Meier) was 88%. There were ten cases of late MI, and 95 patients (9.5%) reported return of angina. Increased rate of angina return was noted in patients with PVD (OR 3.04, 95% CI 1.6–5.77), and in patients younger than 70 years (OR 2.03, 95% CI 1.27–3.33). Eighty-seven patients underwent cardiac catheterization during the follow-up period: 78 because of chest pain and nine consented to elective catheterization within the framework of our learning to use

the composite graft. One hundred and sixty of 176 distal ITA anastomoses (91%) were patent. There were 15 occluded ITAs (11, string sign). Reinterventions included four repeat operations and 20 PTCA's and stents.

Analysis of both early and late mortality showed the following risk factors to be independent predictors of overall mortality: PVD (RR 5.52, 95% CI 3.31–9.2); CHF (RR 2.13, 95% CI 1.31–3.45); and age > 70 years (RR 2.1, 95% CI 1.37–3.47). Similar findings were observed when late mortality was analyzed separately [36].

14.5 Comments

This report summarizes our surgical experience and enlightens the technical aspects of routinely using skeletonized ITA. The patients were typical for an urban population (relatively older) and this technique was used in most (71%) of the patients who underwent CABG in this institution over a short period of time (40 months). The only contraindications for the use of ITA grafts were emergency operations with hemodynamic instability, requiring rapid connection to cardiopulmonary bypass. The immediate operative results are comparable to those described in procedures in which one ITA was used [1].

The report confers significant clinical approval of the basic assumption concerning the skeletonized ITA technique – that it probably causes less damage to the sternal blood flow [10, 11, 18], and therefore the rates of sternal infections and complications are in the lower

range of those reported by others. We found only chronic lung disease and diabetes mellitus to be major risk factors for deep sternal infection [36].

Diabetes mellitus is generally considered to be a major risk factor for sternal complications, especially when bilateral internal mammary artery grafting is used. The risk in these circumstances was estimated to be five times more than in other patients [38]. We found no evidence of this relationship in patients who received bilateral skeletonized ITA. Our results are even more definitive, considering the fact that 30% of our patients had diabetes mellitus.

No difference was found in the occurrence of deep sternal wound infection among female and elderly patients as compared to those without these risk factors. In a previous study, we showed that increased risk of infection among diabetic patients was noted only among obese patients (8.3% vs 1.1% in non-obese patients, $p=0.03$), especially obese females (15% vs 1.4% in diabetics without these risk factors, $p=0.001$) [39]. Explanations for the latter findings in patients with chronic lung disease might include high suture line pressure or collagen abnormalities described in smokers [19]. In another publication from our group, there was no difference in the occurrence of deep sternal wound infection between the non-insulin-treated (9/468, 1.92%) and the insulin-treated (2/47, 4.26%) diabetic patients [40]. Occurrence of sternal infection among insulin-treated patients with BITA was similar to that of insulin-treated patients with single ITA (4% vs 2.7%, $p=1.00$). On the other hand, they had significantly lower rates of leg infection in the SVG harvesting site (0% vs 24%, $p=0.000$) [41]. In the orally treated subset of diabetics, early outcome of BITA versus single ITA was comparable, including the incidence of deep sternal infections (1.8% in both groups). During follow-up (range 4–7.5 years, median 5 years), there were less repeat revascularizations (4.4% vs 12.3%, $p=0.025$) and major adverse cardiac events (MACE) (11.2% vs 36.8%, $p<0.0001$) in the BITA group. At 7 years, survival (Kaplan-Meier) (75% vs 59%, $p=0.006$, log-rank), freedom from cardiac mortality (92% vs 68%, $p<0.0001$), and freedom from MACE (70% vs 59%, $p=0.004$) were superior in the BITA group. Multivariate analysis identified the use of BITA as a protective factor against the occurrence of late cardiac mortality (OR 0.2, 95% CI 0.06–0.6) and MACE (OR 0.3, 95% CI 0.1–0.66) [42].

Our study clearly defines two subgroups of patients with increased operative and overall (early and late) mortality. Patients with PVD and CHF are probably those with a diffuse and advanced form of atherosclerotic involvement of the heart and peripheral vessels. This may probably partly explain the unfavorable early and late results [35, 36].

An interesting subgroup of the above cohort was the subgroup of elderly patients. There were 433 patients

older than 70 years (70–92 years). Their operative mortality (3.6%) and occurrence of sternal infection (3.4%) were no different from those of the younger age group. However, their late (6 years) mortality was increased (11.5%) and age over 70 was found to be an independent predictor (Cox model) for overall (early + late) mortality [35].

The use of bilateral ITA in the elderly is controversial. He et al. reported an operative mortality of 24% in elderly patients (≥ 70 years) who underwent bilateral ITA [13]. Moreover, use of bilateral ITA in the older patients in their report was found to be a major risk factor for operative mortality, since mortality in the patients receiving one ITA was only 6.8% ($p<0.007$). It is important to note that the ITA in their report was used as a pedicled conduit and, as the authors stated, the fact that only 4% of the patients were grafted with bilateral ITAs might have explained the higher operative mortality and increased use of postoperative IABP (16.2% vs 5.9%, $p<0.015$) [35].

In the study by Lytle et al. [21], the number of patients older than 60 years operated upon with bilateral ITA was relatively small; however, bilateral ITA grafting improved survival of this subset of older patients when compared to patients older than 60 years with a single ITA graft.

The only large series (1,467 patients) comparing bilateral with single ITA in the elderly was reported by Galbut et al. [19]. In this study, patients with bilateral ITAs had lower hospital mortality rates (3.1%) compared to 6.4% in patients with a single ITA, and the late survival rate (mean 43 months) was also better (69.7% vs 60.7%).

In summary, routine use of bilateral skeletonized ITA for left-sided arterial grafting seems to be a safe technique for patients undergoing CABG, not only in terms of early and mid-term mortality, but also in morbidity, especially sternal infection. However, in patients with chronic lung disease and in obese diabetic patients, the risk of sternal infection is still unacceptably high and for them we advocate the use of single ITA plus SVGs instead of bilateral ITAs.

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15 Free Compared with Pedicled Right Internal Thoracic Arteries for Coronary Artery Bypass Grafting

J. TATOULIS, B.F. BUXTON, J.A. FULLER

15.1 Introduction

Bailey and Hirose [1] reported the use of the right internal thoracic artery (ITA) as a bypass graft in 1968. Shortly after its introduction, it became obvious that the pedicled right ITA could not always reach the appropriate target artery. Many surgical techniques were developed which aimed to maximize the length of the right ITA; for example, lengthening the pedicle by performing transverse fasciotomies, harvesting the ITA as a skeletonized graft, tunneling the graft through the transverse sinus and passing the graft anterior to the aorta across the midline to the left anterior descending artery (LAD) or diagonal [2–5]. In 1973, Barner et al. [6] and Loop et al. [7], independently of each other, transected the upper end of the ITA pedicle so that it could be used as a free graft. By anastomosing the proximal end to the ascending thoracic aorta, the free right ITA was able to be grafted to almost any distal coronary artery. The range and application of the free right ITA was further enhanced by the development of the T graft technique, whereby the proximal end of the free right ITA was anastomosed to the side of the left ITA [8]. Proximally, the right ITA has been anastomosed to the distal left ITA as an extension graft [9]. Sequential distal anastomoses further extended the use of the free ITA [10, 11]. The right ITA can be used as the proximal, “inflow” portion of an extension graft (RITA-LITA or RITA-radial), to reach distally to the distal right coronary (RCA) distribution, particularly if the ascending aorta is to be avoided [9].

Use of the right ITA has increased in popularity with wider applications in off pump coronary bypass surgery (OPCAB) – pedicled right ITA to the RCA, LITA-RITA T or Y grafts, and extension grafts RITA-RA – all avoiding proximal aortic anastomoses and manipulation.

There are a number of theoretical objections which may limit the use of the ITA when used as a free graft. Disease in the ascending thoracic aorta may create difficulty in performing the anastomosis between a thin walled ITA and a thick walled, or even calcified aorta [12]. Some surgeons have suggested, therefore, that the free right ITA should be anastomosed where possible to the left ITA [8, 13] or another appropriate graft, such as

the saphenous vein. Vasa vasorum occupy the adventitia but not the media or intima of the ITA. Ligation of the venous drainage results in a venous infarct of the free pedicle including the outer layer of the ITA, causing fibrosis. Loss of the sympathetic nerve supply may alter the vasoreactivity, and reduction of lymphatic drainage prevents the removal of large protein molecules from the pedicle and causes lymphedema. Despite these theoretical objections, Loop and colleagues [14] reported 91% (32/35) patency of the free ITA when anastomosed to the ascending thoracic aorta in a group of 156 patients restudied after more than 18 months (mean 94 months).

The Austin & Repatriation Medical Centre and Epworth Hospital, Melbourne (University of Melbourne), Australia, adopted a policy of bilateral ITA grafting in 1985. This paper compares the survival and angiographic patency data of 2,010 patients who received a pedicled right ITA, with 2,787 patients who received a free right ITA graft as part of a bilateral internal thoracic artery coronary bypass operation.

15.2 Materials and Methods

Between 1985 and 2002, 5,034 patients received a right ITA graft, 2,082 patients received a pedicled right ITA and 2,952 patients a free right ITA graft as part of a primary coronary artery reconstruction. All data were entered into a computerized database at the time of operation, at discharge and on routine follow-up. In 2,010 (96.5%) patients the pedicled right ITA was part of a bilateral ITA reconstruction; 2,787 (94.4%) patients received a free right ITA as part of a bilateral ITA reconstruction. A total of 4,797 patients had a bilateral ITA coronary bypass reconstruction. In a further 237 patients, the right ITA (72 pedicled; 165 free) was used without an additional left ITA, particularly when only the distal right coronary artery required revascularization. Reoperations and combined procedures, such as valve replacement or repair of a ventricular aneurysm, were not included. Myocardial revascularization was completed using saphenous vein (pre 1995), inferior epigastric or radial artery grafts.

15.3

Indications

The decision to use both ITAs was at the discretion of the surgeon and the indications varied. While a single left ITA graft to the LAD was almost universal, the right ITA was employed in only half the patients [15]. Currently, we perform total arterial grafting using both ITA grafts in patients younger than 70 years, supplemented by radial artery grafts when necessary. In general, bilateral ITA grafting was avoided in the elderly, obese patients, those with insulin-dependent diabetes, and in patients with severe lung disease.

The proportion of free ITA grafts varied during this study. Initially, only pedicled right ITAs were used. Commencing in 1987, the free right ITA was used with increasing frequency until the radial artery was introduced as an alternative in 1995. The number of right ITA grafts decreased after 1995, particularly in elderly patients [16]. At present, the policy is to leave the right ITA as a pedicle and attach it to the left system if possible. If there is any difficulty with the length of the pedicle when the heart is fully distended prior to commencement of cardiopulmonary bypass, the right ITA is transected and used electively as a free graft. The free right ITA is attached proximally to the aorta. If the aorta is diseased or additional length is required, the right ITA can be attached to the left ITA as a Y graft [8].

15.4

Surgical Technique

The left ITA was harvested with a wide pedicle after a median sternotomy. Since 1995 the left ITA has been harvested as a “semi-skeletonized” conduit which contains only the ITA and the medial vein. A “flap” of en-

dothoracic fascia was left in situ and covered the ITA ‘bed’ – assisting in hemostasis and in infection prophylaxis. This was facilitated using the Delacroix-Cabrol retractor (Paris, France). Side branches were clipped adjacent to the left ITA and the distal end cauterized, except for large branches, which were clipped at both ends and divided with scissors. The left ITA was completely mobilized from the level of the subclavian vein above, to its bifurcation distally. Dilation was achieved with intraluminal 1 mmol/l papaverine mixed with equal quantities of heparinized Ringer’s lactate and arterial blood (40 mg/100 ml at 37°C). Additional papaverine was sprayed onto the surface of the artery. The ITA was also loosely wrapped in a papaverine soaked gauze and placed between the left lung and pericardium until use. The distal end was clipped and the vessel allowed to dilate under pulsatile arterial pressure.

The right ITA was mobilized in a similar fashion to the left ITA and since 2000 has been harvested as a skeletonized conduit, and dilated with intraluminal papaverine (as indicated above). If the right ITA was to be converted to a free graft, the distal end was divided first at the ITA bifurcation and the unobstructed flow checked. Dissection of the upper end was completed by division of the right internal thoracic vein between medium hemoclips. Proximally, the right ITA and right IT vein (medially placed) are widely separated (Fig. 15.1). The right internal thoracic vein drains into the right brachiocephalic vein near its junction with the superior vena cava. The proximal right ITA was divided; usually, it was necessary to clip and divide the pericardiophrenic branch where it branches from the ITA just below the level of the subclavian vein. The proximal right ITA was divided after being double clipped at the level of the right subclavian vein, just before it was to be used for grafting.

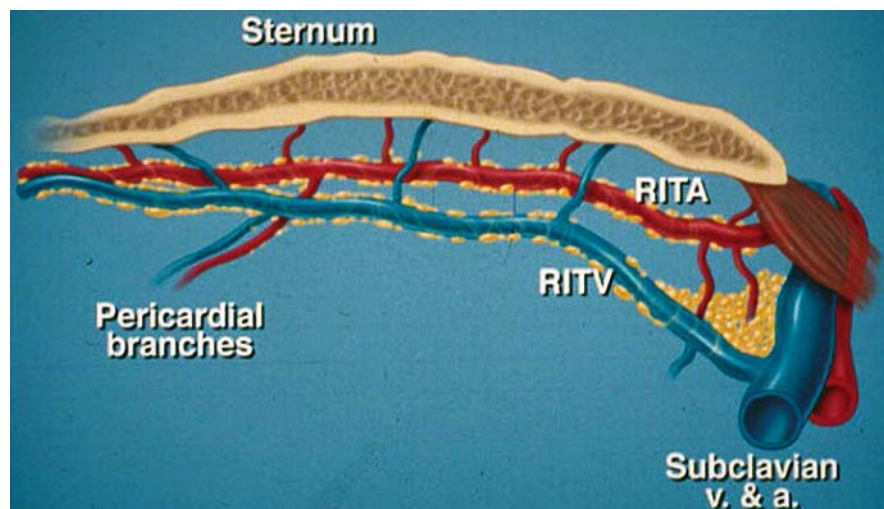


Fig. 15.1. Surgeon’s view of the right internal thoracic artery and vein. Note the wide separation between the internal thoracic artery and vein proximally

Cardiopulmonary bypass was initiated by cannulating the distal ascending thoracic aorta and right atrium. A separate cannula was placed in the coronary sinus for retrograde cardioplegia. Between 1985 and 1990 cardiopulmonary bypass was performed at 28°C, more recently (since 1991) it has been performed at 32–34°C. Antegrade blood cardioplegia was used initially at intervals of approximately 20 min and temperatures of 15–20°C and proximal anastomoses—including the free right ITA—were performed using a side biting clamp. However, since 1991, combined antegrade and retrograde blood cardioplegia has been given at 20°C. Both proximal and distal anastomoses were performed under a single cross clamp with the myocardial temperature kept at 25°C. Additional doses of retrograde blood cardioplegia were given after completion of each anastomosis and prior to release of the aortic clamp. The heart was vented through the aortic root. Vein grafts were usually placed first, followed by other non-ITA arterial grafts, the right ITA and, finally, the left ITA.

The strategy adopted for grafting was to suture the left ITA to the LAD and the right ITA to the second most important artery (Fig. 15.2). The distribution of pedicled and free right ITA grafts is shown in Table 15.1. Af-

Table 15.1. Distribution of RITA grafts ($n = 4,797$)

Coronary artery	Pedicled RITA ($n = 2,010$)	Free RITA ($n = 2,787$)
LAD (%)	29.5	8.2
DIAG/INT (%)	10.8	12.0
MARG (%)	15.2	48.8
RCA (%)	32.6	7.9
PD (%)	11.9	19.9
PLV (%)	0	3.2

RITA right internal thoracic artery, *LAD* left anterior descending coronary artery, *DIAG* diagonal branch, *INT* intermediate, *MARG* circumflex marginal branch, *RCA* right coronary artery, *PD* posterior descending branch, *PLV* posterior left ventricular branch of the right coronary artery

ter each distal anastomosis, the pedicle was secured with interrupted 7/0 polypropylene sutures to prevent rotation. Proximal anastomoses were performed directly with the ascending thoracic aorta to an elliptical opening created by a 3.5-mm punching using 6/0 polypropylene. If the aorta was atheromatous, the proximal anastomosis was performed directly with the left ITA as a “Y” graft or to another graft proximally. A vein patch was not used in any patient. After completion of cardio-

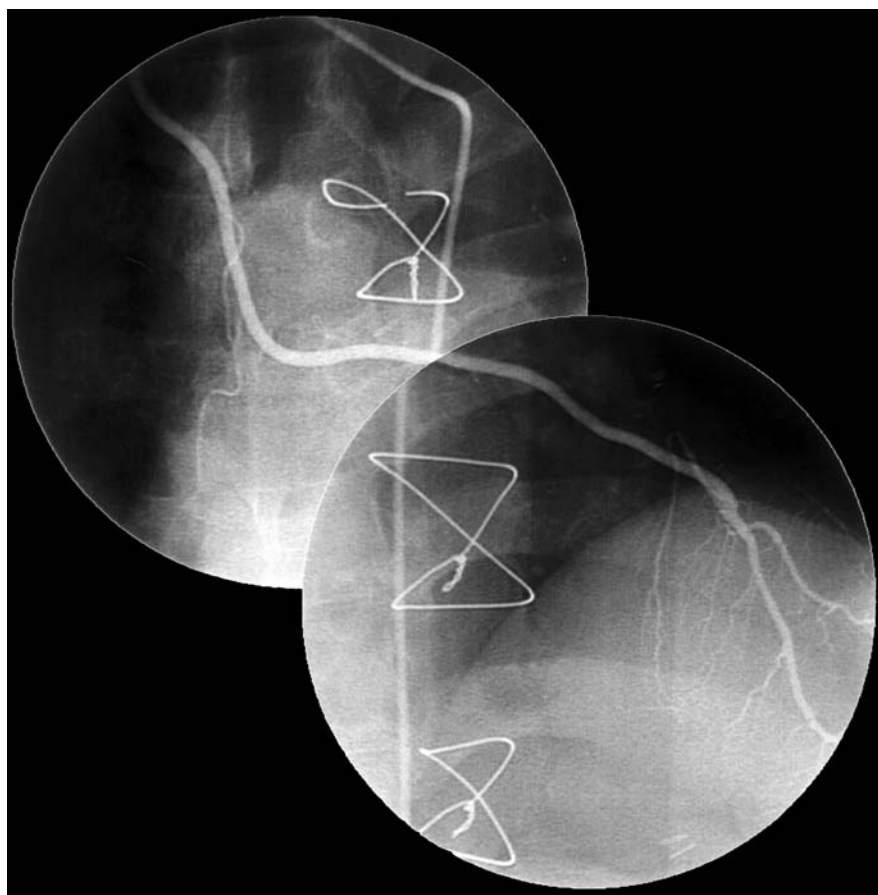


Fig. 15.2. Angiogram of a pedicled (in situ) right internal thoracic artery graft passing through the transverse sinus to the circumflex marginal

pulmonary bypass, blood pressure was kept at a mean of greater than 70 mm Hg and a systolic pressure greater than 110 mm Hg. A Swan-Ganz catheter was used routinely to maintain a cardiac index of 2.5 l/min/m² and a systemic vascular resistance of 800–1,200 dynes/s/cm⁵. The thymus, pericardium and pleurae were closed routinely with a drain in either pleural space and the anterior mediastinum.

15.5 Follow-up

Postoperative reviews were conducted during an office visit to the surgeon, cardiologist or family practitioner and by telephone interview. Postoperative coronary angiography was performed in response to symptoms suggestive of myocardial ischemia. Postoperative coronary angiographic data were collected directly from the cardiologist and catheterization laboratory, and each angiogram was reviewed by the cardiologist, radiologist and surgeon.

All data were placed on a computerized database and analyzed using the Statistical Package for Social Sciences (SPSS/PC). The significance of discrete variables was determined using the chi-square test; continuous variables were assessed using Student's *t*-test and expressed as mean $\pm$ one standard deviation. Survival curves were constructed using the Kaplan-Meier method. Differences between survival curves where the probability (*p*) was <0.05 using the log rank statistic were considered significant.

15.6 Results

The demographics of patients in the pedicled and free right ITA groups were very similar, except that the pedicled ITA group was younger and had a greater proportion of patients with a low ejection fraction compared with the free ITA group.

The distribution of grafts in the groups differed. Pedicled right ITA grafts were usually attached to the right coronary artery, posterior descending artery, LAD or diagonal branches. Free grafts were commonly anastomosed to the circumflex marginal or the posterior or descending branch of the right coronary system (Table 15.1).

Postoperative complications were similar in both groups and were low, with death and most serious complications having an incidence of approximately 1% each (Table 15.2). At 5 years after surgery, actuarial survival did not differ significantly and was excellent, with 5-year survivals of 95% and 94% respectively ($p=NS$) (Table 15.3).

Table 15.2. Postoperative complications ($n=4,797$ patients)

Complication (%)	Pedicled ITA ($n=2,010$)	Free ITA ($n=2,787$)	<i>p</i> value
Death	18 (0.9)	34 (1.2)	0.38
MI	36 (1.8)	31 (1.1)	0.08
Stroke	20 (1.0)	39 (1.4)	0.28
Bleeding	29 (1.5)	38 (1.4)	0.83
Sternal infection	10 (0.5)	17 (0.6)	0.62
CKMB	34.2 $\pm$ 47	20.7 $\pm$ 33	<0.001

ITA internal thoracic artery, MI perioperative myocardial infarction, CKMB creatine kinase isoenzyme myocardial band fraction (normal <20 IU/l), Bleeding return to operating room for hemostasis, Sternal infection deep infection requiring intravenous antibiotics or operation

Table 15.3. Probability of survival of patients with RITA grafts (4,797 patients)

Years	1	3	5	7	<i>p</i> value
Pedicled RITA ($n=2,010$)	99	97	95	91	NS
Free RITA ($n=2,787$)	98	97	94	89	

RITA right internal thoracic artery, NS not significant

Table 15.4. Probability of graft patency, free versus pedicled RITA grafts – 636 graft angiograms

Grafts	2 years	4 years	6 years	8 years	10 years
Pedicled RITA ($n=323$)	98	94	92	88	84
Free RITA ($n=313$)	96	93	89	82	79

RITA right internal thoracic artery
Reangiography performed for evidence or symptoms of ischemia, $p=NS$

Overall, graft patency following reangiography performed for symptoms or evidence for ischemia revealed the pedicled right ITA grafts to have similar patency compared with the free right ITAs at 10 years after operation ($p=NS$). A total of 636 right ITA grafts were studied angiographically, a mean of 80 months postoperatively; 562 (88.4%) were patent; 74 grafts (11.6%) had failed. Of the failed grafts, 3% had an 80–99% stenosis, and 8.6% were completely occluded. Right ITA graft patency was 89–92% at 6 years and 79–84% at 10 years (Table 15.4), with no significant difference for pedicled compared to free right ITA grafts.

There was a hierarchy of patency for right ITA grafts, according to the vessel to which they were grafted. Patency to the left anterior descending was best, being 96% (and similar to left ITA grafts to the left anterior descending – 97.2%, $p=NS$). Right ITA patency to the diagonal was 93%, to the intermediate and circumflex marginal vessels 90%, posterior descending coronary artery 87%, and right coronary artery 79% (Ta-

Table 15.5. Right ITA – relationship between target coronary artery and patency

Target artery	Number (<i>n</i> = 636)	% Patency
LAD	96	96
DIAG	48	93
Int, OM, OM2	226	90
RCA	141	79*
PDA, PLV	125	87

LAD left anterior descending artery, DIAG diagonal, Int intermediate, OM, OM2 1st and 2nd circumflex marginal arteries, RCA right coronary artery, PDA posterior descending branch (of right coronary), PLV posterior left ventricular branch (of right coronary)

* $p < 0.01$ for comparison of RITA-RCA and all other target arteries

ble 15.5). Patencies to the right coronary were clearly inferior.

When pedicled (in-situ) RITA grafts were compared to free right ITA grafts, patencies were similar for the left anterior descending and diagonal as target vessels (95 % vs 96.3 %, $p = \text{NS}$). However, patencies were better with free right ITA grafts when grafted to the circumflex system (84.7 % vs 91.9 %) and also to the right coronary system (79.2 % vs 90.9 %, $p < 0.02$) (Table 15.6).

There was a tendency for the degree of native coronary artery stenosis to affect right ITA conduit patency. In general, the more severe the native coronary artery stenosis, the greater the probability of patency. For the right ITA, the threshold effect for this was a 60 % coronary target vessel stenosis. In 605 right ITA conduits, where this information was studied, patency was 65 % (44/66) where the target coronary stenosis was < 60 %, and patency was 91 % (490/539), $p = 0.01$, where the target coronary artery stenosis was > 60 %.

For the right ITA conduits, there was a gradual decline of patency over time. Ten-year patency data comparing the pedicled right ITA and free right ITA are shown in Table 15.4. The results of grafting the LAD, diagonal or circumflex marginal using a right ITA were significantly better than when grafted to the right side ($p < 0.05$). A review of the patency of RITA grafts from the literature is shown in Table 15.7, displaying patencies of 90–94 % at 5 years and 86–90 % at 10 years postoperatively.

15.7 Discussion

The bilateral ITA reconstruction is a logical extension of single ITA grafting and follows the excellent late results and patency of pedicled left ITA grafts attached to the LAD [17–19]. The results of the pedicled right ITA as a coronary bypass graft are less consistent, especially if it is grafted to the right side [20], although excellent results have followed the use of a pedicled right ITA graft passing through the transverse sinus or anterior to the aorta to reach the left side [3, 4]. Grafting the pedicled right ITA to a major coronary artery is more difficult because of the asymmetry of the heart. Difficulty was encountered in judging the length of the right ITA pedicle, particularly when grafted to the right side. Often, the RCA, though patent at the site of intended anastomosis, was diffusely diseased and thick walled and the intended anastomotic site found to be unsuitable, thus requiring grafting more distally, usually to the posterior descending coronary arteries, often resulting in unintended tension on the right ITA. For this and other technical reasons the procedure was largely abandoned in later years. In many patients, therefore, the right ITA was used electively as a free rather than a pedicled graft [15, 16].

The theoretical advantages of the pedicled ITA are the maintenance of the normal arterial supply and venous drainage. Venous drainage of the arterial wall is by vasa vasorum and the internal thoracic veins and if obstructed causes edema of the outer layer of the arterial wall and other structures of the pedicle, which may lead to fibrosis. An intact lymphatic drainage may prevent lymphedema of the pedicle. An intact sympathetic nerve supply to the pedicle may also assist in the adaptation of the blood supply of the pedicle to varying physiologic demands. Implantation of a pedicled right ITA requires a single anastomosis, thereby eliminating any problems that may occur at the proximal anastomosis. This may be of particular importance if there is heavy calcification or thickening of the ascending thoracic aorta.

A free graft, on the other hand, can bypass almost any artery. It can be used on the left or right side and is normally of sufficient length to avoid tension, even

Target artery	Pedicled RITA (<i>n</i> = 323 angiograms)		Free RITA (<i>n</i> = 313 angiograms)	
	Total	% patency	Total	% patency
LAD, DIAG	113	94.7	29	96.4
Int, OM, OM2	54	84.8	174	92.0*
PDA, PLV, RCA	156	79.3	110	91.0*
Total	323	85.7	313	91.2
For total $p = 0.56$				

LAD left anterior descending artery, DIAG diagonal, Int intermediate, OM, OM2 1st and 2nd circumflex marginal arteries, RCA right coronary artery, PDA posterior descending branch (of right coronary), PLV posterior left ventricular branch (of right coronary). * $p < 0.02$

Table 15.6. Comparison between pedicled (in-situ) and free right ITA patencies (*n* = 636 at mean of 80 months postoperatively)

Table 15.7. Probability of graft patency – series

Series	Proximal anastomosis	Distal anastomosis	6 months	1 year	2 years	3 years	5 years	10 years
Free RITAs								
Loop et al. 1986 [14]	Aorta			31/40 (77%)				
Chocron et al. 1994 [22]	LITA (Y graft) LITA (Y graft)		39/62 (63%) 27/34 (75%)					
					10/12 (83%)			
Chow et al. 1994 [32]	Aorta							
Barra et al. 1995 [13]	LITA (Y graft)			52/61 (85%)				
Dion et al. 1996 [3]	Aorta			39/49 (80%)				
Tatoulis et al. 1997 [16]	Aorta					67/71 (94.5%)		259/284 (91%)
Late series 2004 [27]	Aorta							
Pedicled RITAs								
Buche et al. 1995 [24]		Circumflex via transverse sinus		73/74 (99%)				
Chow et al. 1994 [28]	LAD Non-LAD via transverse sinus				28/30 (93%) 26/35 (74%)			
Dion et al. 1993 [3]		Circumflex via transverse sinus		168/181 (93%)				
Ura et al. 1998 [37]			111/114 (97%)				62/67 (90%)	
Puig et al. 2004 [38]							46/50 (92%)	
Tatoulis et al. 2004 [27]								275/321 (86%)

LITA left internal thoracic artery, *RITA* right internal thoracic artery, *LAD* left anterior descending coronary artery

when grafted to the distal right coronary artery, the posterior descending coronary artery or the posterolateral branches from either the right or distal circumflex coronary arteries [16]. Where a more proximal coronary artery is to be grafted, the lower 1–3 cm of the right ITA, which contains increasing amounts of smooth muscle towards the lower end, is excised [21]. This leaves the proximal part of the right ITA, which is larger in caliber and less prone to spasm [21]. Recently, it has become popular to attach a free right ITA to the pedicle of the left ITA (LITA-RITA T or Y graft) to maximize the length or to avoid an aortic anastomosis and achieve efficient conduit use. This is also an extremely useful technique to avoid aortic manipulation and clamping in off-pump coronary bypass [9, 21–24].

Pedicled grafts were more frequently attached to a proximal site on a larger coronary artery, in contrast to free grafts which were anastomosed more often to the posterior descending artery, posterolateral branches of the right coronary artery and circumflex marginal branches on the left. Any valid comparison between the outcome following pedicled and free right ITA grafting, therefore, must take into account these differences in graft distribution.

Angiographic studies following surgery suggest that a pedicled right ITA has a greater patency compared with a free right ITA [3, 25, 26]. Our results show similar patencies when pedicled or free right ITA grafts are placed to the left system – and indeed are comparable to patencies achieved by the left ITA to the branches of the left coronary system [27]. The results of attaching a pedicled right ITA to the right system were not as satisfactory. On the right side, free grafts appear to be more satisfactory than pedicled grafts, and have the advantages that they can reach the distal vessels without tension and are easy to suture [16, 27].

As coronary territory grafted affects the patency of the right ITA (LAD diag > OM > RCA), there may be benefits of RITA grafting to branches of the left coronary artery [26].

The routine mobilization of the right ITA as a skeletonized graft guarantees a further 2–4 cm in length, enabling construction of a more distal anastomosis if an intended more proximal anastomotic site is unsuitable. Early concerns regarding the skeletonization technique (trauma and disruption of vascular supply to the ITA wall) have been discounted by excellent angiographic results [28]. As native coronary artery stenosis (threshold 60%) appears to influence right ITA patency (as well as left ITA and radial artery patencies), it follows that the best long-term patency results with the right ITA will be achieved when it is grafted to tightly stenosed and important coronary vessels [26, 27]. The mode of failure of right ITA grafts is different from the intimal hyperplasia, atheroma and thrombosis seen in aortocoronary saphenous vein grafts. Right ITA grafts

(and other arterial grafts) fail by either developing total occlusions (possibly due to technical factors), string signs (most likely due to competitive flow and autoregulation) or localized stenoses (localized trauma or wall disease) [27].

Survival differences between bilateral and single ITA reconstructions have been difficult to demonstrate and the validity of benefits remains controversial [3–6, 29–31]. Different grafting techniques, for example, pedicled or free grafts [15, 16], attaching the right ITA to the left or to the right sided vessels [4, 26, 32], grafting to dominant or non-dominant arteries [33], and the use of T graft techniques, have clouded the interpretation of the results. In general, however, it appears that using both ITAs – whether the right ITA is pedicled (in-situ) or free, – confers a survival benefit to patients [34–36].

Currently we prefer to use bilateral internal thoracic arteries in patients 70 years or younger, and based on current clinical and patency results, we would recommend placement of the left ITA to the left anterior descending, the right ITA either as a pedicled (if it reaches comfortably) graft or a free graft to the circumflex marginal system, and use of a radial artery to the distal right coronary artery, or preferably the posterior descending coronary artery.

15.8 Conclusion

This study confirms that the right ITA is an excellent conduit for coronary artery bypass grafting. Excellent patency of the right ITA was observed when it was grafted to the LAD, diagonal, intermediate or proximal circumflex marginal branches, suggesting that preference should be given to the use of a right ITA when grafting to one of the coronary arteries on the left side (after the LITA). However, there were differences in patency between pedicled and free right ITAs when grafted to the right side. Free right ITA grafts are recommended for grafting the distal right coronary artery or its branches, and for bypassing the distal circumflex marginal branches because of their greater flexibility. Survival after bilateral ITA grafting was excellent, whether the right ITA was pedicled or free.

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Radial Artery Grafting

History and Operative Technique

C. ACAR

16.1 History

In 1971, Carpentier used for the first time the radial artery (RA) to bypass the coronary arteries [1]. A series of 30 patients were then operated upon using the RA. Four years later, at the Annual Meeting of the American Association for Thoracic Surgery in New York, Carpentier reported that one-third of the RA grafts were occluded [2]. He suggested that occlusion of this arterial conduit was due to spasm of the denervated vessel and concluded that the RA should no longer be used as a graft until this physiological problem had been resolved. Other reports from small series [3, 4] confirmed these results and the use of the RA was completely abandoned.

In 1989, Carpentier received from a referring cardiologist an angiographic follow-up of a patient operated on 14 years earlier using the RA anastomosed to the LAD, which at that time was considered to be occluded. The recent follow-up showed a perfectly patent RA graft revascularizing the LAD with no evidence of graft disease. Five additional angiographic follow-ups of patients operated on in the early 1970s using the RA showed perfectly patent RA grafts 13–18 years postoperatively (Fig. 16.1). He hypothesized that the technique of preparation of the RA had been responsible for graft failure. The RA was dissected alone separately from the satellite veins. Moreover, progressive instrumental dilatation of the vessel was performed using metallic probes which might have caused intimal damage. At that time, no antispastic drug was available.

In view of the advances in arterial revascularization together with an improved understanding of the vasoreactivity of arterial conduits, he decided that the use of the RA for coronary bypass should be reinvestigated. Harvesting of the vessel was performed using a perfectly atraumatic technique. The artery was dissected “en bloc” with the satellite veins similar to the internal mammary artery (IMA) dissection and no instrumental maneuver was performed. Conversely, the artery was dilated using blood and papaverine at a low pressure and antispastic drugs (diltiazem) were administered. Both early [5] and 5-year [6] clinical and angio-

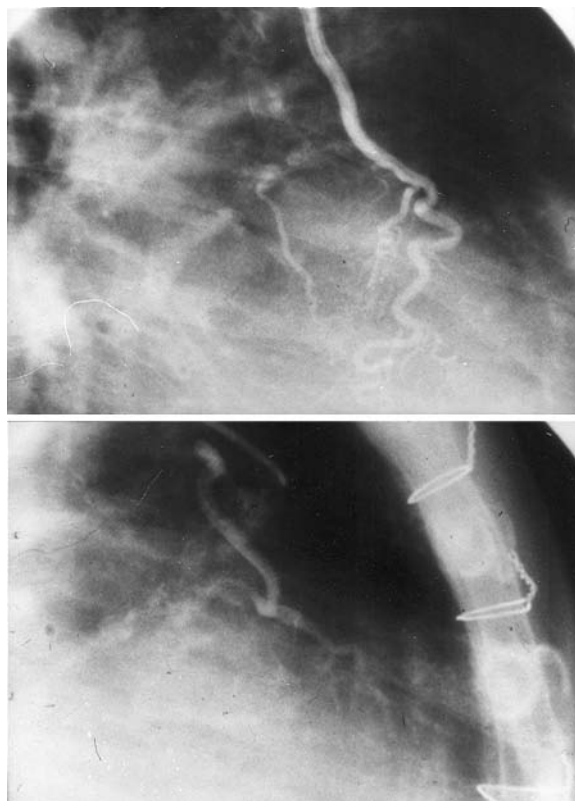


Fig. 16.1. Two radial artery grafts in the same patient followed up at 18 years (from *Ann Thorac Surg* 1992; 54:652–660 with permission)

graphic results were satisfactory and the RA was rehabilitated as a graft of choice for coronary surgery.

16.2 Preoperative Assessment

16.2.1 Risk for Hand Ischemia

In 1929, Edgar V. Allen [7] described a clinical test for evaluating the respective contribution of the ulnar and radial arteries to the blood supply to the hand. The fist is clenched, and both the radial and the ulnar arteries

are occluded by manual compression, until complete exsanguination of the hand is obtained. The occlusion of the ulnar artery is released and the time needed for return of the coloring of the extremity is measured. The Allen test is considered positive whenever full coloring of all fingers is not obtained beyond 6 s. This test has been used extensively prior to catheterization of the radial artery. In reality, a number of studies have shown that the Allen test is not reliable due to the frequency of false-positive and false-negative results [8] with failure to predict collateral blood flow through the palmar arches.

Many attempts at increasing the sensitivity of the Allen test have been made. By means of a digital oximeter using a probe at the thumb, oxygen saturation in the radial artery territory was measured [9]. Occlusion of both forearm arteries abolished the normal oxygen saturation curve, and failure of a normal tracing to reappear following ulnar artery reopening would translate into inadequate blood flow.

Similarly, measurement of the digital pressure at the thumb was performed using a pressure cuff placed at the proximal phalanx. A systolic digit pressure below 40 mm Hg was interpreted as a positive test [10]. Others have proposed flow assessment of the main artery of the thumb (princeps pollicis artery) using Doppler ultrasound. Alteration of the normal (triphasic) signal would mean a poor collaterality from the ulnar artery [11–14].

Finally the superficial palmar arch flow was directly measured by means of a Doppler probe placed at the third metacarpal head. A persistent decrease of the audible Doppler signal in the palmar arch following RA compression was considered as a predictor of insufficient ulnar artery back flow [15–18].

Application of the classic Allen test or its modifications described above would lead to the exclusion of a number of potential candidates for radial artery removal (20–40%). Little correlation has been found between the Allen test and the anatomy of the blood supply to the arm. In the author's experience, the Allen test has completely failed to identify the potential limitations for RA removal and there has not been a single contraindication for RA removal due to fear of hand ischemia. However, in two patients, a technical error resulted in stenosis at the origin of the ulnar artery due to proximal ligation of the RA and required rapid surgical reintervention with no further consequences. Even in patients whose job requires vigorous use of the upper limb, removal of the RA has been proven to be safe and has not resulted in any significant functional incapacity [19]. The same has been found for elderly patients [20]. Large anatomical studies with angiographic correlations of arterial variations in the upper limb have shown that the ulnar artery is invariably present and that the risk for ulnar artery agenesis is virtual. Pre-

and postoperative flow measurements using either plethysmography or Doppler ultrasound have demonstrated an adaptation of the blood supply distribution in the forearm following RA removal. The flow in the distal brachial artery in the elbow region reflects the blood supply to the forearm; it has remained unchanged following RA harvesting. This is made possible by an increased flow in the ulnar artery during the early postoperative period, although no change in size of this artery could be detected [21]. The lack of peripheral resistance related to radial artery flow competition through the palmar arches probably accounts for the increased flow while the caliber of the ulnar artery remains unchanged. Conversely a few months later, vasodilation of the ulnar artery becomes apparent with a significant and persistent increase in size (approximately 15%) [21].

In summary, the decision for using or not using this conduit should no longer rely on the Allen test. The author's experience has shown that the RA can safely be removed in all cases with no evidence of hand ischemia provided that the operative technique is correct. Other groups have also reported extensive use of the radial artery graft with no ischemic complications [19]. This does not signify that the RA is a suitable graft in all situations. Contraindications for using the RA are not infrequent; however, these are related to the anatomy of the RA itself rather than to the variability of the blood supply distribution to the upper limb.

16.2.2

Contraindications for Using the RA as a Coronary Graft

16.2.2.1

Anatomical Variations

Anatomical variations of the RA are rare and concern mainly the origin of the vessel merging from the brachial or axillary artery [22–24]. An abnormality in the origin or a variation in the course of the RA does not preclude using it as a graft; it requires slight changes in the operative technique which are described below. The size of the RA is almost always perfectly matched with that of the coronary vessels. In exceptional female cases (<0.5%), however, a severe hypogenesis of the RA defined as an RA diameter below 1.5 mm in spite of spasm release maneuvers can be encountered and constitutes a contraindication. It is then probably preferable to use a saphenous vein since the internal mammary arteries are usually also undersized.

16.2.2.2

Pathology of the RA

The main contraindications for using the RA are due to the pathological involvement of this artery, which is more frequent than that of the internal mammary ar-

tery. In patients with severe diabetes mellitus, the RA can be the site of mediocalcinosis (non-obstructive calcifications of the RA wall). In patients with multifocal atherosclerosis, atheromatous stenosis and occasionally thrombosis of the RA can be observed. The incidence of macroscopic RA calcification among patients requiring coronary bypass grafting is approximately 5%. Histological studies have found evidence of microscopic calcification in up to 13% of the cases [25, 26]. Not surprisingly, age and smoking have been identified as risk factors for RA calcification. The proximal portion of the RA lying underneath the brachioradialis muscle is less frequently affected by the calcifying process. Calcification of the vessel wall, whether mild or moderate, must preclude the use of the RA.

In patients who have undergone prior catheterization of the RA (blood gases, pressure monitoring), focal fibrosis or dissection of the distal portion of the vessel can be observed. Again, the proximal part of the RA is usually intact. Similarly, the RA approach for coronary angiography which is increasingly used by cardiologists can potentially create traumatic lesions to the intima due to the spastic reaction of the artery on the guidewire. A report including control angiograms showed a decreased early patency of RA grafts in patients having undergone transradial catheterization [27]. Until more data are available, preoperative retrograde catheterization of the RA should be considered as a relative contraindication for using this conduit.

Preoperative Doppler ultrasound assessment of the RA can evaluate the quality of the RA wall and its patency with a good sensitivity, thus avoiding an unnecessary skin incision. Therefore, this test is recommended prior to any RA harvesting. In addition, Doppler study can verify the integrity of the other arteries of the upper limb. In case of a tight stenosis of the subclavian artery, brachial artery or ulnar artery RA harvesting is not advised. Finally, in severe renal insufficiency that may require chronic hemodialysis, it seems preferable to preserve the use of the RA for an arteriovenous fistula. On the whole in the author's series, the frequency of non-usable RA grafts was 7%.

16.3

Operative Technique

16.3.1

Harvesting and Preparation of the RA

The left radial artery is harvested in right-handed individuals and vice versa. The patient is positioned with the arm at a 90° angle to the longitudinal axis of the body. Arterial blood pressure is monitored using a radial artery catheter on the opposite side. No intravenous catheters are inserted on the side of RA harvesting because section of the superficial veins would produce

a back flow from the infusion line in the operative field. The dissection of the RA is performed simultaneously with that of the IMA.

The incision starts laterally 2 cm above the wrist and extends medially to the interline of the elbow (Fig. 16.2). The antibrachial fascia is incised above the vascular pedicle. In the upper third of the forearm the RA runs deep underneath the brachioradialis muscle, which is retracted laterally without being divided (Fig. 16.3). The numerous collateral branches are occluded using metallic clips, and the vascular pedicle is harvested "en bloc" with the artery and both satellite veins. Most of the dissection can be carried out without electrocautery.

Anatomical variations of the RA require slight technical changes. Rarely, the distal part of the vessel lies superficially above the antibrachial fascia [28]; this is a usual location of the accessory RA in exceptional cases of duplication of this vessel RA; however, the operative technique remains unchanged. The RA can be harvested up to the bifurcation of the brachial artery depending upon the number of grafts required and their respective length. The only potential hazard that might be encountered is damage to the ulnar artery. In fact, the bifurcation of the brachial artery is usually located below the elbow and the origin of the ulnar artery lies deep posteriorly hidden by the muscle belly of the pronator teres (Fig. 16.3). Injury to this vessel must be avoided during the dissection or the proximal ligation of the RA graft. Two anatomical landmarks indicate the proximity of the bifurcation of the brachial artery: the emergence of the recurrent radial artery and a dense venous network around the RA (Fig. 16.3). It is recommended to keep a distance of 1 cm from the brachial bifurcation.

Rarely, the RA originates either from the proximal brachial artery or from the axillary artery (14% of cases [22]). This anatomical variation is clinically relevant since if the origin of the RA is not found in the elbow, the incision should not be extended further proximally. The skin healing process can be altered when the interline of the elbow has been divided.

Following explantation, the RA is usually vasoconstricted and should not be immediately used for bypass. It should first be stored in a solution of blood, heparin and papaverine. The proximal end of the RA is then catheterized using a 16-gauge Cathlon catheter and hydrostatic dilatation is achieved at a low pressure using the same mixture (Fig. 16.4). Thus, the surgeon can visualize complete release of the spasm and check hemostasis of small collateral branches. It has been shown that this procedure does not damage the vessel wall and in particular the intima [28].

Some authors have reported modifications to the aforementioned harvesting technique including RA skeletonization, use of an ultrasonic scalpel or endo-

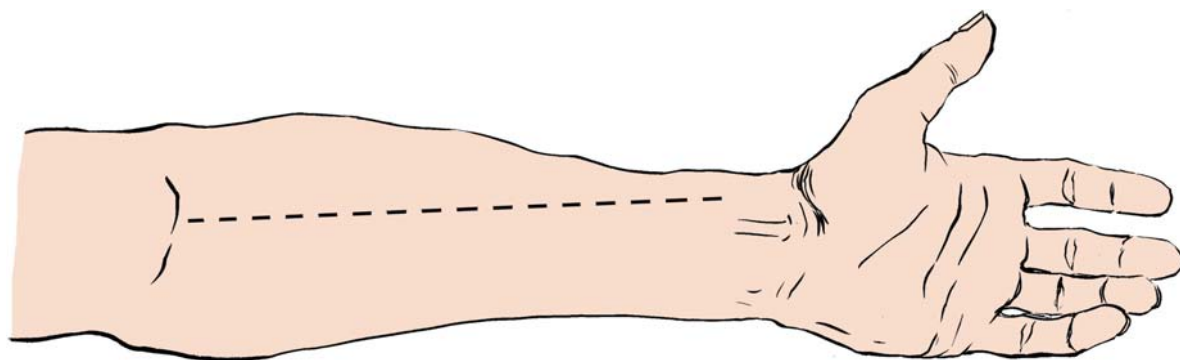


Fig. 16.2. Incision extends from lateral at the wrist to median in the elbow region



Fig. 16.3. The brachioradialis muscle is retracted. The ulnar artery lies deeply hidden by the pronator teres muscle. The radial artery is removed en bloc with the satellite veins

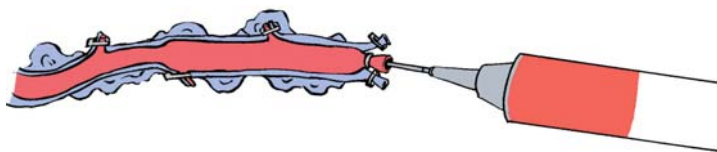


Fig. 16.4. Spasm is released using gentle injection of a mixture of heparinized blood with papaverine

scopic techniques [29–31]. The advantages of these techniques over the conventional approach are questionable.

16.3.2

Technique of Coronary Bypass Using the RA

The surgical technique of coronary bypass using the RA presents few distinctive characteristics. The distal anastomosis is performed in the usual manner using 7/0 or 8/0 Prolene depending on the wall thickness and diameter of the target vessel. When repeating cardioplegia care should be taken to clamp the RA in order to avoid steal through the graft, which contains no valves. Proximal anastomosis is performed directly on the ascending aorta using a side-biting clamp. When the target vessel is a proximal obtuse marginal one, the RA graft is anastomosed to the posterior aspect of the aorta via the transverse sinus. In other

cases, the anastomosis is constructed on the anterior aspect of the aorta. A 4-mm circular aperture is created in the aortic wall using a punch and the RA is sutured directly to the aorta using 7/0 Prolene. The RA graft can be used for sequential revascularization; it also constitutes an excellent site for proximal anastomosis of other arterial grafts (additional RA graft or free ITA).

First described by Calafieri [32], proximal anastomosis of the RA to the ITA is an alternative technique of creating a composite arterial graft. This technique is technically challenging and dysfunction of one graft can occur in the case of geometric distortion. The site of anastomosis between the two vessels is important. The best location is the initial part of the left ITA graft lying against the pleural proximally to the pericardial cavity. The length of the RA graft should also be carefully measured as it is a potential source of traction on the IMA pedicle (if too short) or kinking of the RA con-

duit (if too long). Ideally the anastomosis is completed so as to orientate the two arteries in parallel.

As a rule, the author favors proximal anastomosis of the RA to the ascending aorta rather than to the ITA. The results of the two techniques are discussed elsewhere.

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17 Radial Artery Grafting: Clinical Antispastic Protocols

G.-W. HE

Various arterial grafts have been used for coronary artery bypass grafting, but there is no unanimous opinion as yet about the best use of these grafts, except that the internal mammary artery (IMA) has been accepted as the first choice, usually for the left anterior descending artery (LAD) if the artery needs to be grafted [1, 2].

The patency rate of the radial artery (RA) is more dramatic. A disappointing 35 % incidence of narrowing or occlusion of the RA has been reported [3, 4]. With modified technique, avoiding skeletonization and using calcium antagonists, the early patency increased to 93.5 % at 9 months in Acar's group [5] and 93.1–95.7 % in other groups [6, 7] at 3–21 months in the early stage of the use of RA. Latterly, Acar and colleagues reported that the patency rate of the radial artery grafts was 83 % at 5 years [8]. In addition, Tatoulis and associates reported that the radial artery patency at 1 year was 96 % and at 4 years it was 89 % [9]. The higher patency of the RA was associated with greater coronary stenosis.

Arterial grafts are not uniform in their biological characteristics (see Chaps. 3, 4). The difference in the perioperative behavior of the grafts and in the long-term patency may be related to different characteristics. According to our functional classification [10, 11], the RA belongs to the Type III arterial graft – a type of graft that is more spastic than Type I arteries (such as IMA and inferior epigastric artery, IEA). In our experience and according to the experience of others [5, 12, 13], the RA contraction (or spasm) is almost inevitably encountered during the surgical dissection or even in the postoperative course [3, 14]. The spastic character-

istic of the RA is related to its differences in the endothelial function compared to the IMA, involving either nitric oxide [15] or prostacyclin [16] and the smooth muscle contraction [17, 18]. Therefore, the characteristics of the RA warrant the use of vasodilators during harvesting and postoperative course. In fact, the use of vasodilators is a key step in the revival of the RA [5]. In the standard protocol suggested by Acar et al. [5], diltiazem is used as the systemic vasodilator and papaverine is used topically during harvesting.

On the other hand, the long-term patency of the coronary bypass grafts in general depends on the endothelial function. If the endothelium is damaged, thrombosis formation and platelet aggregation occur and this is closely related to the occlusion of a graft [19].

Due to the importance of antispastic protocols in the preparation of RA and postoperative care, a number of protocols have been clinically used. The existing technique to overcome spasm of the radial artery is listed in Table 17.1. These protocols involve using calcium antagonists and nitroglycerin (NTG), although the choice of systemic and topical use varies [20–25], based on the comparison of the effect of these drugs on the RA [26–34].

An ideal antispastic protocol should fulfill the following criteria: (1) excellent antispastic (vasorelaxant) effect; (2) maximal preservation of the vascular endothelial function; (3) readily used perioperatively; and (4) no major side effects.

Table 17.1. Existing techniques to overcome spasm of the radial artery [26]

Authors	Topical	Systemic	Postoperative oral
Acar et al. [5]	Papaverine + blood	Diltiazem	Diltiazem
Dietl et al. [20]	Papaverine diltiazem “if spasm is noted”	Diltiazem	
Reyes et al. [21]	Papaverine 60 mg + 60 ml blood	Diltiazem	
He [22, 23]	VG (verapamil + nitroglycerin)	Nicardipine ^a	One calcium antagonist ^b
Esmore [24]	VG (verapamil + nitroglycerin)	Nitroglycerin	
Tatoulis [9]	Papaverine	Nitroglycerin	Amlodipine

^a Nicardipine is used in the modified protocol, instead of the previous use of verapamil

^b One calcium antagonist (nifedipine/nicardipine/diltiazem/verapamil) is used according to the availability, the patient condition, and the preference of the cardiologist

17.1

GWH Protocol (Previously University of Hong Kong Protocol)

To search for such a method, we systematically studied the effect of a number of vasodilators on arterial grafts [29, 30, 32–49; see also Chap. 6]. To choose a calcium antagonist [50, 51] to be used for RA grafting, we reviewed our previous pharmacological studies which compared the effect of calcium antagonists from three chemically divergent groups – dihydropyridine (nifedipine, etc.), phenylalkylamines (verapamil, etc.), and benzothiazepines (diltiazem, etc.) in the human IMA [35] and other vascular tissues (canine coronary arteries [36]). We demonstrated that the combination of verapamil and nitroglycerin solution (VG solution), balanced to pH 7.4, may provide a rapid onset, complete relaxation, and long-lasting vasorelaxant effect [23], and maximal preservation of endothelial function [24], when used to prepare the RA for grafting. In addition, verapamil has other advantages in coronary diseases [52], inhibiting platelet thrombus formation in humans [53], inhibiting neointimal smooth muscle cell proliferation and ameliorating vasomotor abnormalities in experimental vein bypass grafts [54].

17.1.1

Comparison of Four Calcium Antagonists in the Radial Artery (Figs. 17.1, 17.2)

We compared the vasodilator effect of four commonly used calcium antagonists from three chemically divergent groups – dihydropyridine (nifedipine and nicardipine), phenylalkylamines (verapamil), and benzothiazepines (diltiazem) in the human RA [33].

All calcium antagonists induced a full relaxation (97.8–100%) with higher sensitivity to nifedipine ($-7.37 \pm 0.20 \log M$) than nicardipine ($-6.43 \pm 0.39 \log M$), verapamil ($-6.08 \pm 0.13 \log M$), and diltiazem

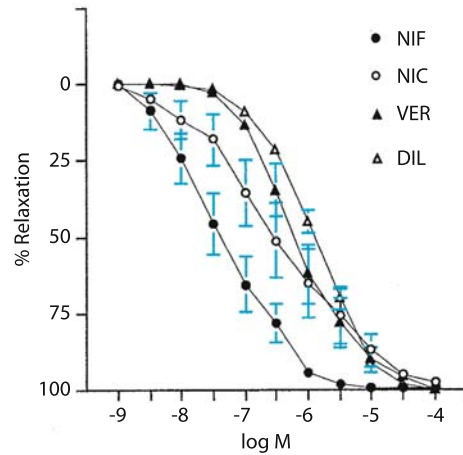
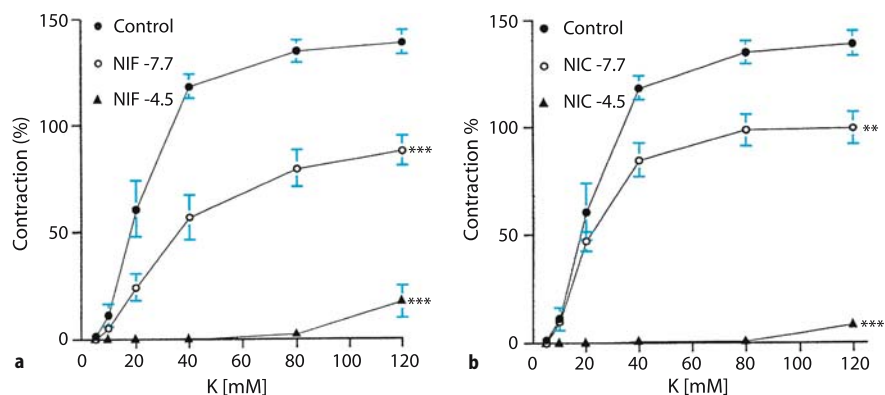


Fig. 17.1. Mean concentration ($-\log_{10} M$)-response (% relaxation) curves for four calcium channel antagonists in the human radial artery precontracted by potassium chloride (K^+ , 25 mM; $n=6$ for NIC, $n=6$ for NIF, $n=5$ for VER and DIL). The rings were taken from at least three patients in each group. Vertical error bars are 1 SEM of mean values (NIF nifedipine, NIC nicardipine, VER verapamil, DIL diltiazem). (Reproduced from *J Thorac Cardiovasc Surg* 2000; 119:94–100 with permission)

($-5.87 \pm 0.07 \log M$). Pretreatment with the plasma concentration of the CCA (60 nM for diltiazem and 20 nM for the others) inhibited the K^+ -induced contraction by nicardipine (from $138.6 \pm 5.8\%$ to $101.4 \pm 7.6\%$) and nifedipine (to $87.7 \pm 6.8\%$) but not by verapamil (to $140.3 \pm 15.2\%$) or diltiazem (to $132.8 \pm 7.3\%$), although at higher contraction ($-4.5 \log M$) all the four calcium antagonists abolished the contraction. We therefore concluded that although all calcium antagonists have an antispastic effect in the RA, the vessel has a different sensitivity to them. Dihydropyridine derivatives may be the most potent ones and are therefore recommended for clinical use for this purpose.

Taking together the aforementioned information, we designed a new protocol [GWH Protocol, previously named the University of Hong Kong (UHK) Protocol]

Fig. 17.2. Mean concentration ($-\log_{10} M$)-contraction (percentage of 100 mM K^+ -induced contraction) curves for four calcium channel antagonists: NIF **a**, NIC **b**, VER **c**, and DIL **d**. Rings were allocated to each treatment. One ring was the control (solid circles) without pretreatment of calcium antagonists. The second ring was treated with the plasma concentration of the particular calcium channel antagonists (open circles): 20 nM ($-7.7 \log_{10} M$) for NIF **a**, NIC **b**, and VER **c**; 60 nM ($-7.2 \log_{10} M$) for DIL **d**



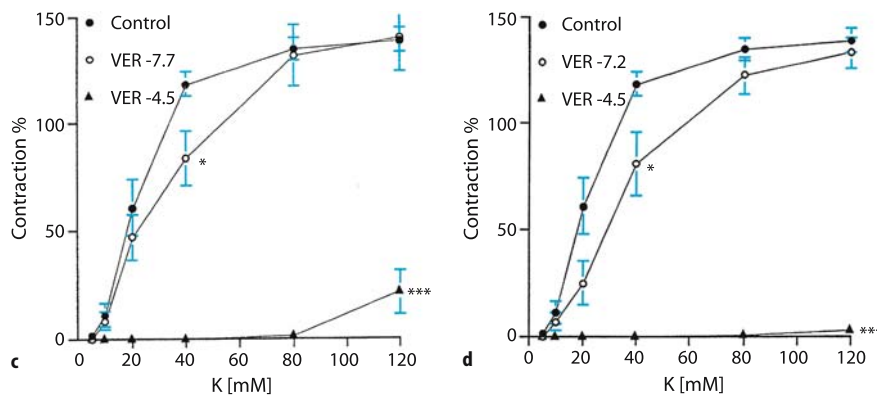


Fig. 17.2. (Cont.) The third ring was treated with a high concentration of the calcium channel antagonists (solid triangles, $30 \mu\text{M} = -4.5 \log_{10} M$), which implies the topical use of the drug. The drug was added to the organ bath 20 min before the start of the concentration-contraction curve. Symbols represent data averaged from six rings (from six patients) for each calcium antagonist. Vertical error bars are 1 SEM of mean values. Comparing the three curves at maximal contrac-

tion, $p=0.0002$ for NIF **a**, $p=0.003$ for NIC **b**, $p=0.9$ for VER **c**, and $p=0.5$ for DIL **d** (ANOVA). * $p<0.05$; ** $p<0.01$; *** $p<0.001$, compared to control (Scheffe F -test) (NIF nifedipine, NIC nicardipine, VER verapamil, DIL diltiazem). (Reproduced from He GW and Yang CQ: *J Thorac Cardiovasc Surg* 2000; 119:94–100 with permission)

to use the RA as a graft for coronary artery bypass grafts (CABG) [24]. This protocol has been used routinely in our practice, and recently we have modified the protocol. This is based on two considerations: first, when verapamil is given systemically (either IV or orally), its effect of bradycardia is often the indication to withdraw and it cannot be used together with β -blockers. Secondly, because our new study comparing calcium antagonists on the human RA [33] demonstrated the superiority of dihydropyridine derivatives to other types of calcium antagonists and the fact that nicardipine, as a dihydropyridine derivative, is available both in IV and oral preparations, we have changed the systemic calcium antagonists from verapamil to nicardipine.

The purpose of this section is to review the antispastic effect of the GWH Protocol and its effect on endothelial function in the RA.

17.1.1.1

The GWH Protocol (Modified UHK Protocol)

The protocol includes pre-, intra-, and postoperative management.

Preoperative

1. The Allen test for both arms
2. The Doppler flow examination for the ulnar artery during the Allen test and for the RA flow to demonstrate its patency

Intraoperative

1. Use verapamil plus nitroglycerin (VG) solution (see below) topically during harvesting
The components of the VG solution are as follows [23, 24, 37, 42]:
 - Verapamil hydrochloride: 5 mg

- NTG: 2.5 mg
 - Heparin: 500 units
 - 8.4% NaHCO_3 : 0.2 ml
 - Ringer's solution: 300 ml
- This solution gives a concentration of about $30 \mu\text{mol/l}$ of verapamil or NTG in an isotonic solution of pH 7.4.
2. The radial artery is removed as soon as dissected from the arm and stored in the VG solution at room temperature.
 3. Once the harvesting of the radial artery is started, low dose nicardipine (0.5 mg/h; 5 mg in 100 ml D5 W, IV at the rate of 10 ml/h) is given systematically.

Postoperative

1. Nicardipine IV at the same dose until the patient is able to take oral calcium antagonists
2. Low oral dose of one of the calcium antagonists for at least 6–12 months. This can be nicardipine 20 mg twice a day; or nifedipine (retard preparation) 20 mg/day; or verapamil 120–240 mg/day (a test dose of 120 mg is recommended); or diltiazem at an appropriate low dose. The choice of calcium antagonist (nifedipine/nicardipine/diltiazem/verapamil) is based on availability, patient condition particularly heart rate, and the preference of the cardiologist.
Beta-blockers should be used with caution when some of the calcium antagonists are given.

17.1.1.2

Harvesting Technique for the Radial Artery

The surgical dissection of the RA basically follows the technique described previously [5, 22] except that we now use two small incisions with a skin bridge between them instead of one long incision for minimally inva-

sive purposes. Once the harvesting of the radial artery is started, low dose nicardipine (0.5 mg/h) is given intravenously. A short skin incision (4 cm long) parallel to the distal RA course is used. The RA is carefully dissected with its accompanying veins and the connective tissue. The side branches are carefully identified and clamped by small size hemoclips. During harvesting, VG solution may be used to bath the RA. Leaving a skin bridge, a proximal skin incision (4 cm long) is made along the RA course that is identified from the distally dissected RA. The artery is removed as soon as it is dissected out. The RA is immediately placed into a bowl containing a large enough volume of VG solution to be completely immersed. Gauze-wrap technique is not used, for it may not be as efficient as the immersion method to allow the artery (both the adventitia and the intima) to have complete contact with the solution. The RA is checked after at least a 15-min immersion in the VG solution, allowing full relaxation of the artery [23, 24]. A 24-gauge plastic arterial puncture needle sheath is inserted into the RA (usually proximal end) and the artery is gently held with the fingers. A clean VG solution is injected through the needle to flush (not distend) the RA with the other end freely open. This gentle flush at low pressure will not distend the artery and its purpose is to flush out any possible blood clots in the artery and to test the patency of the artery. This flushing procedure is not done specifically for detecting side branch leakage, but some large branches may be detected at this time. For easy detection of leakage, one may use heparinized blood to flush the RA lumen, then use VG solution to flush again. In our experience, there is no need to flush the RA lumen with blood for this purpose. If the RA is to be used after vein grafts, it is placed back in clean VG solution and stored in the bowl until use. The distal end of the RA is anastomosed to the coronary artery with a 7-0 Prolene running stitch. When the heart is resuscitated, usually there is back flow from the proximal end. Side branch bleeding may be easily detected during this period and stopped by a hemoclip. A 3.6-mm punch is used to make an oval hole in the ascending aorta. The proximal end is directly anastomosed to the aorta with a 6-0 Prolene stitch.

17.1.1.3

Antispastic Effect of GWH Protocol

A series of in vitro experiments using the human RA segments taken from CABG patients receiving the RA as a graft were designed to investigate the antispastic effect of VG solution and the acting duration of the solution. The experiments were conducted in organ baths [23, 24]. The effect of nicardipine on RA was also demonstrated [33].

Effects of VG Solution and Comparison to Papaverine [14]. After the normalization procedure, the vascular rings were equilibrated for at least 1 h. K^+ (potassium chloride, 25 mM) was added to the organ bath. After the contraction reached a stable level, VG (30 μ M verapamil and 30 μ M NTG) or papaverine (30 μ M) was added. VG solution induced a more rapid relaxation than papaverine. After 10 min, however, there was no statistical difference between the rings treated with VG solution and those treated with papaverine with regard to the magnitude of the relaxation. In fact, both solutions induced full relaxation. However, papaverine has some limitations in preparation [55] and it is acidic (see Chap. 6), which is known to damage the endothelium [56].

Examination of Acting Duration After Treatment with VG Solution [23]. To examine whether the effect of VG solution would last for prolonged period after topical use, segments were taken from the RA that had been immersed in the VG solution before use for CABG. The VG treatment time was 45 min. Control segments were taken from the RA that was not treated with VG solution. Both the VG-treated and non-treated segments were immersed in oxygenated Krebs solution and stored in a refrigerator at 4°C for 24 h. The contraction to K^+ in rings ($n=5$) treated with VG solution for 45 min during surgery was almost abolished 24 h later. This result demonstrates the long antispastic action of the VG solution, which may cover the most critical period – the early postoperative period.

17.1.1.4

Endothelial Function in RA Using the GWH Protocol

Surgical harvesting, including use of a vasodilator solution, may injure the RA endothelium. Except the direct injury due to surgical handling, endothelial damage is also related to vasospasm. When a vessel is in spasm, a higher pressure is needed to distend or dilate the vessel before it can be used for grafting. This “classical mechanism” was recognized many years ago [19]. Therefore, an antispastic therapy (systemic and topical) is necessary to preserve the endothelium. However, topical use of antispastic drugs may also damage the delicate endothelium. Therefore, we designed experiments to test the endothelial function after treatment with the VG solution.

Endothelial Function in VG-Solution-Treated RA Compared to Control RA [24]. There was no difference in either receptor-mediated endothelium-dependent relaxation by acetylcholine (ACh) or non-receptor-mediated endothelium-dependent relaxation by A23187 (calcium ionophore) between VG solution-treated RA and control RA.

Comparison Between VG and Papaverine Solution in Preservation of Endothelial Function in RA [24]. RA segments were either immersed in VG solution as mentioned above or in papaverine solution (60 mg in 60 ml normal saline as used clinically) at room temperature for 45 min. The pH of the papaverine solution measured in this study was 5.75. The arteries were then tested in the organ-bath setting.

In the papaverine-treated RA, ACh-induced relaxation was almost abolished ($3.3 \pm 2.6\%$ compared with $23.9 \pm 3.9\%$ in the VG treatment, $p < 0.001$, unpaired t -test; 95% CI: 0.5%, 9.8%). In addition, A23187 induced significantly less relaxation ($39.7 \pm 5.2\%$) than that ($62.3 \pm 8.4\%$) in the VG-treated RA ($p = 0.02$, unpaired t -test; 95% CI: 0.4%, 7.4%) (Fig. 17.3).

These results demonstrate the superior protective effect of VG solution to papaverine solution in the RA. However, it is unclear what the effect is of blood mixed papaverine on the endothelial function of the RA.

We have previously reported the excellent relaxation effect of VG solution in human saphenous vein [42] and IMA [37]. In our practice, we use only one solution to prepare all coronary bypass grafts and this is extremely convenient for the surgical team.

17.1.1.5

Early Clinical Results of the GWH Protocol

Results from in vitro experiments can only be carefully transferred to the clinical setting. Although the above studies have demonstrated the efficacy of the GWH Protocol in antispastic therapy and in preservation of the endothelial function, the influence of the GWH Protocol on long-term patency needs to be studied. We have performed a mid-term study to examine the angiographic patency of the RA grafts.

We have now used the GWH Protocol in 131 patients who have undergone elective RA grafting by a single surgeon (Guo-Wei He) [57]. The operative mortality was 1.5% (2/131). There were 109 male and 22 female

patients aged 61.5 ± 8.5 years. The average number of grafts was 3.1 per patient. The RA was grafted to the left anterior descending (LAD, 33 patients due to very small size of LIMA), diagonal (22), intermediate (20), obtuse marginal (OM)1 (30), OM2 (9), right coronary or posterior descending artery (RCA/PDA, 16), or left ventricular branch (1). LIMA was mainly grafted to LAD (86), and SV, to OM (83) or RCA/PDA (60). Seventy-eight patients (59.5%) had recatheterization on the postoperative day of 210.9 ± 64.3 (42~532 days). In these patients, the patency was 92% for the LIMA (46/54), 88.4% for the RA (61/69), and 92.3% (84/91) for the SV, respectively ($p = 0.67$), and there were no significant differences between any two of these groups (Fisher's exact test: $p = 0.28 \sim 0.59$). However, there were four patent SV grafts showing more than 50% stenosis but this was not seen in either LIMA or RA grafts. Using this protocol, we have always seen a "fully relaxed" RA before performing anastomosis. In this group, we encountered spasm of the RA and IMA perioperatively only in one patient, who was salvaged by intraluminal injection of verapamil and NTG through the coronary catheterization urgently performed immediately after the CABG surgery [58].

17.2

Discussion

Operative results (early mortality and long-term patency) of CABG in general depend on the function of the graft. For the RA, the major concern is its spastic characteristic, which led to the early abandonment of this arterial graft. As to the long-term patency, apart from the necessary spasmolytic treatment, preservation of endothelium is vitally important. Vascular endothelium derives a number of endothelium-derived relaxing factors (EDRFs) that play an important role in vasorelaxation and in inhibition of platelet aggregation. When endothelium is impaired, the antiplatelet func-

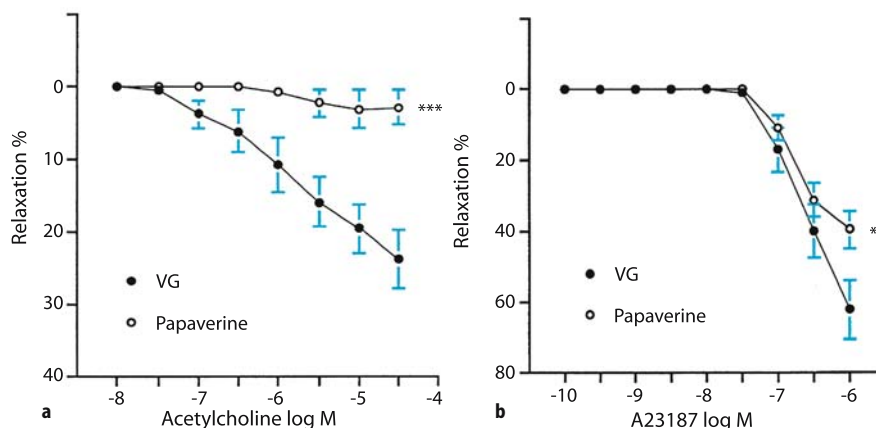


Fig. 17.3. Endothelium-dependent relaxation in the radial artery is maximally preserved after incubation with verapamil + nitroglycerin solution but impaired after papaverine incubation. (Reproduced from He GW: *J Thorac Cardiovasc Surg* 1998; 115: 1321–1327 with permission)

tion of EDRFs [such as nitric oxide (NO) and PGI_2] is lost and platelets attach to the area denuded or impaired of endothelium. The coagulation cascade is activated by aggregating platelets and by thrombin. Thrombus then forms. This becomes the basis for later growth and development of atherosclerotic plaque and may lead to graft occlusion. Therefore, an ideal method to harvest the RA should be (1) antispastic and (2) able to maximally preserve the endothelial function. These principles urged us to search a method fulfilling these criteria in the harvesting of the RA.

The reported methods of harvesting the RA include (1) systemic use of diltiazem once harvesting is started and (2) use of papaverine alone [19] or mixed with blood [5, 21] for “gentle hydrostatic dilation” of the artery to achieve an antispastic effect and to check leaking. However, if a graft is fully relaxed, there is no need to mechanically dilate it since mechanical distention (dilation) may impair the endothelium or smooth muscle, particularly when the distention pressure is high. In fact the distention pressure is difficult to control during harvesting.

The advantages of using VG solution over papaverine in the RA include (1) a more rapid onset and (2) a neutral pH. Our experiments have shown a more rapid relaxation induced by the VG solution than papaverine within the first 10 min (Fig. 17.4). Perhaps more importantly, VG solution is neutral ($\text{pH}=7.4$), whereas papaverine is acidic as measured in this study ($\text{pH}=5.75$ at a clinically used concentration in the saline solution). It has been reported [55] that a white precipitate sometimes forms when papaverine is added to electrolyte solution (Plasma-Lyte; pH approximately 7.4) and papaverine is relatively unstable in nonacidic solution. Acidic solution has been shown to damage the endothelium [56]. This is more important in the preparation of the RA than of the IMA because the IMA is usually used as a pedicle and most surgeons only spray the vasodilator solution on the surface of the pedicle. Therefore, the vasodilator does not directly come into con-

tact with the endothelium of the IMA unless the intraluminal injection is used. However, the RA is used as a free graft. No matter how the RA is immersed in the solution either as we do or wrapped in a gauze with vasodilator solution, it is inevitable that the endothelium more or less comes into contact with the solution.

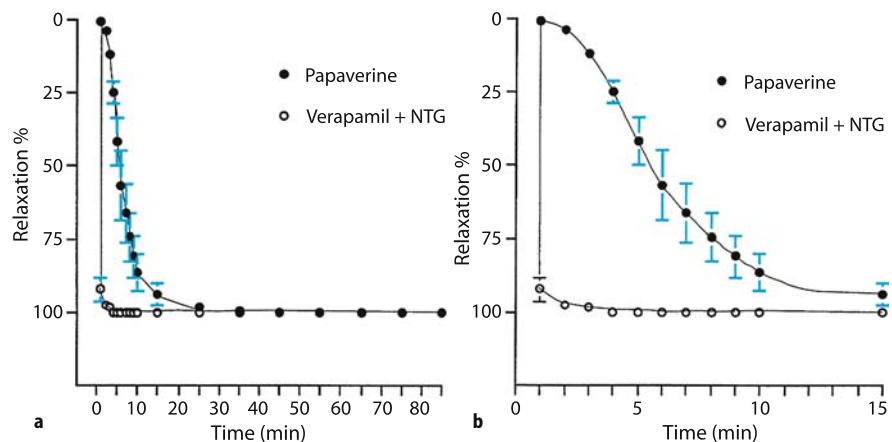
In general, the advantages of calcium antagonists are (1) high potency to inhibit the voltage-operated calcium channel (L-type calcium channel), which is the primary mechanism for regulation of intracellular calcium concentration of vascular smooth muscle [50] and (2) long duration.

The effect of three chemically different calcium antagonists [51] has been compared in the coronary artery and coronary bypass grafts [35, 48], particularly using the RA [33]. Among the three calcium antagonists, diltiazem is the least potent one. For example, nifedipine is 15-fold more potent than diltiazem with regard to the vasorelaxant effect in the most commonly used human arterial coronary bypass graft – the IMA, as demonstrated in our previous study [35]. However, nifedipine is not available for IV or topical use. Verapamil is more potent than diltiazem in the canine IMA (EC_{50} -5.73 vs. -5.38 log M) and saphenous vein (-6.74 vs. -6.30 log M) [48]. We have also found that in the human saphenous vein [42] diltiazem is significantly less potent than verapamil (EC_{50} -6.62 vs. -6.96 log mol/l). Therefore, we studied the effect of verapamil and NTG initially in the human IMA [37, 42] and then in the human RA [23, 24].

Apart from those mentioned above, other advantages of verapamil have been reported. It has been suggested to be antiplatelet and antithrombotic in patients with coronary artery disease [53], to improve prognosis in postinfarction patients [52], and to inhibit smooth muscle cell proliferation in experimental vein bypass grafts [54].

The common disadvantages of calcium antagonists, on the other hand, are (1) that a high vasoconstrictor selectivity may limit their effect under some circum-

Fig. 17.4. Comparison of verapamil + nitroglycerin solution and papaverine solution on the vasorelaxation of the human radial artery in vitro. Both induced full relaxation but verapamil + nitroglycerin solution has more rapid onset compared with papaverine solution. (Reproduced from He GW and Yang CQ: *Ann Thorac Surg* 1996; 61:610–4 with permission)



stances when a vessel is contracted through receptor mechanisms and (2) that there is a relatively (compared to NTG) slower onset of action although the onset is more rapid than papaverine [23]. As demonstrated in the human IMA [37], saphenous vein [42] and RA [23], a combination of calcium antagonists with NTG may combine the advantages of both.

A major question related to any solution used topically for grafts is whether, in addition to the full relaxant effect, the preparation maximally preserves the endothelial function. Our studies, testing two mechanisms of endothelium-dependent relaxation, demonstrated that the VG solution does not impair the endothelial function after full exposure (immersion) during surgery. This is probably due to the neutral pH and the isotonic nature of this solution. In addition, NTG is an exogenous nitric oxide (NO) donor. It releases NO when it diffuses into the vascular smooth muscle [59], which is identical to endothelium-derived NO – one of the three major EDRFs [60]. Therefore, NTG would enhance but not impair the EDNO-mediated endothelial function.

In contrast, after papaverine treatment, the endothelial function in the RA is impaired. This is most likely due to the acidic characteristic of papaverine solution (pH = 5.75), as already mentioned above.

Another advantage of the GWH Protocol is that the excellent vasorelaxing effect of VG solution also exists in the human saphenous vein [42] and IMA [37]. In our practice, we use only one solution to prepare all coronary bypass grafts and this is extremely convenient for the surgical team.

The GWH Protocol includes other aspects during the pre-, intra-, and postoperative period. In this article, we have focused our discussion on the effect of the intraoperative topical antispastic treatment using VG solution.

As mentioned above, after we developed the VG solution, we specifically investigated and compared the vasodilator effect of the four commonly used calcium antagonists from three chemically divergent groups – dihydropyridine (nifedipine and nicardipine), phenylalkylamines (verapamil), and benzothiazepines (diltiazem) in the human RA [33]. We demonstrated that although all calcium antagonists have an antispastic effect in the RA, the vessel has a different sensitivity to them. Dihydropyridine derivatives may be the most potent ones and are therefore recommended for clinical use for this purpose. We have therefore changed the systemic drug from verapamil to nicardipine, which is a dihydropyridine derivative readily available for IV clinically. The systemic use of calcium antagonists was suggested by the initial experience when the use of the RA was revived [5]. This was due to the high incidence of occlusion of the graft during Dr. Carpentier's early experience in the 1970s when calcium antagonists were not available. The exact role of the systemic use of calci-

um antagonists awaits future justification. However, taken together with the early experience, in the GWH Protocol, systemic administration of verapamil or recently nicardipine has been an active part in order to reduce possible vasospasm and occlusion during the peri- and postoperative period.

Although some authors have now given up oral administration of calcium antagonists after RA grafting [25], due to the spastic characteristics and possible clinical spasm of the RA graft [3, 14, 58], we believe that the oral administration of a dihydropyridine derivative or other calcium antagonists for at least 6–12 months is beneficial. However, an adequate period for oral calcium antagonists beyond 6–12 months still has to be determined.

We conclude that the use of the GWH Protocol for the RA in CABG may provide a method that may have full antispastic effect on the graft and maximally preserve the endothelial function of the RA. Therefore, this protocol eliminates the need for mechanical distention or “hydrostatic dilation” during the preparation, has excellent clinical results and mid-term patency, and may provide an effective and safe method for using the RA for CABG. Other protocols proven to be effective are also alternatives for the use of RA in CABG.

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Radial Artery: Clinical Results

C. ACAR

Since July 1989, the radial artery (RA) has been used extensively for coronary bypass surgery in the author's practice [1]. In 1994, as the 5-year results showing excellent patency rates became available, the use of the RA graft was further expanded [2]. At present it is systematically considered in all cases and has been applied in over 1,200 cases.

18.1

Early Results

18.1.1

In Hospital Mortality

In the author's experience with coronary artery bypass using the RA, in hospital mortality and incidence of perioperative myocardial infarction have been low (1% and 2% respectively) [1] and have appeared comparable to coronary bypass surgery using other types of conduits. No deadly complications occurred that could be related to the use of the RA. Many reports in the literature confirmed the safety of using the RA as a graft with no increased risk of perioperative death or infarction [3–5]. Studies specifically focused on high risk patients with either left ventricle dysfunction [6] or coronary reoperation [7] and the risk of postoperative death and infarction remained unchanged when using the RA. Furthermore, one report [8] suggested that exclusive arterial conduits including the RA in combination with the internal thoracic arteries (ITAs) was associated with a reduced in hospital mortality when compared to patients in whom vein grafts had been used.

18.1.2

Spasm of the RA

Spasm of arterial conduits is a reality and RA spasm needs to be addressed (see Chap. 17). However, in the author's series, there was no clinical episode suggesting myocardial ischemia, EKG change or enzyme elevation that could be attributed to a spasm of the RA. Occasionally, routine angiographic findings displayed a localized spasm of the RA conduit early in the postoperative course [1]. This finding did not translate into clinical

symptoms or EKG changes. It has been interpreted as a reaction to a mechanical stimulus, which could have been either an incomplete release of the spasm at the time of harvesting or a selective catheterization of the graft during angiography. As already mentioned, it is important to use a RA conduit totally free of spasm at the time of construction of the coronary anastomoses, and pharmacological or mechanical maneuvers are warranted so as to obtain a fully dilated vessel.

The prescription of calcium channel inhibitors in patients receiving ITA grafts is a widespread practice although no study clearly demonstrated its beneficial effects on graft patency. Because of the propensity to spasm of the RA observed both in the operating room and in the catheterization laboratory, calcium channel blockers (diltiazem) have been recommended in all patients receiving a RA graft [1]. From 1989 to 1994 diltiazem was administered both intravenously in the intensive care unit and then orally. Patient follow-up revealed that the cardiologists had not always followed the initial recommendations and 5 years after surgery, only 60% of the patients with a RA graft were still receiving a calcium inhibitor [2]. Although the subset of patients was limited in number, angiographic data failed to show any benefit of calcium blockers concerning graft patency. Because it carries a risk of negative inotropic effect, the use of intravenous calcium blockers in the intensive care unit was then abandoned. Other studies based on clinical evaluation, stress myocardial scintigraphy and angiographic analysis [9, 10] also failed to demonstrate any advantages of using calcium antagonists beyond the first postoperative year [9]. Knowing the spastic characteristics of the RA and the innocuousness of diltiazem when prescribed orally, we believe that this treatment is still recommended during the early postoperative period (< 1 year) until more data are available.

18.1.3

Wound Complications

In the author's experience, the skin incision at the forearm usually healed remarkably rapidly and the onset of local infection was an exception. Reexploration for he-

matoma formation was also very unusual and the overall incidence of local complications was approximately 1%. Several studies have confirmed this finding; furthermore the risk of leg complications at the vein harvest site (infection, dehiscence) was demonstrated to be much higher than forearm complications particularly in elderly patients. The protective effect of using the RA rather than a vein resulted in a reduced length of stay and readmission, therefore reducing hospitalization cost [11, 12].

Other reports have compared the postoperative outcome of coronary bypass with the right ITA versus the RA as a second arterial graft to complement the left ITA to LAD. Patients receiving a right ITA had a higher incidence of sternal wound infection or dehiscence [13–15]. In addition, these patients had more postoperative bleeding and a prolonged hospitalization stay [13–15].

18.1.4 Neurological Complications

A potential complication is damage to the superficial branch of the radial nerve which runs in close relation to the RA. This was observed in 8% of cases in the author's series and resulted in numbness and paresthesia of the thumb that almost invariably resolved within 6–12 months [6, 16]. In no instance did this minor complication result in any significant functional incapacity. Exceptional cases of intense and persistent pain in the forearm have been reported [17], no anatomical support has been identified and this "causalgia" was most probably related to postoperative psychological disorder. Rarely, transient dysesthesia in the territory of the ulnar nerve (fourth and fifth fingers) occurred due to traction on the brachial plexus secondary to a

poor positioning of the upper extremity with excessive stretch on the elbow during harvesting. In spite of these minor complications, quality of life studies have confirmed the safety of RA removal, which was responsible for minimal discomfort [11].

18.2 Late Results

18.2.1 Survival and Cardiac Events

The first 102 patients operated on in the author's experience (1989–1993) were reviewed and followed for a period up to 15 years postoperatively. At 5.27 years, the actuarial survival rate at 5 years was 92% [2]. Others have reported 86% survival at 8 years [18].

The actuarial rate of patients free from angina at 5 years was 89% (Fig. 18.1) and the incidence of myocardial infarction and congestive heart failure was 1% and 6% respectively [2]. The EKG stress test is considered as the gold standard for detecting silent ischemia in coronary artery disease. This test is of limited value in the follow-up of patients having undergone coronary bypass surgery because of the frequency of contraindications related to the patient's age or associated disease. In the author's experience, at 5 years, the EKG stress test was performed in half of the cases and showed a negative result in 73% of the cases, EKG changes alone in 21% of cases and clinically positive results with chest pain in 6% of cases [2]. A positive stress test could be interpreted as a progression of the coronary disease or a graft dysfunction (RA or non-RA).

The use of the RA did not preclude the later possibility of percutaneous transluminal coronary angioplasty (PTCA) [19]. The need for PTCA either on the RA graft

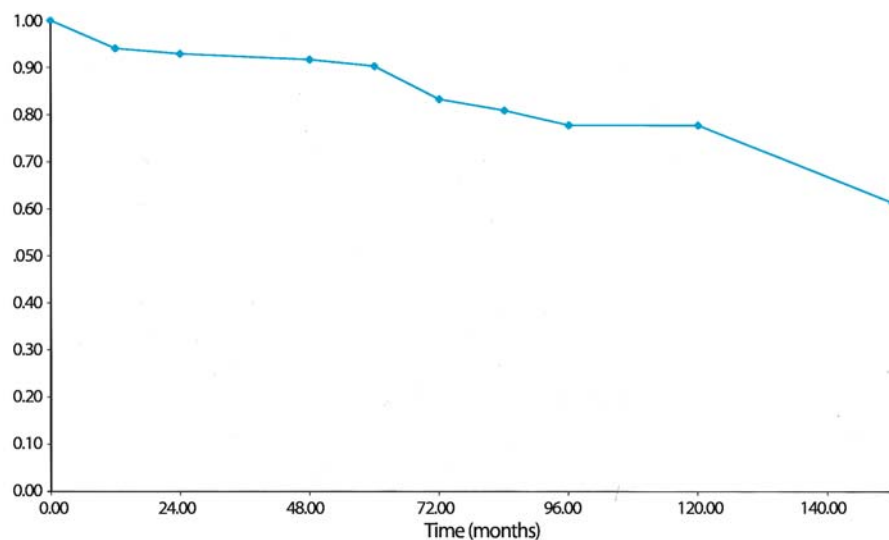


Fig. 18.1. Fate of radial artery grafts. Actuarial patency rates were 94%, 90% and 78% at 1 year, 5 years and 10 years respectively

or on the native coronary vessel to which it had been anastomosed was 3% at 5 years in the author's series [2].

18.2.2

Clinical Results of RA Versus Other Conduits

Because of the multiplicity of confounding parameters, even sophisticated statistical methods have difficulty in identifying the graft selection itself as risk factor for early death and cardiac events. An important case matched study including patients with identical demographics receiving either a RA or a vein as a second graft to complement the left IMA to LAD has recently been published [20]. For the first time it has been shown that using the RA as opposed to a vein graft decreased the incidence of late death especially beyond the third postoperative year. This finding confirms the clinical efficacy of RA coronary artery bypass and urges a wider use of this conduit rather than vein grafts.

When compared to the right ITA, the RA offers many advantages: (1) it is a versatile conduit whose size and quality of wall make it perfectly suitable for coronary anastomoses, (2) it can be harvested simultaneously to the left ITA, saving operating time, and (3) it can reach all target areas even the most distal coronary arteries. The only disadvantage is the fact that contraindications to its use are more frequent mainly because graft atherosclerosis is encountered more often with the RA than with the ITA. A study compared the clinical benefits of using the RA rather than the right ITA to

complement the left IMA to LAD graft [13]. Patients in the RA group were older and had more risk factors (low ejection fraction, diabetes, NYHA class). Nevertheless, statistical analysis showed that the RA use reduced the perioperative morbidity (myocardial infarction, atrial fibrillation, postoperative transfusion and ICU stay) as compared to the right ITA. In addition, at 18 months, the RA offered a stronger protective effect against cardiac death than the right ITA. This study reflects the experience of one center and its conclusions remain a matter of debate [21, 22]. However, knowing that RA use offers fewer wound complications than the right ITA [13–15], the selection of this conduit as the second graft of choice to complement the left IMA to LAD graft is a valuable option.

18.2.3

RA Graft Patency

The control angiogram has for a long time been the only technique capable of completely analyzing the characteristics of a conduit, the patency being the ultimate criterion of success. At present, CT scan and nuclear magnetic resonance imaging can provide information regarding graft patency, and these noninvasive techniques will play a major role in the future. However, a new surgical strategy must be validated by a conventional method. In the author's experience repeated angiograms have been performed in order to analyze the fate of the RA conduits (Fig. 18.2).



Fig. 18.2. Sequential and Y radial artery grafts at 5 years

At 1 year the patency rate of the RA graft was $94 \pm 2\%$, which appears to be equal to or higher than that of vein grafts constructed in the same conditions (i.e., on non-LAD coronary arteries) [23]. At 1 year, intimal hyperplasia had little time to develop; thus graft failure is unlikely to be related only to modifications of the vessel wall, and abrupt graft thrombosis is probably a frequent mechanism. When compared to a vein, the RA has superior hemodynamic characteristics which can translate into a lower thrombosis rate. Its size is close to that of the coronary arteries and the diameter ratio between the graft and the target vessel never exceeds 2/1. In addition, this graft is free of valvula and its caliber is homogeneous throughout its whole course with a slight decrease in diameter from the proximal to the distal end.

Conversely, the diameter of the vein is invariably larger, frequently leading to a discrepancy with the coronary artery (diameter ratio 4/1). Furthermore the saphenous vein lumen contains valvula and its diameter is variable with abrupt changes at the level of collateral branches. The diameter of the vein increases from the proximal to the distal end. These relatively unfavorable hemodynamic characteristics probably lead to a higher risk of thrombosis when used on small target vessels. Although several studies have tended to show an advantage of using the RA [3–6], the superior patency rate of the RA over the vein graft has not yet been clearly established.

In the author's series, 5- and 10-year patency rates of RA grafts were $90 \pm 3\%$ and $78 \pm 6\%$ (Figs. 18.1–18.3). Other authors have reported similar or higher 5-year

patency rates (95% at 5 years for Calafieri [18] and 88% at 8 years for Possati [24]).

In comparison, saphenous vein grafts are more frequently affected by graft disease with progressive intimal hyperplasia responsible for stenosis and occlusion, and their reported patency rate [7] seems to be lower than that of the RA. Quoting the title of Carpentier's original article in the 1973 *Annals of Thoracic Surgery* issue, the radial graft whose ultrastructure is used for the systemic pressure regimen could be a "*technique avoiding pathological changes in grafts*." A definitive answer concerning patency of RA versus vein grafts will be provided by prospective randomized studies currently in progress [25].

In most series, the patency rate of the RA graft was slightly lower than that of the left IMA graft [2–5]. However, the interpretation of angiographic data must take into consideration the implantation sites of the grafts. Whichever conduit is used [23, 26], the extent of the distal runoff is a major factor influencing graft patency. Interestingly when used on similar target vessels such as the RA, the 5-year patency of the free ITA graft (84% according to Loop [27]) has been reported to be equal to that of the RA graft in our series. As for veins and ITAs [23, 26], the patency of radial artery conduits has been directly influenced by the size of the coronary vessel [28–30]; as a result RA anastomosed to the right coronary artery has a lower reported patency rate [28–30].

In the author's series [2] as well as in a number of other studies [10, 28–30], a lesser degree of stenosis on the target artery has been shown to decrease RA graft

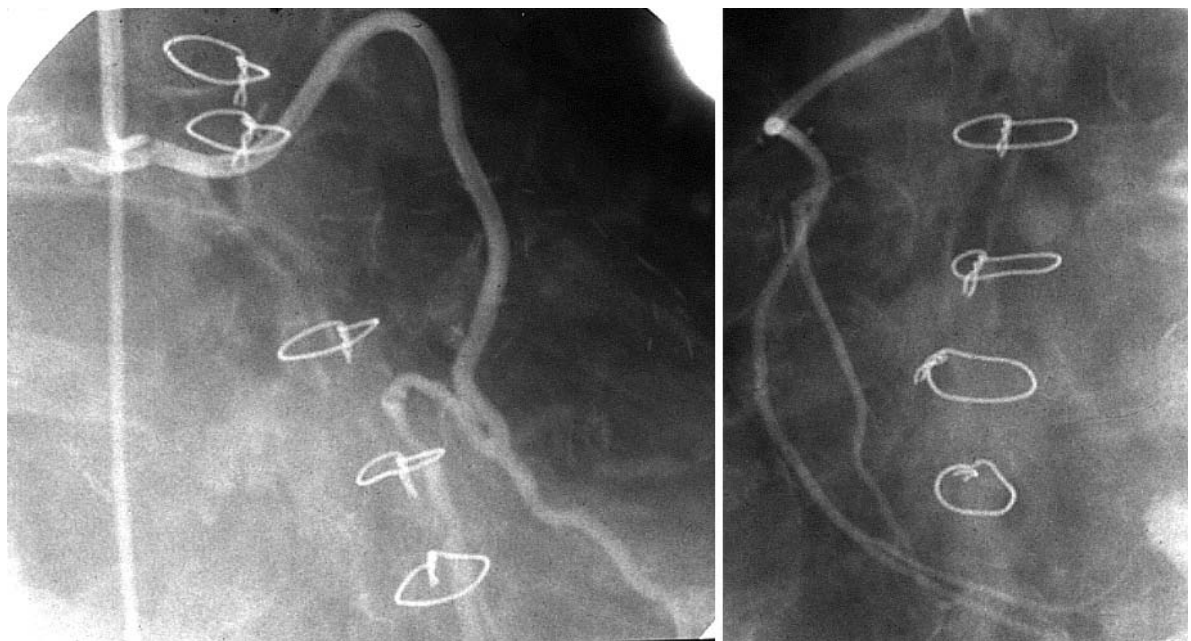


Fig. 18.3. Radial artery to obtuse marginal and to right coronary artery at 12 years

patency. Competitive flow from the native coronary vessel diminishes the amount of blood flowing through the graft and increases the risk for early thrombosis. The critical degree of stenosis to which patency starts to decline has not been clearly established, and is certainly below 60% and probably below 90% [10]. This observation is not specific for the RA graft; it applies also to other free grafts including the internal mammary artery [28, 31].

Similarly, isolated proximal coronary stenosis of the left main coronary artery is usually revascularized using one or more grafts in addition to the left ITA to LAD bypass. If no restriction of flow exists beyond the left main stenosis, the left ITA graft can supply most of the distal run-off including the lateral wall, and occlusion of the other grafts constructed on this network can ensue due to competitive flow. This situation has been occasionally met in the author's series [2].

Whether the use of a RA proximally anastomosed to the pedicled IMA rather than to the aorta improves graft patency remains debatable. The proponents of this method [32] claim that the shear stress is increased when the RA is anastomosed to the aorta whose diameter is larger than that of the vessel from which the RA naturally originates. Although the use of composite arterial conduits with the RA anastomosed to the IMA has gained a wide acceptance [33–35], its superiority over direct RA anastomosis to the aorta has not been demonstrated. In fact, reports comparing the two techniques found either the same [36] or the opposite angiographic results [29]. In this last study, ITA anastomosed RA grafts were more vulnerable with a higher occlusion rate in case of competitive flow when compared to RA directly anastomosed to the aorta [29].

18.2.4

Very Long Term Evaluation

From Carpentier's original series, five grafts were followed up angiographically from 14 to 23 years later, which displayed a perfectly patent and fully dilated radial artery. Another 23-year patency of a radial artery graft was recently reported by De Oliveira [37]; reoperation required for valve surgery showed a radial artery conduit free of atherosclerosis.

18.3

Conclusion

Use of the RA for coronary bypass grafting has stood the test of time and offers excellent clinical and angiographic results in the long term. Routine use of this conduit in combination with the left IMA is safe and can be recommended. There is increasing observational evidence that the RA protects against wound compli-

cations observed with the saphenous vein or with the right ITA. Some studies have suggested that the use of the RA has decreased early mortality and cardiac events as compared to the saphenous vein and the right ITA. Similarly to the other conduits, radial artery patency is decreased when used on small target vessels or with a low degree of stenosis. In order to clarify which is the best conduit to complement the left ITA to LAD, comparative randomized studies with early and long term patency data are needed.

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Angiographic Studies of the Radial Artery Graft

C.A. DIETL

19.1 Introduction

The radial artery graft was first used as an alternative conduit for coronary revascularization in 1971, by Carpentier and associates [1]. However, its use was abandoned 2 years later, because postoperative angiographic studies showed that 35% of the radial artery grafts were diffusely narrowed or occluded [2]. The high failure rate was attributed to spasm of the denervated radial artery. Other authors [3–5] also reported high failure rates of the radial artery graft, caused by intimal hyperplasia.

The use of the radial artery graft was revived by Acar and colleagues of Carpentier [6], in Paris, in 1989. They observed that several patients had widely patent radial artery grafts on postoperative angiographic studies obtained more than 15 years after the operation. Several patients had patent radial artery grafts, which were initially thought to be occluded. Acar and associates [6] observed a 93.5% angiographic patency rate of the radial artery graft. Their improved results were attributed to a modified surgical technique, avoiding skeletonization and dilation of the radial artery, and to the routine use of calcium channel blockers to prevent arterial spasm. Since then, several authors [7–10] have reported angiographic studies demonstrating mid-term (5-year) radial artery graft patency rates ranging from 91% to 95%.

Our initial experience with the radial artery graft between 1992 and 1994 was reported elsewhere [11]. Several modifications to our original surgical technique have been introduced since then.

from 34 to 82 years (mean age 61.3 years). This series included 113 female (27.0%) and 306 male (73.0%) patients. There were 134 (31.9%) patients with diabetes mellitus, 79 (18.8%) patients with severe left main stenosis, 48 (11.4%) patients with left ventricular ejection fraction less than 0.3, and 48 (11.4%) patients who underwent a coronary artery bypass reoperation.

Initially, use of the radial artery graft was limited to patients with unavailable or unsuitable saphenous veins, and to patients with calcified ascending aorta, and patients with peripheral vascular disease (to spare their saphenous veins for revascularization of the lower extremity), as well as patients who had undergone a previous coronary artery bypass. Other indications to use the radial artery graft include the use of at least two arterial grafts to the left coronary system, in combination with the left internal mammary artery (LIMA) graft, and to achieve total arterial revascularization, in combination with the LIMA and the right gastroepiploic artery (GEA) graft. In our series, total arterial revascularization, using arterial grafts exclusively, was accomplished in 332 (79.2%) patients. In 87 (20.8%) of our patients, one or more vein grafts were used concomitantly, with a mean of 3.25 distal anastomoses per patient.

Contraindications for using the radial artery graft included patients on hemodialysis, previous trauma to the non-dominant hand or forearm, or Raynaud's disease. The modified Allen test was performed routinely before the operation, with the patient's hand flexed and relaxed, as recommended by Ejrup et al. [12], to avoid false-positive tests. Segmental Doppler studies were performed if the Allen test was positive after 5 s.

19.2 Patients and Methods

Between November 1992 and July 2004, we used the radial artery graft in 419 patients who underwent isolated coronary artery bypass grafting (CABG) at Geisinger Medical Center, in Danville, Pennsylvania, USA, and at the University of New Mexico Health Sciences Center, in Albuquerque, New Mexico, USA. Their ages ranged

19.3 Surgical Technique

The radial artery graft was harvested from the non-dominant arm, using a technique previously described [11]. Bilateral radial arteries were harvested in 11 (2.6%) patients. The antebrachialis fascia was opened longitudinally, following the medial edge of the brachioradialis tendon and muscle. The two satellite veins

and the surrounding fat were left attached to the radial artery, to avoid skeletonization. The middle portion of the radial artery pedicle was freed first, and a bulldog clamp was applied briefly to occlude the radial artery. A palpable pulse in the radial artery, distal to the clamp, indicated adequate collateral blood flow supplied by the ulnar artery. An absent pulse, on the contrary, suggested inadequate collaterals, and the radial artery was not harvested in those patients.

We prefer to use the harmonic scissors to dissect the radial artery pedicle and to divide the side branches. The electrocautery was not used, to prevent thermal injury to the radial artery. During the dissection, the radial artery pedicle was sprayed several times with a solution containing 125 mg of diltiazem in 125 ml of D5 W, and the radial artery graft was stored in the same solution, at room temperature, until it was used. Currently, we do not use systemic intravenous diltiazem in the operating room.

Off-pump CABG with the radial artery graft was done in 23 (5.5%) patients in this series. However, cardiopulmonary bypass with mild systemic hypothermia at 32°C was used in most patients. Myocardial protection was accomplished with intermittent antegrade cold blood cardioplegia earlier in our series. At present, we use continuous retrograde cold blood cardioplegia. In patients with a calcified ascending aorta, no clamps were applied, and total arterial revascularization was performed either off-pump, or on pump with a beating heart, using a “no-touch” technique [13].

The radial artery graft was used as a single graft (in 260 patients), as a sequential graft (in 121 patients), as a Y graft (in 27 patients), or as bilateral radial artery grafts (in 11 patients), for a total of 578 distal anastomoses in 419 patients (mean 1.38 distal anastomoses per radial artery). The radial artery graft was anastomosed distally to the obtuse marginal branches of the circumflex artery in 348 patients, and to the intermediate branch in 64 patients; and frequently, both vessels were grafted sequentially with the same radial artery graft. All the distal anastomoses were performed with continuous 7-0 polypropylene suture. A concomitant coronary endarterectomy was done in 13 patients.

Earlier in our experience, the proximal end of the radial artery graft was anastomosed to the ascending aorta, using continuous 6-0 polypropylene suture, except for patients with calcified ascending aorta, in whom the proximal anastomosis was performed end-to-side to the LIMA graft, using continuous 7-0 polypropylene suture. During the past 5 years, however, all the proximal anastomoses of the radial artery graft were done end-to-side to the LIMA graft, before going on cardiopulmonary bypass. In off-pump CABG patients, the proximal radial artery to LIMA anastomoses were performed before any of the distal anastomoses.

19.4 Results

No permanent ischemic or functional complications occurred in the hand or arm after removal of the radial artery in the present series. Only one patient had temporary ischemia of his left hand during the early postoperative period. Angiography of the arm vessels revealed spasm of the ulnar artery, which resolved with an increased dose of systemic intravenous diltiazem at 20 mg/h, in addition to systemic heparinization. Another patient, in whom the antebrachialis fascia was closed, developed a postoperative compartment syndrome, secondary to a hematoma, which required surgical drainage. This was the only patient who had temporary weakness in the involved hand. Usually, we do not close the antebrachialis fascia to avoid this complication. In addition, three patients developed superficial wound infections, and cellulitis was noted in another two patients, managed with oral antibiotics.

Only three patients (0.7%) had a new Q-wave myocardial infarction in the distribution of the vessel grafted with the radial artery graft. In addition, two patients had marked ST-T wave abnormalities during the early postoperative course, requiring an urgent cardiac catheterization and coronary angiography, and immediate reoperation in one of these two patients (see below, “Angiographic Studies”).

The overall 30-day mortality in the present series was 2.4% (10 patients). Six of these were cardiac related deaths, of which only one was attributed to failure of the radial artery graft, secondary to spasm. Two deaths occurred in patients who suffered a cerebrovascular accident, one patient suffered a fatal pulmonary embolism, and one patient died of sepsis secondary to mediastinal infection.

19.5 Angiographic Studies

Two patients required urgent cardiac catheterization and coronary angiography within 12 h of the operation, because they had marked ST-T wave abnormalities, and new wall motion abnormalities in their postoperative echocardiogram. The coronary angiogram was normal in one of these patients (Fig. 19.1). The EKG changes and the echocardiogram returned to normal within 24 h. The other patient had a stenosis of the LIMA graft, immediately distal to the radial artery to LIMA end-to-side anastomosis (Fig. 19.2a, b). He underwent an urgent reoperation, to divide the adventitial bands, which were kinking the LIMA graft immediately distal to the anastomosis with the radial artery.

During a mean follow-up period of 48.4 months (range 2–96 months), 20 patients who developed re-

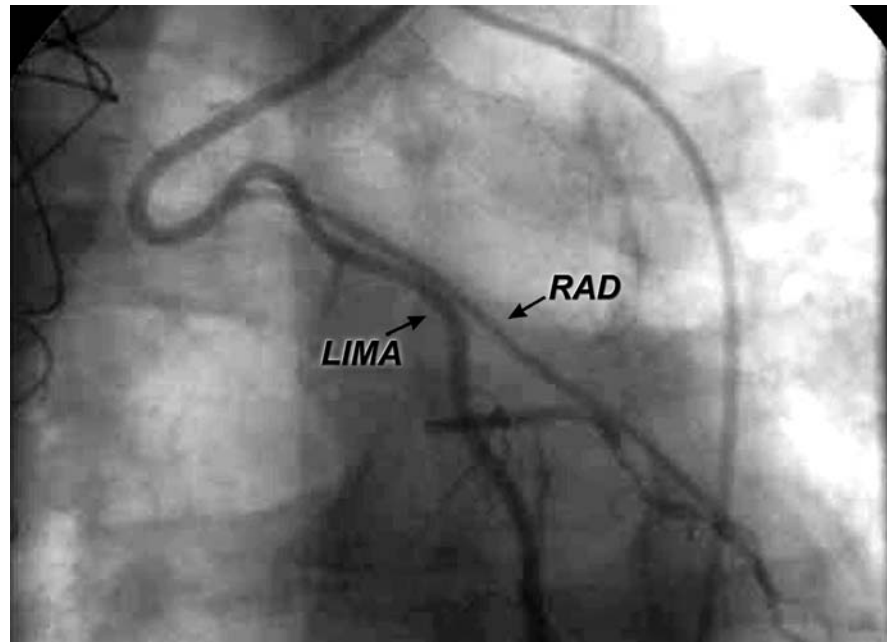


Fig. 19.1. Normal postoperative coronary angiogram (*LIMA* left internal mammary artery, *RAD* radial artery graft)

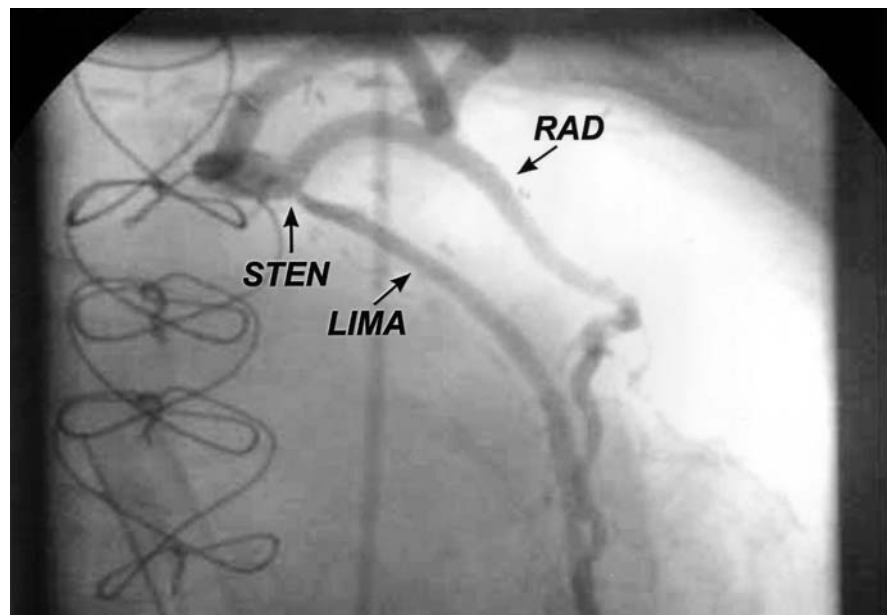


Fig. 19.2a. Postoperative coronary angiogram, showing a stenosis of the LIMA graft, immediately distal to the radial artery to LIMA end-to-side anastomosis (*LIMA* left internal mammary artery, *RAD* radial artery graft, *STEN* stenosis)

current angina underwent coronary angiography at an interval of 2–48 months (mean 22.7 months) after CABG. The radial artery graft was completely occluded in 4 patients, and showed a “string sign” in two other patients, and was widely patent in the remaining 14 patients (Figs. 19.3–19.5).

Radionuclide exercise studies were performed 12 months after surgery in 265 patients, of whom only

seven (2.6%) patients had stress-induced reversible defects in areas revascularized with a radial artery graft. Two of these patients underwent coronary angiography, which showed patent radial artery grafts. The perfusion defects were attributed to old myocardial infarctions.

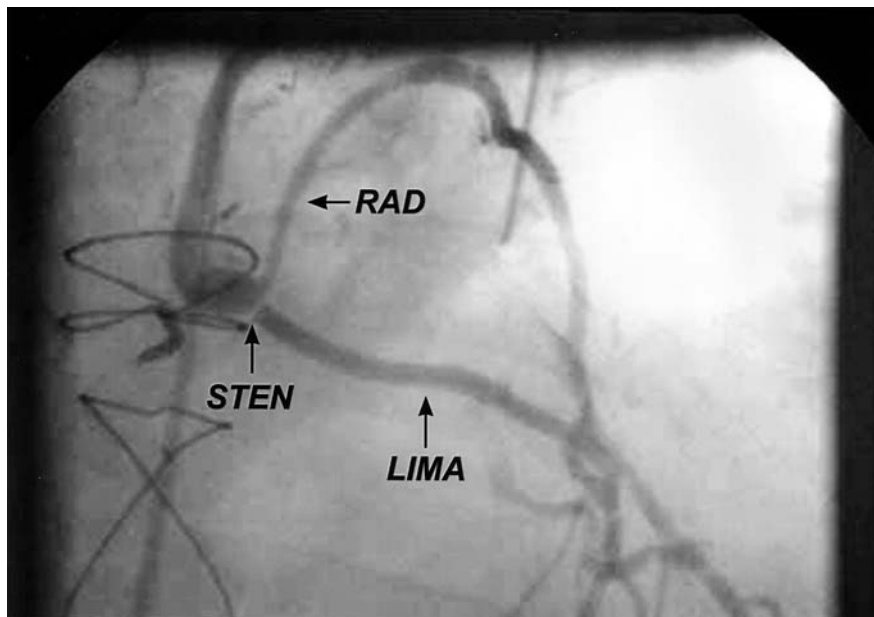


Fig. 19.2b

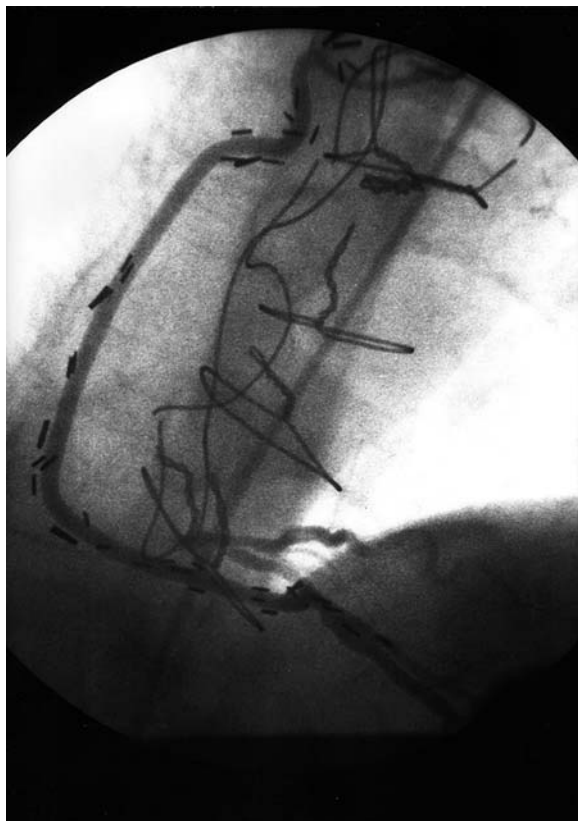


Fig. 19.3. Postoperative coronary angiogram of a radial artery graft to the right posterior descending artery, obtained 24 months after surgery. [Reproduced from Dietl CA (1999) *Angiographic studies of the radial artery graft*. In: He GW (ed) *Arterial grafts for coronary artery bypass surgery*, 1st edn. Springer-Verlag, Singapore, Chap. 19, p. 265, Fig. 1]

19.6 Discussion

The left internal mammary artery is the best conduit available for coronary artery bypass grafting, with a patency rate of 90–95% after 10 years [14, 15]. Late cardiac events, such as recurrent angina, myocardial infarction, and reoperation, are less prevalent when at least one internal mammary artery is used for revascularization [15].

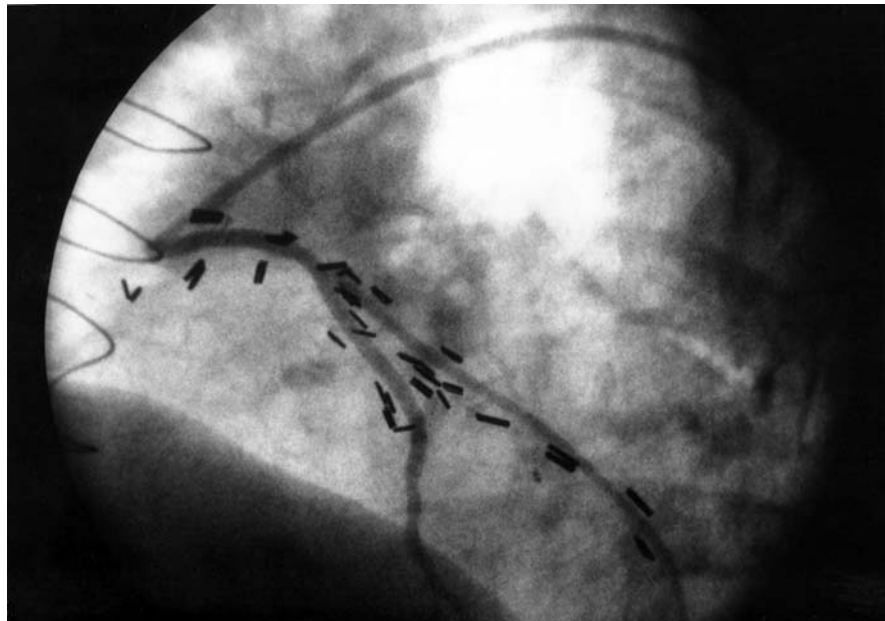
Mid-term patency rates of other arterial conduits are lower than the LIMA graft, yet they compare favorably to vein grafts. For example, Suma and co-workers [16], and Hirose and associates [17], have demonstrated an angiographic 5-year patency rate of 80% and 84%, respectively, for the gastroepiploic artery, when used as a pedicled graft.

However, patency rates of “free” (aorta-coronary) arterial grafts are significantly lower than pedicled (or “in-situ”) grafts. For example, only 75% of free GEA grafts were patent after 12 months [18], and only 77% of the free internal mammary artery grafts remained patent after 18 months [19]. Free arterial grafts may fail because of spasm, secondary to an increased reaction to norepinephrine, as a consequence of total denervation of the artery [3], and because the vasa vasorum are disrupted at both ends [5]. Free arterial grafts are also more prone to develop diffuse intimal hyperplasia [3]. Carpentier’s initial experience with the radial artery graft resulted in a high failure rate, which was attributed to a combination of spasm and intimal hyperplasia [2]. To minimize the risk of intimal hyperplasia, Acar and co-workers [6] recommended avoidance of intimal trauma by dilation, or by excessive skeletonization, to

Fig. 19.4. Postoperative coronary angiogram of a sequential radial artery graft with side-to-side anastomosis to a diagonal branch, and end-to-side anastomosis to an obtuse marginal artery, obtained 14 months after surgery. [Reproduced from Dietl CA (1999) *Angiographic studies of the radial artery graft*. In: He GW (ed) *Arterial grafts for coronary artery bypass surgery*, 1st edn. Springer-Verlag, Singapore, Chap. 19, p. 266, Fig. 4]



Fig. 19.5. Postoperative coronary angiogram of a radial artery used as a Y graft, with proximal anastomosis to the ascending aorta, and distal anastomoses to two obtuse marginal branches of the circumflex artery, obtained 36 months after surgery. [Reproduced from Dietl CA (1999) *Angiographic studies of the radial artery graft*. In: He GW (ed) *Arterial grafts for coronary artery bypass surgery*, 1st edn. Springer-Verlag, Singapore, Chap. 19, p. 267, Fig. 5]



preserve the vasa vasorum. They also advocated the routine use of calcium channel blockers during and after surgery, to prevent spasm of the radial artery graft.

In a previous report, Calafiore and colleagues [20] suggested that the main reason for radial artery graft failure was the proximal anastomosis to the ascending aorta, and recommended using the LIMA for the proximal anastomosis. However, Iaco and associates [9], from Calafiore's group, and also Lemma and colleagues [21], observed more recently that the site of the proximal anastomosis of the radial artery graft did not influence early or late patency rates.

Earlier in our experience, the proximal end of the radial artery graft was anastomosed to the ascending aorta, except for patients with calcified ascending aorta. Also, use of the radial artery graft was limited to patients with unavailable or unsuitable saphenous veins, and to patients with peripheral vascular disease (to spare their saphenous veins for lower extremity revascularization), and to patients who had undergone a previous coronary artery bypass. In patients with a calcified ascending aorta, and in patients with peripheral vascular disease, we prefer to achieve total arterial revascularization.

Currently, we prefer to do all the proximal anastomoses of the radial artery end-to-side to the LIMA graft, before going on cardiopulmonary bypass. In off-pump CABG patients, the proximal radial artery to LIMA anastomoses were performed before any of the distal anastomoses. A word of caution when anastomosing the radial artery to the LIMA, is to divide completely all the adventitial bands along the undersurface of the LIMA, from the divided distal end, all the way up to the site for the proximal radial artery anastomosis, to avoid kinking of the LIMA graft, as occurred in one of our patients.

At present, we use the radial artery graft in combination with the left internal mammary artery in all age groups, whether the saphenous veins are suitable or not, and regardless of the total number of distal anastomoses. We use the pedicled LIMA graft routinely for the left anterior descending (LAD), and the radial artery graft for the obtuse marginal branch, the intermediate branch, or for both. For the right coronary artery and its branches we prefer to use a saphenous vein graft if it is a large artery, or a pedicled right gastroepiploic artery graft, if there is a severe proximal stenosis of the native coronary.

According to several authors, using two arterial grafts for myocardial revascularization decreases the prevalence of late cardiac events and the need for reoperations. Lytle and colleagues [22] observed that death and reoperation were more frequent for patients undergoing single rather than bilateral internal mammary artery grafting. However, Khot and associates [23] from the Cleveland Clinic observed a 33% occlusion rate for the radial artery graft, compared to 4.8% occlusion rate for LIMA grafts, in angiographic studies performed in a group of 310 selected patients with a radial artery graft, with recurrent angina. Their findings are in sharp contrast with the widespread information available in the literature, demonstrating a high patency rate of the radial artery graft [7–10]. A limitation in their study is that this group of 310 patients does not represent the entire population of patients with a radial artery graft at the Cleveland Clinic during the 5-year study period. In addition, the poor patency rates observed by Khot and colleagues [23] could be explained by the fact that the radial artery graft was frequently used for secondary targets with poor run-off, and for targets with competitive flow because of moderate stenosis of the native coronary.

In conclusion, several authors [7–10] have reported a high patency rate of the radial artery graft in postoperative angiographic studies. We believe that using at least two arterial conduits for myocardial revascularization is beneficial. In fact, Zacharias and associates [24] recently demonstrated improved survival in patients with radial artery grafts as a second arterial conduit, compared to patients with LIMA and vein grafts

only. Their study may help confirm the hypothesis that two or more arterial conduits may decrease the incidence of late cardiac events, and improve survival.

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Gastroepiploic Artery Grafting

Right Gastroepiploic Artery Grafting: History and Operative Techniques

J. PYM

20.1 Introduction

The right gastroepiploic artery has been successfully used as a coronary artery bypass graft since 1984. It is a very versatile conduit. When harvested appropriately, it provides approximately 20 cm of useable length. As a pedicled graft based on its gastroduodenal origin, it is capable of reaching all areas of the heart. It is usually used to graft the posterior descending branch of the right coronary artery, and seems to be the ideal arterial conduit for this purpose. Alternatively, segments can be used as free grafts, either aortocoronary grafts or composite grafts (Y- or T-grafts) with the internal thoracic arteries. It may also be used as the inflow source of a composite graft constructed with free segments of radial or internal thoracic arteries.

The only absolute contraindication to use of the right gastroepiploic artery is previous complete or partial gastrectomy. Harvesting is quite feasible even in morbidly obese patients. In patients who have had previous upper abdominal surgery – even hiatus hernia repair – adhesions around the stomach are usually sparse.

20.2 Anatomy

The right gastroepiploic artery is the largest branch of the gastroduodenal artery, which usually arises from the right hepatic artery. The gastroduodenal artery runs anteriorly and inferiorly between the pancreas and the duodenum from its hepatic artery origin and gives rise to branches to the anterior and posterior surfaces of the pancreas. It then divides into the superior pancreaticoduodenal and right gastroepiploic arteries. It should be noted that a major anastomotic channel between the celiac and superior mesenteric systems is via the superior and inferior pancreaticoduodenal arteries. After its origin from the gastroduodenal artery, the right gastroepiploic artery turns superiorly, giving off branches to the head of the pancreas and duodenum. There are usually several large branches to the pylorus.

The right gastroepiploic artery then runs towards the greater curvature of the stomach. After a short segment relatively free of branches, there are multiple branches to the antrum. The artery then runs between the layers of the greater omentum, 2–3 cm from the greater curvature of the stomach. It gives off large branches, usually in pairs, to the anterior and posterior surfaces of the body of the stomach, and the main artery becomes correspondingly smaller. There are also single branches to the greater omentum.

To the left of the midpoint of the greater curvature of the stomach, the right gastroepiploic artery usually becomes relatively small, often after giving off a leash of large gastric branches, and then anastomoses with the left gastroepiploic artery.

Significant anatomical variations occur in approximately 5% of patients, the most common being an origin from the superior mesenteric artery. This should be kept in mind if the right gastroepiploic artery cannot be visualized on postoperative celiac angiography.

20.3 History

The era of arterial revascularization of the heart began with Arthur Vineberg's surgical implantation of the internal thoracic artery into the myocardium. Although this was performed clinically from the early 1950s with notable symptomatic relief in some patients, prior to the advent of coronary angiography, the technique could only be validated by postmortem examination. The formation of collaterals between an implanted internal thoracic artery and the coronary circulation was first demonstrated angiographically at the Cleveland Clinic in 1962, and resulted in increased enthusiasm for the procedure. Bilateral internal thoracic artery implants were performed, but these reached only the anterior and lateral walls of the heart, so alternative conduits for revascularization of the posterior wall of the heart – right gastroepiploic and splenic arteries – were introduced.

In 1966, Charles P. Bailey reported the first use of the right gastroepiploic artery as a Vineberg implant for re-

vascularization of the posterior portion of the heart [1]. Further experience, with good clinical results [2, 3] and demonstrated angiographic patency [4], led to its acceptance as the implant of choice for the posterior wall of the heart. However, with the advent of direct revascularization with aortocoronary saphenous vein grafts, this promising conduit was ignored for almost a decade and a half.

Direct anastomosis of the left internal thoracic artery to the left anterior descending artery was reported by Kolessov in 1967 and pioneered in North America by George Green in 1968. In the same year, anastomosis of the right internal thoracic artery to the right coronary artery was performed by Bailey and Hirose (pioneers of the right gastroepiploic implant). Why did use of the right gastroepiploic artery for direct coronary anastomosis not follow? The most obvious explanation is technical: methods of microvascular anastomosis were still in evolution. The left anterior descending and main right coronary arteries are easily accessible anterior structures, allowing use of the operating microscope, as advocated strongly by George Green and others at the time. This, however, may be an oversimplification. Despite the fact that internal thoracic artery grafts were not widely used for many years, while aortocoronary saphenous vein bypass grafting was accepted early and dominated the field, there *was* an ongoing interest in alternative arterial conduits. However, early results of these grafts were generally disappointing.

The history of the radial artery graft in the early 1970s is well known: endothelial damage due to mechanical dilation led to unacceptable early failure rates. Subsequently, in the 1990s, it was rehabilitated as a viable conduit when the role of the endothelium in arterial function and the consequences of endothelial damage were recognized. Another arterial conduit introduced at that time was the splenic artery, pioneered by W. Sterling Edwards [5]. This was the first reported use of an abdominal artery for direct revascularization of the posterior wall of the heart. The splenic artery is large, but apparently more prone to atherosclerotic disease than other abdominal vessels, and may be more difficult to harvest. It was felt at that time that the right gastroepiploic artery was too small to use as a bypass graft: "We have explored the possibility of using the left gastric and the gastroduodenal arteries instead of the splenic, but these branches have always appeared too small and too short" [6]. Edwards confirmed this in conversation with me in 1987, although others have subsequently said that he did one unreported gastroepiploic artery bypass. An addendum to Edwards' 1973 paper [6] noted the requirement for splenectomy in most cases of splenic artery harvesting because splenic infarcts had been seen in two patients in whom the spleen had not been removed. There were also anecdotal reports of pancreatitis, either mechanical or ische-

mic, and concerns about the degree of atherosclerosis in some splenic arteries. For these reasons, among others, the technique was not developed further and fell into disuse. Thus, there was a long hiatus in the use of arterial conduits – apart from the few dedicated advocates of the internal thoracic artery.

In 1983, while at Queen's University in Kingston, Ontario, I was referred a 55-year-old woman (EK) requiring grafts to the left anterior descending and right coronary arteries. She had undergone bilateral long and short saphenous stripping, and had no useable arm veins. Her symptoms settled on medical management, but her case stimulated a search for alternative conduits. We noted the old reports of successful right gastroepiploic Vineberg implants and evidence that it was, like the internal thoracic artery, spared from atherosclerosis [7]. My senior colleague, Dr. R. Beverly Lynn, a retired cardiac surgeon, told us of his experience with the right gastroepiploic artery as an implant, and mentioned the extensive experience in Ottawa in the 1960s. To our surprise, we could not find any evidence in the literature that the right gastroepiploic artery had ever been used for direct coronary revascularization. Its use seemed quite feasible after dissection in the autopsy suite and palpation of the artery in a number of patients. The next question was how we should investigate it further. Fate took a hand. In September 1983, I met both Dr. G.M. Fizzgibbon, a senior Ottawa cardiologist, and Dr. Arthur Vineberg. In the course of our conversation, Dr. Fizzgibbon asked Dr. Vineberg about the long-term clinical efficacy of right gastroepiploic implants. The reason for his interest was that he had just performed celiac angiograms in two such patients, 17 and 19 years postoperatively: the implants were both angiographically patent.

The implications were obvious: if the right gastroepiploic artery behaved like the internal thoracic artery, remaining patent and free from occlusive disease as an implant, its behavior should be similar when it was directly anastomosed to a coronary artery. When the original patient (EK) who had started this train of thought presented again with symptoms refractory to medical management, informed consent was obtained and a right gastroepiploic to right coronary bypass, together with a left internal thoracic to left anterior descending bypass, was performed on 20 June 1984. Her recovery was uncomplicated, and angiography on the eighth postoperative day showed widely patent grafts. A brief article on the technique by a medical reporter appeared in the well-known Canadian natural history magazine *Equinox* in January 1985 [8] and was picked up by the lay and medical press, both in Canada and internationally. Incidentally, EK returned with recurrent angina 7 years later. Repeat angiography showed a patent left internal thoracic artery graft, but marked progression of distal left anterior descending artery dis-

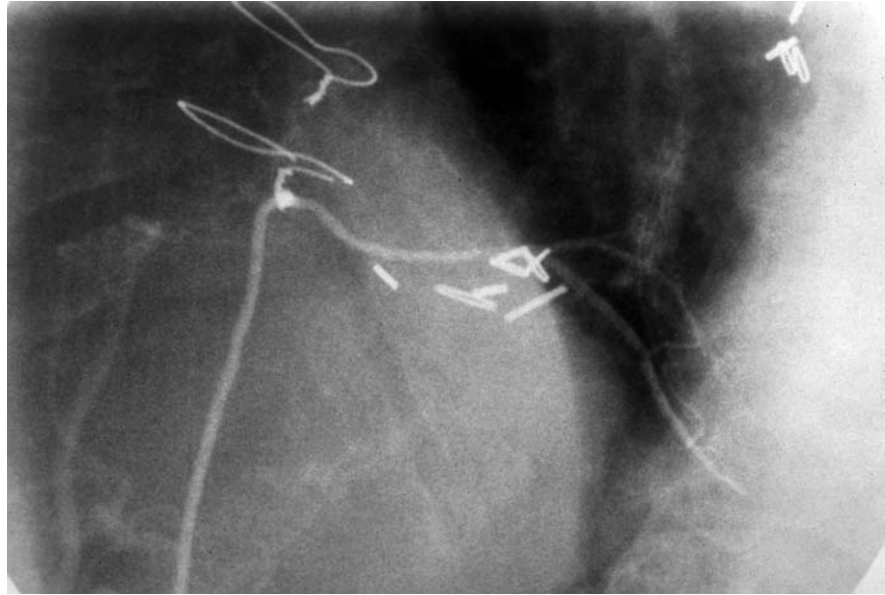


Fig. 20.1. Angiogram of the first right gastroepiploic to coronary artery bypass graft at 15 years

ease. The right gastroepiploic artery graft to the main right coronary artery was widely patent and smooth walled. The same excellent appearance of the right gastroepiploic artery was seen on angiography in February 1999, almost 15 years after surgery (Fig. 20.1). At that time, the left anterior descending artery was found to be occluded, and she underwent an off-pump right internal thoracic artery graft to the distal left anterior descending artery. Since then, she has continued to do well – I last spoke with her in March 2005, almost 21 years since her original surgery.

Initially, we used the right gastroepiploic artery only in patients without alternative conduits for posterior wall vessels. Early postoperative angiography was performed on all patients. Our first academic presentation, a report of two cases, was made at the Annual Scientific Meeting of the Royal Australasian College of Surgeons in Sydney, Australia, on 2 May 1985. This stimulated Martin Carter to begin a small series of patients, which he presented at the 1986 Australian meeting. Also, after our early discussion of the technique with Dr. Vineberg, a small series was begun in Montreal by Normand Poirier. Bruce Lytle at the Cleveland Clinic began using the right gastroepiploic artery in early 1986.

Meanwhile, in Tokyo, Hisayoshi Suma independently began his work on the right gastroepiploic artery in late 1985. His elegant study, based on a review of 100 celiac artery angiograms and histological specimens from five patients, showed the anatomic feasibility of routinely using the right gastroepiploic artery as another arterial conduit for coronary bypass surgery. He found that the artery supplied at least half the length of the greater curvature of the stomach in 95% of patients and was at least 1.5 mm in internal diameter in 96%.

Only one atherosclerotic stenosis was found. Suma then performed two clinical cases in March and October 1986, both successful reoperations in which the right gastroepiploic artery was used as a graft to the left anterior descending artery.

Our report of nine cases with early clinical and angiographic results was accepted by the *Journal of Thoracic and Cardiovascular Surgery* in August 1986 and published in 1987 [9]. Suma's study was accepted by *Annals of Thoracic Surgery* in April 1987 and published later that year [10].

Carter's series was also published in 1987 in Australia [11]. Other groups adopted the technique, and there were three further publications in 1989 [12–14]. Additional reports of very large series in the early 1990s by Suma [15] and Grandjean [16] confirmed the efficacy of the procedure. Our 10-year experience was presented to the American Heart Association in 1994 [17]. There was lasting symptomatic improvement and 10-year actuarial survival was 86.6%. There were no short term or long term complications related to the use of the right gastroepiploic artery.

In 2000, Suma published a series of 935 patients with right gastroepiploic artery grafts in which patency was 91.4%, 80.5% and 62.5% at 1, 5 and 10 years respectively [18]. These results are excellent, considering that the vast majority of right gastroepiploic artery grafts were used for the right coronary distribution, which gives the lowest long-term patency for any conduit. Also, late angiography was only performed in symptomatic patients. An important observation was that, while progression of disease was seen in the coronary arteries, luminal irregularities in the right gastroepiploic artery were rare. Our experience has been the same. The

smooth-walled appearance of a 15-year-old right gastroepiploic artery graft, almost unheard of in a venous graft to the right coronary system, is seen in Fig. 20.1.

The history of the right gastroepiploic artery would not be complete without mentioning the International Symposia organized by Jose Roquette in Portugal. The first was held in Lisbon in early June 1990, immediately following the successful symposium on arterial grafting in Toulouse, France. Most of the early users of the right gastroepiploic artery were present and have maintained contact with each other ever since. A second International Symposium was held in Lisbon in March 1994.

20.4

Harvesting Technique

The right gastroepiploic artery may be harvested as a pedicle, together with the right gastroepiploic vein and surrounding fat, or skeletonized, taking the artery alone, with no surrounding tissue. I strongly believe in the former approach, as skeletonization has no real advantage in terms of length, if a pedicle is harvested correctly. Furthermore, skeletonization risks damage to the arterial wall, and may render the vessel prone to perioperative spasm.

The right gastroepiploic pedicle can be harvested through a small midline extension to a conventional median sternotomy or a lower hemisternotomy. If exposure of the heart is through one of the minimally invasive approaches, it can also be harvested through a small separate upper abdominal incision. Since most coronary bypass surgery is performed via a median

sternotomy, this is the approach which will be described in detail. If there has been previous upper abdominal surgery, the peritoneum can be opened at the lower end of a standard sternotomy incision, and the extent and severity of intra-abdominal adhesions assessed before committing to a longer incision.

The median sternotomy incision is extended inferiorly by 5–7 cm beyond the tip of the xiphoid process. The sternal spreader is moved towards the lower end of the sternum, and a Balfour retractor is positioned so that it is held either by the divided xiphoid process on each side or the blades of the sternal retractor. Strong inferior traction on the Balfour blade then provides excellent exposure of the stomach (Fig. 20.2). A nasogastric tube is used to empty the stomach completely. This facilitates harvesting of the right gastroepiploic artery and allows full mobilization through only a small addition to the standard median sternotomy incision.

The right gastroepiploic artery is located by palpation. Dissection of the omental border of the pedicle is begun in the midline, 1–2 cm from the artery, using low intensity electrocautery or, preferably, the Harmonic Scalpel shears (Ultracision, Johnson & Johnson) (Fig. 20.3). The few large omental branches are clipped and then divided. The lesser sac of the peritoneum is entered. With a hand in the lesser sac holding the stomach and the artery between finger and thumb, keeping its position known at all times, dissection is carried down towards the pylorus. A key technical point is to fully mobilize the stomach by dividing all adhesions in the lesser sac. This allows the stomach to be drawn up into the incision, giving access to the proximal portion of the artery. After reaching the pylorus, dissection is carried out to the left of the midline according to the

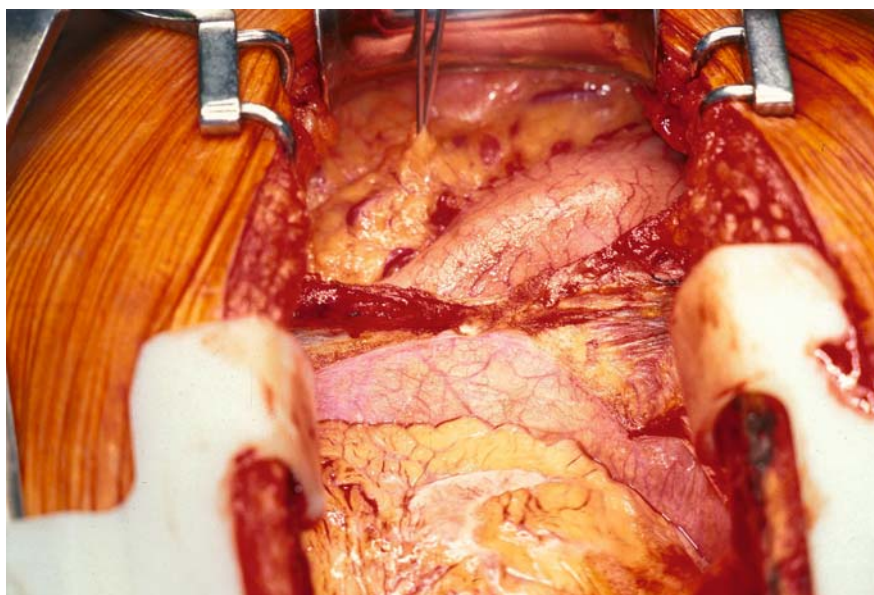


Fig. 20.2. View from patient's head showing heart, diaphragm and stomach, with forceps holding the omentum near the right gastroepiploic artery

Fig. 20.3. Dissection of the omental border of the pedicle with low-intensity electrocautery

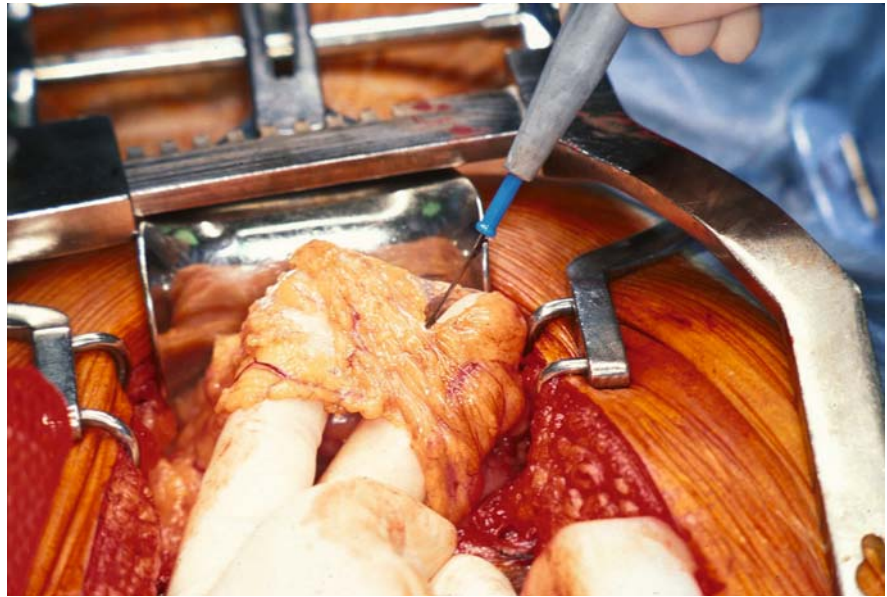
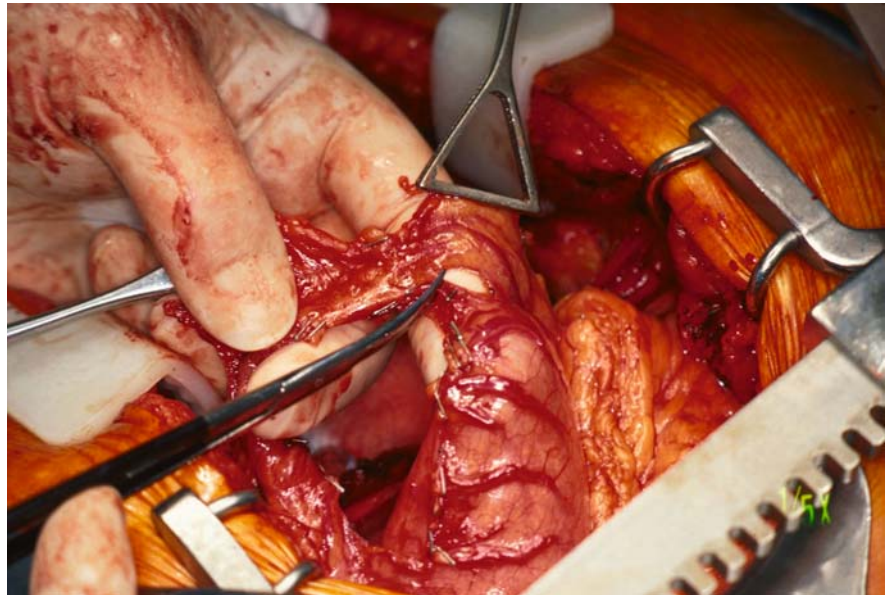


Fig. 20.4. Dissection of the gastric border of the pedicle, individually clipping and dividing the branches to the stomach



length of graft required. Usually, for a pedicle graft to the inferior wall of the heart, only a few additional centimeters are required, if full proximal mobilization has been performed. It should be noted that the right gastroepiploic artery usually gives off a leash of large gastric branches near the midpoint of the greater curvature of the stomach, and becomes significantly smaller after this.

The stomach is then lifted superiorly, and mobilization of the gastric side of the pedicle is begun. The visceral peritoneal layer is divided with the Harmonic Scalpel shears, which can then be used to dissect out gastric branches. This can also be done with scissors or low-intensity electrocautery, using the spatula as a dis-

secting tool to isolate the gastric branches. Care must be taken to avoid the use of electrocautery close to the gastroepiploic artery itself, or to divide branches with it, because of the risk of thermal and electrical injury to the artery.

Branches of the artery, which usually arise in pairs, are *individually* clipped and divided (Fig. 20.4). Alternatively, large branches can be clipped and the remaining smaller branches and fat divided with the Harmonic Scalpel (Fig. 20.5). Whatever the method used, it is vitally important to divide the branches individually, clipping or ligating them without including any surrounding tissue. This allows the pedicle to elongate, so that a more proximal portion of larger diameter can be



Fig. 20.5. Use of the Harmonic Scalpel to mobilize the right gastroepiploic pedicle



Fig. 20.6. Typical elongation of the right gastroepiploic pedicle seen when appropriate harvesting techniques are used

used for coronary anastomosis. After all, the stomach is an extremely distensible organ, and the greater curvature elongates markedly as the stomach fills. If gastric branches are mass ligated or the gastric border of the pedicle is stapled, the pedicle length is essentially fixed at the size of the empty stomach. Dissection, ligation or clipping, and division of individual branches in this manner also avoids the risk of a vessel slipping back inside a sheath of visceral peritoneum, leading to a potentially troublesome hematoma in the pedicle. Typical elongation of the right gastroepiploic pedicle is seen in Fig. 20.6.

Branches to the distal portion of the antrum are more easily approached from the anterior surface.

There are multiple smaller arterial branches in this area, and use of the Harmonic Scalpel greatly facilitates this part of the dissection. There is usually a relatively avascular window just before the pylorus. Branches to the pylorus itself are usually divided; this significantly increases mobility and length of the pedicle, allowing anastomosis with a larger diameter segment of artery. There appears to be no advantage in terms of length to be obtained by dividing branches to the duodenum, because the right gastroepiploic artery is running directly cephalad at this point. Furthermore, there is at least the theoretical risk of ischemic damage to the head of the pancreas, which is partially supplied by branches from the artery at this point.

If the pedicle is too bulky, it may be trimmed of excess fat using the Harmonic Scalpel. It is easier, faster and safer to do this with the pedicle fully mobilized. Once sufficient length of pedicle has been mobilized, it is left in situ and wrapped in gauze soaked in nitroglycerin/verapamil solution until ready for division. At this point, it is usual to create the appropriate diaphragmatic opening, depending on the coronary artery to be grafted, as discussed below.

20.5

Preparation of the Artery

After other grafts have been harvested and the patient heparinized, the right gastroepiploic pedicle is divided. The distal end of the artery is cannulated with a soft 22-gauge Angiocath and 3–4 ml of dilute nitroglycerin/verapamil solution gently infused. The end of the artery is then clipped and the artery is allowed to dilate under its normal perfusion pressure. Hemostasis of the pedicle should be checked at this time, as small branches may open under the influence of a vasodilator. The pedicle may also be trimmed of excess tissue, using the Harmonic Scalpel. At this point, it is useful to bring the graft through the diaphragmatic incision, carefully checking its orientation using the line of clips along the gastric border of the pedicle. After checking the length and leaving enough to permit the necessary cardiac displacement, excess length is trimmed. Since the right gastroepiploic artery decreases in diameter much more rapidly over its length than the internal thoracic artery, it is important to use the more proximal portion of the artery for grafting. The distal end of the artery is

clipped again to allow continued perfusion until it is required for anastomosis. The right gastroepiploic vein is also clipped.

Since the right gastroepiploic pedicle is usually larger and heavier than that of other arterial grafts, there is potentially more risk of kinking of the anastomosis if it is unsupported. In order to maintain the orientation of the pedicle at the anastomosis, the artery is left within it, rather than being partially skeletonized. For this purpose, the artery is exposed 2 cm proximal to the end of the pedicle (Fig. 20.7).

20.6

Routing the Pedicle

The pedicle is either brought anterior or posterior to the pylorus, depending on the lie of the stomach and size of the liver. In most patients, the anterior route is used. For grafts to the left anterior descending artery, the pedicle is brought anteriorly through a small slit in the diaphragm. For all other coronary vessels, it has always been my practice to bring the right gastroepiploic artery anterior to the liver and through a cruciate incision in the diaphragm opposite the atrioventricular groove (i.e., between the midline and the inferior vena cava; Fig. 20.8). The artery then lies in the pericardium parallel to the atrioventricular groove, and is brought down to the target vessel in a smooth curve. There is no significant advantage in terms of length to be obtained, even in reaching distal circumflex branches, by bringing the pedicle posteriorly. In fact, if the heart needs to be elevated significantly to perform the anastomosis, additional length will be required. Furthermore, with



Fig. 20.7. Preparation of the right gastroepiploic artery – exposure of the artery within the distal end of the pedicle

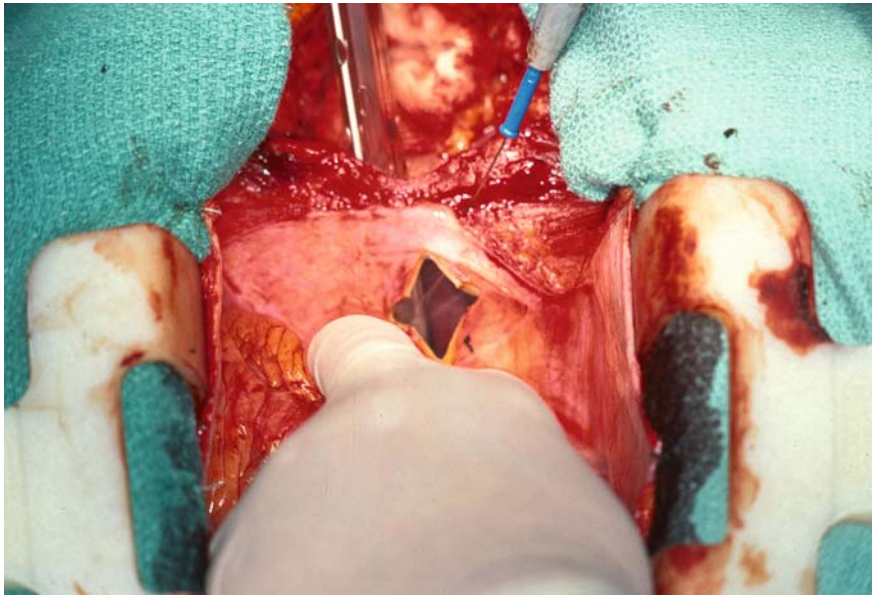


Fig. 20.8. Cruciate incision in the diaphragm opposite the atrioventricular groove for passage of the right gastroepiploic pedicle. The liver is seen through the incision

the anterior approach, the whole pedicle remains easily accessible to check orientation and hemostasis. The diaphragmatic incision should be cruciate, rather than a slit, so that it will allow free passage of the pedicle and will splay open when the diaphragm contracts. An opening in this portion of the diaphragm will always be protected by the liver, thus minimizing the risk of a diaphragmatic hernia.

20.7

Anastomotic Technique

More than 85% of our experience with the right gastroepiploic artery has been with its use as a graft to the posterior descending artery. There is usually an excellent size match between the two vessels, and excellent exposure can be obtained for the anastomosis. Furthermore, the posterior descending artery is almost always less atherosclerotic than the main right coronary artery, rendering a graft to this vessel less vulnerable to progression of distal coronary disease.

For right gastroepiploic artery grafts to coronary arteries on the inferior and inferolateral walls of the heart, the heart is held vertically, apex to ceiling. In my experience, this gives the best exposure and most convenient orientation for anastomosis. Also, for off-pump grafting, this position of the heart is extremely well tolerated, requiring only slight head-down (Trendelenburg) positioning to maintain normal hemodynamics. Even this may not be necessary if an apical suction heart positioner (such as a Medtronic Starfish) is used. Alternatively, as for access to the right main coronary artery, the acute margin of the heart can be rolled over

and elevated, but this does not give as good an exposure as the vertical position.

After making an arteriotomy in the coronary artery, an undersized intraluminal Flo-Rester is inserted. This soft atraumatic device keeps the arteriotomy free of blood and allows gentle manipulation of the vessel without trauma to its wall. When the procedure is performed off-pump, an intracoronary shunt is usually used.

The right gastroepiploic artery, having previously been brought through the diaphragm and its orientation checked, is transected obliquely within its pedicle, and the end spatulated (Fig. 20.9). Free blood flow is visually assessed. The anastomosis is constructed using a two-stitch technique with continuous 7-0 or 8-0 Prolene (Fig. 20.10). Five bites of continuous open suture are placed in a counterclockwise direction at the heel of the anastomosis, after which the right gastroepiploic artery is drawn down onto the coronary artery and flushed to check outflow. Next, the toe of the anastomosis is sewn with five bites of continuous open suture in the same direction. This suture is then tightened, and the shunt or Flo-Rester removed, verifying patency of the anastomosis. If the two arteriotomies have been correctly sized, the arterial walls then lie parallel to each other with intimal apposition, and the remaining stitches along the lateral aspects of the anastomosis can be rapidly completed.

A key technical point is to protect the anastomosis from kinking from cardiac and diaphragmatic movement and the weight of the pedicle. This can be prevented if the anastomosis is performed with the right gastroepiploic artery remaining within the pedicle. The pedicle is sutured to the epicardium on either side of the coronary artery, just proximal to the heel of the

Fig. 20.9. The pedicle is passed through the diaphragm and the artery is divided within the pedicle and spatulated ready for anastomosis to inferior or inferolateral wall vessels

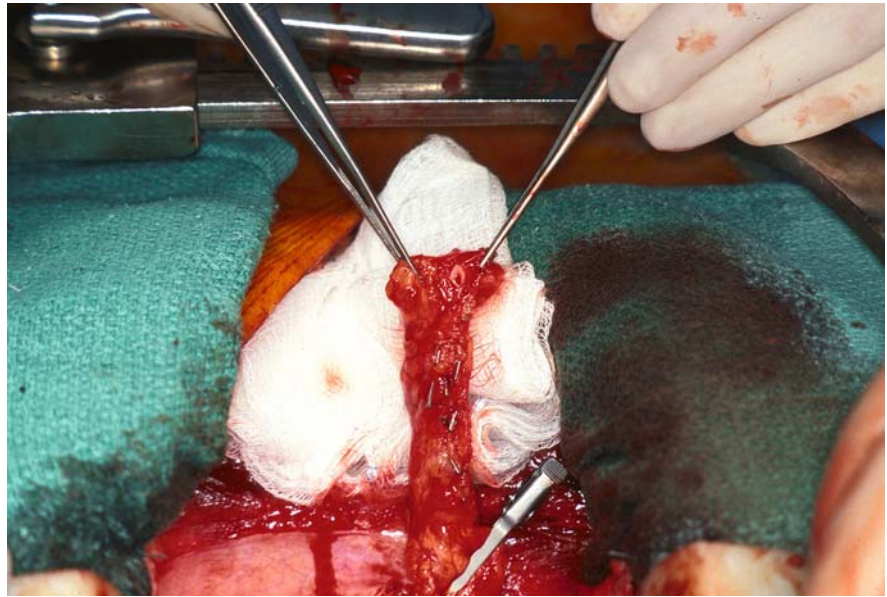


Fig. 20.10. Right gastroepiploic anastomosis to the posterior descending branch of the right coronary artery



anastomosis. The distal end of the pedicle is then brought over the anastomosis and sutured to the epicardium distally in the line of the graft. This three point fixation securely maintains the correct orientation of the graft. If there are any concerns about hemostasis, one of the fixation stitches can easily be cut and the anastomosis inspected.

When the heart is returned to its anatomic position, excess graft length, if any, is returned to the abdomen. However, when the graft is brought through the diaphragm in this course and position, the length required to reach the posterior descending artery is almost identical whether the heart is held vertically or placed in the anatomic position. The completed right gastroepiploic

bypass is seen from the surgeon's perspective in Fig. 20.11. An angiogram (at 63 months) of a right gastroepiploic bypass to the posterior descending branch of the right coronary artery (Fig. 20.12) shows the graft running in a smooth curve from the abdomen into the pericardium and to the coronary artery. In most situations, the right gastroepiploic artery is anastomosed to the coronary artery in an antegrade fashion (i.e., in the direction of normal coronary blood flow). For grafts to the left anterior descending artery the right gastroepiploic artery is brought anteriorly across the diaphragm and anastomosed in the opposite direction to normal coronary blood flow. A retrograde anastomosis is sometimes preferable for grafts to the main right coro-

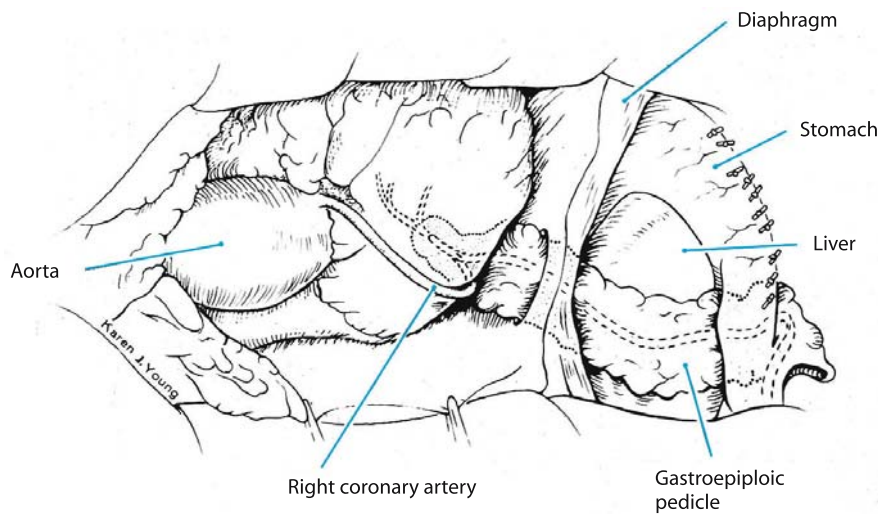


Fig. 20.11. Surgeon's perspective of completed right gastroepiploic artery bypass

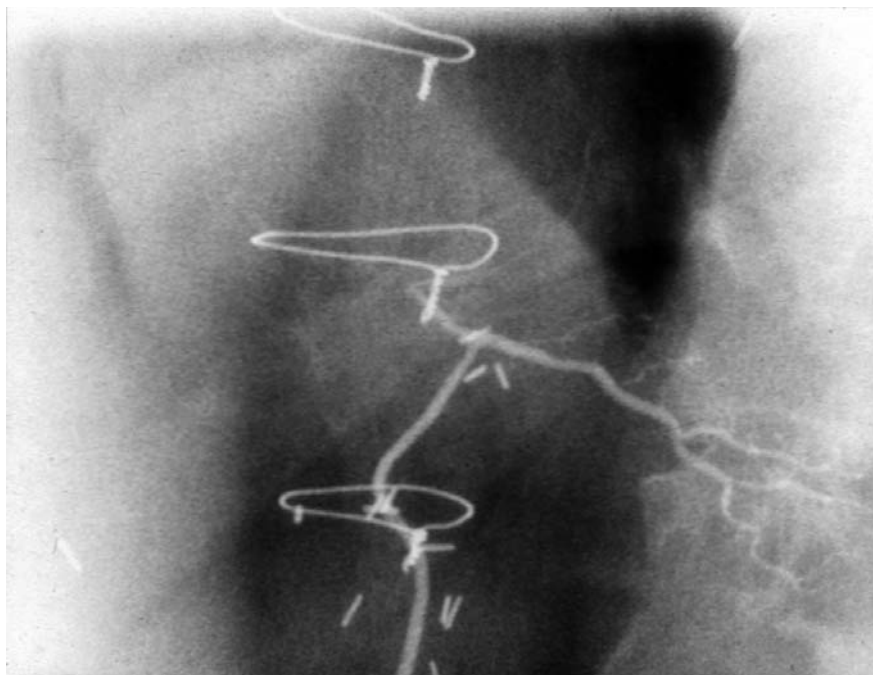


Fig. 20.12. Angiogram (at 63 months) of right gastroepiploic artery bypass to posterior descending branch of the right coronary artery, showing smooth curve from abdomen into pericardium and to coronary artery

nary artery. Sequential grafts with the right gastroepiploic artery are feasible but are difficult if the pedicle is very fat. The Harmonic Scalpel is useful to debulk the pedicle without risk of damage to the artery. For side-to-side anastomoses in sequential grafts, it is useful once again to use an intraluminal Flo-rester in each artery to help with exposure and avoid excessive direct manipulation of the arterial walls.

Segments of the right gastroepiploic artery may also be used as free grafts, although long term results of these are not available, and I have rarely used them. For an aortocoronary free graft, the proximal anastomosis should be to a pericardial or venous patch in the aorta, or to the hood of a saphenous vein graft, rather than di-

rectly to the aorta itself. Alternatively a segment of the right gastroepiploic artery may be used to construct a composite graft, such as a Y- or T-graft from the left internal thoracic artery for grafting the diagonal branch of the left anterior descending or obtuse marginal branch of the circumflex. The use of composite grafts rather than free grafts has the advantage of arterial size and compliance matching at the proximal anastomosis. Also, much less graft length is required between, for example, a left internal thoracic artery to left anterior descending graft and a circumflex branch than for an aortocoronary graft to the same vessel.

If it is decided to use a composite Y-graft, it is constructed prior to cardiopulmonary bypass. The distal

anastomosis of the “donor” graft – usually the left internal thoracic artery – is performed first. The free Y-segment is then tailored to length and its distal anastomosis carried out.

The RGE artery may also be used as the “donor” artery for a composite graft. A segment of another vessel, usually the radial artery, may be anastomosed to the right gastroepiploic artery in a Y- or T-configuration. Alternatively, a bridge between two coronary arteries may be made with, for example, a segment of radial artery, and the right gastroepiploic artery anastomosed to that bridging segment.

Although the right gastroepiploic artery can be used in creative arterial grafting as described above, its primary role is as a pedicled graft to the right coronary system, usually to the posterior descending artery.

20.8

Perioperative Management

Flow in arterial grafts depends on both blood pressure and vascular tone. The right gastroepiploic artery is a muscular vessel, and contracts much more strongly than the internal thoracic artery. Thus, any conditions such as hypovolemia and hypothermia, which have vasoconstrictor responses, should be prevented or corrected rapidly. Adrenoceptors in the right gastroepiploic artery are largely α_1 , with a variable and weak β response. Pure α -agonists or inotropes having a largely α effect may increase blood pressure at the expense of a disproportionate increase in vascular tone, resulting in vasoconstriction in an arterial graft. There have been anecdotal reports of severe graft vasoconstriction with concomitant intraoperative use of an α -agonist and a β -blocker. The use of these agents together should be avoided.

Postoperatively, it has been our practice to use a low dose intravenous nitroglycerin infusion (10–30 $\mu\text{g}/\text{min}$) for 12–18 h [19]. Hypertension is managed with nitroglycerin, supplemented with nitroprusside if required. If inotropic support is required, dobutamine or dopamine is used at doses not exceeding 10 $\mu\text{g}/\text{kg}/\text{min}$. When this is inadequate, either an isoproterenol/epinephrine infusion or intra-aortic balloon pump may be used.

Perioperative spasm of right gastroepiploic artery grafts has not been a problem in our experience. Avoiding excessive manipulation of the artery and damage to the arterial wall are key points. We have not used prophylactic calcium channel blockers. If arterial graft spasm is suspected, an intravenous milrinone infusion is recommended.

Nasogastric tube drainage is used routinely to prevent acute gastric dilatation which may cause tension on the anastomosis. We have not seen prolonged ileus

as a consequence of right gastroepiploic harvesting and the tube is usually kept in only overnight. It should be emphasized that, although there have been a number of potential intra-abdominal complications postulated as a consequence of right gastroepiploic artery harvesting, these are extremely rare.

20.9

Conclusion

The right gastroepiploic artery has been used as a coronary artery bypass graft for almost 21 years, with excellent short term and long term results and freedom from graft atherosclerosis. Despite this, it is underutilized, particularly in North America, and deserves further attention. The combination of pedicled internal thoracic artery grafts to the left coronary system and a pedicled right gastroepiploic artery graft to the right coronary system allows total arterial revascularization of the heart with three separate inflow sources and the avoidance of aortic manipulation. The right gastroepiploic artery should become the graft of choice for the posterior wall of the heart.

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The Right Gastroepiploic Artery Graft

H. SUMA

21.1

Introduction

The right gastroepiploic artery (RGEA) was used for indirect myocardial revascularization by Bailey [1], Vineberg [2], and their colleagues in the 1960s, and Sterling Edwards utilized the RGEA for coronary artery bypass grafting in the early 1970s [3]. One and half decades later, the RGEA was revived as a new arterial conduit following general recognition of the superiority of the internal thoracic artery (ITA) over the saphenous vein (SV) graft in coronary artery bypass grafting [4, 5].

The GEA is detached as a pedicle or in skeletonized fashion along the greater curvature of the stomach. Usually the GEA is taken down to two-thirds of the greater curvature. Detachment of the GEA at the proximal site should be limited to the lower margin of the pylorus. Endoscopic Doppler flow study has shown no ischemia in the greater curvature after detachment of the GEA from the stomach [6]. Prior to the anastomosis, 3–4 ml diluted papaverine hydrochloride (40 mg in 10 ml physiological saline) is injected into the GEA lumen from the distal cut end to relieve spasm. Because the GEA is a muscular artery, strong spasms frequently occur by manipulation for take down. Intraluminal papaverine is an essential procedure to obtain good caliber and flow for successful anastomosis.

The GEA pedicle is then introduced into the pericardial space through the hole in the diaphragm made by electrocautery, passing the anterior surface of the stomach and the liver. Anastomosis between the GEA and coronary artery is made by 8-0 suture similar to that of the ITA. The GEA is occasionally used as a free graft. The harvesting technique is the same as that of an in situ GEA graft as described above.

21.2

Clinical Results

The patency rate of the in situ GEA graft was 95% in 783 grafts at the early postoperative period (within 1 year, mean 2 months) and 88% in 138 grafts at late re-

study (1 year to 15 years, mean 6 years) (Table 21.1, Fig. 21.1).

In our 18-year experience with 1,118 patients since 1986, 942 patients have been men and 176 women with a mean age of 61 years, ranging from 6 to 83 years of age (Table 21.2). The sites of GEA grafting were 70 anterior descending, 7 diagonal, 174 circumflex and 889 right coronary arteries (Table 21.3). ITA was used in 1,080 patients (97%) concomitantly. Also, inferior epigastric artery, radial artery and saphenous vein were combined in 46,128 and 523 patients, respectively. Mean number of bypasses was 3.1 and mean number of arterial grafts was 2.4 per patient. There were 17 early deaths (1.5%). New Q wave was noted in 13 patients (1.2%) (Table 21.4).

The free GEA graft has been less commonly used in our practice and its patency rate was 80% in 15 grafts at

Table 21.1. Right gastroepiploic artery graft patency

Period	No. restudied GEAs	No. patent GEAs	Patency rate
Early (<1 year)	783	744	95
Late (1 ~ 15 years)	138	121	88

Table 21.2. The right gastroepiploic artery graft

No. of patients	1118
Male/female	942/176
Age (years)	61 (6–83)
Coronary lesion	
Single	9 (1%)
Double	179 (16%)
Triple	749 (67%)
LMT	181 (16%)
Previous MI	682 (61%)
Previous CABG	92 (8%)
Ejection fraction	0.51 (0.24–0.80)

Table 21.3. The right gastroepiploic artery graft

Site	No. of GEA anastomoses
LAD	70
Diagonal	7
Circumflex	174
RCA	889

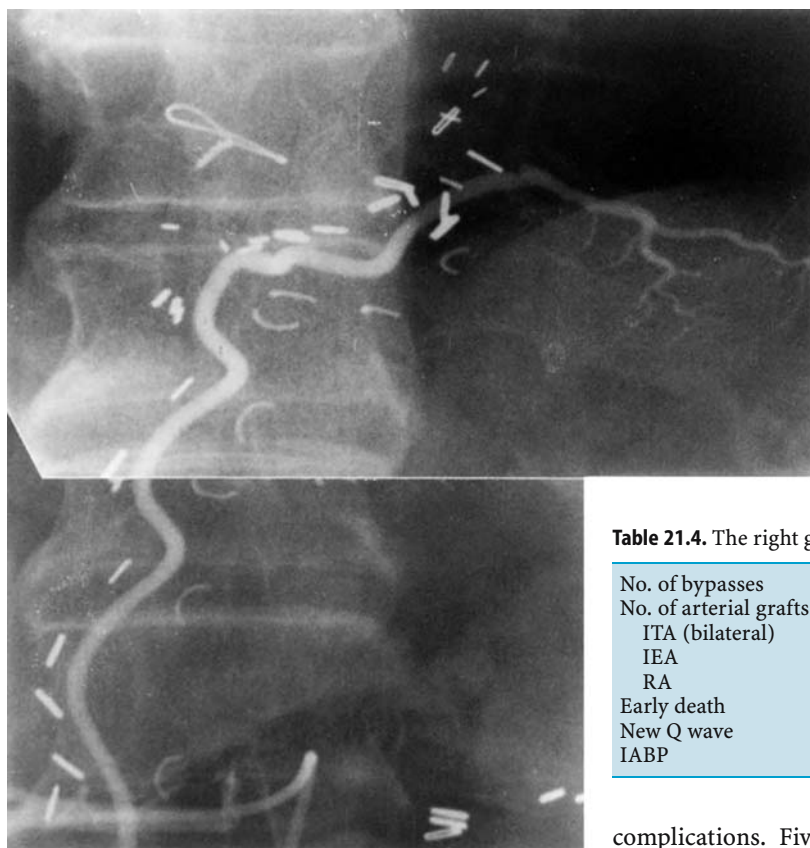


Fig. 21.1. GEA graft: 10 years

Table 21.4. The right gastroepiploic artery graft

No. of bypasses	3.1
No. of arterial grafts	2.4
ITA (bilateral)	1,080 (321)
IEA	46
RA	128
Early death	17 (1.5%)
New Q wave	13 (1.2%)
IABP	19 (1.7%)

the early postoperative period. Durability of the free GEA graft has not yet been investigated sufficiently.

Regarding postoperative exercise tolerance, Kusukawa [7], Isomura [8] and their colleagues have shown that the in situ GEA graft has sufficient flow capability under maximal stress. Thallium-201 washout rate significantly improved at the GEA grafted area.

The mid term results of the GEA graft were reported by Suma [9] and co-workers in 200 patients, followed up from 6–7 months with a mean of 27 months. Early mortality was 3% and early patency rate was 96% in 152 in situ grafts.

Regarding late clinical outcome, Grandjean and colleagues [10] reported that 5-year actuarial survival rate in 256 patients who were operated on with bilateral ITA and GEA grafts was 95.5%. Nishida and colleagues [11] have shown that 5-year survival with the combined GEA and bilateral ITA without other conduits was 92.9% and the cardiac death free rate was 97.8% in 239 patients.

In the report of Hirose and colleagues [12], in-situ GEA grafts were generally used to bypass the posterior descending coronary artery in association with internal thoracic artery to the anterior descending artery bypass in 1,000 isolated CABGs during a 10-year period. Operative mortality was 0.8% with no abdominal

complications. Five-year survival and cardiac event free rates were 92.6% and 84.2%, respectively. The 5-year graft patency rates of GEA and left internal thoracic artery grafts were 84.4% and 97.0%, respectively. Tavilla et al. [13] reported 10-year survival rate was 87% in 201 patients, with triple vessel disease treated by using bilateral ITA and GEA grafts.

Late angiographic patency of the GEA graft reported by Voutilainen et al. [14] was 82% in 26 grafts restudied 5 years postoperatively. In our recent investigation with 936 patients having a GEA graft [15], cumulative patency rate of the in situ GEA graft was 91.4%, 80.5%, and 62.5% at 1, 5, and 10 years, respectively. The most common cause of late occlusion of the graft was primary anastomotic stenosis and anastomosis to the coronary artery with a low grade stenosis (competitive flow). In other words, a good anastomosis to the critically stenotic coronary artery improves GEA patency. In angiograms 10–15 years after operation, wall irregularity or a new stenotic lesion was uncommon in GEA conduits and this suggests less graft disease than in the saphenous vein (Fig. 21.1).

As a recent fashion, skeletonization of GEA, which was introduced by Dr. Vincent Dor [16], seems to have superior patency at the early postoperative period even for off-pump CABG [17, 18]. The GEA pedicle has recently been investigated as a new biological graft as an omental wrapping with basic fibroblast growth factor [19].

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22 Technique and Results for Skeletonized GEA Using the Harmonic Scalpel in Combination with Other Arterial Grafts in Off-Pump Coronary Bypass Surgery

T. ASAI

22.1 History of GEA Skeletonization

The history of using the right gastroepiploic artery (GEA) in coronary revascularization started in the 1960s, when Bailey reported the Vineberg implantation of the GEA into the posterior area of the heart [1]. Since direct coronary artery bypass procedures became the standard revascularization method, the GEA to coronary artery anastomosis has been reported by Pym [2] and Suma [3] in 1987.

Some long-term results from the GEA bypass procedure have been reported [4, 5]. Suma demonstrated that the patency rate of GEA was 80.5% at 5 years and 62.5% at 10 years. There has indeed been some criticism since the data were not much better than the late patency results for saphenous vein grafts. However, if we read the publication carefully, the author noted that the causes of late occlusion were related to primary anastomotic stenosis or grafting to only mildly stenotic coronary arteries. We suspect that the anastomotic stenosis may have come from inadequate dilation of vasoconstricted GEA

during preparation and construction of the anastomosis. Another reason for the mediocre late results may be the indiscriminate use of GEA bypass to only mildly stenotic coronary arteries. However, the angiographic study reportedly rarely showed late-developing stenosis in GEA trunks in the long term.

Since then, in 1998, the use of skeletonized GEA has been reported for coronary bypass conduit [6]. Skeletonization prevents vasospasm, facilitates visual inspection, and makes sequential anastomosis easy. However, the skeletonization technique is cumbersome and time-consuming with ordinary methods using electrocautery, scissors and hemoclips. In 2001, we developed a simple and safe technique for harvesting skeletonized GEA using an ultrasonic scalpel (Harmonic Scalpel, Ethicon Endo-Surgery, Cincinnati, Ohio) [7]. Our clinical results with skeletonized GEA and the internal mammary artery (IMA) using a Harmonic Scalpel in off-pump coronary artery bypass (OPCAB) were presented at the Sixth Meeting of the International Society for Minimally Invasive Cardiac Surgery in San Francisco in 2003.

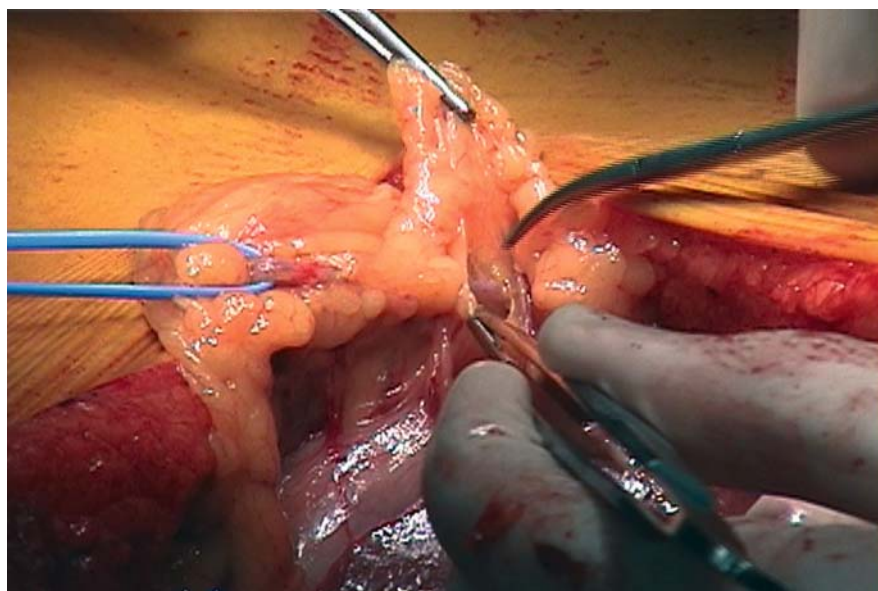


Fig. 22.1. The first step is to pass thin vessel loops under the GEA at 5-cm intervals

22.2

A Technique for Skeletonizing GEA Using the Harmonic Scalpel

A median sternotomy is extended about 5 cm caudally from the xiphoid process. Prior to harvesting one or both IMAs, the peritoneal cavity is opened by cutting down the diaphragm vertically rather than making a large midline upper abdominal incision. This significantly facilitates the exposure of the inferoposterior area of the heart for anastomosis in OPCAB, and is later closed simply with a 3-0 Vicryl running suture. The GEA is inspected and palpated to confirm it as a suitable conduit.

After skeletonizing one or both IMAs using the Harmonic Scalpel with the dissecting hook tip, GEA is harvested in skeletonized fashion using the Harmonic Scalpel with the coagulating shears tip. The first step of this stage is to pass thin vessel loops under the GEA at 5-cm intervals (Fig. 22.1). The anterior layer of the greater omentum is incised using an electrocautery. The soft tissue between the GEA and its satellite vein is carefully undermined using “mosquito” forceps and only the artery is encircled with the rubber vessel loops. This is carried out through the entire necessary length from the level of the pylorus.

The second step is to unroof the tissue surrounding the GEA (Fig. 22.2). The anterior layer of the greater

Fig. 22.2. The second step is to unroof the anterior layer of the surrounding tissue

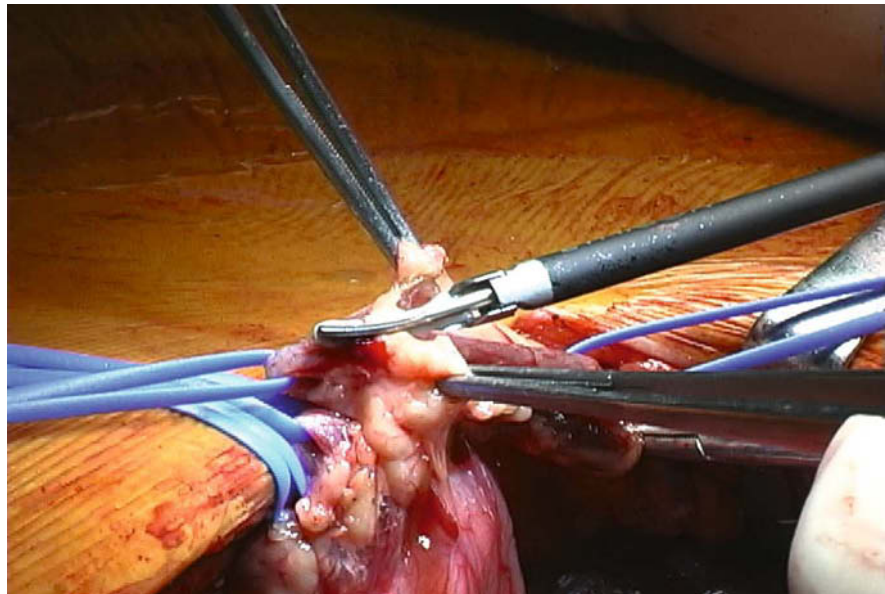
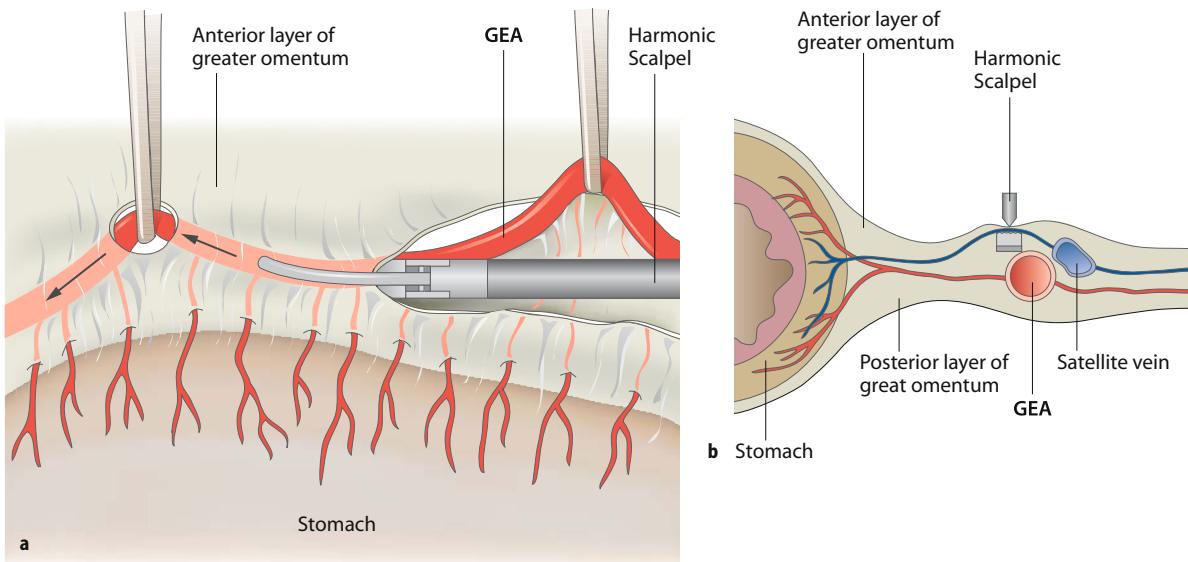


Fig. 22.3. a The anterior layer of the greater omentum is incised just above the right gastroepiploic artery (GEA) using a Harmonic Scalpel with coagulating shears. **b** The cross-sectional view demonstrates how the GEA is protected from heat damage by the “tissue pad” of the Harmonic Scalpel. (Fig. 22.3 is reproduced from ref. [7])



omentum is divided with the Harmonic Scalpel coagulating shears between the vessel loops. The “tissue pad” jaw of the shears is inserted through the soft tissue (Fig. 22.3) in such a way that the GEA trunk is protected from heat energy during use of the Harmonic Scalpel. With this step, the GEA is exposed throughout its entire length. When we occasionally encounter omentum thick with adipose tissue, we clear away the fat around the GEA by stroking it gently with the activated tip of the Harmonic Scalpel.

The GEA gives off thin-walled gastric and omental branches. The next step then is to seal and sever all the branches together with the soft tissue (Fig. 22.4). By gently pulling up the vessel loops, the whole surrounding tissues are detached by coagulating shears approximately 2 mm away from the GEA (Fig. 22.5). During dissection, we rarely encounter bleeding from the satellite vein or any other vessels. The whole skeletonization of the GEA takes a short time, ranging from 7 to 13 min, without injuring the arterial trunk, in our experience.



Fig. 22.4. The next step is to divide all the arterial branches together with soft tissue 2 mm away from the GEA

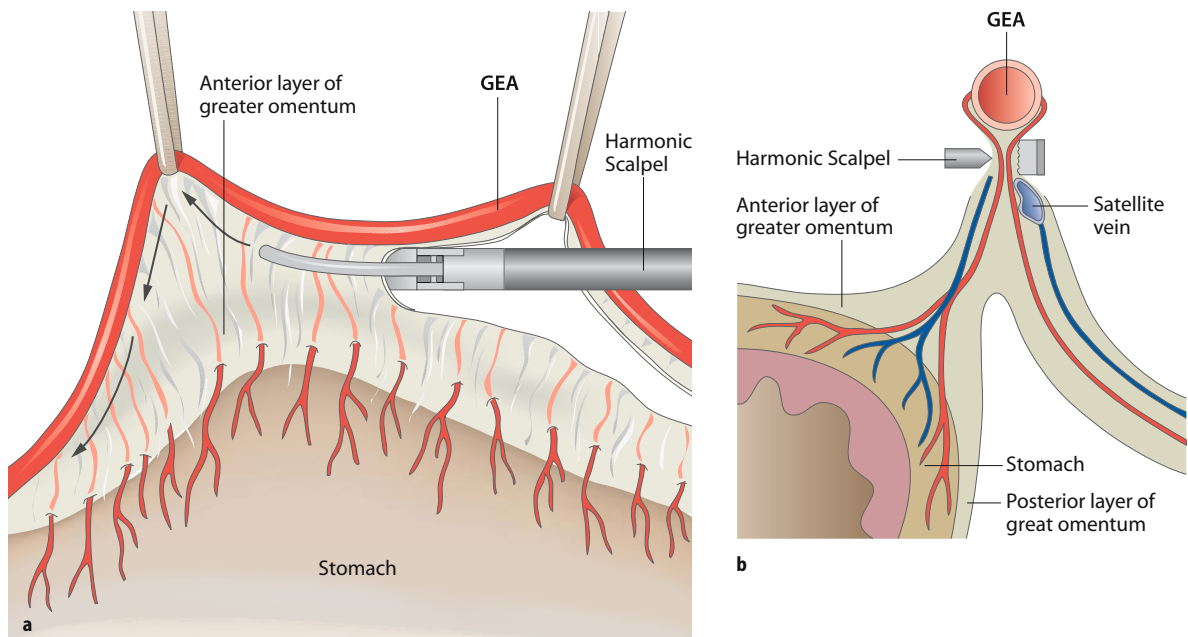


Fig. 22.5. **a** Vessel loops are pulled up gently; thus all arterial branches and veins are detached approximately 2 mm away from the GEA by the Harmonic Scalpel. **b** The cross-sectional view shows how the surrounding tissues are divided from the GEA. (Fig. 5 is reproduced from ref. [7])

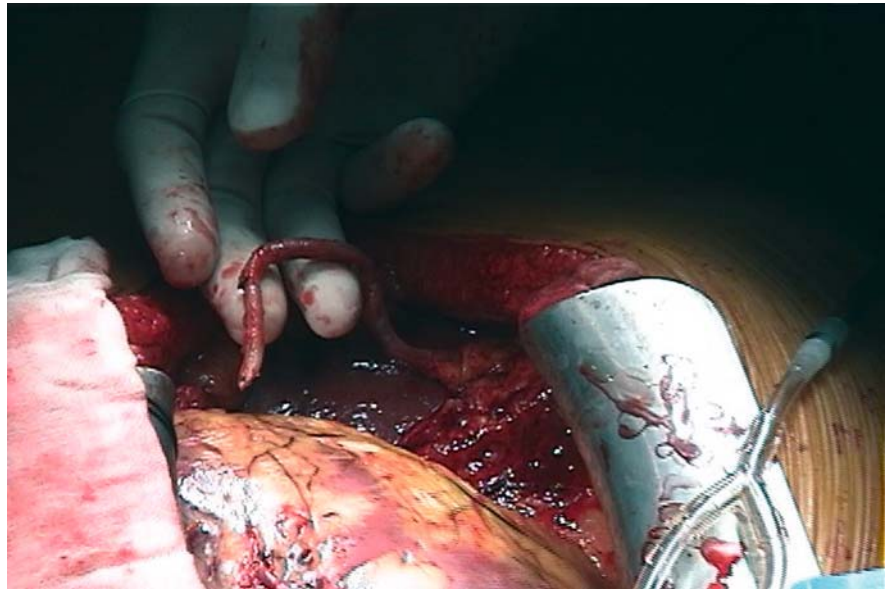


Fig. 22.6. The skeletonized GEA becomes a markedly dilated arterial conduit

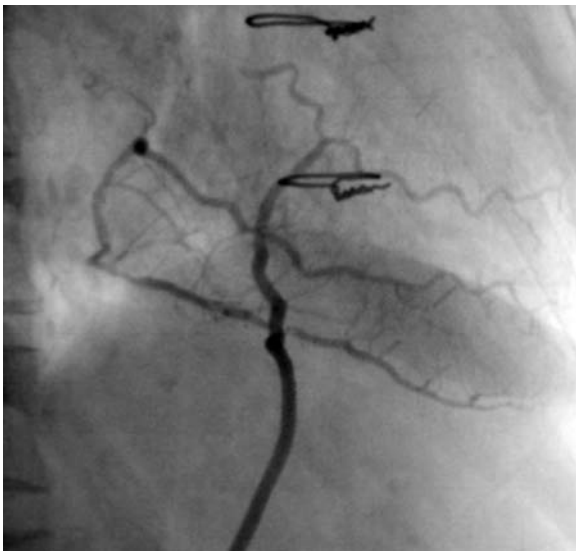


Fig. 22.7. The GEA sequentially anastomosed to the posterior descending artery, the left ventricular branch of the RCA, and the circumflex artery

After making sure the omentum is hemostatic, we give intravenous heparin. The distal end of the graft is then divided, and papaverine solution is instilled in it, and a hemoclip is applied. The skeletonized GEA is then wrapped in a papaverine-soaked sponge. With the papaverine preparation, the GEA becomes a maximally dilated, spasm-free arterial conduit (Fig. 22.6). We have obtained surprisingly dilated GEA with this technique. This makes sequential grafting with skeletonized GEA much easier (Fig. 22.7).

The skeletonized GEA is brought anteriorly to the pylorus through the vertical incision in the diaphragm to reach the heart.

22.3

Results of Skeletonized GEA in Combination with Skeletonized IMA in OPCAB

We have performed 115 consecutive isolated coronary artery bypasses with skeletonized GEA since January 2002; all were completed without cardiopulmonary bypass. The patients were 96 men and 19 women, with a mean age of 66 years (range 43–87 years). The mean number of distal anastomoses per patient was 3.67 (range 1–6). This series represents 44.4% of our whole OPCAB series. In five other patients, we found GEAs with atherosclerotic changes and did not use these GEAs. GEA was only used for in-situ grafts (i.e., no free GEA was used). In this series, then, GEA grafts were used for the right coronary artery territory and sometimes the posterolateral area of the circumflex artery, in cases with greater than 90% stenosis.

We grafted these 115 skeletonized in-situ GEAs to 160 inferoposterior aspect sites, including 43 conduits sequentially grafted for a total of 88 anastomoses. We used skeletonized IMA, with or without sequential grafting, predominantly at target sites in the left coronary artery. Concomitantly, left and right IMA (LIMA, RIMA) and saphenous vein grafts were used in 107, 85 and 6 patients respectively, to 161, 92 and 9 anastomoses respectively. Sequential grafting of conduits was liberally employed but composite grafts were very rarely used. No other arterial conduits were used in the series.

There was no hospital mortality. Two superficial wound infections, cured by antibiotics, and one perioperative infarction were noted. Angiographic study was conducted in 81 patients (289 sites) in the early postoperative period. The graft patencies were 98.2% ($n=113$) in LIMA, 100% ($n=64$) in RIMA and 99.1%

($n=112$) in GEA respectively. Only one GEA to the left ventricular branch of the RCA was not visible by angiogram. There was no gastrointestinal complication noted in the series.

22.4

Comments

The size of the skeletonized GEA has surprised us since we have been using the technique described above. It has ranged from 2.5 to 6.5 mm in internal diameter at the site of the distal anastomosis. This is quite different from the sizes of conventionally prepared GEA with surrounding tissues, which were reported to be 1.25–2.5 mm in earlier work [4]. The difference implies that skeletonization may play an important role in dilating GEA maximally. I believe it is most important that we prepare each GEA conduit at its maximal dilatation prior to anastomosis.

In contrast to the IMA, the GEA has fewer elastic lamellae in its media, and is classified as a muscular artery [8]. What we have found since we started the skeletonization technique is that the first appearance of GEA does not predict the potential size of the artery. The vascular tonus of GEA can vary significantly during an operation. Care should be taken not to underestimate the size of GEA at the beginning. In no case was a GEA too narrow for use after the proper skeletonization technique.

Use of Harmonic Scalpels has recently become popular in cardiac surgery [9]. Skeletonization of IMAs [10] and harvesting of radial arteries [11] are reported to be safe. However, the GEA has a larger satellite vein and many more fragile arterial branches, compared to IMAs. Our method, using a Harmonic Scalpel with coagulating shears, is essential to prevent bleeding and to achieve simple and safe harvesting of skeletonized GEA. This technique facilitates effective use of skeletonized GEA combined with skeletonized IMA [12]. We

demonstrated excellent early outcomes in OPCAB with these arterial conduits. With the skeletonization and proper selection of target sites, we may expect GEA to demonstrate significantly improved late patency.

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Inferior Epigastric Artery Grafting

Inferior Epigastric Artery Grafting: History, Anatomy and Surgical Techniques

L. BORO PUIG, S. ALMEIDA DE OLIVEIRA

23.1 Historical Note

Vineberg initiated study of the use of arterial grafts for myocardial revascularization in 1946, with implantation of the left internal thoracic artery (LITA) into the left ventricle [1]. In 1954, Murray and associates demonstrated use of the LITA as a direct bypass graft to the anterior interventricular branch (AIVB) in an experimental model [2]. Kolessov reported the first clinical success with this method in 1964, using a LITA-to-AIVB bypass graft without extracorporeal circulation in six patients [3]. In a 3-year study involving 165 patients, Green expanded the clinical experience with this method of direct myocardial revascularization [4].

Despite these early studies, the advantages of using the LITA-to-AIVB system versus saphenous vein grafting only became evident at the beginning of the 1980s; they include higher long-term patency rates, greater resistance to atherosclerosis, and significant decreases in the rates of angina, nonfatal myocardial infarction, reoperation, and mortality. In addition to the LITA, the AIVB deserves credit in the success of this revascularization technique; functionally, the AIVB is the most important branch of the left coronary artery.

The gratifying results obtained with LITA-to-AIVB grafts have stimulated interest in the use of other types of arterial grafts. For example, the right internal thoracic, radial, gastroepiploic, inferior epigastric, laterocostal, and inferior mesenteric arteries may be used in situ or as free grafts to the right coronary artery or its branches and to the other branches of the left coronary artery. In this way, improved long-term graft patency due to more effective myocardial revascularization may be achieved.

23.2 Inferior Epigastric Artery

Puig and associates first proposed use of the inferior epigastric artery (IEA) as a free graft for myocardial revascularization in 1987 [5]. The IEA is a double graft with a diameter similar to that of the coronary

branches. With proximal anastomosis on the aorta, the IEA graft can generally reach the AIVB, diagonal, circumflex, and right coronary arteries. With proximal end-to-side anastomosis on the LITA or right internal thoracic artery (RITA), the IEA graft can reach the diagonal, diagonalis, and marginal branches of the left coronary artery. If end-to-end LITA-IEA anastomosis is performed, this composite graft may reach the right coronary artery or its branches, depending on the length of these two conduits. In this respect, the use of one of the two terminal branches of the LITA permits lengthening of the composite graft.

23.3 Anatomy of the Epigastric Artery

The IEA originates at the anterointernal side of the external iliac artery, slightly above the inguinal ligament; it heads transversally and medially, passing over the external iliac vein and following obliquely upward and towards the inside. After reaching the abdominal rectum-muscle, the IEA passes between the fascia transversalis and peritoneum. Its initial course is horizontal. In approximately 10% of cases, atherosclerotic plaques in various degrees of evolution are observed in this initial segment of the IEA.

Three collateral vessels originate closely to the iliac artery: the funicular, suprapubic, and anastomotic branches of the obturator. The initial course is related to the presence of a ductus deferens in men or a round ligament in women. The IEA is used as a free graft after this initial segment, which does not need to be dissected, making it easier to harvest the arteries. The useful segment varies in length from 8 to 13 cm, but occasionally it is 17–19 cm long and has proximal and distal diameters of 2–3 mm and 1.5–2 mm, respectively.

In regard to vessel structure, the distance from the lumen to the outer media of the IEA is approximately 250 μ m below the critical wall thickness established by Geiring. Therefore, the IEA is nourished by diffusion from the lumen [6] and is not dependent on the adventitial blood supply. The IEA is considered a muscular artery due to the predominance of muscular fibers ver-

sus elastic fibers in its medial layer. Elastic tissue is limited to fenestrated elastic sheets, i.e., the internal and external elastic lamina. Similar to the internal thoracic artery, the internal elastic lamina of the IEA has few fenestrations, thus discouraging the growth and migration of smooth muscle cells (from the media into the intima), intimal thickening, and atherosclerosis [7, 8].

23.4

Surgical Technique

23.4.1

Graft Preparation

The IEA needs less handling when harvested than the internal thoracic artery. It can be approached through a midline infraumbilical incision or a transverse suprapubic incision; an advantage of the latter is that it allows the simultaneous dissection of both inferior epigastric arteries [9]. When only one graft is needed, a transverse lateral incision is preferred, and a 2–4 cm length of open skin is enough to permit dissection of the IEA. This transverse incision results in a cosmetic scar.

The incision comprises skin, subcutaneous tissue, and the aponeurosis. The rectus muscle is medially retracted, and the inferior epigastric vessels are identified in the preperitoneal fat. The dissection is extended

until the graft has a suitable diameter to perform the graft-coronary anastomosis.

The dissection of the IEA pedicle preserves the surrounding preperitoneal fat to avoid physical injury of the arterial graft. Larger collateral branches are controlled with metal clips or are tied. Care must be taken to damage the IEA by the electrocautery close to the metal clip.

The IEA pedicle is sprayed with papaverine solution (20 mg of papaverine in 50 ml of saline solution). It is maintained at its own site to protect against hypoxia and to help maintain function in regulating membrane permeability, lipid transport, vasomotor tone, coagulation, fibrinolysis, and inflammation [10]. The pedicle is also measured to determine its most useful length.

Once the anastomosis sites are chosen before starting the extracorporeal circulation, the supposed route of graft is measured to determine if there is a suitable length and an acceptable diameter of IEA. The pedicle is harvested at the time that it will be used. Large metal clips are located in the proximal and distal ends and then the IEA is transected. The proximal aspect is then observed to identify any abnormality in the vessel wall. Finally, the papaverine solution is gently injected, without pressure, into the IEA.

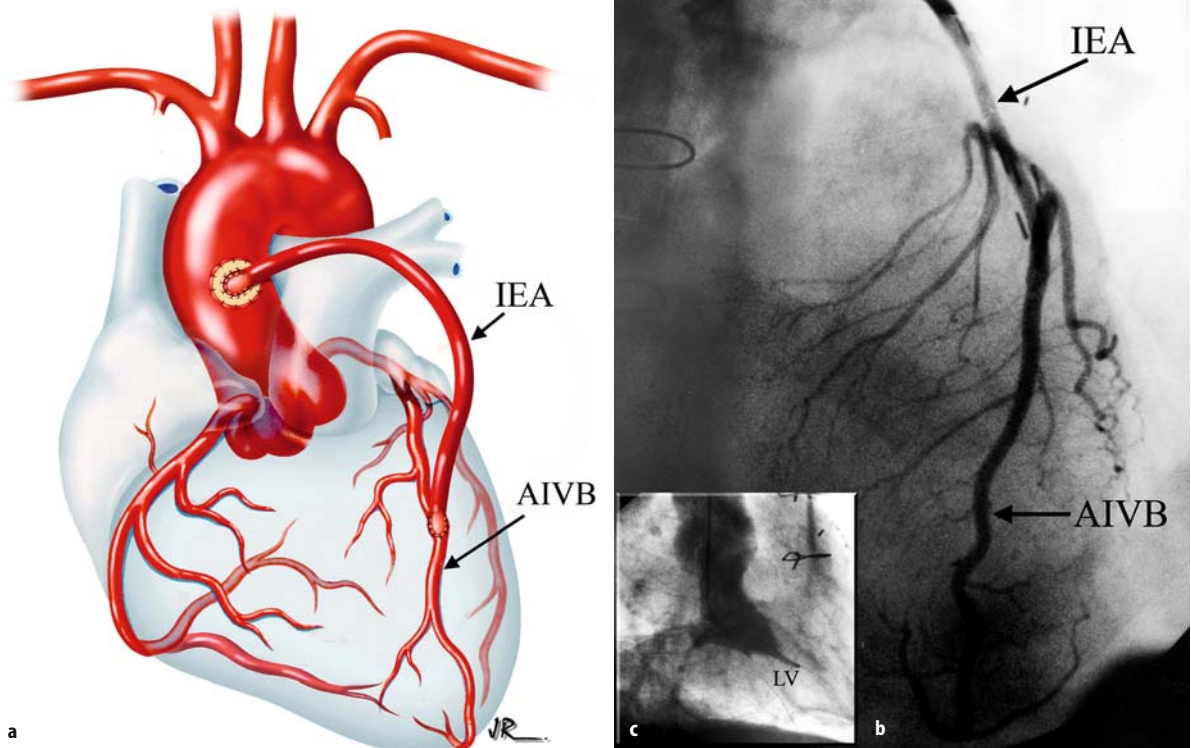


Fig. 23.1. **a** The bovinus pericardial patch between both the aorta and the IEA, and the grafting to the anterior interventricular branch (AIVB). **b** Angiographic aspect of the IEA: AIVB 16 years after surgery, showing the smooth wall of the IEA graft, and uniformity in diameter. **c** The normal systolic aspect of the left ventricle

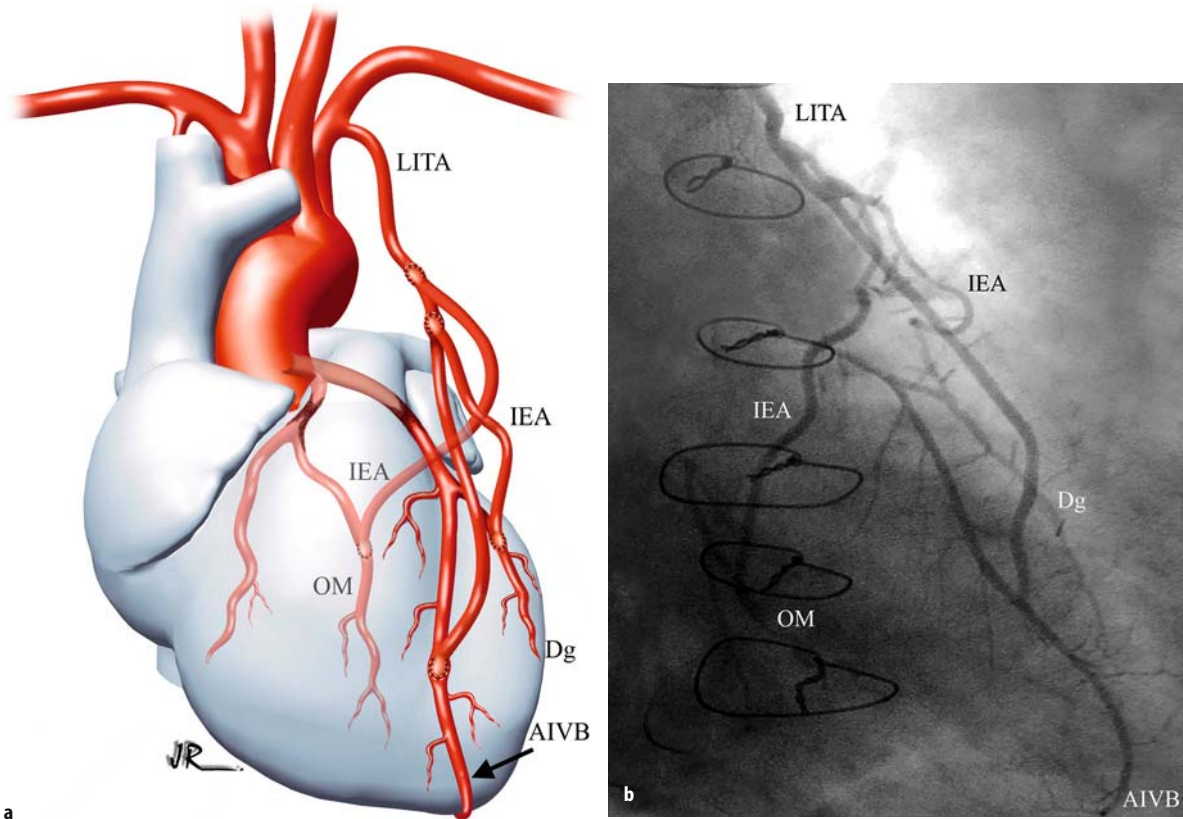


Fig. 23.2. a Both IEA grafts to diagonal and obtuse marginal branches, with end-to-side anastomosis between the left internal thoracic artery (LITA) and the IEA. The LITA is connected to the AIVB. **b** Angiographic illustration of this composite graft in the early postoperative stage suggesting effective myocardial revascularization

23.4.2

Proximal and Distal Anastomosis

Lateral clamping is used to construct the proximal anastomosis between the IEA and aorta. When the wall of the aorta is thick or calcified, we use a patch made of bovine pericardium or saphenous vein between the aorta and IEA. Using running suture, we first anastomose the patch to the aorta and then anastomose the IEA to the patch (Fig. 23.1a).

Direct anastomosis onto the aorta results in graft occlusion in some cases; this is probably because of the difference in wall thicknesses, making this surgical technique difficult. When the wall of the aorta is thickened by atherosclerotic plaques at the site of the anastomosis, the risk of failure is high. In cases of reoperation, the proximal anastomosis of the IEA may also be onto the initial part of a new or an old saphenous vein graft. For composite grafts, the proximal anastomosis with the internal thoracic artery can be performed end-to-side or end-to-end (Figs. 23.2a, 23.3a). The use of the superior epigastric or musculophrenic arteries permits lengthening of a composite graft.

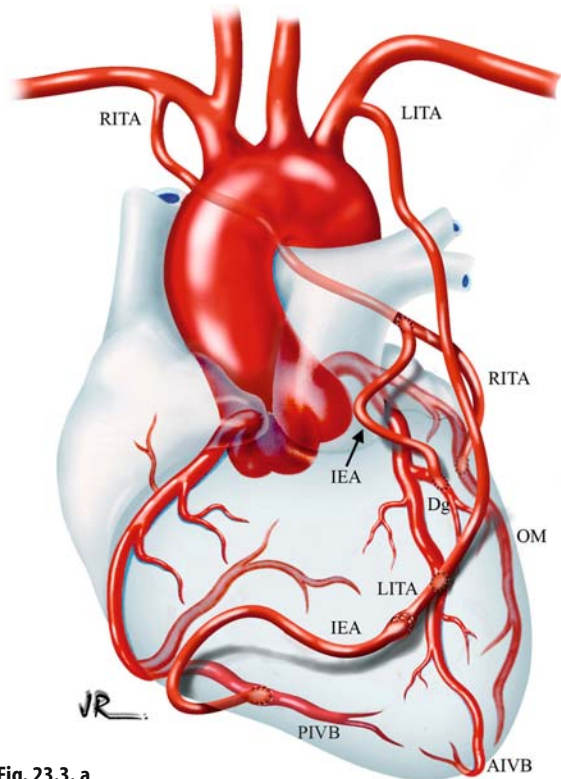


Fig. 23.3. a

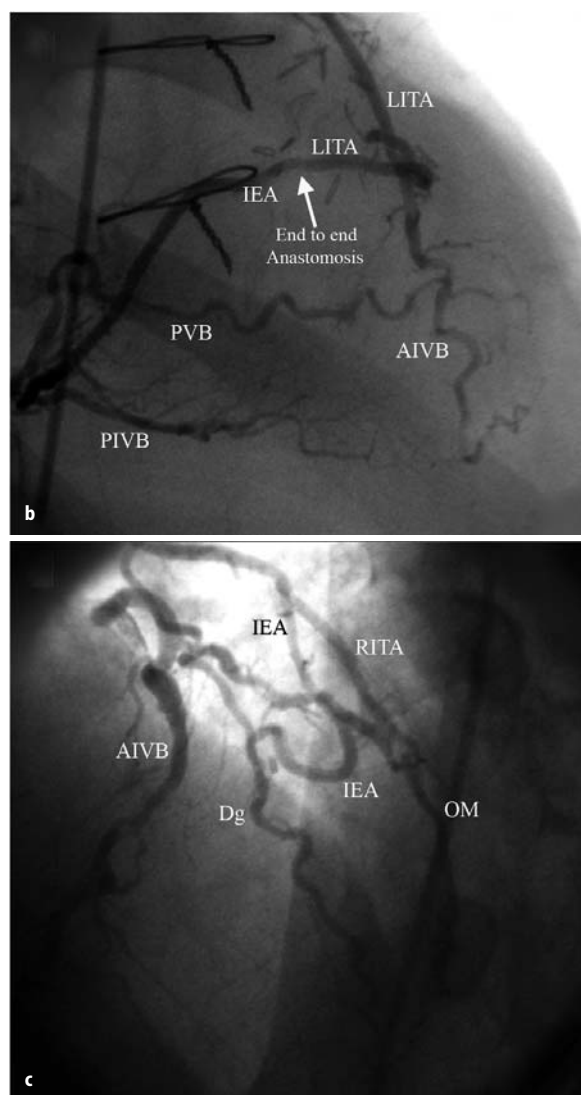


Fig. 23.3a–c. Both IEA grafts with end-to-side and end-to-end anastomosis between RITA and LITA respectively. These grafts are connected to the diagonal and posterior interventricular branches, while the RITA and LITA are connected end-to-end to obtuse marginal and side-to-side to the AIVB respectively. **b, c** Angiographic aspect of this procedure with composite grafts, 3 months after surgery

23.5

Postoperative Angiography

There is a wealth of published information about the early and intermediate rates of patency of this IEA graft [5, 11–17] (Table 23.1). The early postoperative angiography of the IEA grafts in 8 years of clinical experience reflects different points of the learning curve and includes cases of graft occlusion when the IEA was directly anastomosed to the atherosclerotic disease of the aorta. The early patency rate of the IEA to anterior interventricular and diagonal branches was 85.7% [17]. The up-to-date late patency rate from 3 to 192 months (mean 91 months) is 87%. Considering the composite grafts with end-to-side or end-to-end anastomosis the patency of the grafts reached 94%. The postoperative uniformity of the IEA graft wall further suggests that it is a “live” conduit receiving nourishment from the lumen, consistent with an appropriate wall thickness (Figs. 23.1b, 23.2b, 23.3b).

Figure 23.1B shows the late angiographic study, 16 years after the operation, where we can see uniformity of the IEA diameter.

23.6

Remodeling of the IEA

Remodeling of the arterial wall in response to changes in flow (increase or decrease) occurs over weeks to months [18]. The postoperative remodeling of the IEA graft seems similar to that of the internal thoracic artery graft, with changes in graft diameter seen on late angiographic studies [19] (Fig. 23.1B). In the whole series, early patent but narrowed IEA graft was observed in a few cases. These patients studied in the late postoperative showed evidence of an increase in diameter (remodeling of the grafts) and uniformity of the wall, suggesting early vasoreactivity of the IEA graft that disappears weeks or months after surgery [20]. There has been no sign of degenerative processes involving the wall of the IEA graft.

	No. of IEA grafts	Early angiography (N)	Early angiography (%)	Intermediate angiography (N)	Intermediate angiography (%)	Follow-up (months)
Louagie et al. [11]	83	69	98	27	88	6
Cremer et al. [12]	50	–	–	23	82.6	1–6
Perrault et al. [13]	18	–	57	–	–	–
Schroeder et al. [14]	–	90	–	87	24	–
Calafiore et al. [15]	124	70	95.7	25	100	25
Buche et al. [16]	157	135	97.7	29	96.5	13–14
Puig et al. [5]	22	17	88	–	–	–
Puig et al. [17]	–	–	85.7	–	85.7	81.2

Table 23.1. Early and intermediate angiographic findings after revascularization with the epigastric artery

23.7

Clinical Experience

Our clinical experience consists of 263 patients who underwent IEA grafting as a complement to myocardial revascularization between 1987 and 2003. Of the 827 grafts employed (3.1 grafts/patient), 665 (80.5%) were arterial grafts (Table 23.2). The IEA graft was employed to the anterior interventricular, diagonal, obtuse marginal, and posterior interventricular arteries as well as to the right coronary artery (Table 23.3). Thus, it is possible to revascularize almost all of the branches of the left and right coronary arteries using one or both IEAs.

Table 23.2. Graft types

No. patients	Graft types						Total
	LITA	RITA	RA	IEA	GEA	SV	
263	259	95	27	282	2	162	827

LITA left internal thoracic artery, *RITA* right internal thoracic artery, *RA* radial artery, *IEA* inferior epigastric artery, *GEA* gastric epiploic artery, *SV* saphenous vein

Table 23.3. Inferior epigastric artery to coronary arteries

Coronary arteries	Number	%
Anterior interventricular branch	58	20.5
Diagonal branch	136	48.2
Obtuse marginal branch	56	19.8
Posterior interventricular branch	9	3.2
Right coronary artery	23	8.1

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24 Inferior Epigastric Artery Grafting: Clinical Results

F. DAGENAIS, L.P. PERREAULT, M. CARRIER

24.1 Introduction

In the early 1980s, Grondin et al. [1] from our institution, the Montreal Heart Institute, demonstrated the long-term superiority of the pedicled internal thoracic artery (ITA) compared to the saphenous vein graft. Such findings stimulated interest in identifying other arterial conduits harboring anatomical and physiological characteristics comparable to the ITA graft. In 1988, Puig et al. reported the use of the inferior epigastric artery (IEA) as a bypass conduit for myocardial revascularization [2]. The anatomy, physiology and operative technique of the IEA graft have been detailed in previous chapters. The present chapter addresses the clinical results obtained with the IEA graft.

24.2 Indications, Perioperative Mortality and Myocardial Infarction Rate

In the early 1990s, the IEA graft was selected as an alternative conduit in patients with inadequate saphenous veins, who had undergone bilateral saphenous vein stripping or previous harvesting for lower limb or myocardial revascularization procedures, who had severe peripheral vascular disease or in whom ITA grafts were unavailable. Following the initial encouraging clinical experience with the IEA, indication was extended to young (<60 years) patients with three-vessel disease and diabetic patients in an attempt to achieve complete arterial revascularization [3]. Since the length of the IEA (range: 8–17 cm) frequently limits its use for revascularization of distal territories [4], the IEA graft is mainly anastomosed to the right coronary system, diagonal branches or to a proximal obtuse marginal artery. The IEA graft is rarely used for anastomosis to the left anterior descending artery since the ITA is the graft of choice.

The hospital mortality rate for patients revascularized with at least one IEA graft is between 0% and 5.5% and is not increased over coronary artery bypass grafting (CABG) with conventional conduits [5–8]. Range

in mortality among the different series is more related to patient selection. No death attributable to an early postoperative IEA graft occlusion has been observed in the different studies reported. Gurne et al. [9] reported one early death following hemorrhage from an IEA anastomosed to a fragile ascending aorta. Although not always stated, the perioperative myocardial infarction rates among series reporting use of the IEA graft fluctuate between 0% and 8.5% [5, 8, 10, 11]. No perioperative infarct in the territory of the IEA graft has been clearly demonstrated.

24.3 Morbidity Related to IEA Harvesting

The IEA is harvested through a paramedian incision although other techniques such as a transverse suprapubic incision have also been described [12]. The most frequent complication associated with the IEA harvest is an abdominal or retroperitoneal hematoma. The incidence varies among the different series. In our series, three patients (3/18, 17%) developed a postoperative hematoma of the abdominal wall; none requiring surgical drainage [11]. Buche et al. reported abdominal wall hematoma necessitating drainage in 3.8% (6/157) of patients [4]. To minimize hematoma formation, the abdominal wound should not be closed until heparin has been reversed with protamine. In addition, a closed-suction drain may be left behind the rectus muscle and another in the subcutaneous space in the case of an obese patient. Abdominal wound infections are rare after IEA harvesting although the incidence among obese or diabetic patients may be higher. Meticulous surgical technique, prevention of hematoma formation and appropriate antibioprophylaxis diminish this complication. Incisional hernias were reported in two patients by Buche et al. in a series of 157 IEA grafts [4]. Another potential complication during the IEA harvest is injury to the vas deferens relating to its proximity to the external iliac artery.

Ischemic complications related to IEA harvesting are rare. Barner et al. [5] reported two cases of skin and rectus muscle necrosis requiring debridement follow-

ing bilateral ITA and IEA harvesting. It is noteworthy that both patients had a history of peripheral vascular disease. Tsui et al. [13] reported an unusual case of bilateral lower limb ischemia following bilateral ITA and IEA harvesting in a patient with a long-standing occlusion of the abdominal aorta. Thus, presence of a severe peripheral vascular disease is a contraindication to bilateral ITA and IEA harvesting. Furthermore, unilateral epigastric with bilateral mammary artery dissection was shown to cause significant although partial and temporary sternal ischemia at sternal bone tomography 7 days and 1 month after surgery [14]. The hypoperfusion lasts longer when the epigastric artery mobilization is added to bilateral mammary artery harvesting. Thus bilateral mammary and epigastric artery grafting should be avoided when other risk factors for wound complication are present.

24.4

Patency Rates

24.4.1

Early Patency

The first angiographic results were reported by Puig et al. [15] and Mills et al. [3] with, respectively, 15/17 (88%) and 3/3 (100%) of patent IEA grafts within 10 days of the operation (Table 24.1). Patency rates were corroborated by others [16, 17] and by a larger angiographic follow-up published by Buche et al. in 1992 [7] in which 61 of 69 (88%) IEA grafts were patent within 10 days of operation. At the Montreal Heart Institute, we reported our initial clinical experience with 18 IEA grafts performed in 18 patients [11]. Among the 14 patients who underwent early angiographic control, eight IEA grafts were patent (57%). Different technical factors may influence the early patency of the IEA graft. Difficulty in performing the proximal anastomosis has been evoked to explain early graft thrombosis. Mismatch between a thick aortic wall and a small IEA may induce an anastomotic stenosis thus making the graft prone to early failure. Different options are possible to circumvent this technical difficulty. Direct aortoepigastric anastomosis should be performed only in presence of a smooth and thin aortic wall. On the other

hand, when facing a diseased aorta, apposition of a pericardial or saphenous vein patch with subsequent implantation of the IEA graft on the patch may prevent proximal anastomotic problems. Vincent et al. [18] have advocated removal of a cuff of the external iliac artery with the IEA to facilitate construction of the proximal anastomosis. However, the distal iliac vessels are frequently atherosclerotic rendering closure of the iliac artery an intricate procedure. Furthermore, proximal aortic anastomosis incorporating atherosclerotic lesions is not optimal. Other options available are construction of a Y graft with a saphenous vein or an ITA graft. Atherosclerosis of the proximal IEA segment has been documented in up to 24% of patients and may definitely decrease early patency [19–21].

In addition to the surgical technique and conduit type, early graft patency is also influenced by the quality of the vessel bypassed. We have encountered on one occasion during our angiographic follow-up a diffuse narrowing (“string sign”) of an IEA graft anastomosed to the right coronary artery (Fig. 24.1). This “thinning-down phenomenon” has been observed by others [15, 22, 23]. Such a phenomenon is thought to be an adaptive response to a decrease in IEA flow secondary to a competitive flow through the native coronary vessel. Rona et al. [23] demonstrated dilation of a string-like IEA graft during rapid induced atrial pacing or nitroglycerin injection. Furthermore, Buche et al. [22] showed reversal of an angiographically narrowed IEA graft on a control study in which the stenosis on the bypassed coronary vessel had significantly increased. The ultimate fate of these string-like IEA graft remains to be elucidated. In addition to the severity of the target vessel stenosis, the run-off capacity of the recipient coronary artery influences early patency. In light of these different determinants of early graft patency, Buche et al. [22] have developed specific criteria to select the IEA graft as a bypass conduit: use of the IEA requires a severe stenosis on the vessel to be bypassed as well as an adequate distal run-off. This selective approach may explain the high early patency rate reported in their series [21].

Considering the important muscular component of the IEA graft, spasm has been implicated in early graft failure [10]. Calcium channel blockers have been rec-

Table 24.1. Early angiographic patency rates of the IEA graft

Authors	Year of report	Time of study	No. of grafts studied	No. of grafts patent
Puig et al. [15]	1990	< 10 days	17/22 (77%)	15/17 (88%)
Mills et al. [3]	1991	< 10 days	3/19 (16%)	3/3 (100%)
Perrault et al. [11]	1993	< 10 days	14/18 (82%)	8/14 (57%)
Cremer et al. [16]	1993	< 6 months	23/50 (46%)	19/23 (83%)
Teerenhovi et al. [6]	1994	< 3 months	18/18 (100%)	13/18 (72%)
Manapat et al. [17]	1994	5 days – 13 months	21/130 (16%)	18/21 (86%)
Gurné et al. [9]	1994	< 14 days	135/153 (88%)	132/135 (97%)
Total			231/410 (56%)	208/231 (90%)

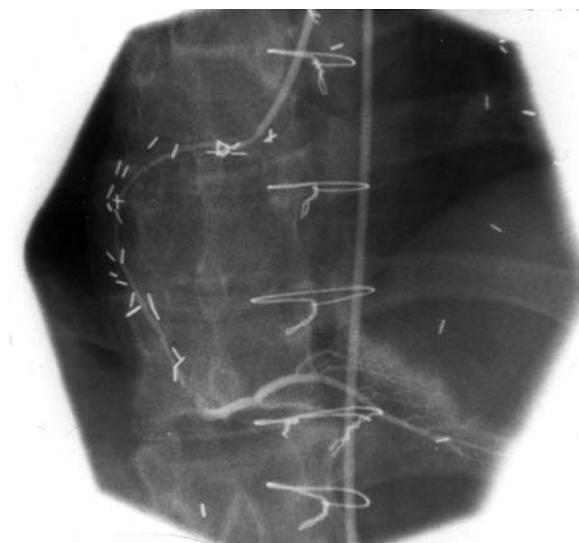


Fig. 24.1. Follow-up coronary angiogram of an IEA graft anastomosed to the right coronary artery showing a diffuse narrowing of the graft

ommended to counteract the tendency of the radial artery for spasm in the early postoperative period [24]. Such an approach could be beneficial with the IEA graft. Furthermore, a decreased postoperative vasodilatory response to nitrates has been documented with the IEA graft possibly due to smooth muscle cell injury secondary to surgical manipulations [9]. Undue traction or intraluminal overdilatation of the IEA graft during harvesting may disrupt the endothelial and muscular linings, rendering the IEA graft more prone to thrombosis.

24.4.2

Mid-term Patency Rates

Few reports assess mid-term (>6 months) angiographic patency rates of the IEA graft. Buche et al. studied 48 patients between 6 and 15 months (mean 8.5 months) after surgery [22] (Table 24.2). Among the 48 IEA grafts, four were occluded and 44 were patent. Of these 44 patent IEA grafts, eight were diffusely narrowed and 36 (75%) had normal angiographic appearance. Twenty-nine other patients were recatheterized at a mean of 25 months after surgery. One IEA graft was occluded, three were diffusely narrowed and 25 (86%) were perfectly normal. Five other IEA conduits studied at a mean of 39 months postoperatively were patent and intact. Donatelli et al. reported angiographic follow-up in 23 patients with the use of IEA. At an average of 21.2 months 52.2% (12/23) were patent [25]. On the other hand, Buche et al. reexamined by angiography 29 IEA grafts at an average of 25 months postoperatively and 28/29 were patent [22]. These results have been substantiated by Puig et al., who reported an 85.7% pa-

Table 24.2. Mid-term (>6 months) angiographic patency rates of the IEA graft

Authors	Year of report	Time of study	No. of grafts studied	No. of grafts patent
Buche et al. [22]	1995	8.5 months	48	44/48 (92%) ^a
		25 months	29	28/29 (97%) ^b
		39 months	5	5/5 (100%)
Puig et al. [25]	1997	81.2 months	16	14/16 (87.5%)

^a Eight IEA grafts were patent, but diffusely narrowed

^b Three IEA grafts were patent, but diffusely narrowed

tency rate of the IEA to the diagonal and left anterior descending territories at a mean follow-up of 81 months [26]. These authors have further stressed the problems with the proximal anastomosis in the mode of graft failure.

24.5

Composite Grafts Using the IEA

Calafiore et al. reported use of the IEA graft in composite arterial conduits [27, 28]. Early angiographic study (<12 months) demonstrated that 96% (67/70) of IEA grafts were patent while late study (>12 months) showed a 100% (25/25) permeability. More recently, Ayabe et al. have reported a 94.9% (37/39) patency rate early postoperatively [29]. These excellent patency rates of composite ITA-IEA grafts are similar to other composite arterial grafts using the ITA as an inflow graft, suggesting a benefit of connecting a free arterial graft to an in situ ITA. Furthermore, using a composite graft technique, the proximal aortic anastomosis complications are avoided.

In the era of “minimal invasive” cardiac surgery, authors have reported bypass procedures using composite ITA-IEA grafts through a mini-thoracotomy or sternotomy incision without cardiopulmonary bypass [30–32].

24.6

Conclusion

The IEA graft offers acceptable early patency rates. Reliance on precise surgical technique and grafting to severe stenotic coronary arteries with acceptable distal run-off optimizes early patency. Although the composite IEA-ITA graft technique appears attractive, longer and more complete angiographic follow-ups are required to better define the rate of IEA atherosclerotic changes and patency. Furthermore in light of the arterial conduits now available for CABG, the indications for IEA use remain limited.

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Rarely or Possibly Used Arterial Grafting

X

Splenic Artery Grafting

B. BLAKEMAN, J. PICKLEMAN, G.-W. HE

Increasing numbers of complex redo revascularizations face the cardiac surgeon. The standard vessels for coronary artery bypass are the internal mammary arteries and the greater saphenous vein. Interest in recent years has been directed towards radial arteries, gastroepiploic arteries, and lesser saphenous veins. Other choices for conduit have been basilic vein, inferior epigastric artery, and cadaver vein. Edwards et al. offered the splenic artery as a conduit in 1973 [1, 2]. Further use of the splenic artery as a free graft was offered by Mueller in 1992 [3].

25.1

Case Report

An example of one early patient is provided to demonstrate a likely situation in which a splenic artery may be considered. The patient was a 67-year-old woman who came to the emergency department complaining of chest pain, dyspnea, and orthopnea. The patient had undergone coronary artery bypass grafting on four occasions – the two most recent with cadaver veins. Coronary angiography showed thrombosis of the cadaver veins to the left anterior descending and obtuse marginal arteries. An intra-aortic balloon pump was inserted and thrombolytic therapy was attempted without success. No angioplasty or stent procedure could be attempted because of unfavorable anatomy. During previous procedures, all greater saphenous vein, lesser saphenous vein, cephalic vein, inferior epigastric, and both internal mammary arteries had been used. The patient had no radial pulses because of severe peripheral vascular disease, so this conduit source was unsuitable. Cadaver veins had been used for the two most recent operations.

Aortocoronary artery bypass was performed using *in situ* the right gastroepiploic artery to the obtuse marginal artery, and a free splenic artery to the left anterior descending artery. Excellent Doppler pulses were present in both grafts.

An adenosine thallium stress test was obtained postoperatively at 6 months showing no areas of reversible ischemia. The patient remains pain free at 4 years. Be-

cause of severe peripheral vascular disease, it was decided not to repeat coronary angiography. In fact, since the fifth open heart operation, the patient has required an axillobifemoral artery bypass graft.

25.2

Technique

The operation using the splenic artery is performed through a standard midline sternotomy. The incision is extended down 4–5 cm towards the umbilicus (Fig. 25.1). The same incision can also be used for the

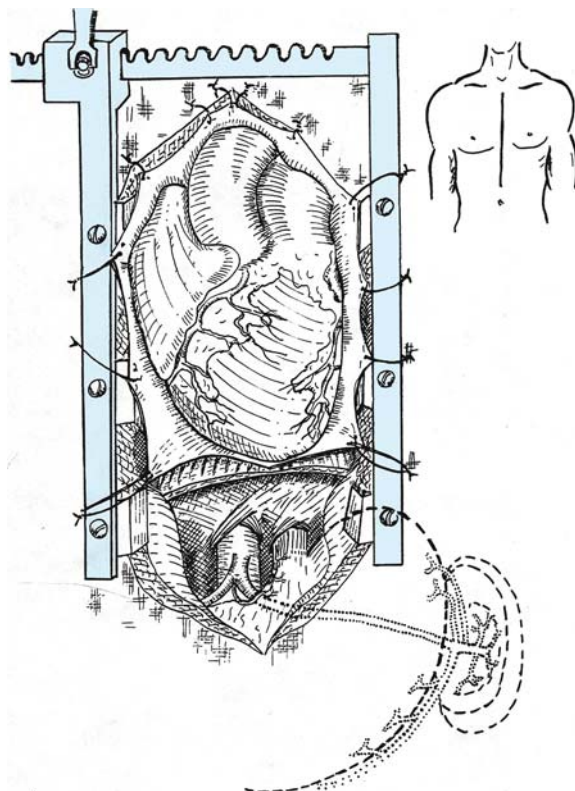


Fig. 25.1. The midline sternotomy is extended 4–5 cm below the xiphoid process. Exposure is facilitated by inverting the chest retractor. (Illustrations by Sasha Alexander)

gastroepiploic artery. The splenic artery is approachable through the lesser sac between the stomach and the transverse colon. If the gastroepiploic artery is also to be harvested, it is suggested it be done before the splenic artery.

The splenic artery is visible near the mid portion of the pancreas. The harvest should begin here and proceed toward the celiac origin of the vessel. Multiple branches pass from the splenic artery to the pancreas. It is suggested the branches be tied on the splenic artery side and suture ligated on the pancreas. This must be done meticulously in order to prevent injury to the pancreas. At our institution, one of the general surgeons familiar with pancreatic surgery is asked to harvest the splenic artery. Once the celiac origin is reached, the surgeon should then proceed towards the hilum of the spleen. The dissection proceeds in a similar fashion as described. When the splenic artery branches at the hilum, the dissection is completed. If no injury occurs to the spleen, it can be preserved. Short gastric arterial supply should be sufficient to preserve the spleen. If the spleen on inspection after interrup-

tion of splenic artery blood is compromised it should be removed. Removal of the spleen will be necessary if the gastroepiploic artery is also harvested because of compromise to the short gastrics. About 15 cm of arterial conduit can be consistently harvested.

The splenic artery is very tortuous and has multiple adventitial bands, which should be divided to increase length. If the artery is to be used for the inferior wall to the posterior descending artery, it can be used in situ. The vessel can be tunneled behind the stomach (Fig. 25.2) through the central tendon and anastomosed to the posterior descending vessel. As an in situ vessel, the splenic artery can only reach the inferior wall of the heart. The artery can also be used as a free graft. Due to limitations on length, it is sufficient for bypasses to the anterior descending, diagonal, ramus intermedius, or main right coronary arteries.

25.3

Use of the Splenic Artery Under Other Situations

25.3.1

Takayasu's Disease

Yamaguchi and associates [4] reported that in a patient with ostial stenoses of coronary arteries and heavy aortic calcification caused by Takayasu's disease, intraoperative examination revealed that the entire wall of the ascending aorta had severe calcification considered to be unsuitable for arterial cannulation or aortic clamping. Two saphenous vein grafts were anastomosed to the splenic artery and the superior mesenteric artery as the proximal pedicle graft. The distal ends of the vein grafts were then anastomosed to the left anterior descending artery (LAD) and posterolateral branch using the off-pump coronary artery bypass (OPCAB) technique with a cardiac tissue stabilizer. The right gastroepiploic artery was anastomosed to the posterior descending branch of the right coronary artery. The postoperative coronary angiogram showed patent grafts 2 weeks postoperatively.

25.3.2

Reoperative CABG Using Off-Pump Coronary Artery Bypass

In reoperative coronary artery bypass graft (CABG) in patients with patent internal mammary artery (IMA) grafts, injury to patent IMA graft could be catastrophic. To prevent injury from sternal reentry, a thoracotomy approach with off-pump technique can be used to graft the circumflex branches. Baumgartner and associates [5] in the reoperative CABG used the splenic artery as the inflow source in off-pump CABG through a left thoracotomy. In one patient who had a densely calcified

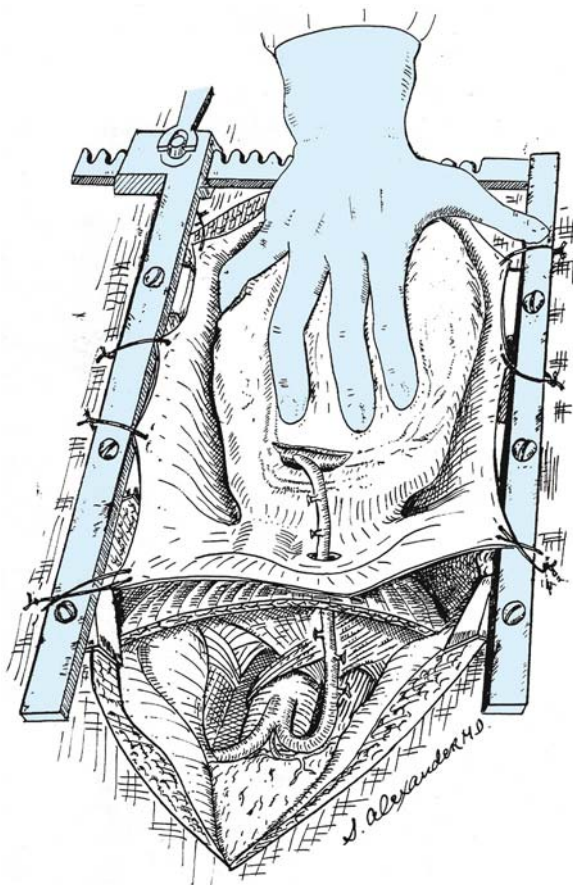


Fig. 25.2. The splenic artery as an in situ vessel can be tunneled behind the stomach and through the tendinous diaphragm to bypass the posterior descending coronary artery. (Illustrations by Sasha Alexander)

descending thoracic aorta, the graft originated from the splenic artery rather than the aorta. In this patient the left hemidiaphragm was incised to gain access to the splenic artery.

Similarly, the splenic artery may also be used for the right coronary artery in this situation by using the OPCAB technique. This was reported by Machiraju and colleagues [6] in an 80-year-old woman who had undergone open heart CABG previously presented with unstable angina as a result of stenosis of the right coronary artery. The LIMA graft to the LAD and vein graft to the marginal branch of the circumflex placed at her previous operation were patent. Through a small subxiphoid incision, the authors used the splenic artery as the inflow source and formed a composite graft with a segment of saphenous vein, anastomosed to the right coronary artery.

Occasionally, the splenic artery is indicated in other situations. For example, it was reported [7] that in a 74-year-old patient who had in situ right gastroepiploic artery graft to the posterior descending artery during coronary arterial bypass grafting. He later underwent total pancreatectomy. At celiotomy, the splenic artery was first anastomosed to the right gastroepiploic artery graft in an end-to-side manner; then a total pancreatectomy was performed with resection of the gastroduodenal artery and the proximal portion of the right GEA. The patient recovered well without evidence of cardiac ischemia.

25.4 Discussion

Six technical aspects of using the splenic artery merit discussion. The majority, but not all, the tortuosity can be eliminated by dividing surrounding tissue and adventitial bands. As mentioned earlier, the tortuosity contributes to limitations in length. The intima is extremely friable near the splenic hilum. This friability necessitates extremely meticulous suturing of the distal anastomosis. Though our standard suture technique is a running suture, it may be necessary to use interrupted sutures in some situations. The splenic artery also possesses calcium plaques scattered throughout its length, which may make placement of sutures more difficult. Extremely meticulous technique must be used in harvesting the splenic artery to avoid injury to the pancreas and potential pancreatitis. The splenic artery is larger than many saphenous veins, and may pose a size mismatch to the vessel for bypass. As mentioned, it may be necessary to do a splenectomy. If only the splenic artery is harvested, the probability of splenectomy will be about 5%. The surgeon can visually assess the

spleen after division of the artery to assess the need for removal. If the right gastroepiploic artery is also harvested, this further compromises short gastric blood supply, thus increasing the likelihood for splenectomy. Our policy would be to also harvest the gastroepiploic maximizing conduit through the abdominal incision. Greater length of the gastroepiploic artery also provides for more flexibility of vessels to be bypassed than the splenic artery.

The splenic artery has advantages over some other arterial grafts such as radial artery and inferior epigastric artery due to its anatomical characteristics so that it is used as a pedicle graft. This gives its use in OPCAB, as described above.

25.5 Conclusion

The splenic artery is a rarely used conduit for extremely complicated redo revascularization cases. Difficult harvest technique, potential for pancreatic injury, limitations in length, and friability of intima will limit the use of this conduit to infrequent situations. No long term follow-up on patency for the splenic artery has been noted in the literature. In recent years, the splenic artery has gained use in OPCAB for reoperative CABG either as a pedicle graft or as the inflow source as a part of a composite graft for the lateral or inferior wall of the heart.

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26 Use of the Subscapular-Thoracodorsal Artery for Coronary Artery Bypass Grafting

G.-W. HE, N.L. MILLS

The subscapular-thoracodorsal artery is not usually used as a primary arterial graft because of the availability of more frequently used arterial grafts, left and right internal mammary artery (IMA), radial arteries, the gastroepiploic artery, and inferior epigastric arteries plus saphenous veins, which already meet the needs of primary and most reoperative coronary artery bypass grafts (CABGs). These arteries are also easier or more convenient to be taken during surgery. However, in some reoperative CABG patients, when other conduits are exhausted, the subscapular-thoracodorsal artery can be used. This has been demonstrated by Mills [1], who reported the successful use of the subscapular-thoracodorsal artery in five reoperative CABG patients.

26.1

Anatomical Notes

The largest branch of the axillary artery is the subscapular artery. It arises from the last third of that artery to course downward and in a medial direction along the anterior border of the subscapularis muscle. It tracks the edge of the latissimus dorsi. The circumflex scapular artery is the first branch of the subscapular artery and is usually a sizeable vessel. The subscapular artery becomes the thoracodorsal (dorsal thoracic) artery after the circumflex scapular artery origin (Fig. 26.1). It offers numerous branches supplying thoracic muscles as it courses inferiorly. Its harvest as a free graft does not harm the latissimus dorsi muscle because of generous collateral from intercostal branches. The vena comitantes drain the area and unite with the circumflex scapular vein to enter as a single vessel into the axillary vein. The subscapular artery in its upper third ranges from 3.25 to 4.5 mm in internal diameter. The lengths of these arteries as free grafts range from 12 to 14 cm. The graft should be used only if the distal internal diameter at the point of the planned anastomosis is 2 mm or larger.

The thoracodorsal artery is, in fact, the continuation of the subscapular artery (75%), but it could also be a direct branch from the axillary artery in 25% of patients [2, 3]. The mean length is reported to be about

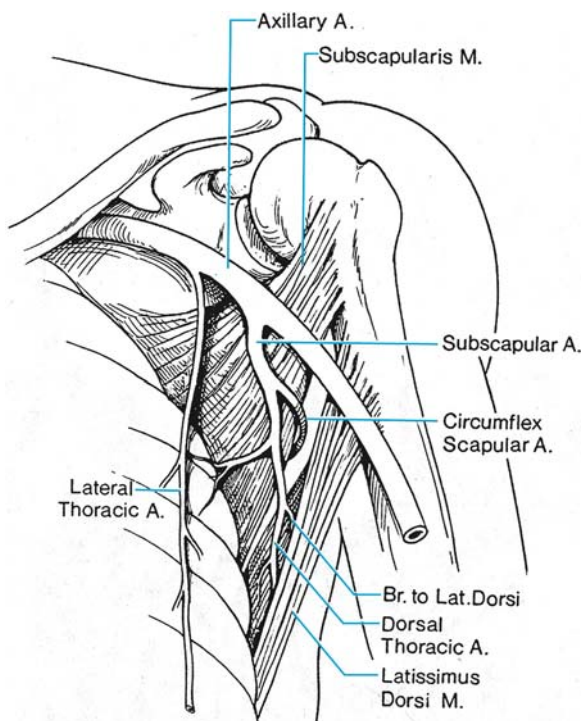


Fig. 26.1. Anatomy of the subscapular artery

128 mm and the proximal-distal diameter ratio is about 3.44 ± 1.49 [4, 5]. We therefore describe the subscapular artery and thoracodorsal artery together as a coronary bypass conduit.

26.2

Historic Notes

Disappointing long-term results with the saphenous vein for coronary artery bypass grafting have resulted in an intensive search for other arterial grafts for coronary artery bypass conduits. The results of new arterial grafts, as well as old resurrected (i.e., radial artery) grafts, must be compared to the internal mammary artery, which is the gold standard of all arterial CABGs. Saphenous vein grafts to bypass a circumflex coronary

artery system by way of a left thoracotomy have been used since the 1980s [6]. Although the indications for use of the left thoracotomy for a coronary artery bypass are only in the range of 2%, such an approach can be very advantageous in reoperative coronary artery surgery [7]. That technique has certain advantages. It allows the surgeon to avoid time consuming and potentially dangerous dissection of adhesions that coexist with reoperative median sternotomy. Such dangers include embolization of old vein grafts and damage to critically functioning saphenous vein grafts. Even more importantly, injury to an internal mammary artery graft imbedded in scar tissue may be prevented. Median sternotomy operations may be avoided when the patient has had previous mediastinitis. Through this approach concomitant pulmonary lesions in the left hemithorax may be easily addressed.

Plastic surgeons have used transplanted latissimus dorsi muscle grafts for reconstructive operations for many years. Both the subscapular artery and vein are anastomosed in these operations to provide a viable implant. The latissimus dorsi muscle based on the thoracodorsal neurovascular bundle has been used for dynamic cardiomyoplasty since 1985. These experiences indicated that the subscapular artery was an appropriate size and length for use in CABG. Thus it began to be used clinically as a free graft for coronary artery bypass surgeries when a left thoracotomy was indicated for other reasons in patients requiring reoperation [8].

More recently, another strategy has been used to take the subscapular-thoracodorsal artery. Simic and associates [9] described an approach for preparation and use of thoracodorsal artery as a free graft for coronary artery bypass grafting. The preparation and removal of thoracodorsal artery were performed through the right axilla when the patient was placed in the lateral decubitus position. The thoracodorsal artery, as a free graft, had 14 cm of length with an internal diameter of about 2.5 mm, and the artery wall had a better consistency than the mammary artery. The right axilla incision was closed and the patient was positioned in the supine position for harvesting of the radial artery and then CABG was performed through median sternotomy.

A more recent report [10] describes the use of subscapular-thoracodorsal artery in the primary minimally invasive direct coronary artery bypass (MIDCAB) for multiple vessel disease. Watanabe and associates used a small left thoracotomy to harvest the subscapular-thoracodorsal artery and the left IMA as well as to perform CABG. They anastomosed the left IMA to LAD and used a free radial artery to create a subscapular-thoracodorsal artery-radial artery composite graft and anastomosed this composite graft to the obtuse marginal branch.

26.3

Harvest of the Subscapular Artery

As described before, there are two ways to harvest the subscapular-thoracodorsal artery.

26.3.1

Through Left Thoracotomy

If the CABG is going to be performed through the left thoracotomy, as described by Mills, a standard left lateral thoracotomy is carried out. Prior to entering the left thoracic cavity, the latissimus dorsi muscle is identified. Initially, a vertical incision up into the axilla in line with the leading border of the latissimus dorsi muscle was made. However, with experience it was found that the graft could be harvested without a vertical incision extension using appropriate retraction of the muscles in that area. Arterial branches and the venae comitantes supplying the latissimus dorsi muscle are identified and traced retrograde to identify the thoracodorsal artery as it lies under the cover of the latissimus dorsi muscle. The narrow Deaver retractors work well to obtain exposure for harvest of this graft. The branches of the thoracodorsal artery are ligated along with the venous branches with 4-0 silk and divided. The dissection is carried out superiorly and the circumflex scapular artery is identified. That artery is ligated and the subscapular artery is traced to its origin from the axillary artery and doubly ligated near that point. After ligating and dividing the subscapular artery proximally and distally, it is dilated gently with an intraluminal solution of body temperature papaverine hydrochloride in normal saline (60 mg in 40 ml of normal saline). A 1-mm olive tip needle tied into the distal vessel is used to introduce the solution into the subscapular artery. At that time, it is important to check for and ligate any missed branches that might bleed after reinstituting blood flow through the graft. A fenestrated suction drain apparatus (Hemovac) is placed along the bed of the harvested graft to prevent a hematoma and is brought out through a separate stab wound. It is removed on the first postoperative day unless there is significant persistent drainage. The muscles are routinely closed anatomically and the subscapularis muscle is not divided.

26.3.2

Through Small Left Thoracotomy

If MIDCAB is used, as Watanabe and associates [10] described, the patient is placed in the right lateral position. An incision of approximately 3 cm is made over the fourth intercostal space along the anterior margin of the left latissimus dorsi muscle. The subscapular-thoracodorsal artery courses between the latissimus

dorsi muscle and the serratus anterior muscle and is easily visualized when the latissimus dorsi muscle is retracted laterally. The right radial artery (RA) is also harvested. The left subscapular-thoracodorsal artery is divided distally after heparinization and anastomosed to the free RA. The subscapular-thoracodorsal artery-RA composite graft is introduced through the fourth intercostal space via the major fissure of the left lung. Stay sutures are applied to the pericardium and pulled upward, thus providing adequate exposure of the coronary arteries.

26.3.3

Through Right Axilla

As described by Simic and associates [9], if the CABG is going to be performed through the median sternotomy as usual, the subscapular-thoracodorsal artery is harvested through the right axilla incision. The patient is positioned in the lateral decubitus position with the arm abducted at the shoulder and the elbow flexed at 90°. The forearm is suspended in the drape bar. It is important not to stretch the shoulder to prevent brachial plexus injury. The proximal third of forearm, axilla and thorax are prepared and draped. A zigzag incision is placed in the axilla with a short incision, following the posterior border of the latissimus dorsi muscle. First, the most distal part of thoracodorsal artery is identified. It is then traced in the depth of the axillary space for about 10 cm. The artery is accompanied by two comitantes veins and the thoracodorsal nerve. After identifying the circumflex scapular artery entering the triangular foramen, it can be ligated or harvested if a y-graft is needed. The triangular foramen is retracted and additional length can be obtained. The wound is closed with suction drainage.

26.4

Cannulation

If standard median sternotomy is used, the routine cannulation method is used.

26.4.1

Cannulation in Left Thoracotomy

Cannulation for cardiopulmonary bypass from the left thoracotomy approach has become fairly standard. Arterial cannulation may be carried out through either the femoral artery or the descending aorta. The preference of one of the authors (Mills) and colleagues for venous cannulation has been the common femoral vein at the origin of the saphenous vein. A number 28-32 Argyle chest drainage tube with multiple holes cut with a rongeur is used for venous drainage. Cardiopulmonary by-

pass with mild hypothermia is used, the heart is fibrillated and the anastomosis performed using decreased bypass flow if necessary. The technique is inexpensive, affords excellent venous drainage, and has been used by one of the authors (Mills) successfully over 200 times. The length of the chest tube is appropriate, as the tip of the tube is invariably just above the origin of the inferior vena cava. A sterile guidewire is routinely used to pass this catheter above the pelvic brim after its introduction into the femoral vein. Pulmonary artery monitoring is used to insure that left heart decompression is not necessary. The exposure is adequate for the operation to be performed with a warm beating heart if the surgeon desires. However, such techniques may offer a greater chance for anastomotic technical error.

26.5

Clinical Notes

The use of the subscapular-thoracodorsal artery as a conduit for CABG has been rarely performed by cardiac surgeons. Mills has experience with five male patients. A sixth 50.1-kg female patient had an attempted harvest of the subscapular artery, but that artery was found to be too small to consider its use as a bypass graft as the distal thoracodorsal artery was less than 1.5 mm in internal diameter. When reviewing the anatomy of the subscapular artery, one finds that the incidence of that vessel being too small (less than 1.5 mm internal diameter distally) appears to be in the range of 3–4% in the average sized human. Although angiography of the left subscapular system was not performed in any of these cases, a preoperative angiogram would be a wise decision if all other conduit possibilities had been eliminated and the operation depended solely on the fact that the patient's subscapular artery was of adequate size. All patients in this series were undergoing reoperations. Their ages ranged from 53 to 66 years and all had incapacitating angina pectoris. The length of graft necessary for a bypass to the circumflex system is relatively short. Although 12–14 cm of graft may be easily harvested, 10 cm or less is usually the final length of the graft when it is in place. The descending aorta was used for the proximal anastomosis in all patients, and in three of these it was brought anterior to the hilum of the lung to the bypass branches of the circumflex system. Two patients had atherosclerosis of the descending aorta and in one of these it was necessary to perform a pericardial patch to the aorta prior to anastomosing the graft to it. There was a large natural "Y" bifurcation in one graft and it was used as a "Y" graft. An artificial "Y" was used in a second patient, making a total of seven anastomoses in the five patients. Distal anastomoses were performed using 8-0 Prolene (Ethicon, Inc., Summerville, New Jersey, USA). All proximal

Table 26.1. Subscapular artery to coronary artery bypass

Patient	Indication	Restudy	Artery bypassed	Approach
1 ^a	Reop. ×4; no conduit	Early patency	Circumflex marginal and old SVG	Left thoracotomy
2 ^a	Reop. ×2; early failure and poor quality SVG	Refused	Circumflex marginal	Left thoracotomy
3 ^a	Reop. ×2; no available conduit	Patent on late restudy	Circumflex marginal ×2 thoracotomy	Left
4 ^a	Reop.; no graft available	Patent on late restudy	Circumflex marginal thoracotomy	Left
5 ^a	Reop. ×3; failed PTCA and stents	Refused	Circumflex marginal	Left thoracotomy
6 [9]	Reop. ×2; SVG occluded, LIMA stenotic	Not mentioned	LAD	Median sternotomy
7 [10]	First CABG			
	As STA-RA composite graft	Not mentioned	Circumflex marginal (left thoracotomy)	MIDCAB

^a Patients of Noel Mills [1]

SVG saphenous vein graft, PTCA percutaneous transluminal coronary angioplasty, STA subscapular-thoracodorsal artery, RA radial artery

anastomoses were performed using 6-0 Prolene. Loop magnifications (3.5 power) were used in these cases. There was no mortality or distal arterial embolism, and the patients had basically uneventful postoperative courses. Follow-up has been from 4 to 7 years. Angina improved significantly in one patient, who by necessity had an incomplete revascularization. A second patient has had progressive atherosclerotic disease with angina recurring after 5 years of a symptom free existence. Three patients have remained asymptomatic. A post-operative angiogram was performed from 1 week to 4 years after the operations in three patients and widely patent grafts were found to target vessels (Table 26.1).

Table 26.1 also shows two more cases reported by other surgeons. The case was reported by Simic and colleagues, who used a right axilla incision to take the subscapular-thoracodorsal artery and used the standard median sternotomy to perform the reoperative CABG. The patient had occluded saphenous vein graft and stenotic left IMA. They grafted the subscapular-thoracodorsal artery to the LAD and the radial artery to the RCA with success.

The case reported by Watanabe and associates [10] used the MIDCAB method without cardiopulmonary bypass. Interestingly, the subscapular-thoracodorsal artery was used as a composite graft with radial artery to become a pedicle graft to the obtuse marginal branch.

26.6

Comment

Although atherosclerosis was present in 8% of subscapular arteries studied in 50 fresh cadavers (mean age of 66 years), no occlusive disease was found [11].

When harvesting this artery, it is wise to be aware that the thoracodorsal artery often bifurcates significantly in its lower portion in as many as 86% of patients. This may allow use of a natural “Y” graft, which offers a more efficient use of arterial conduit. Although there have been no histologic studies on this artery to compare it with IMA grafts, a cursory study by our group has shown relatively few breaks in the internal elastic membrane and a moderate amount of elastic tissue as compared to internal mammary grafts. Although this operation will never be used to any significant degree, it is a wise “trick” to have up one’s sleeve when one is faced with a patient who needs a second to fourth reoperation with a functioning left internal mammary arterial conduit densely adhered to the undersurface of the sternum. A catastrophic result may result from damage to such a graft. The consistent origin of the subscapular artery from the axillary artery, and the fact that it is an arterial graft (especially when there has been early venous graft failure), make this an attractive and effective conduit when coronary revascularization is planned using a left thoracotomy. All patients in the experience of one of the authors (Mills) had a functioning left internal mammary artery. We did not see atherosclerosis in any of the grafts that we harvested [12]. Diltiazem was used postoperatively to prevent spasm in the last three patients because of the experience from France which reported the importance of use of this drug when free radial artery conduits are used as coronary artery bypass grafts [13]. However, due to the fact that the thoracodorsal artery is a Type I artery (see Chapter 4), this may be unnecessary. It is important to use external patches placed on the chest preoperatively to defibrillate the heart when using the cold fibrillation technique. None of the patients had aortic insufficiency nor

was cardiac distention a problem. If it occurs, the surgeon must remain prepared to cannulate the left atrial appendage during the period of ventricular fibrillation. All proximal anastomoses were performed with a partially occluding clamp and a beating heart while the patient was rewarming. Although the initial experience with use of this conduit has been rewarding, caution must be used in evaluating any new arterial graft especially of the non-pedicle type [1].

As to the role of the subscapular-thoracodorsal artery in the primary CABG, although it was reported by Watanabe and associates [10] that the artery was used as inflow (pedicle) composite (with a radial artery) graft in a MIDCAB case, the limited number of patients and the difficulty of the technique may prevent its widespread use in the future. In fact, since 1998 [10], no further such cases have been reported.

Probably, when there is a need for use of subscapular-thoracodorsal artery in reoperative CABG, the method described by Simic and colleagues [9], i.e., harvesting the artery through an axilla incision and performing CABG through the usual median sternotomy is a feasible method for most surgeons.

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Inferior Mesenteric Artery Grafting

P. SHATAPATHY, B.K. AGGARWAL

Update Note by the Editor

GUO-WEI HE

The most recent search through “Medline [Pub Med]” for the key words “*inferior mesenteric artery and coronary bypass surgery*” and “*inferior mesenteric artery and coronary bypass*” and “*inferior mesenteric artery and coronary surgery*” up to 5 August 2005 found that the original report by the authors in *J Thorac Cardio-vasc Surg* 1997; 113:210–211 remains the only clinical report on the inferior mesenteric artery used as coronary artery bypass graft. This information indicates that currently the clinical use of the inferior mesenteric artery is extremely rare. Even in the reoperative coronary artery bypass graft (CABG) in which the primary and secondary conduits such as IMA, SVG, GEA, radial artery, and inferior epigastric artery are used up, the availability of rarely used conduits such as ulnar artery, scapular-thoracodorsal artery, or splenic artery may be chosen prior to the consideration of using the inferior mesenteric artery. This is obviously due to the potential risk of colonic ischemia if the inferior mesenteric artery is used as a coronary bypass graft.

27.1

Introduction and Anatomic Considerations

Superior late patency of the grafts utilizing the internal thoracic artery (ITA), also known as the internal mammary artery, over the venous grafts for bypassing obstructed coronary arteries, has led to the search and increasing use of additional arterial conduits. Both muscular and visceral arteries have been used for this purpose. We have preferred to use the isolated inferior mesenteric artery with its left colic and superior rectal branches as conduit material for direct aorta to CABG for a variety of reasons [1].

The *inferior mesenteric artery* (IMA) is an unpaired branch of the abdominal aorta arising approximately 3–4 cm proximal to its bifurcation (Fig. 27.1). After traversing subperitoneally downward and to the left, it divides into two. The superior division continues as the left colic artery (LCA) in about two-thirds of cases. In

the remaining cases, it may give up one or two sigmoid arteries (SA) as well. The inferior division, after giving rise to one to three sigmoid branches, continues as the superior rectal artery. The length of the mainstem of the IMA varies from 3 to 4 cm and its internal diameter is between 3 and 5 mm in an average adult. Our histological studies showed that, unlike the internal thoracic artery (ITA), it has media consisting of predominantly smooth muscles and limited by elastic laminae. As in other muscular arteries, there are fenestrations in the internal elastic lamina.

The *left colic branch* (LCA) also runs subperitoneally to the left, somewhat laterally and superiorly or sharply upward, towards the descending colon to divide into two branches. The ascending branch is crossed by the inferior mesenteric vein and passes into the transverse mesocolon, where it anastomoses with the left branch of the middle colic artery. The descending branch anastomoses with the highest SA. The ascending branch may divide early into two vessels, one of which approximately parallels and supplies the descending colon. The LCA in its natural position measures between 6 and 9 cm in length and about 2–3 mm in caliber.

The *sigmoid branches* (SA), usually two or three in number, descend obliquely to the left, under the peritoneum, anterior to the left ureter and the testicular or ovarian vessels. Besides anastomosing with each other, the highest SA anastomoses above with the descending branch of the LCA, and the lowest SA (sometimes referred to as the rectosigmoid artery) with the branches of the superior rectal artery, thus forming arterial arcades before a ‘marginal artery’ can almost invariably be visualized (Fig. 27.2) on selective mesenteric arteriograms [2]. Continuity of this marginal chain of vessels is rarely interrupted. Even near the sigmoid-rectal junction, occasionally when it cannot be recognized, there is still anastomosis, through various tenuous vessels, easily overlooked in dissection [3].

The *superior rectal (hemorrhoidal) branch*, a continuation of the inferior mesenteric, descends into the pelvis in the sigmoid mesocolon, crossing the left common iliac vessels. It divides, usually at the level of the third sacral vertebra, into two descending branches, one on each side of the rectum. About halfway, they di-

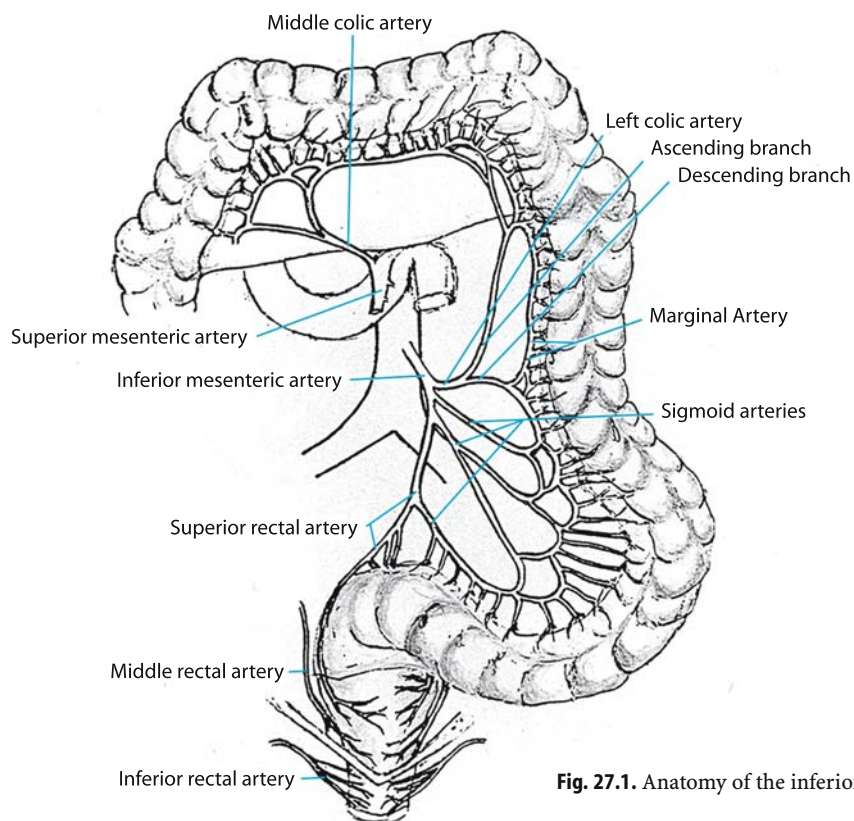
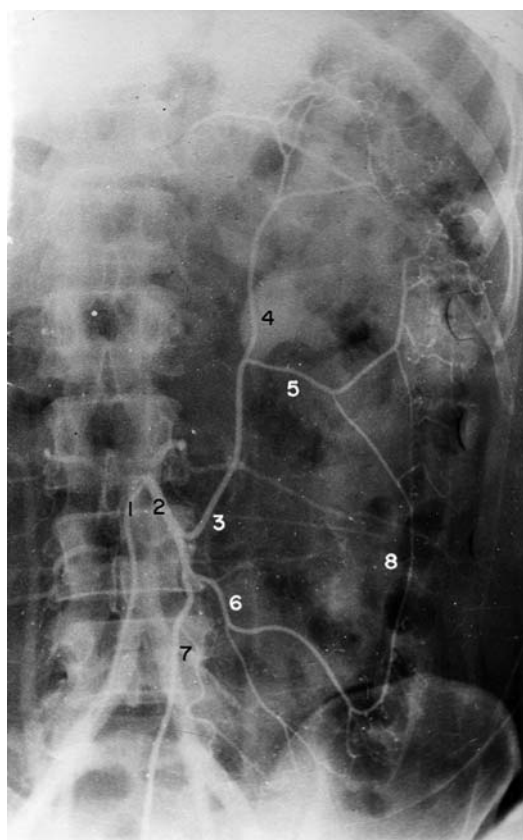


Fig. 27.1. Anatomy of the inferior mesenteric artery and its branches



vide into smaller branches, which form loops around the lower rectum, by communicating with the middle rectal artery, a branch of the internal iliac, and with the inferior rectal branch of the internal pudendal artery. The length of this inferior division of the IMA with its superior rectal continuation approximates 12 ± 2.5 cm with a caliber of 2–3 mm at its distal end.

27.2

Physiopathologic Considerations

Velocity profiles of blood in smaller arteries, such as the radial and mesenteric arteries, are known to be essentially parabolic while that in the human abdominal aorta is blunted (practically unchanged all across the aortic diameter). As per Poiseuille's law, in a parabolic flow profile, the velocity is highest in the center of the stream and becomes progressively lower towards the inner wall such that the thin layer of blood in contact with the wall is stationary [4]. This creates a shear rate at the wall and corresponding shear stress on the endo-



Fig. 27.2. Selective inferior mesenteric angiogram (1 tip of catheter in the inferior mesenteric artery, 2 inferior mesenteric artery, 3 left colic artery, 4 ascending branch of left colic artery, 5 descending branch of left colic artery, 6 sigmoid arteries, 7 superior rectal artery, 8 marginal artery)

thelial surface. The wall shear increases as the mean velocity increases or the radius decreases. Apparently, the endothelium in some way senses the increasing shear, causing the release of endothelium derived relaxing factor (EDRF), which in turn relaxes the smooth muscles of the arterial wall, allowing the vessel to expand [5].

Endothelial cells are aligned and are overlapped in the direction of the wall shear stress [6]. In areas with decreased shear, and where the direction of shear oscillates during pulse cycle, the orientation of these cells is distorted and the pattern of overlap is disrupted. The endothelial barrier may in turn be more susceptible to penetration by smooth muscle cells owing to the distorted alignment of the cells and the instability of the cellular junctions [7]. Besides, when a peripheral arterial free graft is transferred into an aorta to coronary artery position, it will be subjected to a dp/dt higher than that in its natural site, and this new dynamics of pressure produces wall stretching which could lead to intimal disruption and to a subsequent recovery by means of the migration of the smooth muscles through the fenestrated internal elastic lamina [8]. Histologic research has established that this is the first stage of intimal thickening leading to the development of stenosis [9].

The IMA, being a direct branch of the aorta with a markedly significant drop in radius, carries a much higher velocity of blood flow than any of the peripheral branch arteries. Much like the coronary arteries, it is used to the direct aortic pressure with higher and more rapid upstroke (rate of pressure rise) and, therefore, experiences a higher shear rate at the wall so that the relatively stagnant layer of blood in contact with its wall would be even thinner with shortened fluid "residence time," and there should be less likelihood of disruption in the alignment and overlap of its endothelial cells. The EDRF released by the cells, in response to high shear, makes vessel spasm only a remote possibility. All these factors are expected to discourage mass transport of atherogenic substance from the lumen into the wall and the adherence of platelets and macrophages to the endothelial surface [7]. Understandably, there is a sharp drop in shear at the origin of the IMA and for a few millimeters of its "entrance length" before the flow is "developed." Atherosclerotic lesions would, therefore, be more frequent in this location and, indeed, our vascular surgical experience and the observations of Mikkelsen [10] confirm that atheromatous plaques are invariably confined to the proximal 1 cm or so of the IMA.

27.3

Harvesting of Inferior Mesenteric Artery

In the supine position, while one team of surgeons performs the median sternotomy and harvests the left ITA, a second team enters the peritoneal cavity, usually

through a lower abdominal midline incision. The left lower para-median incision may have the merit of avoiding the second incision to go through the linea alba, which necessarily gets incised in its cephalad portion by the inferior extension of the median sternotomy incision.

With a self-retaining abdominal retractor in place, the small intestines are packed off on the right side of the abdominal cavity. The peritoneum and fat layer overlying the IMA and its two divisions are incised to expose the vessels. The mainstem of the IMA is dissected free. The process of skeletonization, leaving behind as little fat adherent to the artery as possible, continues along the superior division until the LCA bifurcates into the ascending and descending branches. At this point, the primary arcade of anastomosis between the left branch of the middle colic artery and the branches of the LCA must be visible. In the event of a well formed secondary arterial arcade being present, the ascending or the descending branch of the LCA can also be skeletonized, depending upon whichever is of larger size, to gain extra length. The dissection then proceeds along the inferior division of the IMA. The sigmoidal branches, excluding the lowest SA, are ligated and divided close to their origins. If one of these branches is of good caliber and has appreciable length before it joins the anastomotic arcade, then it too can be harvested for possible use as a side-arm for additional coronary anastomosis. The superior rectal branch is skeletonized well into the lesser pelvis. One to three small branches may be encountered during this dissection, which stops just before the lowest SA takes origin. The IMA is then divided close to its take-off from the abdominal aorta, after thoroughly securing its proximal cut end with appropriate suture ligature. The left colic and the superior rectal branches are then divided after ligating their continuations at the distal ends of the dissection. When one of the branches of the LCA is included in the graft then the other branch is also divided between ligatures.

With a cannula in place, the IMA and its two branches are flushed with heparinized saline and then temporarily distended with dilute papaverine solution (1:10) before being wrapped in a papaverine soaked gauze piece. This step seems to be essential as the IMA and its two branches, after their disconnection, shrink in length and look much shorter than they actually are in their native site. After this, openings, if any, in the mesocolon are closed with chromic catgut sutures. Hemostasis is ensured and the abdominal incision is closed in layers, irrespective of whether the patient has been, by then, fully heparinized in preparation for the CABG. No drainage is left behind. The average time taken for completing this procedure is around 45 min and could become shorter with practice.

As already alluded to, either the mainstem of the IMA is directly anastomosed to the ascending aorta for

a natural 'Y' graft bypass of obstructing lesions in two different graftable coronary vessels, on the left ventricular surface. Alternatively, almost the entire length of the IMA is excised and the cut end is oversewn with 5-0 Prolene suture. Thereafter the two connected branches are as nearly straightened as much as possible. The entire graft can then reach any of the target coronary arteries on the left ventricle or on the inferior surface of the heart, by anastomosing the left colic end to either the aorta or the side of the left ITA. The choice of single or sequential anastomosis is dictated by the circumstances of the case. A still longer length of the graft and a non-turbulent linear blood flow can be obtained by retaining the mainstem IMA for the proximal anastomosis, disconnecting the left colic branch at its origin and reanastomosing it end to end with the superior rectal artery.

27.4

Clinical Experience

Not until November 1994 did we come across a case that satisfied all the ethical considerations for using the free IMA graft for CABG. In this 42-year-old man, we used in-situ right ITA to the mid-right coronary artery, in-situ left ITA to the large obtuse marginal branch (OM) of an obstructed circumflex artery, and free IMA to the mid portion of the totally occluded left anterior descending artery (LAD). He had an uneventful hospital course. Since then, for reasons other than academic ones, we have used this conduit for CABG only on three more patients, all with complete success. The first of the three received IMA as 'Y' graft to bypass the 1st diagonal (D) and the 1st OM branches. In the second patient, the left colic branch was disconnected and reanastomosed end to end to the superior rectal artery. The proximal end of the IMA was anastomosed to the ascending aorta and then the D and the 3rd and 4th OM branches were bypassed in sequence. The last patient had free IMA graft to the circumflex territory and an in-situ left ITA to the LAD. All four patients have remained asymptomatic, with no demonstrable evidence of recent myocardial ischemia, 20–42 months after surgery. Follow-up angiograms in two of the four patients, after 5 months and 31 months respectively, have demonstrated patent IMA grafts.

27.5

Closing Comments

Even though our clinical series is pathetically small, from the experience gained and based on the anatomic and physiopathologic considerations, we are inclined to believe that the inferior mesenteric artery with its left colic branch and superior rectal continuation is a superior free graft conduit for coronary artery bypass surgery and would prove to be a perfect complement to the left internal thoracic artery in-situ graft. We visualize that the only limitations for using this graft routinely are the necessity of ensuring that the other two visceral arteries, particularly the superior mesenteric artery and its middle colic branch, do not have any obstructive lesions and no complex abdominal pathology or history of previous colonic surgery is present. A careful abdominal examination and selective superior and inferior mesenteric arteriographic studies, therefore, become prerequisites for this purpose.

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Ulnar Artery as a Coronary Artery Bypass Graft: Five-Year Experience

28

A. NEWCOMB, E. OQUELI, B.F. BUXTON

28.1 Introduction

In 1992, Acar [1] rekindled interest in the use of the radial artery (RA) as a coronary artery bypass graft when he reported widely patent grafts many years after the original surgery. Since that time, RA grafting has become more common [2, 3] and, in turn, has led to interest in the other forearm artery – the ulnar artery (UA). Although the RA can be removed from most patients, there are some in whom the RA is the dominant supply for the forearm and cannot be removed safely. In many of these patients, the UA is of sufficient size and quality to be harvested and thus used as a bypass graft.

28.2 Anatomy

The UA originates in the cubital fossa as one of two terminal branches of the brachial artery. It passes along the medial aspect of the flexor compartment of the forearm between the cubital fossa and the flexor retinaculum. The UA curves from its origin to the medial side of the forearm, lying directly on the lateral side of the ulnar nerve until its termination. A line joining the medial epicondyle of the humerus to the lateral side of the pisiform bone represents its course in the distal half of the forearm. In the cubital fossa, the UA lies on brachialis and the median nerve crosses the UA from its medial side to lie laterally. The UA leaves the cubital fossa deep to pronator teres and the median nerve, which passes between the two heads of the muscle.

In the flexor compartment of the forearm, the UA lies on flexor digitorum profundus, to which it is bound by fascial bands. Prior to accompanying the ulnar nerve, the artery passes deep to flexor digitorum superficialis under a fibrous arch between its humero-ulnar and radial origins and the overlying flexor carpi radialis and palmaris longus. In the middle third of the forearm it is deep to flexor carpi ulnaris, while in the distal third it is lateral to the tendon of that muscle, covered only by deep fascia, superficial fascia and skin. On the flexor retinaculum, the artery lies deep to palmaris

brevis and the palmar cutaneous branch of the ulnar nerve.

Throughout its course the UA is accompanied by a pair of veins linked by numerous cross branches. Sympathetic twigs from the ulnar nerve supply the UA at multiple levels.

28.2.1 Branches

The UA has three named branches near its origin and three near its termination, as well as a variable number of smaller branches to surrounding muscles and to the ulnar nerve.

The anterior and posterior ulnar recurrent arteries arise in the cubital fossa and take part in the anastomosis around the elbow joint. The common interosseous artery is a short trunk arising just distal to the radial tuberosity, 2–3 cm from the origin of the UA. The common interosseous artery divides into the anterior and posterior interosseous arteries at the proximal border of the interosseous membrane. These arteries supply the bones of the forearm and muscles, as well as contributing to anastomoses around the elbow and wrist joints. The anterior interosseous artery gives off the median artery, a long branch of which accompanies the median nerve and which is sometimes much enlarged to reinforce the superficial palmar arch.

The posterior and anterior ulnar carpal arteries arise near the pisiform bone to take part in the posterior and anterior carpal arches, respectively, which form an anastomosis around the wrist joint. The deep branch of the UA accompanies the deep branch of the ulnar nerve and completes the deep palmar arch.

The UA provides numerous muscular branches. Some of these cross the ulnar nerve, particularly near the wrist, before sending a recurrent branch to supply the nerve [4]. The UA provides small branches to the ulnar nerve (*arteriae nervorum*). In a study of 37 forearms by Sunderland [4], the mean number of branches was 7 (range 2–19). They were usually short and stout, resulting in the ulnar nerve being securely attached to the UA, particularly in the distal half of the forearm.

28.2.2

Anastomoses

The main anastomoses with the RA are via four arches in the hand and wrist (the superficial and deep palmar arches, and the anterior and posterior carpal arches) and between their metacarpal and digital branches.

28.2.3

Variations

A superficial UA is usually associated with a high origin and passes over the muscles arising from the common flexor origin. It is generally covered by deep fascia, but occasionally is even superficial to the deep fascia. The radial trunk gives off the common interosseous and recurrent arteries.

A variation in the size of the UA is generally accompanied by a compensatory variation in the size of the RA. A typical superficial palmar arch is present in about 30% of cases and may be formed solely by the UA. The median artery enters into its formation in about 8% of individuals [5].

28.3

Patterns of Arterial Supply to the Forearm and Hand

Normally, either the radial or the UA can be removed from the forearm with safety. They are of similar size and there is normally an excellent collateral circulation between these arteries, both in the forearm and in the hand. Assessment of the blood supply to the forearm and hand revealed that there are several patterns that dictate whether the radial, or the ulnar, or neither can be removed safely (Table 28.1). It has long been thought that the ulnar is the larger of the two forearm arteries, but a recent article involving assessment of 24 cadaver limbs showed that the radial artery is indeed the larger, being some 3.2 ± 0.5 mm vs. 2.5 ± 0.5 mm on the right and 3.0 ± 0.5 vs. 2.4 ± 0.5 mm on the left [4]. However, in some patients, the radial is the only source of blood supply to the hand [7, 8]. Using Doppler ultrasound, Little and colleagues found that in 6% of patients there was a drastic reduction in the blood flow to the hand when the RA was occluded at the wrist. Pola and colleagues also found that 11 out of 188 (6%) patients had a poor collateral circulation. These patients are candidates for UA harvesting. In some patients with distal disease, such as those with diabetes, Buerger's disease (thromboangiitis obliterans) or following trauma, the collateral supply between the two major forearm arteries is poor; the RA supplies the thenar side of the hand and the UA supplies the hypothenar aspect of the hand. In these patients, neither artery can be removed safely (Table 28.1).

Table 28.1. The pattern of circulation in the forearm and hand determines the availability of the radial or ulnar artery as a coronary artery bypass graft

Graft	Mixed	Dominant radial	Dominant ulnar	Independent
Radial artery	✓	x	✓	x
Ulnar artery	✓	✓	X	x

x not useable, ✓ useable

Table 28.2. Target vessels for ulnar arterial anastomoses

Left coronary territory	Right coronary territory		
Marginal branches	9	RCA	5
Diagonal branches	4	PDA	4
Intermediate branches	1	Left ventricular branch	2

RCA right coronary artery, PDA posterior descending coronary artery

28.4

Surgical Technique

The UA may be harvested as an isolated procedure before opening the chest, or removed at the same time as the median sternotomy and mobilization of the left ITA. In patients where there was a different arterial pattern on each side, the UA was removed at the same time as the RA was harvested from the other arm.

The arm is abducted to 90° and placed in full external rotation with the hand supinated. The incision commences about 3 cm above the wrist along a line between the lateral border of the pisiform bone and the medial epicondyle. The incision runs along the lateral border of the tendon of flexor carpi ulnaris. Near the midpoint of the forearm the incision curves anteriorly in the direction of the bicipital tendon and stops approximately 3 cm below the elbow joint (Fig. 28.1a). The posterior branch of the medial cutaneous nerve of the forearm may be seen lying subcutaneously as it passes anterior to the medial epicondyle before turning around to the back of the forearm and descending to the wrist.

The UA is removed by commencing the dissection distally. The pedicle containing the artery and its adjacent veins is identified after dividing the deep fascia where it lies between the tendons of flexor carpi ulnaris medially, and flexor digitorum superficialis laterally (Fig. 28.1b). In the distal two-thirds of the forearm the vascular pedicle containing the UA is closely applied to the adjacent ulnar nerve (Fig. 28.1c). Care is required to avoid handling the ulnar nerve, which may be obscured by the UA and the venae comitantes. Division of small branches of the UA to the ulnar nerve (arteriae nervorum) is not avoidable and so far has not been associated with any neurologic dysfunction. The vascular pedicle is mobilized by dividing the small arterial and venous branches between clips. The pedicle is dissected

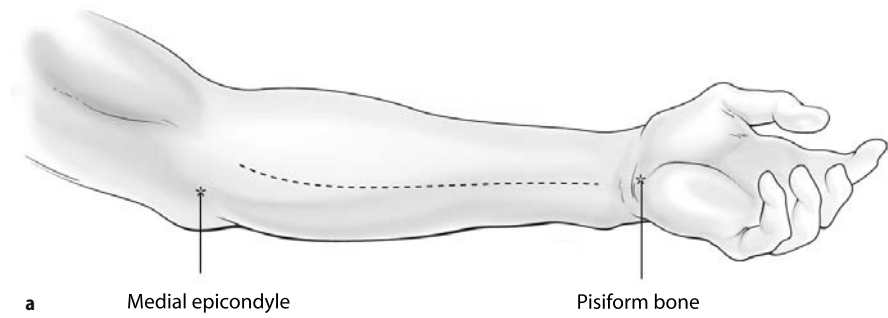
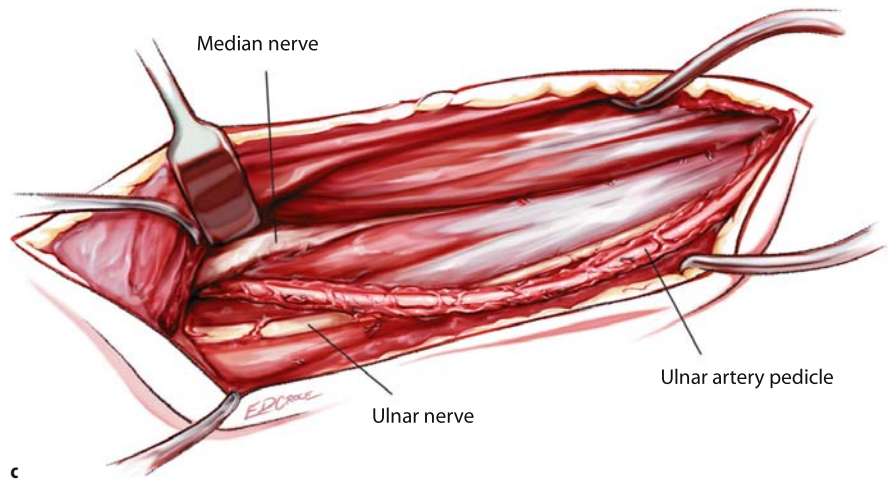
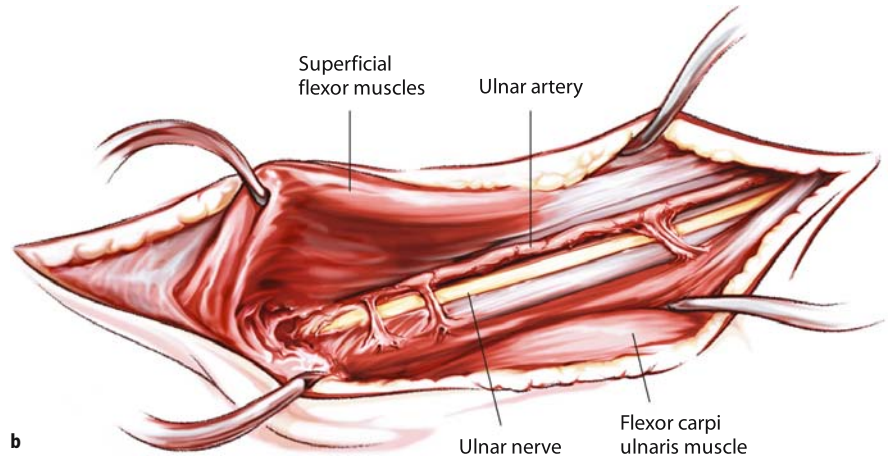
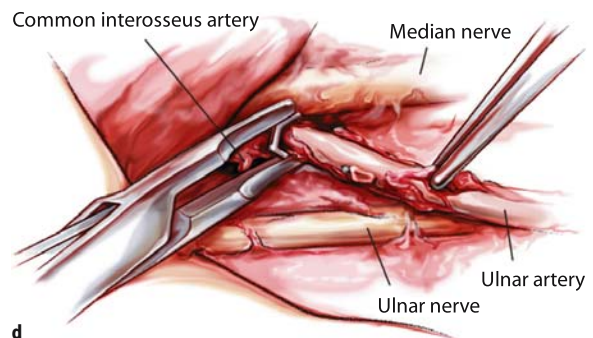


Fig. 28.1. **a** Incision commences 3 cm above the level of the wrist joint along a line lateral to the tendon of the flexor carpi ulnaris in the direction of the medial epicondyle before curving forward towards the bicipital tendon terminating 3–4 cm below the elbow joint. **b** In the lower third of the forearm the ulnar artery lies beneath the deep fascia. The middle third is covered by the flexor carpi ulnaris muscle. Note the proximity of the ulnar artery to the ulnar nerve. **c** Surgical exposure of the left ulnar artery in the anterior compartment of the left forearm. Note the flexor digitorum superficialis is retracted laterally and the flexor carpi ulnaris is retracted medially to expose the ulnar artery. **d** Harvesting of the ulnar artery is completed by clipping and dividing the artery distal to the median nerve, immediately below the origin of the common interosseous artery. (© 1997, The Cardiac Surgery Publishing Office)



proximally by separating flexor carpi ulnaris from flexor digitorum superficialis. The artery is followed until it disappears beneath the muscles arising from the medial epicondyle. Before mobilizing the upper end of the UA, the artery and its collateral veins are divided distally and clipped, leaving a stump of 2 cm above the level of the wrist joint. The cut artery is injected in a retrograde fashion with a solution containing equal parts of heparinized blood and Ringer's lactate solution, with a final concentration of papaverine of 1 mmol/l, or 40 mg/l. After clipping, the UA is allowed to dilate passively.



The upper end of the UA is dissected to the level of the median nerve and common interosseous artery. The UA separates from the ulnar nerve in the proximal third of the forearm before passing beneath flexor digitorum superficialis and the overlying palmaris longus and flexor carpi radialis. As it passes proximally, the UA lies on flexor digitorum profundus, from which it is transected and the artery stored in the papaverine solution (Fig. 28.1d). It is important that it is divided distal to the origin of the common interosseous artery, which is an important collateral supply to the forearm. The wound is closed and bandaged.

28.4.1

The Superficial Ulnar Artery

In one patient from our series the UA had a high origin from the brachial artery. The UA was found crossing the superficial flexor muscles arising from the medial epicondyle, where it lay immediately beneath the deep fascia. It was followed distally, where it was divided 2–3 cm above the wrist joint. The superficial UA was not closely related to the ulnar nerve until it reached the distal fourth of the forearm. This facilitated removal of the artery because it was not directly related to the ulnar nerve. The superficial UA was harvested without handling the ulnar nerve.

28.5

Results

28.5.1

Patients

Between 1997 and 2003, 25 patients had a UA harvested. In these patients, the UA was found to be of sufficient size and quality for use as a bypass graft (22 males, 3 females; average age 69.2 years). All patients had a combination of one or both internal thoracic artery (ITA) and UA grafts, and many had radial arteries harvested from the contralateral arm. The left ITA and the UA were used in all patients. One patient had bilateral ITA and UA grafts and in two patients saphenous vein graft was used to complete the reconstruction. The average number of grafts per patient was 3.1 and ranged from 2 to 4. The aorta was the site of the proximal anastomosis for the majority of these conduits (18). Four were fashioned as Y grafts from the radial artery or ITA, and three were used as composite grafts to extend the range of other conduits such as the pedicled right ITA.

Fifteen of the 18 UAs harvested were satisfactory for use as an arterial graft. The average length of these grafts was 15 cm, approximately 3 cm less than the average length of RA. The mean diameter was 2.4 mm, similar to that of the RA and an excellent size for a coronary artery conduit.

28.5.2

Target Vessels

Ulnar arteries were grafted to all three coronary territories of the heart (Table 28.2). One UA was used as an extension graft (Fig. 28.2). This was attached distally to the posterolateral branch of the right coronary artery and proximally to the pedicled right ITA, after passing behind the vena cava. The other segment of UA that was anastomosed distally to the posterolateral branch of the right coronary artery was attached proximally to a RA grafted to the posterior descending coronary artery (Fig. 28.3).

All patients were removed from cardiopulmonary support without difficulty and there was no evidence of myocardial infarction. None of the patients had evidence of hand ischemia following removal of the UA. One patient had severe pain in the distribution of the ulnar nerve, suggesting that there may have been ischemic injury to the nerve.

28.5.3

Ulnar Nerve Ischemia

One patient with diabetes had persisting pain in the left ulnar nerve distribution along the medial side of the fourth finger and involving the fifth finger. The sensitivity remains although there has been some reduction

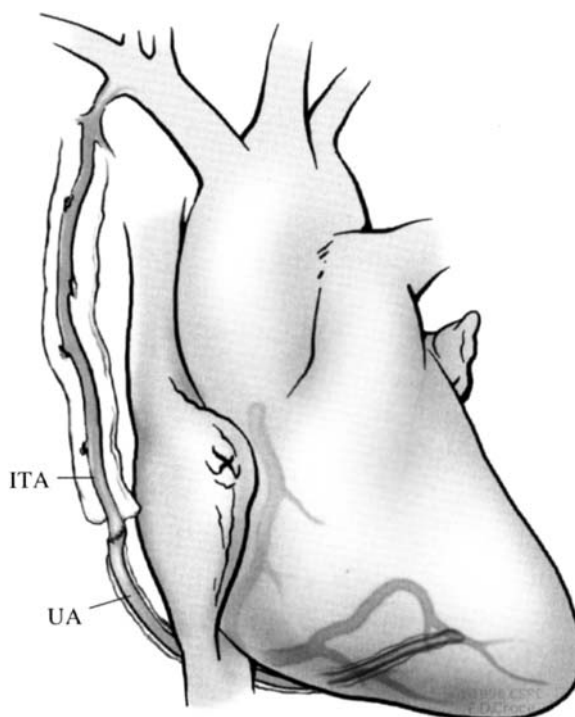


Fig. 28.2. Ulnar artery (UA) extension graft from a pedicled right internal thoracic artery (ITA) graft. (© 1998, The Cardiac Surgery Publishing Office)

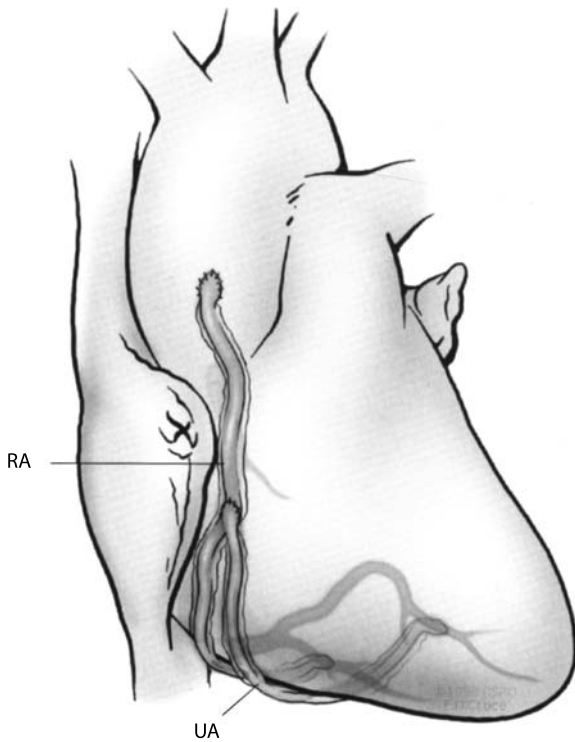


Fig. 28.3. Ulnar artery (UA) and radial artery (RA) Y graft. (© 1998, The Cardiac Surgery Publishing Office)

in the pain over the 8 years since the surgical procedure; he still has occasional episodes of severe pain. He has no cardiac symptoms and his exercise capacity is normal. He is walking one hour a day without angina or shortness of breath. Diabetic control is good and his blood sugar levels are 5–6.5 mmol/l. He has some mild weakness of fine movement of the small muscles. These findings suggest that he has an ischemic injury to the ulnar nerve from the time of surgery.

28.6 Discussion

The UA is frequently available for use as a coronary artery bypass graft in patients who have a dominant RA circulation in the forearm and hand, and in whom the removal of the RA is unsafe.

There is an inverse relationship between the blood supply of the RA and UA. It cannot be assumed that either can be removed satisfactorily and careful clinical testing is required. Removal of the UA should be confined to those patients who have a dominant RA circulation on Allen testing. Other diagnostic modalities, such as the use of arterial Doppler, plethysmography, digital blood pressure testing and angiography, may be of value in assessing the dominance of the UA circulation.

The ulnar nerve is closely related to, and receives its blood supply from, the UA. Removal of the UA demands great care and should not be delegated to a junior member of the operating team. The ulnar nerve supplies both motor and sensory fibers to the hand and therefore injury to the nerve at this level may have serious consequences. The presence of longitudinal vascular anastomoses within the nerve may protect it from ischemia; however, the presence of adequate collateral blood supply cannot be assured as one patient developed evidence of nerve damage, which may have been due to ischemia. Removal of the UA as a bypass graft should therefore be confined to patients in whom there are no alternative conduits.

The UA, like the RA, has a thick muscular media and is therefore prone to spasm. Careful preparation and handling to avoid intima damage are essential prerequisites for use of the UA as a coronary artery bypass graft. If these principles are adhered to, then these grafts may remain patent for a long period of time as shown in the angiogram performed as a follow-up 6 years after surgery (Fig. 28.4). Other problems related to the use of arterial grafts, such as competitive flow and poor runoff, will affect these grafts also. Evidence of this is seen in Fig. 28.5, which shows a tight stenosis at the midpoint of the graft prior to successful angioplasty.

The early data suggested the use of the UA relatively as safe and reliable, with no evidence of myocardial ischemia although 1/25 patients has persisting ulnar nerve ischemia. There are neither long-term clinical data nor any angiographic data to indicate the efficacy of this vessel as a coronary artery bypass graft. It is rec-

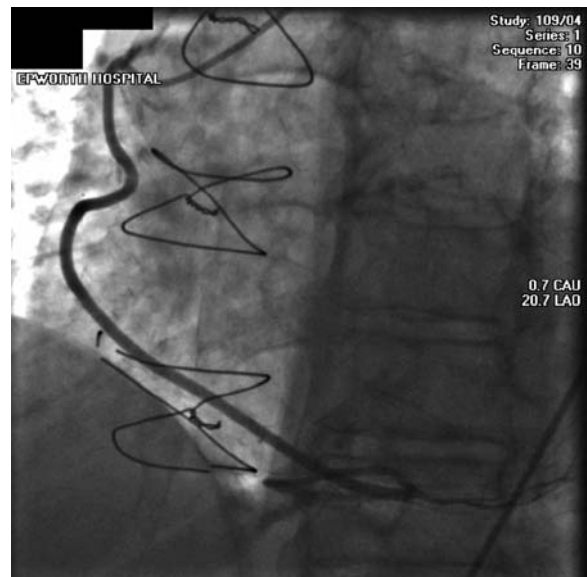


Fig. 28.4. Ulnar artery graft to posterior descending artery at 6 years postoperatively

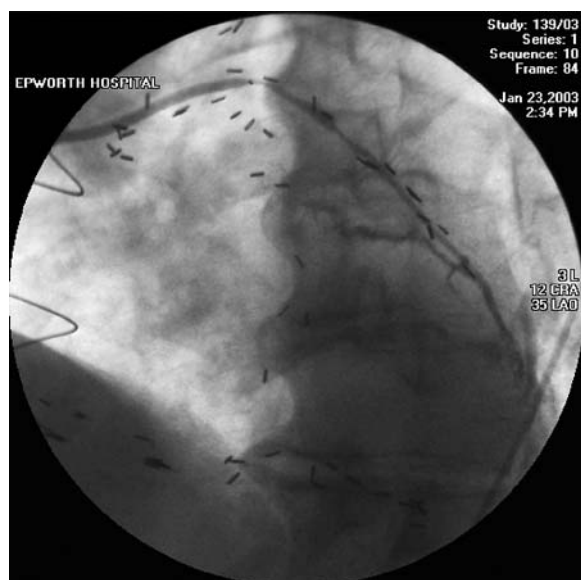


Fig. 28.5. Ulnar artery to OM1 6 years postoperatively with tight stenosis at its midpoint, and a poor runoff

ommended that the UA be removed only in the absence of other arterial conduits. The UA is used in a similar fashion to the RA and it is anticipated that its use may be extended by using T or Y-grafting techniques in the future.

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Descending Branch of Lateral Circumflex Femoral Artery Grafting

T.O. TATSUMI, S. MINOHARA, K. KONDOH

29.1

Introduction

The lateral circumflex femoral artery (LCFA) is one of the branches of the deep femoral artery. The LCFA has three major branches: the ascending, transverse and descending branches. The ascending branches of the LCFA have a large diameter and do not taper like those of the radial arteries [1]. The descending branch of the LCFA has an attractive caliber and length.

The LCFA has been used to supply composite tissue of skin and/or muscle in the field of plastic and reconstructive surgery [1–4].

Now, with the trend toward complete myocardial revascularization using the autologous arterial conduits, the descending branch of the LCFA can be used as an alternative arterial graft.

29.2

Anatomy

The LCFA typically arises from the lateral side of the upper end of the deep femoral artery, but in some 15% or so of instances it begins by the femoral artery above the deep femoral artery [5]. The LCFA runs laterally across the front of the iliopsoas muscle, between the branches of the femoral nerve, to pass behind the sartorius and rectus femoris muscle. Here, the LCFA divides into the three major branches: the ascending, transverse and descending branches (Fig. 29.1).

The ascending branch ascends along the intertrochanteric line, under the tensor fasciae latae, lateral to the hip joint; it anastomoses with the superior gluteal and deep circumflex iliac arteries, supplying the greater trochanter, and forms an anastomotic ring round the femoral neck and head.

The transverse branch, the smallest, passes laterally anterior to the vastus intermedius, pierces the vastus lateralis to wind round the femur, just distal to the greatest trochanter, anastomosing with the medial circumflex, inferior gluteal and first perforating arteries, which is the *cruciate anastomosis* in the buttock.

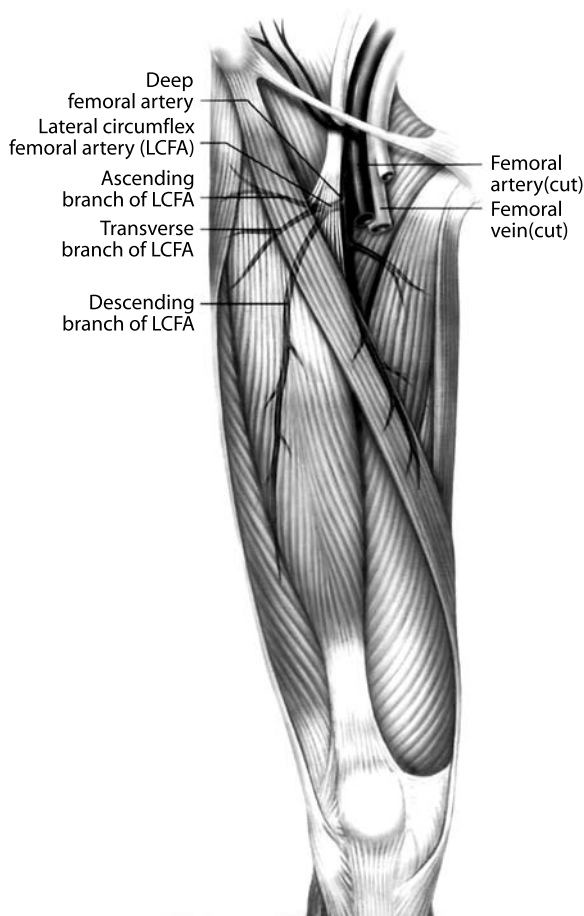


Fig. 29.1. The right lateral circumflex femoral artery and its three major branches

The descending branch, which sometimes runs from the deep femoral artery or the femoral artery, descends posterior to the rectus femoris, along the anterior border of the vastus lateralis, which it supplies; a long ramus descends in the vastus lateralis to the knee, anastomosing with the lateral superior genicular branch of the popliteal, accompanied by the nerve to the vastus lateralis.

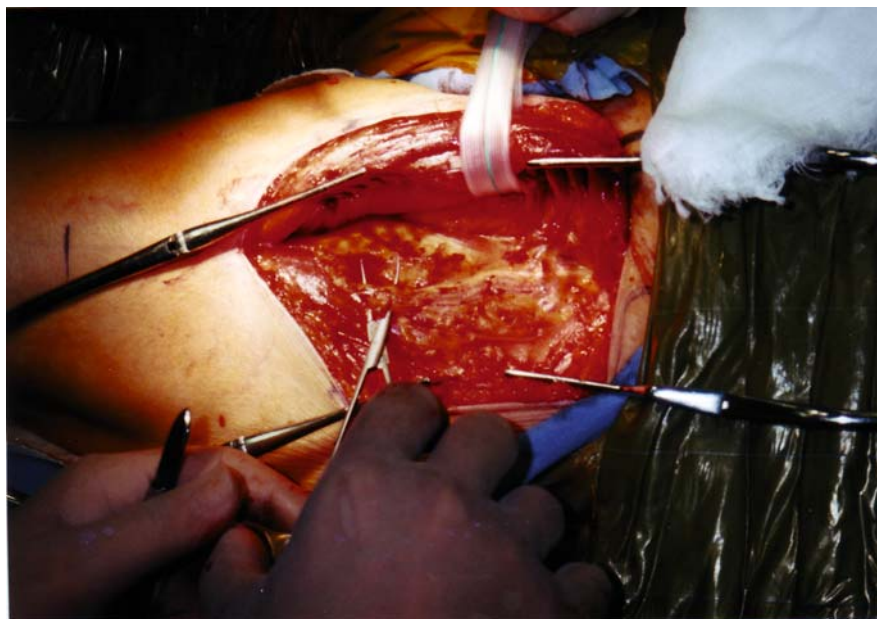


Fig. 29.2. The descending branch of the left LFCA between the rectus femoris and the vastus lateralis muscle

29.3 Surgical Procedure

The harvest of the descending branch of the LCFA can be performed simultaneously while the internal thoracic artery is isolated. It can be done before or after the harvest of the same side of the greater saphenous vein on the same position of the lower extremities.

The incision to harvest the descending branch of the LFCA is made in the middle third of the thigh along the lateral margin of the rectus femoris muscle. The subcutaneous tissue and the fascia latae are opened longitudinally along the length of the incision, so you can see the space between the rectus femoris muscle and the vastus lateralis muscle.

The descending branch of the LCFA courses between the rectus femoris and the vastus lateralis muscle and is easily visualized when the rectus femoris muscle is retracted medially and the intermuscular space is explored. In general, you will find the descending branch of the LCFA is simply running straight to distal with little surrounding tissue (Fig. 29.2).

The pulsation of the descending branch of the LCFA should be ensured by palpation to avoid applying the poor graft conduit to coronary artery bypass grafting (CABG). Poorer pulsation of the artery would be considered to indicate its obstruction or stenosis caused by some organic disorder of the artery.

After the descending branch of the LCFA is isolated carefully from the surrounding tissue, the muscle branches are the descending branch of the LCFA tied and cut individually with hemoclips. Once mobilized, it is wrapped in a papaverine-soaked sponge and kept until the anastomosis.

The descending branch of the LFCA is ligated and cut near its origin with silk proximally, and cut off distally at the appropriate length for bypass grafting; that is usually 10–15 cm. The descending branch of the LFCA is absolutely free from the patient and is soaked in the preservative solution after the injection of diluted papaverine hydrochloride (40 mg in 10 ml saline) into the free graft through the proximal site of the free graft.

CABG is performed per protocol with or without cardiopulmonary bypass (CPB). The descending branch of the LFCA is grafted to the coronary branch except for the left descending branch. The proximal anastomosis is constructed onto the ascending aorta, saphenous vein graft (SVG) and internal thoracic artery (ITA).

29.4 Results

Twenty of 21 descending branches of the LFCA harvested were satisfactory for use as arterial grafts after the first patient undergoing CABG used the descending branch of the LFCA [6]. The lengths of these grafts were 10–17 cm and the inner diameter measured 1.5–2.0 mm, similar to the ITA of the same patient. CABG with CPB was performed on 11 patients, and the other 9 patients underwent CABG without CPB. The perioperative and postoperative course of all patients was not eventful.

The descending branch of the LFCA was grafted to the diagonal branch, posterolateral branch of circumflex, right coronary artery or the posterior descending branch of the right coronary artery. The proximal anastomosis of these grafts was on the ascending aorta, sa-

phenous vein graft, left ITA or right ITA. The LFCA grafts anastomosed to the right ITA were used as an extension graft (I grafting technique). The LFCA grafts were anastomosed to the left ITA by the end-to-side method (Y grafting technique) (Table 29.1). Figure 29.3

shows the patent LFCA graft anastomosed right ITA grafting to the 4PD (Fig. 29.3). And Fig. 29.4 shows the patent LFCA graft anastomosed left ITA grafting to the diagonal branch (Fig. 29.4). The patency rate of the LFCA graft was 85% at the early postoperative period (Table 29.1). In these cases, we have seen none of the complications of lower limb postulated as a consequence of harvesting the descending branch of the LFCA.

Table 29.1. Sites of proximal and distal anastomoses of LFCA

Proximal	Distal
Aorta 4 (1)	RCA 7 (1)
RITA 7 (1)	4PD 2
LITA 8 (1)	4AV 1 (1)
SVG 1	Diagonal 6 (1)
	PL 3
	OM 2

No. of occluded anastomoses are in parentheses

29.5 Comment

Several points regarding the use of the descending branch of the LFCA as a bypass graft can be addressed. With regard to the quality of the vessel, the descending

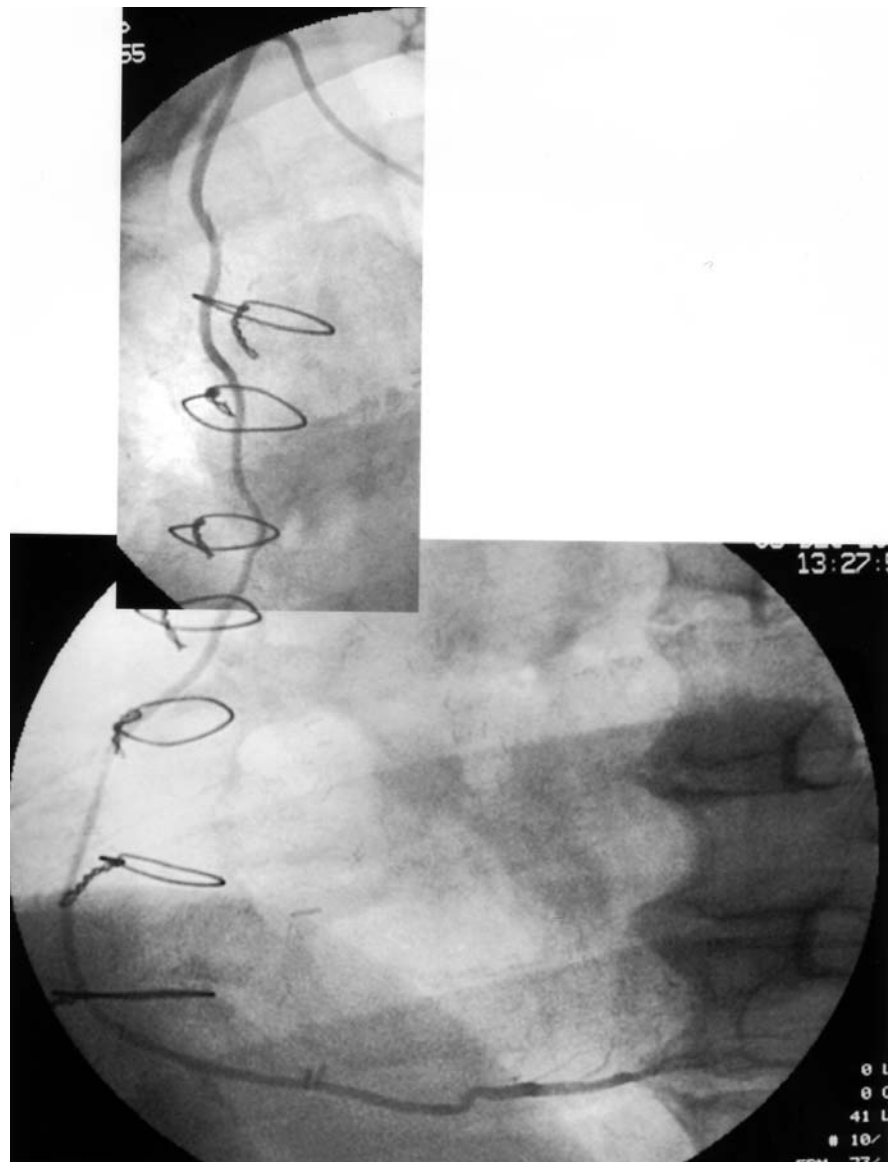


Fig. 29.3. The descending branch of the LFCA anastomosed right ITA is grafting to the 4PD

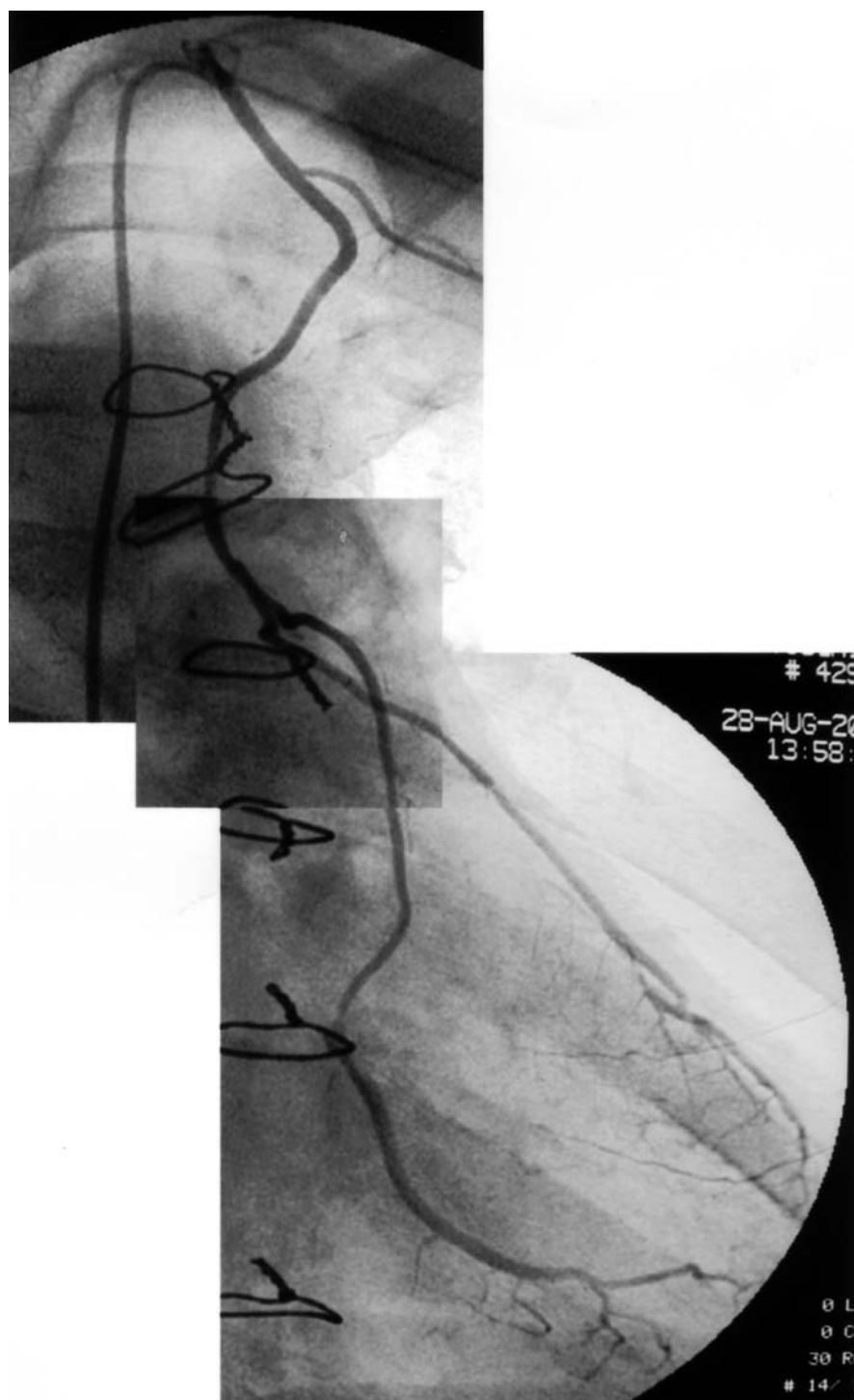


Fig. 29.4. The descending branch of the LCFA anastomosed left ITA by the Y-grafting technique is grafting to the diagonal branch

branch of the LCFA was similar in size to the ITA. Moreover, the descending branch of the LCFA is readily accessible and easier to isolate than the internal thoracic artery, gastroepiploic artery and inferior epigastric artery. Lastly, inasmuch as the muscles of the thigh supplied by the descending branch of the LCFA have a rich

collateral supply, functional deficits associated with the operation are potentially reduced.

Histologically, the LCFA is of the muscular type and contains many smooth muscle cells in the media, similar to the radial artery, inferior epigastric artery and gastroepiploic artery, whereas the ITA has elastic fibers

in the media. There is very little difference in the incidence of arteriosclerosis between the LFCA and these arteries. But the LFCA has one disadvantage. The descending branch of the LFCA cannot be used in patients having arteriosclerosis obliterans, because the LFCA may make the important collateral. Therefore the angiogram of lower limb is necessary preoperatively.

All patients undergoing CABG using the descending branch of the LFCA had no perioperative or postoperative complications such as myocardial infarction, heart failure or operative death. This showed no increase in perioperative risk with the use of the LFCA graft.

The descending branch of LFCA bypass graft offers an acceptable early patency rate. Due to the technical demands involved with descending branch of LFCA harvesting, a learning period may be necessary. Anastomosis of the LFCA graft on the aorta may increase the risk of graft failure, because the wall of the aorta is thicker than the wall of the descending branch of the LCFA. The difference in thickness of their walls made the surgical technique difficult. It is anticipated that use of the descending branch of the LCFA should be extended by using the I or Y grafting technique.

In summary, we believe that the descending branch of the LFCA can be used as an autologous graft for myocardial revascularization.

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30 The Intercostal Artery: An “Ideal” Arterial Graft Awaiting Clinical Application

L.C.H. JOHN

30.1 History

The use of the intercostal artery (ICA) in cardiac surgery predates the development of cardiopulmonary bypass and coronary artery surgery. The first report was in 1946 [1], which described a patient with constrictive pericarditis, whom following pericardiectomy had three intercostal muscles including the arteries sutured to the de-epicardialised heart. Its first application for the treatment of coronary artery disease was reported in 1966 [2]. This was for a Vineberg procedure rather than a direct coronary artery graft. The 5th rib was resected and a pedicle formed based posteriorly, of the intercostal muscles, fascia and periosteum of the resected rib together with the intercostal neurovascular bundle. These ICA pedicles were implanted into a tunnel of left ventricular myocardium in 25 dogs and constrictors placed around the left anterior descending and circumflex coronary arteries. Seventeen of the 25 dogs survived for 3–9 months. Following the initial animal work the technique was used in three patients. In one it was implanted into the anterolateral part of the left ventricle. The other two had implantation into the posterior part of the left ventricle. It was reported that there was symptomatic improvement in all three.

30.2 Potential Advantages of Intercostal Arteries

Since these early reports the literature has been confined to the potential use of the ICA for directly grafting coronary arteries. There are a number of reasons why ICAs are an attractive option and these include the following:

30.2.1 Favourable Histology

The ICA has a relatively thin intima and media, which is elastic or elastomuscular [3]. The elastic nature of the ICA is similar to the internal mammary artery. This is in contrast with other potential arterial conduits inves-

tigated, which are muscular [4]. It has been suggested that the perfect continuity of the internal elastic membrane of the internal mammary artery prevents the migration of smooth muscle cells from the media to the intima thereby explaining its resistance to developing atherosclerosis [5]. The similarity between the histology of the ICA and the internal mammary artery is suggestive that the former would also be relatively protected from atherosclerosis. On this basis the ICA would be expected to have a good long-term patency as a coronary bypass graft.

30.2.2 Favourable Anatomy

Unlike every other potential arterial conduit there are significantly more than two ICAs available for coronary grafting. Thus assuming adequate lengths the entire coronary artery system could theoretically be grafted using them. In addition because of their intrathoracic location they are suitable for use as “in situ” arterial grafts rather than “free” grafts. Although disputed [6] there is evidence that “in situ” arterial grafts have a long-term patency advantage compared with “free” grafts. In one study looking principally at radial artery patency, the 9-month patency of “free” internal mammary artery grafts was 69.3% compared to 100% for “in situ” grafts [7]. For gastroepiploic artery grafts the 2-month patency of “free” grafts was only 75% as compared to 95% for “in situ” grafts [8]. At present the most commonly used “free” arterial graft is the radial artery. A recent study [9] has reported that the 4-year patency for radial arteries was 89% as compared to 98% for left internal mammary arteries. This radial artery patency was also inferior to the 5-year patency of long saphenous veins (95%). Thus the suitability of ICAs as “in situ” arterial grafts gives them a potential long-term patency advantage.

30.3 Feasibility Studies

In a human cadaver study the third to eighth ICAs were dissected out bilaterally [10]. The extent of the dissection was from approximately 2 cm lateral to the vertebral bodies to the anterior end of the ICA (internal mammary or musculophrenic arteries). Two routes for in situ grafting of the coronary arteries were examined. For the *superior route* the ICA was brought from its proximal dissection point (adjacent to the vertebrae), superior to the pulmonary hilum and through the pericardium. It was then routed anterior to the proximal descending aorta and main pulmonary artery for a left sided ICA (superior vena cava and ascending aorta for a right sided ICA) and then inferiorly to reach the relevant coronary artery. For the *inferior route* the ICA was brought from its proximal dissection point and inferior to the inferior pulmonary vein (following division of the inferior pulmonary ligament) before passing through the pericardium and directly to the relevant coronary artery. In this cadaveric study the mean length of the ICAs was 27.4 ± 3.2 cm on the right and 27.0 ± 2.9 cm on the left. The longest were the fifth ICA (both right and left). In order to identify which of the ICAs would be optimal for grafting, the mean excess of length for each ICA dissected out when routed as for an in situ graft to each of the major coronary arteries was determined. The greater the excess length then the more proximal the ICA could be divided at the site of potential anastomosis. The more proximal the ICA can be divided then the greater its diameter and hence its suitability for coronary artery grafting. On this basis this study determined that, although any of the right or left third to eighth ICAs can reach the left anterior descending coronary artery by either the superior or inferior routes (apart from the right eighth ICA by the inferior route) the optimum graft and route was the left fifth ICA through the inferior route. Similarly the optimum graft for the lateral circumflex coronary artery appeared to be the left fifth ICA by the inferior route and for the right coronary artery the right seventh ICA by the inferior route.

Intercostal artery grafts have also been investigated in live dogs [11]. In this study the 8th and 9th ICAs were harvested as pedicled grafts in 12 dogs, initially by a thoracic approach and then via a median sternotomy. These pedicled grafts were able to reach branches of both the left circumflex and the right coronary artery. Mean blood flows in the left 8th and 9th ICA grafts were 25 ± 3 and 27 ± 2 ml/min with mean external diameters of 0.44 and 0.48 mm respectively.

30.4 The Future

Despite the evidence, which suggests that ICAs might be an "ideal" arterial conduit, for directly anastomosing to coronary arteries, there are at present no human clinical reports of them being so used. There are a number of potential concerns that have inhibited their use and these include the following:

30.4.1 Diameter and Flow of the ICA

The ICA has a smaller diameter than the average internal mammary artery and it has been questioned whether they are large enough to form a good anastomosis with a coronary artery and whether the flow would be adequate. The free flow of the transected ICA at the mid axillary level has been measured at 80–100 ml/min, which should be more than adequate for coronary artery grafting. The mean luminal diameter of the 5th ICA at autopsy has been reported to be 1.4 ± 0.3 cm at its origin and 0.9 ± 0.2 cm at the distal end [3]. Allowing for a 30–40% reduction in the diameter due to rigor mortis the probable diameter of the ICA at the site of an anastomosis would probably be similar to that of a "small" internal mammary or gastroepiploic artery. In addition the diameter of an arterial graft is not static but may increase when grafted to a large viable myocardial area [12].

30.4.2 Risk of Medullar Ischaemia

The relationship between the proximal ICA and the spinal blood supply raises concerns as to whether harvesting ICAs might result in medullar ischaemia. However, limiting the proximal dissection of the ICA to approximately 2 cm lateral to the vertebral bodies in order to minimise damage to spinal tributaries should reduce this.

30.4.3 Harvesting Technique

The perceived difficulty in harvesting ICAs is a major factor in the reluctance to clinically use them. Potentially they may be harvested through a median sternotomy with the pleura widely open and the lungs collapsed whilst on cardiopulmonary bypass. Alternatively they may be harvested by minimally invasive means using videoscopic thoracoscopy. However, it should be noted that in the early report [2] on the use of ICAs as a tunnelled graft in the left ventricle the technique used involved excising a rib and dissecting out the entire neurovascular bundle together with the intercostal

muscles and periosteum. The fragility of the ICA and the difficulty in dissecting it alone was commented upon.

In summary the ICA is potentially an “ideal” arterial graft. It has as yet not been used clinically. Whether it will or not in the future will depend upon demonstrating that the possible concerns with its use are not justified.

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Arterial Grafting Using Complex Grafts

Complex Arterial Grafts: Operative Techniques

A.M. CALAFIORE, M. DI MAURO

Since the beginnings of direct coronary artery surgery, the use of arterial grafts, such as the internal mammary arteries, has been an option. Perhaps the first description of a myocardial revascularization, as known nowadays, was by Vassili Kolesov, who in 1964 anastomosed routinely the left internal mammary artery (LIMA) to the left anterior descending (LAD) artery without cardiopulmonary bypass via a left anterior thoracotomy [1]. However, the widespread use of cardioplegic techniques and the outstanding early results obtained with the saphenous vein graft (SVG) by the Cleveland Clinic group [2] reduced interest in arterial grafts, since their harvest was longer and more difficult. It took several years until the use of the LIMA to the LAD graft was considered a key point in the survival and event free survival of any patient undergoing myocardial revascularization [3]. In the 1980s the use of multiple arterial grafts, left and right internal mammary arteries, right gastroepiploic artery, radial artery and inferior epigastric artery, was reconsidered, with the purpose of improving long-term results in coronary patients.

31.1

Internal Mammary Artery

This graft, used since the 1960s, is considered the arterial graft of choice, mainly for the LAD; it gained widespread popularity due to its anatomical situation, along the lateral border of the sternum, and on the basis of a long follow-up. The use of the bilateral internal mammary arteries (BIMAs) to increase the benefit of arterial revascularization for the patient was the next step. Although the initial experiences were unable to demonstrate any advantage of BIMA over LIMA [4–7], more recently higher freedom from death [8, 9], cardiac death [10–12] and cardiac-related events [10–12] in the case of BIMA grafting have clearly been reported.

In our opinion, the use of the second IMA is essentially a technical factor: if there is no increase in mortality and morbidity related to its use, there is no reason not to use it.

Some questions still need to be answered:

31.1.1

What Is the Best Use of the RIMA?

The first question is the most important, as the correct use of the right internal mammary artery (RIMA) can modify the strategy of a total arterial myocardial revascularization. Many studies have showed that the most important target for the RIMA is not the right coronary artery (RCA) system, but the lateral wall [9, 10, 13, 14].

The RIMA grafted to the RCA has a low patency rate [15]. In fact the RCA is often calcified or severely fibrotic; we graft the RIMA directly to the RCA only when this vessel is more prominent than the circumflex artery and has a normal wall; the posterior descending artery can be used as the target coronary vessel using the Y-graft configuration.

There is no reason to use the RIMA on a diagonal branch. The conduit can be used on an obtuse marginal (OM) branch via the transverse sinus, but this choice is the cause of some concern: it can be used on the first OM and frequently it is not possible to choose the anastomotic site because of the lack of a proper length of graft. In addition, possible bleeding behind the aorta is potentially dangerous.

31.1.2

How Can the Number of Anastomoses/Patient Be Increased Using BIMA?

To increase the number of anastomoses/patient, since 1994 we have harvested both IMAs skeletonized instead of pedicled. In fact if the IMAs are harvested already skeletonized, additional advantages are guaranteed, as our experience demonstrates: the graft is longer (4–5 cm) and bigger than the pedicled one. The absence of the surrounding structures (fascia, veins, muscle) allows the IMA to increase in both dimensions; moreover, after the intraluminal injection of papaverine that we use as routine [16], any focal injury occurring during the harvesting can be easily detected. In our experience the use of small hemoclips and, if necessary, a low energy cautery allows us to visualize optimally every collateral branch just after their origin, making the risk of focal damage minimal.

The harvesting of the IMA as a skeletonized conduit is not recent. Vineberg [17] used the IMA skeletonized and he was followed by other authors [18–22], who reported this technique in their routine practice. It was demonstrated that the IMA is nourished by the lumen and, since in the media vasa vasorum are not present, devascularization of the conduit does not give any adverse effect [23].

31.1.3

Can Sternal Morbidity Limit the Use of BIMA?

Can Some Subgroups of Patients (e.g., Diabetic Patients) Be Revascularized Using BIMA with a Low Morbidity?

In our experience, BIMA skeletonization strongly reduces the sternal morbidity [24]. In fact, as the collateral circulation to the sternum is well preserved, the incidence of sternal dehiscence is surprisingly low.

Many surgeons have long been reluctant to use BIMA grafting, because of a higher risk of deep sternal problems, especially in diabetic patients [25, 26]. Recently, IMA harvesting as a skeletonized conduit [24, 27–29], together with a better-controlled glucose man-

agement in the postoperative period [30], has been shown to lower the risk of sternal wound problems in diabetic patients who receive BIMA grafting.

Recent reports have demonstrated that the use of BIMA in diabetic patients provides similar early and long term results to single IMA [31, 32], although Endo et al. [33] reported 10-year freedom from all deaths (87.4% vs 75.2%, $p=0.04$; HR=0.61) and freedom from all deaths, re-CABG and AMI (86.6% vs 69.0%, $p=0.0086$; HR=0.53) significantly higher in the BIMA group, with EF > 40%.

31.1.4

BIMA Y Graft

At the beginning we preferred to use the RIMA on LAD and the LIMA to the lateral wall, but sometimes the RIMA was not long enough, so, following the experience proposed by other authors [34], we started to use the RIMA as a free graft, anastomosing it to the LIMA (Y graft) [35].

The Y graft was always constructed before the start of cardiopulmonary bypass (CPB) or, if CPB was not used, at the beginning of the operation (Fig. 31.1). The most suitable point for the anastomosis was chosen. Because the common target vessels for side branches are on the circumflex system, the best point is at the level of the pulmonary artery; for other arrangements, the proximal anastomosis site had to be decided on a case-by-case basis. A longitudinal incision was performed on the in situ IMA, 6–8 mm long. The free graft was prepared, opened obliquely at its tip, and then extended to the internal thoracic artery (ITA). A running stitch with an 8-0 Prolene suture (Ethicon, Inc., Somerville, NJ), starting from the heel of the free graft, was used (Fig. 31.2). The in situ IMA was unclamped and the proximal anastomosis was carefully checked for any bleeding. Graft distortion can be avoided merely by placing the ITA over the heart. The inside pressure will keep the graft in the right orientation.

This technique provides long term angiographic (Fig. 31.3) and clinical results similar to using BIMA in situ [35], but allows the RIMA easily to reach the lateral wall, therefore increasing the number of arterial anastomoses, especially on the left coronary system.

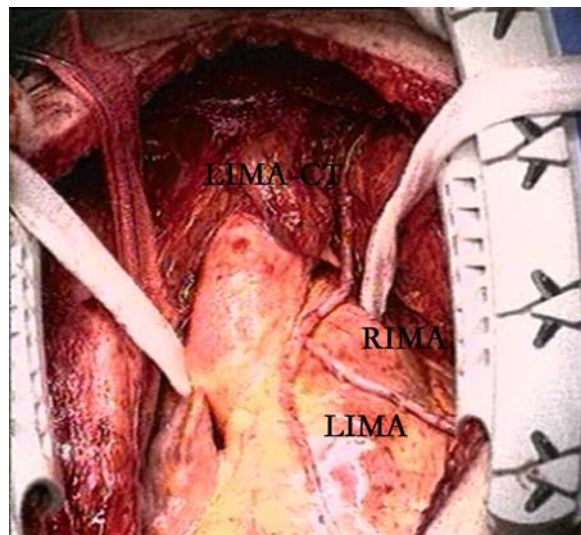


Fig. 31.1. Intraoperative view. Bilateral internal mammary artery preformed as Y graft

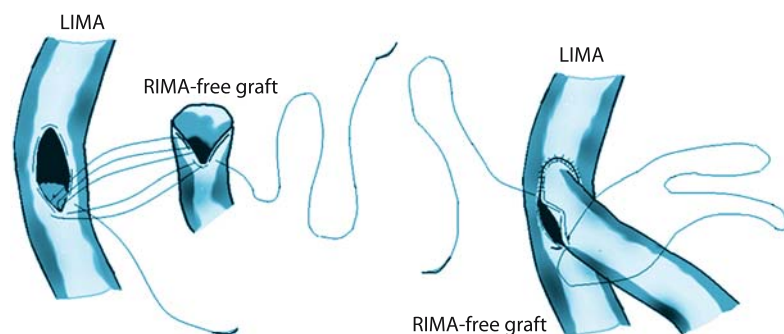


Fig. 31.2. End-to-side anastomosis technique (Y graft) (LIMA left internal mammary artery, RIMA right internal mammary artery)

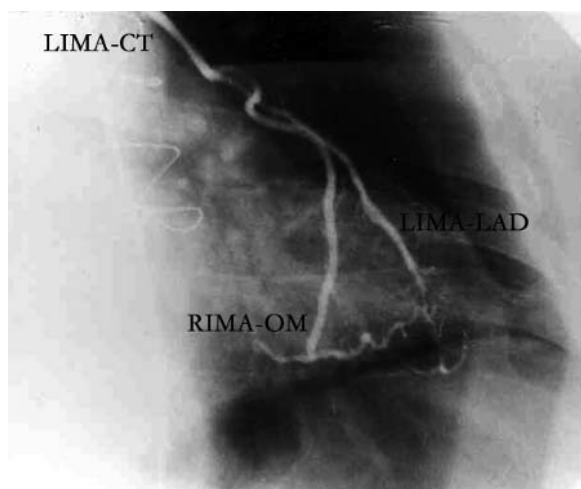


Fig. 31.3. Angiographic control performed 54 months after surgery: LIMA is grafted to the LAD, and LIMA-(Y graft)-RIMA is grafted to the OM

31.2

Right Gastroepiploic Artery

The right gastroepiploic artery (RGEA), which can be utilized as an in situ graft, presents a muscular media layer, different from the IMA [36]. The possibility of its use as an in situ graft avoids the problem of proximal anastomosis. The media structure makes this artery highly prone to spasm either during the harvesting or after the grafting: a careful takedown of the conduit and a high runoff in the target territory are therefore mandatory. This means that the RGEA must be used only down to a severe stenosis or occlusion (high flow situation). In the case of a mild coronary stenosis (low flow, or no flow situation), the graft will immediately adapt to the native flow, reducing its size (string sign) up to the occlusion. In some particular situations (very mild stenosis), the RGEA can be retrogradely perfused, causing a hypoperfusion in that territory, with ischemic changes up to myocardial infarction [37].

In our experience the RGEA is used as follows:

- Always as an in situ graft, to avoid the aortic anastomosis. Only in two cases (too short RGEA) was the graft used on a diagonal branch with the proximal anastomosis on the LIMA, and on the PDA (the RGEA was divided and anastomosed to the aorta with the interposition of an SVG).
- Always in the RCA territory. This solution is the optimal one for this graft, which is very close to this territory. If we cut several centimeters of the free edge we have a suitable graft caliber (up to 3 mm): this is not possible if the anastomotic site is more distant.

31.3

Inferior Epigastric Artery and Radial Artery

These two grafts are treated together because of their many similarities: both conduits are utilized as free grafts and have a similar wall structure (muscular tunica media) [36].

In both cases, the target territory must have a critical stenosis: we must avoid, as for RGEA, the adaptation to a low flow situation (string sign up to occlusion).

The only difference is in the length (6–8 cm for IEA, about 18 cm for RA), whereas distal size is practically similar (about 2.5 mm for IEA, 3.0 mm for RA), so the choice of an IEA instead of an RA depends on the length necessary to reach the anastomotic site (shorter for the IEA, longer for the RA).

Harvesting technique has already been described [16].

31.4

Inferior Epigastric Artery

We would like to stress that we limit the IEA harvesting up to the first muscular branch because the distal size, after this point, becomes less. This technique of harvesting has led us to use the IEA in composite grafts with an IMA as inflow conduit; a proximal anastomosis was performed directly onto the IMA or to the branch of an RA previously connected to an IMA [16]. In the case of end-to-end anastomosis, the extremity of the IEA and that of the inflow graft are both obliquely mouthed, to ensure a wider anastomosis (Fig. 31.4).

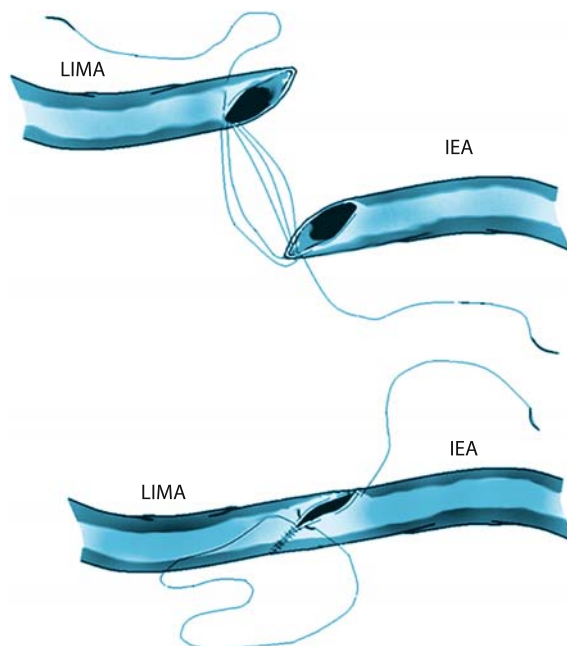


Fig. 31.4. End-to-end anastomosis technique (LIMA left internal mammary artery, IEA inferior epigastric artery)

In more recent experience, the IEA has been used only for lengthening IMA, when this could not reach the anastomosis site, especially in the LAST operation [38]. Indeed, in selected patients the possibility of lengthening an AC with another AC can be a technical solution when the donor graft is too short to reach the target coronary vessel [39].

31.5 Radial Artery

The radial artery (RA) for coronary artery bypass grafting was first introduced by Carpentier and colleagues in 1971 [40]. Two years later the same authors recommended abandoning this graft owing to a high rate of graft failure [41]. At the end of the 1980s the same graft was proposed again with better early and midterm results [42]. The reasons for this favorable outcome were modification of the harvesting technique, use of calcium channel blockers, and a better understanding of the biologic properties of the graft.

The RA shows an important vasoreactivity in comparison with the IMA [43], and its propensity to spasm has some important surgical implications. RA harvesting with the surrounding tissue avoids any touch, and intraluminal injection of a papaverine solution allows the highest dilation possible to be obtained. Whether this tendency to spasm is at the base of the string sign observed in some angiographic controls [42, 44–46] is not clear. However, many authors reported an attenuation or a disappearance of the string sign in serially observed controls [44, 45], as if this aspect were peculiar to the first months after grafting. Possati and associates [44] found at midterm angiographic follow-up that the early RA propensity to spasm after serotonin challenge was markedly decreased. The same group [47] showed that 5 years after surgery the RA graft had a tendency to increase its size significantly, to the same extent as the IMA, and that dilation of these two types of graft in response to acetylcholine administration was similar. It seems that after the first months following surgery, the RA loses its peculiar characteristics of increased vasomotricity.

This graft can be used in all areas, with particular emphasis on the lateral wall. In a study by our group [48], after a maximum follow-up of 8 years, clinical and angiographic results of RA and RIMA grafting in the lateral wall, when the LIMA is anastomosed to the LAD, are similar. This fact enhances the possibility of choice of the appropriate graft when coronary revascularization with multiple arterial grafting is scheduled.

31.5.1 Radial Y Graft

In our experience, the radial artery has been used mainly as a Y graft rather than for lengthening the arterial conduit. The technique performed to anastomose the RA to IMA is the same as reported above for the BI-MA Y graft.

The Y graft can be used when extensive grafting is necessary, providing the target coronary vessel has a degree of stenosis of 80% or higher. If sequential grafting is needed, the intermediate anastomoses can have a lower degree of stenosis if the last territory is severely stenosed. In the case of less severe stenosis, the Y graft is not indicated, but if the RA has to be used, the proximal anastomosis must be performed on the ascending aorta. On the right coronary territory, the best solution seems to be the aortocoronary graft.

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32 Complex Arterial Grafts: Clinical Results

A.M. CALAFIORE, M. DI MAURO

From September 1991 to December 2001, 4,724 patients underwent isolated myocardial revascularization. In 1,215 (25.7%) at least one complex arterial conduit was used:

- End-to-side: 1,113 (91.4%)
- End-to-end: 96 (7.9%)
- End-to-side/end-to-end: 9 (0.7%)

32.1

End-to-Side

In 1,084 cases, a single Y graft was performed. The BIMA Y graft was the main strategy adopted (Table 32.1). In 29 cases, multiple Y graft conduits were performed to achieve a total arterial myocardial revascularization (Table 32.2).

Table 32.1. Strategies for the single Y graft ($n=1,084$)

LIMA Y RIMA	718
LIMA Y RA	170
LIMA Y IEA	77
LIMA Y RGEA	2
LIMA Y LIMA	40
RIMA Y LIMA	26
RIMA Y RA	24
RIMA Y IEA	10
RIMA Y RIMA	5
RA Y LIMA	8
RA Y RIMA	2
RA Y IEA	2

LIMA left internal mammary artery, *RIMA* right internal mammary artery, *RGEA* right gastroepiploic artery, *RA* radial artery, *IEA* inferior epigastric artery

Table 32.2. Strategies for multiple Y grafts ($n=29$)

LIMA (Y-LIMA) (Y) RIMA	2
LIMA (Y-RIMA) (Y) RIMA	5
LIMA (Y) RIMA (Y-RIMA)	8
LIMA (Y) LIMA (Y-IEA)	2
LIMA (Y) IEA (Y-RIMA)	2
LIMA (Y-IEA) (Y) RIMA (Y-IEA)	1
LIMA (Y-IEA) (Y) RA	1
LIMA (Y) RA (Y-IEA)	8

LIMA left internal mammary artery, *RIMA* right internal mammary artery, *RA* radial artery, *IEA* inferior epigastric artery

32.2

End-to-End

In 96 patients a lengthened arterial conduit was mandatory to reach the anastomotic site. Inferior epigastric artery (IEA) was the main lengthening conduit (68 patients, 71%), and in 53 cases lengthened left internal mammary artery (LIMA), in 14 right internal mammary artery (RIMA) and in just 1 case radial artery (RA) was used (Table 32.3).

Table 32.3. Strategies for lengthened arterial conduits ($n=96$)

LIMA+RIMA	4
LIMA+IEA	53
LIMA+RA	6
RIMA+LIMA	1
RIMA+IEA	14
RIMA+RA	17
RA+IEA	1

LIMA left internal mammary artery, *RIMA* right internal mammary artery, *RA* radial artery, *IEA* inferior epigastric artery

32.3

End-to-Side/End-to-End

Nine patients received both the above-mentioned surgical strategies. LIMA represented the main inflow conduit (Table 32.4).

Table 32.4. End-to-side/end-to-end conduits ($n=9$)

LIMA Y RIMA+RA	1
LIMA+IEA Y RIMA+IEA	1
LIMA+RIMA Y IEA	1
LIMA+RIMA Y LIMA	2
LIMA+RA Y RIMA	1
LIMAY RA+LIMA	1
RIMA+IEA Y RA	1
RIMA Y LIMA+IEA	1

LIMA left internal mammary artery, *RIMA* right internal mammary artery, *RA* radial artery, *IEA* inferior epigastric artery

32.4

BIMA Y Graft

From 16 September 1991 to 31 December 2001, a total of 2,072 patients underwent isolated myocardial revascularization grafting with BIMA, 1,308 in situ and 764 with Y graft. By means of the Propensity Score (PS) (goodness of fit²=8.4 *df*=8, *p*=0.81) and sample matching, 1,368 patients (66.5%), 684 for each group and with similar preoperative characteristics, were selected. In Table 32.5 the preoperative characteristics are listed.

The number of anastomoses per patient and especially the mean number of anastomoses performed with BIMA were higher in the BIMA Y group. The latter finding is related to an increased number of anastomoses done using the RIMA branch and in particular is due to a significantly higher number of sequential grafts (Table 32.6).

In the BIMA Y group, most of the LIMAs (92.3%) were grafted to the left descending artery (LAD),

whereas in the BIMA in situ group, the LIMA was mainly used to revascularize the circumflex (Cx) system (57.3% vs 7.4% in the BIMA Y group, *p*<0.001). The right coronary artery (RCA) system was rarely revascularized by the LIMA in both groups (0.4%). The preferable target site of the RIMA was the Cx system in the BIMA Y group (77.9% vs 19.5% in the BIMA in situ group, *p*<0.001). In the latter group the RIMA was used to graft the LAD in most cases (64.7%). The RCA system, and especially the posterior descending artery (PDA), was the target vessel of RIMA grafting in 13.3% of patients in the BIMA in situ group versus just 2.5% in patients who received a BIMA Y graft; *p*<0.001.

Thirty-day results were similar in both groups (Table 32.7). Mean follow-up was 4.6 ± 2.4 years (1.0–11.3 years). Eight-year freedom from death of any cause, cardiac death, acute myocardial infarction (AMI), reintervention (redo or PTCA), cardiac events (cardiac death, AMI and reintervention) and any event were similar in both groups of patients (Table 32.8, Figs. 32.1, 32.2).

After a mean of 2.5 ± 2.7 months, 195 patients underwent angiographic control, checking 655 BIMA anastomoses. Overall patency rate and perfect patency rate (Fitzgibbon) for BIMA were 94.9% and 94.7% respectively. Fifty-two patients had an angiographic control later than the first postoperative year, revealing a pa-

Table 32.5. Preoperative characteristics of patients who underwent BIMA grafting

	BIMA Y 684	BIMA in situ 684	<i>p</i>
Age (years)	61.9±9.0	61.8±8.0	ns
Female	90 (13.2)	85 (12.4)	ns
Diabetes	158 (23.1)	162 (23.7)	ns
COPD	43 (6.3)	32 (4.7)	ns
Previous AMI	303 (44.3)	321 (46.9)	ns
Urgent cases	108 (15.8)	115 (16.8)	ns
ECV	137 (20.0)	159 (23.2)	ns
CRF	20 (2.9)	20 (2.9)	ns
Redo	26 (3.8)	20 (2.9)	ns
EF	57.9±13.2	59.1±12.5	ns
≤35%	41 (6.0)	31 (4.5)	ns
LM	104 (15.2)	106 (15.5)	ns
2-v disease	345 (50.4)	348 (50.9)	ns
3-v disease	339 (49.6)	336 (49.1)	ns
EuroSCORE	3.4±2.7	3.3±2.7	ns

COPD chronic obstructive pulmonary disease, AMI acute myocardial infarction, ECV extracardiac vasculopathy, CRF chronic renal failure, EF ejection fraction, LM left main, v vessel

Table 32.7. Thirty-day outcomes for patients who underwent BIMA grafting

	BIMA Y 684	BIMA in situ 684	<i>p</i>
Deaths	14 (2.0)	14 (2.0)	ns
Cardiac deaths	8 (1.2)	5 (0.7)	ns
CVA	8 (1.2)	9 (1.3)	ns
AMI	6 (0.9)	7 (1.0)	ns
ENPEP	23 (3.4)	25 (3.7)	ns
EMEs	50 (7.3)	36 (5.3)	ns

CVA cerebrovascular accident, AMI acute myocardial infarction, ENPEP early negative primary end-point, EMEs early major events

Table 32.6. Operative details of patients who underwent BIMA grafting

	BIMA Y 684	BIMA in situ 684	<i>p</i>
Anastomoses/pts.	3.2±0.9	2.9±0.8	<0.001
Arterial anastomoses/pts.	2.7±0.9	2.5±0.8	<0.001
BIMA anastomoses/pts.	2.6±0.8	2.3±0.5	<0.001
LIMA anastomoses/pts.	1.2±0.5	1.2±0.5	ns
RIMA anastomoses/pts.	1.4±0.6	1.1±0.2	<0.001
Pt. with at least 1 BIMA seq.	309 (45.2)	166 (24.3)	<0.001
BIMA seq. grafts	370/1,368 (27.0)	178/1,368 (13.0)	<0.001
LIMA seq. grafts	163/684 (23.8)	152/684 (22.2)	ns
RIMA seq. grafts	207/684 (30.3)	26/684 (3.8)	<0.001
BIMA sequential graft			
With 2 anastomoses	336/684 (49.1)	171/684 (25.1)	<0.001
With >2 anastomoses	34/684 (5.0)	7/684 (1.0)	<0.001

BIMA bilateral internal mammary artery, LIMA left internal mammary artery, RIMA right internal mammary artery, pt. patient, seq. sequential

Table 32.8. Eight-year clinical results for patients who underwent BIMA grafting

	BIMA Y 684	BIMA in situ 684	<i>p</i>
Freedom from death of any cause	93.6 ± 1.3	91.5 ± 1.4	ns
Cardiac deaths	96.3 ± 1.4	96.8 ± 0.8	ns
AMI	97.7 ± 0.7	97.8 ± 1.3	ns
Reintervention	96.6 ± 1.2	97.5 ± 0.9	ns
Cardiac events	93.5 ± 1.5	95.2 ± 0.9	ns
Any event	90.0 ± 1.8	89.1 ± 1.5	ns

AMI acute myocardial infarction

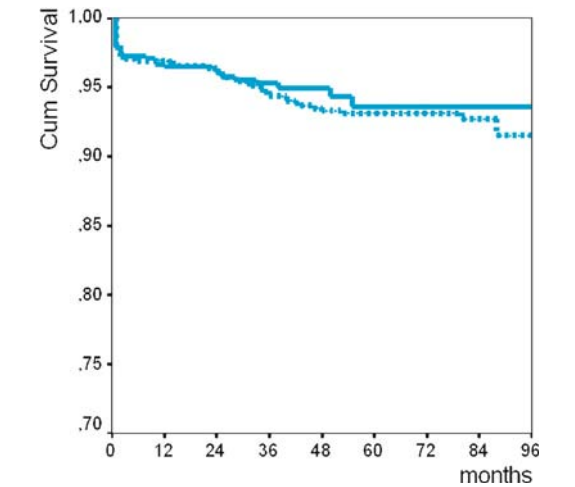


Fig. 32.1. Eight-year freedom from death of any cause in patients who underwent BIMA grafting. BIMA Y graft (—) versus BIMA in situ (···)

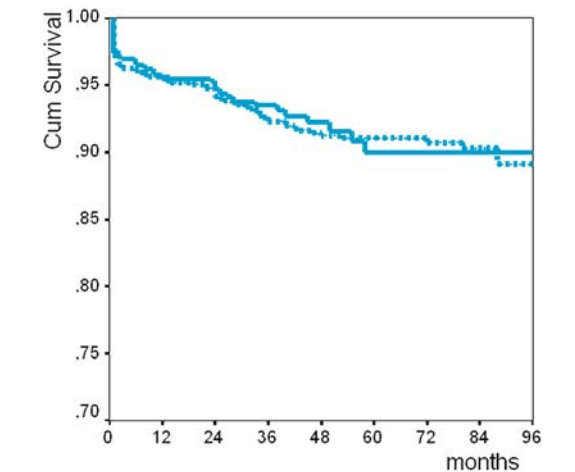


Fig. 32.2. Eight-year freedom from any event in patients who underwent BIMA grafting. BIMA Y graft (—) versus BIMA in situ (···)

tency rate and perfect patency rate of 87.7%. No significant difference was found between the two groups (Tables 32.9, 32.10).

Table 32.9. Early (≤1 year) angiographic results for patients who underwent BIMA grafting

	BIMA Y 85 pts./341 an.	BIMA in situ 110 pts./314 an.	<i>p</i>	Overall 195 pts./ 655 an.
Patency rate				
LIMA	124/129 (96.2)	153/158 (96.8)	ns	277/287 (96.5)
RIMA	120/127 (94.5)	144/156 (92.3)	ns	264/283 (93.2)
BIMA	244/256 (95.3)	297/314 (94.6)	ns	541/570 (94.9)
Y graft	81/ 85 (95.3)	–	–	81/ 85 (95.3)
Perfect patency rate				
LIMA	124/129 (96.2)	153/158 (96.8)	ns	277/287 (96.5)
RIMA	120/127 (94.5)	143/156 (91.6)	ns	263/283 (92.9)
BIMA	244/256 (95.3)	296/314 (94.3)	ns	540/570 (94.7)
Y graft	81/ 85 (95.3)	–	–	–
Follow-up (months)	2.8 ± 3.1	2.2 ± 2.4	ns	2.5 ± 2.7

LIMA left internal mammary artery, RIMA right internal mammary artery, BIMA bilateral internal mammary artery, pts. patients, an. anastomoses

Table 32.10. Late (>1 year) angiographic results for patients who underwent BIMA grafting

	BIMA Y 25 pts./86 an.	BIMA in situ 27 pts./61 an.	<i>p</i>	Overall 52 pts./147 an.
Patency rate				
LIMA	29/32 (90.6)	27/32 (97.0)	ns	56/64 (87.5)
RIMA	23/29 (79.3)	28/29 (96.5)	ns	51/58 (87.9)
BIMA	52/61 (85.2)	55/61 (90.1)	ns	107/122 (87.7)
Y graft	22/25 (88.0)	–	–	22/25 (88.0)
Perfect patency rate				
LIMA	29/32 (90.6)	27/32 (97.0)	ns	56/64 (87.5)
RIMA	23/29 (79.3)	28/29 (96.5)	ns	51/58 (87.9)
BIMA	52/61 (85.2)	55/61 (90.1)	ns	107/122 (87.7)
Y graft	22/25 (88.0)	–	–	22/25 (88.0)
Follow-up (months)	33.6 ± 19.4	63.4 ± 34.1	< .001	49.1 ± 25.2

LIMA left internal mammary artery, RIMA right internal mammary artery, BIMA bilateral internal mammary artery, pts. patients, an. anastomoses

32.5 Radial Artery

From July 1992 to December 2001, 335 patients underwent isolated myocardial revascularization radial artery grafting, from the ascending aorta (Ao-Ra group, *n* = 131) or as a Y graft (ITA-RA group, *n* = 204).

Table 32.11 shows the preoperative characteristics. Mean numbers of anastomoses and arterial anastomoses were 3.1 ± 0.8, and 2.9 ± 0.8, respectively. Average number of anastomoses performed with the radial artery was significantly higher in patients with the ITA-RA Y graft (1.3 ± 0.5 vs 1.1 ± 0.2, *p* < 0.001).

For ascending aorta source the RCA was the preferred target site (89, 61.3% vs 38, 14.6%, *p* < 0.001). For ITA source, Cx was mainly grafted with the RA (187, 71.9% vs 38, 29.0%, *p* < 0.001).

Table 32.11. Preoperative characteristics of patients who underwent radial artery grafting

	ITA-RA 204	Ao-RA 131	<i>p</i>
Age (years)	61.9 ± 8.3	61.6 ± 9.0	ns
Female	22 (10.8)	23 (17.6)	ns
Diabetes	42 (20.6)	29 (22.1)	ns
COPD	8 (3.9)	8 (6.1)	ns
Previous AMI	133 (65.2)	70 (53.4)	ns
Urgent cases	58 (28.4)	27 (20.6)	ns
ECV	35 (17.2)	21 (16.0)	ns
Redo	19 (9.3)	12 (9.2)	ns
EF	58.3 ± 12.0	56.8 ± 12.5	ns
≤35 %	10 (4.9)	8 (6.1)	ns
LM	28 (12.2)	20 (15.3)	ns
1-v disease	7 (3.4)	2 (1.5)	ns
2-v disease	82 (40.2)	48 (38.6)	ns
3-v disease	115 (56.4)	81 (61.8)	ns
EuroSCORE	3.6 ± 2.9	3.7 ± 2.9	ns

COPD chronic obstructive pulmonary disease, AMI acute myocardial infarction, ECV extracardiac vasculopathy, EF ejection fraction, LM left main, v vessel

Table 32.12. Thirty-day outcomes for patients who underwent RA grafting

	ITA-RA 204	Ao-RA 131	<i>p</i>
Deaths	4 (2.0)	0	ns
Cardiac deaths	2 (1.0)	0	ns
CVA	2 (1.0)	2 (1.5)	ns
AMI	3 (1.5)	0	ns
ENPEP	6 (2.9)	2 (1.5)	ns
EMEs	9 (4.4)	6 (4.6)	ns

CVA cerebrovascular accident, AMI acute myocardial infarction, ENPEP early negative primary end-point, EMEs early major events

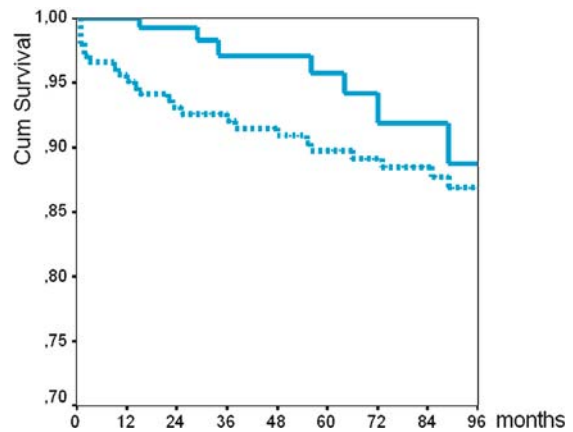
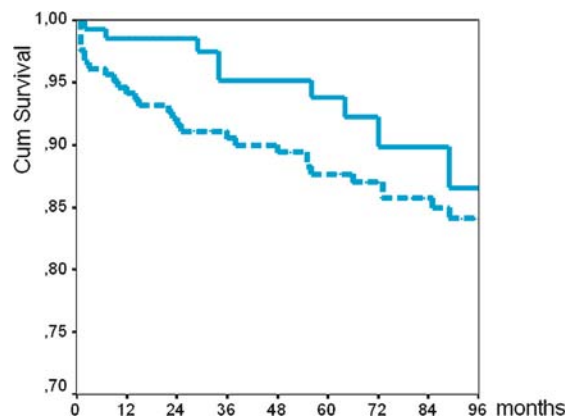
Table 32.13. Eight-year clinical results for patients who underwent RA grafting

	ITA-RA 204	Ao-RA 131	<i>p</i>
Freedom from death of any cause	86.9 ± 2.5	91.9 ± 3.4	ns
Cardiac deaths	93.9 ± 1.8	93.6 ± 3.8	ns
AMI	95.5 ± 1.6	93.8 ± 3.8	ns
Reintervention	97.6 ± 1.5	97.3 ± 1.6	ns
Cardiac events	92.2 ± 2.0	93.5 ± 4.0	ns
Any event	84.1 ± 2.8	86.4 ± 4.8	ns

AMI acute myocardial infarction

The early postoperative events are listed in Table 32.12. Follow-up of survivors ranged from 1.0 to 10.4 years (mean 6.3 ± 2.8 years). Freedom from the all investigated late events results were similar in both groups (Table 32.13, Figs. 32.3, 32.4).

Early and late angiographic controls did not show any difference between the two groups (Table 32.14).

**Fig. 32.3.** Eight-year freedom from death of any cause in patients who underwent RA grafting. ITA-RA (Y) (—■) versus Ao-RA (....●)**Fig. 32.4.** Eight-year freedom from any event in patients who underwent RA grafting. ITA-RA (Y) (—■) versus Ao-RA (....●)**Table 32.14.** Early and late angiographic results for patients who underwent RA grafting

	ITA-RA 55 pts./ 123 an.	Ao-RA 25 pts./ 29 an.	<i>p</i>	Overall 80 pts./ 152 an.
Early angio-graphic controls (≤1 year)				
Patency rate				
RA	67/68 (98.5)	28/29 (96.5)	ns	95/97 (97.9)
Y graft	54/55 (98.2)	—	—	54/55 (98.2)
Perfect patency rate				
RA	67/68 (98.5)	28/29 (96.5)	ns	95/97 (97.9)
Y graft	54/55 (98.2)	—	—	54/55 (98.2)
Follow-up (months)	2.3 ± 2.1	2.3 ± 2.3	ns	2.3 ± 2.2
Late angio-graphic controls (>1 year)				
Patency rate				
RA	59/63 (93.6)	22/24 (91.7)	ns	81/87 (93.1)
Y graft	52/55 (94.5)	—	—	52/55 (94.5)
Perfect patency rate				
RA	59/63 (93.6)	22/24 (91.7)	ns	81/87 (93.1)
Y graft	52/55 (94.5)	—	—	52/55 (94.5)
Follow-up (months)	53.0 ± 30.8	47.4 ± 29.4		49.1 ± 30.0

RA radial artery

32.6

Inferior Epigastric Artery

From September 1991 to December 2001, 163 patients underwent isolated myocardial revascularization grafting of the inferior epigastric artery. Mean age was 61.8 ± 9.4 years. Twenty-three (14.1%) patients were affected by diabetes. Most patients (105, 64.3%) had a history of a previous AMI. Fifty-six were admitted for unstable angina. In 28 (12.2%) cases preoperative angiography showed left main involvement. One vessel disease was present in 42.4% of patients, whereas in 28.4% there was two vessel disease and in 28.2% three vessel disease.

Mean number of anastomoses per patient performed with an inferior epigastric artery was 1.0 ± 0.2 .

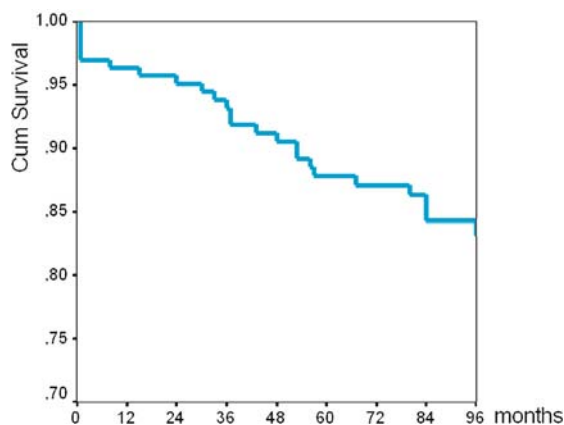


Fig. 32.5. Eight-year freedom from death of any cause in patients who underwent IEA grafting. BIMA Y graft (—) versus BIMA in situ (....)

In 69 cases the IEA graft was used to lengthen the ITA and in 94 patients it was used as a Y graft. Early mortality was 3.1% (five patients), and in four patients it was due to cardiac causes. Morbidity within the first 30 years was 6.1%. After a mean of 7.9 ± 2.5 years, freedom from death of any cause was 83.1 ± 3.2 (Fig. 32.5), from cardiac death 87.7 ± 2.9 , from AMI 90.3 ± 2.7 , from redo/PTCA 97.2 ± 1.4 , from cardiac events 86.3 ± 3.0 and from any event 80.0 ± 3.4 .

Early angiographic controls performed in 63 patients after a mean of 3.2 ± 3.3 months showed a patency rate and a perfect patency rate of 98.5%. All proximal anastomoses were patent. Patency and perfect patency rate after a mean of 48.9 ± 36.0 months were 96.2%. Twenty-two proximal anastomoses out of 23 showed patent results.

32.7

Conclusion

The BIMA Y graft gives the same early and late clinical and angiographic results as BIMA in situ, but the Y graft can produce a higher number of arterial anastomoses. The radial artery can be used from both the ascending aorta and the internal mammary artery. We prefer to use the ascending aorta as the blood source in the case of moderate stenosis of the target coronary artery. In the case of high runoff, the radial artery can be grafted from the internal mammary artery and especially in the case of lateral wall revascularization. The inferior epigastric artery is a good choice in the case of lengthening of the internal mammary artery.

Internal Thoracic Artery T-Grafting: Operative Technique and Long-Term Results

A.J. TECTOR

33.1 Introduction

The internal thoracic artery (ITA) is the ideal coronary bypass graft. This elastic vessel has a near perfect internal elastic membrane, which discourages the production of obstructive atherosclerosis. Early and late survival after coronary artery bypass grafting is significantly enhanced with LITA-left anterior descending coronary artery (LAD) grafting. When both ITA conduits are used, 20-year survival is greater than with single ITA grafting. Our philosophy has been that bypassing all the coronary arteries with the graft with the greatest early and long-term patency should ensure a higher survival and a lower incidence of reintervention in many of our patients.

33.2 Developments Leading to T-Graft Technique

Events leading to total myocardial revascularization with LITA grafts began with implantation of the ITA into the heart muscle in order to increase perfusion of the myocardium by Vineburg [1]. Demikov [2] was the first surgeon to directly anastomose the LITA to the LAD in dogs and also to perform sequential ITA coronary bypass grafts. There is some question about who was the first surgeon to directly bypass a coronary artery with an ITA graft. Shumacker [3] mentions that Longmire did this in 1958, but this work was never published. Goetz anastomosed the RITA to the RCA in 1960 [4]. Kolessov [5] performed the first LITA-LAD bypass in 1967 without a heart lung machine. Green introduced and perfected high power magnification as a vital aid to improving the accuracy of constructing ITA coronary anastomoses [6]. Bilateral ITA grafts were first performed by Sazucki [7] and popularized by Barner [8]. Mills [9] described sewing another bypass graft to the attached LITA in patients with severe ascending aorta atherosclerosis to prevent touching this diseased vessel and to prevent strokes. Sauvage [10] incorporated this technique along with sequential grafting to bypass as many coronary arteries as possible with ITA grafts. We

modified this technique by using the T graft, making it possible to totally bypass most patients with three-vessel coronary artery disease with only ITA grafts [11].

33.3 Advantages of ITA Grafts

The single source ITA graft has been adequately shown to provide ample blood to meet the metabolic requirements of the ischemic myocardium during rest and exercise. It can remain free from spasm, intimal hyperplasia, and atherosclerotic narrowing for the remainder of the patient's entire life. It does not require another incision for harvesting and when properly positioned it is out of the way if sternal reentry is required in the future. A smaller luminal diameter graft has a greater velocity of flow, which enhances patency. Initially surgeons expressed doubts as to whether the single LITA could supply enough blood to the area of myocardium perfused by the left anterior descending coronary artery, and now some surgeons doubt that the single source attached ITA can supply sufficient blood to the ischemic myocardium when all ITA grafts are used for coronary artery bypass grafting. Wendler [12] and associates measured baseline flow and maximum flow after stimulation with adenosine using a Doppler guidewire and calculated critical flow reserve in patients who had total revascularization with T grafts 1 week and 6 months after their operation. Baseline flow measurements were higher in patients with T grafts than those with a single LITA-LAD graft. Maximum flow and critical flow reserve at 6 months were reported to be significantly elevated to normal levels from 1 week after surgery, which occurs with conduit remodeling [13]. Although spasm can occur in any bypass conduit [14], I have rarely seen spasm in ITA grafts and have found inadequate flow in the properly prepared ITA is most often related to technical errors in constructing the anastomoses and securing the pedicle [15]. The ITA releases significant amounts of nitric oxide, which is a potent vasodilator and an inhibitor of platelet adhesions, protecting it from platelet derived vasospasm [16]. Being an elastic artery limits the ITA's

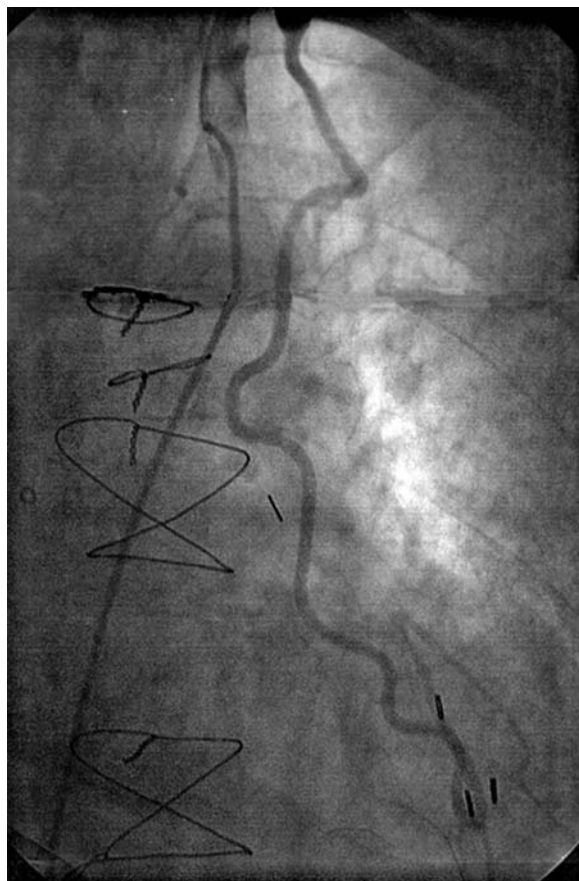


Fig. 33.1. LITA-LAD graft, 30 years postoperatively

vasoregulatory properties, allowing it to function as a reservoir to absorb the vigorous pressure waves in the vicinity of the central aorta [17]. Pathological studies at postmortem have revealed a very low incidence of obstructive atherosclerosis in the ITA [18–20]. Angiograms of LITA-LAD grafts performed 30 years after operation have been completely free of obstruction (Fig. 33.1). The vasa vasorum only supplies blood to the adventitia of the ITA and perfusion of the intima and media comes from within the lumen [21]. The internal elastic membrane is near perfect, producing a tight seal that impairs diffusion of large molecules and formed elements such as muscle and mesenchymal cells from the media into the intima.

33.4

Operative Technique

A median sternotomy incision is always used, the skin, fat and fascia are incised to the bone with a sharp knife, and only bleeding sites are cauterized. It is important to cut the sternum in the midline and to have equal widths of bone on each side to allow for the greatest strength at

the time of closure. The middle of the sternum is usually bisected by the decussation of the pectoral and rectus muscles. Bone wax is not used and, if necessary, pieces of fat from the patient's mediastinal area are pressed into the marrow to control the bleeding from the bone. The pedicle and skeletonized techniques have been used for mobilizing internal thoracic arteries. Although we have employed both methods, we prefer the former because small hemorrhages were noticed in the vascular wall of the ITAs that were skeletonized. A Morse sternal retractor (Codman, Randolph, MA) can spring the left side of the chest wall upwards to the left to improve exposure of the LITA. When dissecting the RITA, we spring the right chest superiorly. Monopolar cautery with all of the blade but the very tip covered with plastic tubing is used at very low amperage to prevent injury to the ITA.

The dissection begins at the sixth intercostal space near the bifurcation of the ITA into the superior epigastric and musculophrenic branches. If the injury to the ITA occurs, it will most frequently be at the beginning of the dissection, leaving enough length to reach the coronary vessels to be bypassed. The dissection proceeds proximally by bluntly separating the ITA and a small pedicle from the chest wall with the cautery tip, cauterizing only the arterial and venous branches and the thoracic fascia. Tension on the pedicle is minimized to prevent tearing of its branches. When approaching the thoracic inlet the surgeon must be careful not to injure the subclavian vein and the phrenic nerve. All superior intercostal arterial branches should be cauterized to eliminate the steal of blood from the ITA postoperatively. If the phrenic nerve is injured on the left side it usually occurs where the slit is made in the pericardium to allow the LITA to enter the surface of the heart. On the right side it often happens where the nerve lies close to the RITA proximal to the site where the internal thoracic vein proceeds medially to the superior vena cava. The RITA is skeletonized from this point to where it is detached at the thoracic inlet. The RITA is secured with a ligature and several vascular clips are applied to secure the ITA distal to the suture. Heparinization is delayed in the event the patient received platelet inhibitors at cardiac catheterization until just before transecting the RITA and the LITA. The fat fascia and muscle are dissected on the posterior surface of the pedicle, exposing the adventitia of the posterior surface of the ITA [15]. This adds length to the ITA and makes it easier to perform the ITA coronary anastomoses. If the ITA is an attached graft, the proximal portion near the thoracic inlet is clamped with a bulldog clamp and a 1/30-papaverine saline or blood solution is infused into the distal end. If the ITA is a free graft, the proximal end is infused with the papaverine solution and the distal end is occluded. Internal luminal diameter, pulse and flow increase dramatically after

administering the papaverine saline or blood solution. The papaverine saline solution is infused through the lumen of the internal thoracic artery instead of spraying it topically because in the ITA only the adventitia is supplied with blood by the vasa vasorum, and the blood supply that nourishes the intima and media comes from inside the lumen.

The RITA is anastomosed to the LITA as a T-graft and, occasionally, it is anastomosed end-to-end as a tandem/sequential graft. If the distal end of the ITA is of small diameter, as sometimes seen in women, the proximal end of the free ITA is closed with a hemostatic clip and an end to side anastomosis, which is larger, is constructed. When the proximal left subclavian artery is obstructed, the LITA can be used as a free graft and anastomosed to the attached RITA. If the LAD is very large and the vessel requires maximum flow, we prefer using the end-to-end or tandem sequential technique. Sometimes, when the left ventricle is dilated and enlarged, attaching the ITAs end to end is the only way the ITAs will reach all the coronaries that need to be bypassed. When the T-graft is constructed, an 8–10 mm arteriotomy is made on the posterior surface of the attached ITA at the level of the left atrial appendage. The site of the T anastomosis can be located proximally or distally to accommodate the position of the first distal coronary anastomoses. The proximal RITA is cut transversely and a 2–3 mm slit is made in the posterior wall. Sewing the ITAs at right angles preserves valuable proximal length and prevents kinking that can occur when a Y anastomoses is constructed. This anastomosis is sewn with a continuous 8-0 monofilament suture. After the anterior row of sutures has been placed, the LITA is then lifted out of the mediastinum exposing the posterior wall and the anastomoses is completed

(Fig. 33.2). When suturing ITAs, it is important to have the tip of the needle enter the artery at a 90-degree angle. This allows the surgeon to make the smallest needle hole in the artery and sew closer to the edge of the artery and include the adventitia, media and intima with the stitch and make the anastomoses as large as possible. The pedicles are attached to each other to prevent any tension or twisting of the anastomosis. If the ITAs are skeletonized, the adventitia of the RITA is sutured to the epicardium proximal to the first anastomosis. The bulldog clamp is released and the pulse and flow is checked in each limb of the graft. If it is insufficient, the anastomosis should be redone and this usually corrects the problem. The T-graft is constructed before going on cardiopulmonary bypass because this allows the surgeon to be certain that the flow in both limbs of the ITA graft is sufficient before completing the distal coronary anastomoses and it reduces time on the cardiopulmonary bypass.

The distal anastomoses can be placed with cardiopulmonary bypass or the off pump coronary artery (OPCAB) technique or using a combination of OPCAB stabilization and cardiopulmonary support. The technique selected should be one that allows the surgeon to construct the most technically perfect distal anastomoses. If cardiopulmonary bypass is used, the ascending aorta or the aortic arch is cannulated and a two-staged venous drainage cannula is placed through the right atrium into the inferior vena cava. A 13-gauge needle is inserted into the ascending aorta for infusion of antegrade cardioplegia and for venting the ascending aorta. A catheter with a self-inflating balloon is introduced into the coronary sinus for infusion of retrograde cardioplegia. Warm substrate enriched blood cardioplegia is used followed by cold blood cardioplegia as described

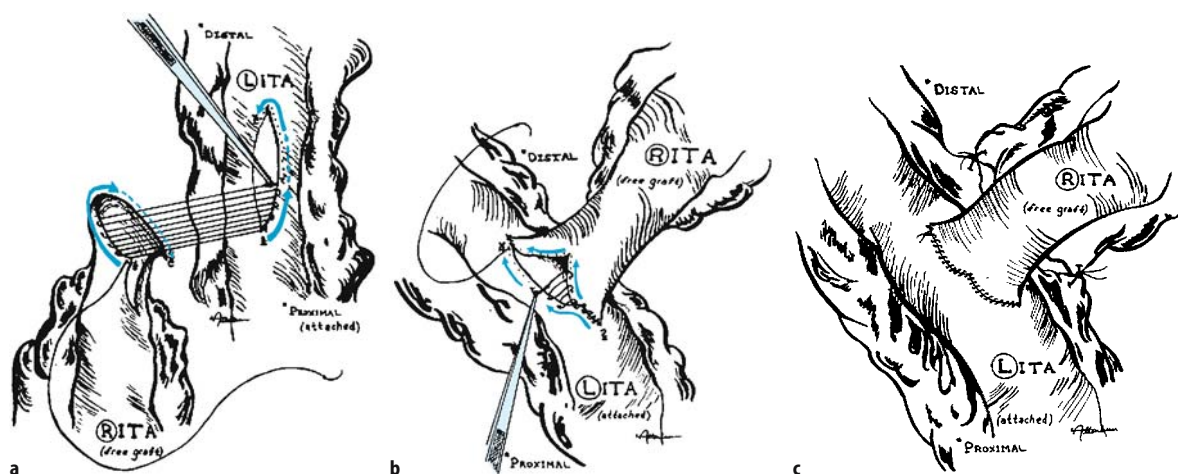


Fig. 33.2a–c. Technique of T-graft anastomosis. A 1-cm parallel incision is made into the attached left internal thoracic artery (LITA). The proximal end of the detached right thoracic artery (RITA) is anastomosed to the side of the LITA with a continuous suture. **a** The interior surface is sutured first. The RITA is then turned over and lifted out of the chest, and **b** the posterior row is completed. **c** Completed anastomosis. (Reprinted from *Annals of Thoracic Surgery* 57:33–39, Tector A, et al.: “Total revascularization with T grafts.” Copyright 1994, with permission from the Society of Thoracic Surgeons)

by Buckberg [22]. Cold maintenance blood cardioplegia is infused antegrade and retrograde every 20 min. After the completion of the last anastomoses while warm blood substrate-enriched cardioplegia is flowing, the anastomoses are checked for bleeding before removing the aortic cross-clamp and are repaired if necessary. It is easier and safer to correct any anastomotic leaking before removing the clamp. When using the tandem sequential or end-to-end method, the right coronary artery and circumflex branches are bypassed with the RITA. The first side-to-side anastomosis is constructed to the most proximal artery bypassed and the end-to-side anastomosis is constructed to the most distal artery to be grafted. The coronary artery sites are identified and these are placed in the more distal part of the coronary arteries. Also, an ample amount of ITA graft between each anastomosis is allowed in order to prevent tension. It makes it easier to measure the proper length from the T anastomoses to the first distal coronary artery target if the LITA has been attached to the epicardium adjacent to the proximal LAD. Parallel ITA coronary anastomoses are preferred; however, if necessary for the ITA to fit properly a perpendicular anastomoses is constructed. Small arteriotomies are made in the ITA and coronary artery in order to prevent constriction at the perpendicular anastomosis. An 8–10 mm opening in the coronary artery and a slightly larger opening in the ITA on the posterior surface are made for the parallel anastomosis. A continuous 8-0 monofilament suture is used beginning at the heel and coming around the toe, and the anastomosis is completed with the other end of the suture. The last anastomosis on each limb of the graft is end-to-side and is created with a continuous 8-0 monofilament suture beginning at the heel and progressing to the toe. If the intima is separated from the other layers of the ITA it can be reattached while performing the graft. The pedicle is secured to the epicardium on each side of the anastomoses to prevent torsion or kinking.

Phrenic nerve injury, sternal infections, hypoperfusion and late subclavian stenosis are complications related to this operation. Identifying and avoiding this nerve before making a slit in the pericardium for the entry of the LITA prevents left phrenic nerve injury. The right phrenic nerve is avoided by skeletonizing the RITA proximal to the origin of the right internal thoracic vein. Redoing the anastomosis of the ITA to the coronary artery where the hypoperfusion is thought to occur and examining the pedicle attachment to the epicardium for producing kinking at the anastomosis usually corrects the rare occurrence of hypoperfusion. If this problem persists, a saphenous vein should be placed to the underperfused coronary artery. Closing the sternum with 12 interrupted stainless steel wires gives added strength to the approximation of the bone until adequate collateral circulation develops after 3 weeks and helps to prevent sternal dehiscence.

33.5 Failure of ITA Grafts

Technical errors occurring during harvesting and construction of ITA coronary anastomoses are the most common causes of early ITA failure [11]. Severe competition of flow mismatches and subtle injuries during harvesting may be responsible for later graft failures. Tearing or cutting a small branch too close to the ITA can usually be repaired with a simple suture. More extensive injuries to the graft from deep cuts in the artery, cautery burns or localized dissections are best fixed by cutting out the injured segment and reanastomosing the ends of the artery. A precise end-to-end reapproximation of the remaining uninjured pieces usually restores satisfactory flow in the repaired artery. Competition of flow is more apt to happen as the flow in the native coronary artery approaches the flow in the ITA; however, the critical point is not known. This phenomenon is more likely to occur when the degree of stenosis in the bypassed coronary artery proximal to the bypass graft is less than 50–70%. Other situations include coronary arteries that have had angioplasty or stenting or in reoperations where the old saphenous vein graft to the artery that is rebypassed with an ITA graft is not occluded. Caution in bypassing arteries with lesser amounts of stenosis is recommended because we have seen a situation where a coronary artery with marginal stenosis was bypassed with a sequential artery; the segment of the graft from the T anastomoses to the minimally stenosed coronary was occluded; and the right coronary artery, which had significant narrowing, was stealing from the coronary artery with the lesser degree of stenosis [11]. We have ligated some partially obstructed saphenous vein grafts with diffuse atherosclerosis in an attempt to prevent competition of flow after coming off cardiopulmonary bypass and observed the patient for 10 or 15 min. If there was evidence of hypoperfusion, the ligature was removed.

In the late 1960s Green postulated that the ITA was superior to the saphenous vein as a coronary bypass graft because as a pedicle it includes its own hemostatic milieu [6]. Subtle injuries to the adventitia and the vasa vasorum of the ITA can cause small areas of hemorrhage and interfere with the blood supply of this graft. These potential injuries could result in late scarring or obstructive atherosclerosis formation. Concerns that skeletonization can produce these minor injuries and result in late ITA failure have been expressed [23]. More frequent bypass graft visualization postoperatively will become possible with the refinement of spiral CT scanners and the development of magnetic resonance coronary angiography. This can make noninvasive coronary angiography a reality and allow these important questions concerning patency of ITA grafts to be answered.

The other obvious late cause of graft failure is the occurrence of new obstructive disease in the native coronary artery distal to the ITA coronary anastomoses. This event happens in about 11% of the patients at 5 years postoperatively [24]. In some instances particularly with the LAD, we have bypassed above and below a nonobstructive but visible area of atherosclerosis in the wall of the artery. The other hope is that the use of cholesterol lowering drugs may reduce the rate of atherosclerotic development in these areas. If significant obstruction occurs in the left subclavian artery later postoperatively and compromises the flow to the ITA, angioplasty or carotid subclavian bypass can be performed to relieve or bypass the narrowing.

33.6

Demographics of T-Graft Patients

Outcomes of coronary revascularization procedures are the true predictors of their success. Early and late mortality and the reduced need for reintervention such as angioplasty, stenting, and reoperation are the most solid indicators of benefit from coronary artery bypass procedures. We reported outcomes of our first 897 patients who had three-vessel coronary artery disease or its equivalent and were completely revascularized with purely internal thoracic artery grafts (PITA) from September 1990 through February 1998 [25].

From September 1990 through February 1998, 897 patients with 70% or more narrowing in all of their coronary arteries determined by coronary angiography underwent total coronary artery revascularization using purely internal thoracic artery grafts (PITA). Patients were not excluded for poor left ventricular function, diffuse disease, increased operative risk, female sex, or older age. One hundred and nine (12.2%) patients were undergoing their first or second reoperation and 195 (22%) had greater than 50% left main coronary stenosis in addition to three-vessel coronary disease. A total of 3,784 ITA coronary anastomoses were fashioned for an average of 4.2 grafts per patient; 837 (93.3%) T-grafts and 60 (6.7%) tandem/sequential grafts were constructed. No other types of arterial or venous conduits were used.

The group included 189 women and 708 men whose ages ranged from 30 to 88 years (mean 64.8 years). Ejection fractions (EF) were measured preoperatively in 578 patients: 221 (38.2%) were normal, 137 (23.7%) had mild dysfunction (EF 0.45–0.54), 151 (26.1%) had moderate dysfunction (EF 0.35–0.44), and 69 (11.9%) had severe dysfunction (EF less than 0.35). Patient risk factors included hypertension (56.2%), smoking (55.6%), preoperative myocardial infarction (33.7%), diabetes (26.5%), peripheral vascular disease (10%), previous cerebrovascular accident (5.9%), chronic ob-

structive lung disease (5.8%), atrial fibrillation (4.8%), chronic renal failure (2.5%), and acute renal failure (1.7%). Patient follow-up ranged from 1 to 102 months and was obtained from questionnaires, recent office visits, and a telephone survey.

33.7

Results

Follow-up was obtained in 894 of the 897 patients (99.7%). The median follow-up was 4.2 years (range 30 days to 8.5 years). There were 21 early deaths (2.3%) and 118 late deaths (13.2%). Early deaths occurred while the patient was in the hospital or within 30 days of the operation; late deaths included all deaths after that period. Survival probability was 86% at 5 years and 75% at 8 years (Fig. 33.3). Sixty of the 118 (50.8%) late deaths were cardiac related, 53 (44.9%) deaths were noncardiac related, and 5 (4.2%) were unknown. Older age, previous CABG, chronic renal failure, and hypothyroidism were significant risk factors for operative death. The 60 patients with tandem sequential grafts were no more likely to experience operative death than those with T grafts ($p=0.992$). The odds ratio and p value for each of these risks are shown in Table 33.1. For all the variables analyzed (Table 33.2), age, severely decreased ejection fraction, acute renal failure, chronic renal failure, carotid disease, deep vein thrombosis and pulmonary embolism, hypertension, and smoking were all significant risk factors for late deaths (Table 33.3). The patients were separated into four age groups (30–54 years, $n=150$ patients; 55–64 years, $n=225$ patients; 65–74 years, $n=375$ patients; and 75–88 years, $n=147$ patients) to determine the influence of age on early and late mortality and outcomes in patients with PITA grafts (Table 33.4).

Analysis of the group based on sex, diabetes, reoperations, and postoperative infection was performed. Separating the group by sex demonstrated that mortality in women was 2.6% early and 13.8% late and in men it was 2.3% early and 13.0% late, $p=0.6757$ and $p=0.8490$, respectively. When comparing diabetic with

Table 33.1. Risk factors for operative deaths. (Reprinted from *Annals of Thoracic Surgery* 72:450–455, Tector A, et al.: “Purely internal thoracic artery grafts: outcomes.” Copyright 2001, with permission from the Society of Thoracic Surgeons)

	Odds ratio (95% confidence interval)	p
Age: 65–74 years	5.81 (1.27–26.5)	0.023
Age: 74–88 years	9.06 (1.81–45.3)	0.007
Previous coronary artery bypass graft	3.17 (1.08–9.32)	0.035
Chronic renal failure	7.41 (1.88–29.1)	0.004
Hypothyroidism	4.07 (1.08–15.3)	0.038

Table 33.2. Variables analyzed for risk factors. (Reprinted from *Annals of Thoracic Surgery* 72:450–455, Tector A, et al.: “Purely internal thoracic artery grafts: outcomes.” Copyright 2001, with permission from the Society of Thoracic Surgeons)

Age range
30–54 years
55–64 years
65–74 years
75–88 years
Acute renal failure
Chronic renal failure
Carotid disease
Deep vein thrombosis and pulmonary embolism
Ejection fraction
Hypertension
Smoking
Abdominal aortic aneurysm
Atrial fibrillation
Previous CABG
Cerebral vascular accident/TIA
Diabetes
Family history
Hyperlipidemia
Hypothyroidism
Myocardial infarction: previous
New York Heart Association class
Obesity
Peptic ulcer disease
Peripheral vascular disease
Sex
Graft type: tandem versus T graft
Ventricular fibrillation

CABG coronary artery bypass grafting, TIA transient ischemic attack

Table 33.3. Risk factors for late deaths. (Reprinted from *Annals of Thoracic Surgery* 72:450–455, Tector A, et al.: “Purely internal thoracic artery grafts: outcomes.” Copyright 2001, with permission from the Society of Thoracic Surgeons)

	Risk ratio (95% confidence interval)	<i>p</i>
Age		
55–64 years	2.60 (1.05–6.40)	0.038
65–74 years	3.76 (1.60–8.85)	0.002
75–84 years	7.18 (2.97–17.3)	0.000
Ejection fraction – severe dysfunction	3.30 (2.01–5.40)	0.000
Acute renal failure	4.80 (1.89–12.2)	0.001
Chronic renal failure	3.05 (1.50–6.17)	0.002
Carotid disease	1.95 (1.04–3.65)	0.037
Deep vein thrombosis and pulmonary embolism	2.66 (1.26–5.61)	0.010
Hypertension	1.65 (1.12–2.43)	0.011
Smoking	1.71 (1.16–2.54)	0.007

	30–54 years	55–64 years	65–74 years	75–88 years	Overall
Early deaths (w/in 30 days)	0	2 (0.9%)	12 (3.2%)	7 (4.8%)	21 (2.3%)
Late deaths	6 (4%)	24 (10.7%)	52 (13.9%)	36 (24.5%)	118 (13.2%)
Cardiac	6 (100%)	12 (50%)	22 (42.3%)	20 (55.6%)	60 (50.8%)
Noncardiac	0	10 (41.7%)	28 (53.8%)	15 (41.7%)	53 (44.9%)
Unknown	0	2 (8.3%)	2 (3.8%)	1 (2.8%)	5 (4.2%)

Number and percent of early versus late mortality and late death by etiology (by age group)

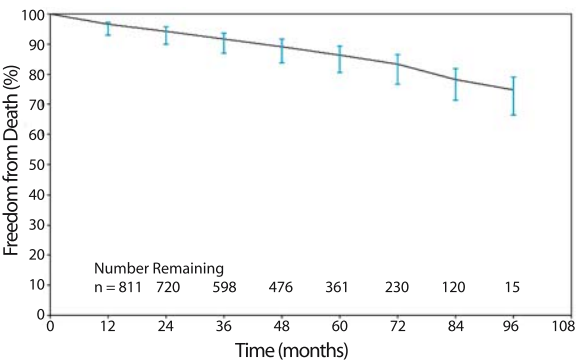


Fig. 33.3. Freedom from death. (Reprinted from *Annals of Thoracic Surgery* 72:450–455, Tector A, et al.: “Purely internal thoracic artery grafts: outcomes.” Copyright 2001, with permission from the Society of Thoracic Surgeons)

nondiabetic patients, 6 of 238 (2.5%) diabetic patients died early compared with 15 (2.3%) of the 659 nondiabetics, $p=0.6110$; also 39 (16.4%) of the diabetics died late compared with 79 (12%) of the nondiabetics, $p=0.6893$, both statistically nonsignificant. Five (4.8%) of the patients who had PITA as a reoperation died early, which was statistically significant. Sixteen (14.7%) died late, a statistically nonsignificant difference. Sternal infections involving the bone occurred in 30 patients (3%) from the group. No patient died because of a sternal infection. Forty-three patients (4.8%) had a stroke, and 14 needed an intra-aortic balloon pump.

Among the surviving patients, 6 of the 876 (0.7%) required a CABG reoperation. One patient was found to have all grafts occluded, including his LITA, and was reoperated on within 9 months. Two patients had RITA obstruction, two had new disease with patent ITAs, and one patient who had poor left ventricular function preoperatively and postoperatively required cardiac transplantation. Two of the patients were reoperated on within 1 year and the others were reoperated on from 15 to 53 months after their first operation. Thirty-seven patients (4.2%) had reintervention with percutaneous transluminal angioplasty or stenting, seven of whom were treated for LITA failure from 20 to 68 months postoperatively. Eighteen of the group had RITA obstruction and 12 had new coronary artery disease. Six of the 37 patients required the procedure within the

Table 33.4. Etiology of deaths. (Reprinted from *Annals of Thoracic Surgery* 72:450–455, Tector A, et al.: “Purely internal thoracic artery grafts: outcomes.” Copyright 2001, with permission from the Society of Thoracic Surgeons)

1st year and the remaining 31 patients between 13 and 88 months postoperatively. Freedom from reintervention was 94% at 5 years and 92% at 8 years (Fig. 33.4). Risk for reintervention was the same in all age groups (Table 33.5). It should be noted that the youngest age category did not have a high enough incidence of reintervention to make a valid estimate. Chronic obstructed pulmonary disease and New York Heart Association classes III to IV were significant risk factors for reintervention (Table 33.6).

Fourteen patients (1.6%) had a documented postoperative myocardial infarction. Fifty-two (5.9%) reported on the questionnaire or during the telephone interview that they had angina postoperatively. Return of angina was more frequent in the 30-to-54 age group (12%) and was evenly distributed in the other groups at 4.5%, 5.2%, and 3.6%. The occurrence of postoperative myocardial infarcts was distributed equally in all the age groups. There was one early death (1.7%) and 9 late deaths (15%) in the 60 patients who had tandem/

sequential grafts. One of these patients had a postoperative myocardial infarct (1.7%), four patients had angina after their operation (6.7%), and none of the group required reintervention.

33.8

Comparison of Results

Most reports concerning the use of bilateral ITA grafts also include other grafts such as saphenous vein grafts or radial artery grafts. Sauvage [26], who was the first person to attach the free RITA to the attached LITA to completely revascularize the heart with ITA grafts, reported on 120 patients who were followed for a mean of 12.1 years. He compared the early outcomes and those at 5 and 8 years with our results at the same time period. Operative 5- and 8-year mortalities were 2.3%, 86% and 75% in our group and 3.2%, 87% and 74% in Sauvage's group. The incidence of reintervention was 90% for the group presented by Sauvage at 12 years and 95% for our patients at 4.2 years. The deep sternal infection rates were 2.3% for Sauvage's patients using the skeletonized method of ITA harvesting and 3% for our patients with the pedicle technique.

Lytle and his associates have compared the up to 20-year outcomes of patients receiving single ITA grafting with those who had bilateral ITA grafting and closely matched the patients according to a propensity scoring technique [27]. They discovered that nearly all patients with bilateral ITA grafting had better outcomes after 10 years from their operation. The best results occurred in the bilateral ITA patients without decreased left ventricular function and cardiac risk factors. Even patients with left ventricular dysfunction had a greater than 10% improvement. The increased prevention of reintervention was stronger than the benefit of protecting against death [28]. Evaluation of outcomes at 15–20 years postoperation will be essential in order to determine the full value of PITA grafting with other techniques.

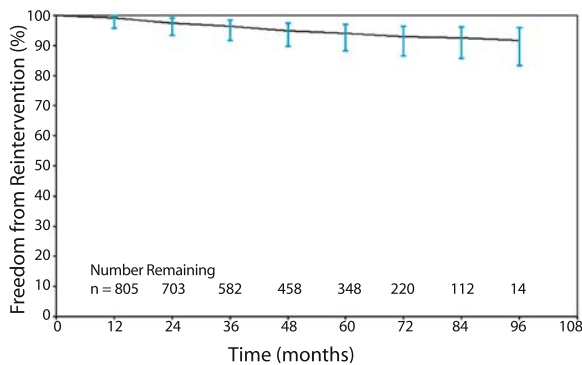


Fig. 33.4. Freedom from reintervention. (Reprinted from *Annals of Thoracic Surgery* 72:450–455, Tector A, et al.: “Purely internal thoracic artery grafts: outcomes.” Copyright 2001, with permission from the Society of Thoracic Surgeons)

Table 33.5. Risk factors for reintervention. (Reprinted from *Annals of Thoracic Surgery* 72:450–455, Tector A, et al.: “Purely internal thoracic artery grafts: outcomes.” Copyright 2001, with permission from the Society of Thoracic Surgeons)

	Risk ratio (95% confidence interval)	p
Chronic obstructive pulmonary disease	2.92 (1.22–7.01)	0.016
New York Heart Association class III–IV	3.10 (1.46–6.59)	0.003

Table 33.6. Reintervention by age (% of age group). (Reprinted from *Annals of Thoracic Surgery* 72:450–455, Tector A, et al.: “Purely internal thoracic artery grafts: outcomes.” Copyright 2001, with permission from the Society of Thoracic Surgeons)

	30–54 years	55–64 years	65–74 years	75–88 years	Overall
Reoperation	0.7%	0.9%	0.8%	0.0%	0.7%
Percutaneous transluminal angioplasty/stents	2.0%	6.7%	4.1%	2.6%	4.2%

33.9

Comment

Failure of CABG procedures is most often the result of bypass graft obstruction, new narrowing in the coronary arteries, or a combination of the two. Connecting the RITA E-S to the attached LITA as a T graft or E-E as

a tandem/sequential graft locates the RITA 10 or more centimeters closer to the coronary arteries on the inferior and posterior surface of the heart. Combining the T graft or tandem/sequential graft with sequential grafting makes it possible for most patients to undergo bypass with PITA grafts. The coronary arteries on the anterior surface of the heart are bypassed with the LITA and the arteries on the posterior and inferior areas are grafted with the RITA. The most important coronary artery in nearly all patients, the LAD, is always bypassed with the graft having the greatest proved patency, that is, the attached LITA. A separate harvesting incision and an aortic anastomosis are not needed. In addition, the bypass conduits are placed out of the way of reentry and are well protected from injury in case the patient needs a repeat sternal incision. Atherosclerotic embolization from old patent ITA grafts during reoperations has not been reported. The results of PITA operations suggest this could be the only invasive procedure some of our patients will ever need.

Acknowledgements. The author would like to thank Kate Senkbeil and Richard Wetzel for their help in preparing this manuscript.

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Internal Thoracic Artery and Radial Artery T-Grafting: Operative Technique and Long-Term Results

H.B. BARNER

34.1 Radial Artery

The radial artery (RA) was used as a coronary bypass conduit in the early 1970s, but was quickly abandoned because of conduit failure. It was reintroduced in 1992 [1] by the same surgeon, Alain Carpentier, who had first used it and who later reported 5-year patency of 83 % [2]. Following the first report its use has expanded more rapidly and widely than that of any arterial conduit.

Multiple Y-grafting with arterial conduits was popularized by Calafiore [3] and T-grafting was introduced by Mills [4], Sauvage [5], and Tector [6]. Our RA experience including T-grafting began in 1993 [7]. The ability to achieve all arterial revascularization with two arterial conduits in most patients is attractive. This approach conserves conduit, allows simultaneous harvest, minimizes aortic trauma (avoids it if done off pump) and avoids bilateral internal thoracic artery (ITA) harvest with its potential complications if one of the conduits is the RA.

34.2 Technique

34.2.1 Radial Artery Assessment

The radial and ulnar arteries are occluded at the wrist with the arm elevated and the hand in a “tight fist” for 15–30 s. The arm is lowered to horizontal and the hand opened to a relaxed position, not hyperextended, and the ulnar artery released. The seconds to capillary refilling of the palm with particular attention to the thumb are noted with a maximum of 12 s allowed. Return of color to the palmar skin is usually easily assessable. If the skin is normally pale and color change not readily apparent, the test is repeated with 1 min of ischemia. If the skin is deeply pigmented and color change not apparent, we rarely find it necessary to use digital oximetry to detect return of perfusion to the thumb. We are not reluctant to harvest the RA from the dominant arm as we prefer to harvest the left RA be-

cause left ITA harvest is facilitated when these concomitant maneuvers are ipsilateral.

About 4% of patients have a bilaterally positive Allen test. We have not utilized ultrasound to assess the RA itself or collateral circulation to the hand. Occlusion of the RA at the wrist is done over a broad area with the three middle fingers to compress distal branches of the RA or a median artery which might provide a false negative test.

34.2.2 ITA Harvest

The left ITA is harvested as a pedicle with low current electrocautery and open pleura from the subclavian vein to the bifurcation and immediately divided between clips at the bifurcation. Branches are not clipped during harvest unless they bleed and larger branches are clipped later. Skeletonization has not been used because the pedicle may stabilize and support the T-anastomosis and avoid angulation.

34.2.3 RA Harvest

The RA is concomitantly harvested by a surgical assistant from its origin to the wrist crease including associated veins and fibrofatty tissue and with a single incision. Initially, we divided the branches between clips and later we used ultrasonic (Harmonic Scalpel, Ethicon) division without clips [8]. Most recently, we have used thermal energy (Cautery Forceps, Starion Instruments) for branch coagulation and division without clips, which is a more rapid and effective technique. Most patients need grafting of the three coronary systems, which requires a full length of the RA (20–24 cm in the male and 2 cm less in the female). The harvested RA is placed in heparinized blood at room temperature containing papaverine 2 mg/ml for 5–15 min (until construction of the T-anastomosis).

The incision is closed immediately after harvest in two layers with continuous absorbable suture and a compressive dressing applied. The arm is then positioned at the patient's side from its abducted position.

34.2.4

T-Anastomosis

The pericardium is opened in the midline and a second incision is started at the level of the pulmonic valve and carried laterally into the “bare area” (no fat) of the pericardium to within 1 cm of the phrenic nerve. The left atrial appendage is usually apparent at the end of this incision, which may be extended 1–2 cm parallel to the phrenic nerve. The ITA is positioned parallel to the phrenic nerve and marked at the apex of the pericardial incision, where it will enter the pericardial space, with two stay sutures in the pedicle to suspend the pedicle with the smooth side (pleural) up in the anterior mediastinum. Heparin 300 U/kg is given and the end of the ITA transected to demonstrate flow and allow heparin to enter.

The ITA is exposed at the level of the stay sutures and a soft, disposable bulldog clamp placed proximally. A 5-mm incision is made just proximal to the stay sutures. The proximal end of the RA is spatulated 2 mm and end-to-side anastomosis performed with continuous 7/0 polypropylene (Fig. 34.1). Tacking sutures at the toe and heel of the anastomosis incorporate the fascia of the ITA pedicle and the adventitia of the RA and are placed to relieve tension on the ITA at the anastomosis. The two conduits are then filled with heparinized blood containing papaverine (as described above) using a 2-mm olive tip plastic cannula (rarely a 1-mm olive tip metal cannula is necessary for a small ITA) and allowed to dilate while exposed to arterial pressure, during cannulation for bypass. Prior to cardiopulmonary bypass the conduits are checked visually for spasm and free flow and the RA is refilled with blood/papaverine before instituting cardiopulmonary bypass. The temperature drifts to 34°C, where it is maintained, and antegrade blood cardioplegia at the same temperature is given (10 ml/kg initially and 7 ml/kg after each anastomosis).

34.2.5

Distal Anastomoses

The most proximal RA anastomosis is done first, usually in parallel, but occasionally as a diamond. It is important to have the proper conduit length from the T-anastomosis by measuring it with the heart in the pericardium or by elevating it and positioning the T-anastomosis 1–2 cm anterior to the left atrial appendage. The latter technique works well for a ramus artery or a proximal marginal artery, but if the first target is more distal, it is best to measure with the heart anatomically positioned. If the measurement is short, then the conduit may be under tension, or if too long, there may not be enough conduit to reach the posterior descending artery. The former situation can be corrected by divi-

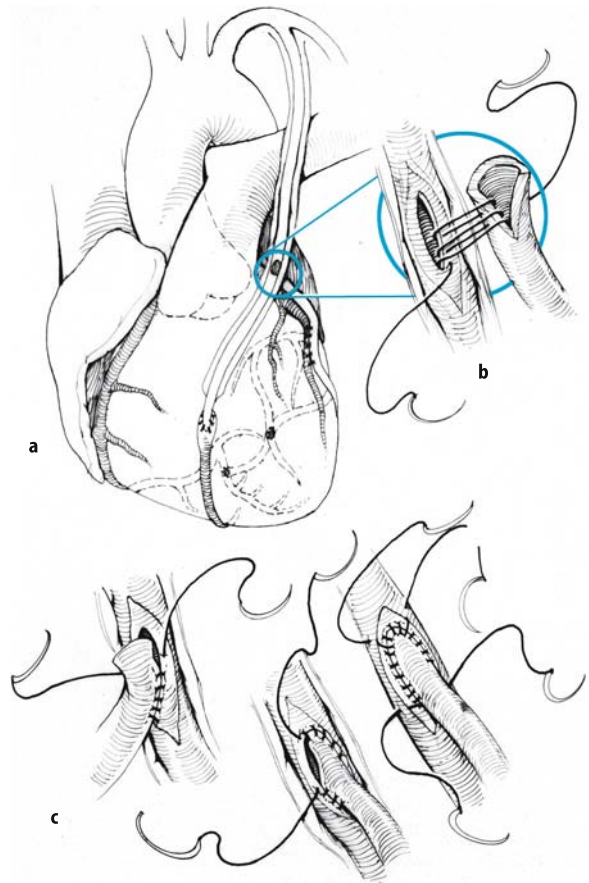


Fig. 34.1. **a** The radial artery (RA) is anastomosed to the left internal thoracic artery (ITA) anterior to the left atrial appendage. The ITA is anastomosed to the anterior descending artery and the RA sequentially to two circumflex branches and the posterior descending artery. **b** Start of the T-anastomosis beginning on the far side of the heel. **c** Completion of the T-anastomosis

sion of the internal mammary vein at its origin and mobilization of the ITA pedicle off of the subclavian vein, which can add 2–3 cm of length in some patients and less in others. A second RA anastomosis to a second marginal artery can be done in parallel with an S-curve between anastomoses or as a crossing (diamond) anastomosis, depending on the distance between anastomoses and their relative positions. Most commonly, after one circumflex anastomosis to a marginal branch, the second anastomosis is to a posterolateral or posterior descending artery with the RA making a gentle loop toward the apex of the heart and then brought parallel to the coronary. If the anastomosis to the posterolateral artery is parallel, the radial artery is looped toward the base of the heart and the distal anastomosis to the posterior descending artery may be in parallel or at a right angle depending on RA length and target location. When three or four RA anastomoses are necessary, the best fit may be with several diamond anasto-

moses. Anastomoses are 3–4 mm in length and 7/0 polypropylene with the 8/0 needle is used. The RA is tacked to the epicardium with multiple sutures of 6/0 polypropylene to maintain position of conduit curves and prevent angulation from occurring at the anastomoses.

In 30% the left ITA is anastomosed to the diagonal artery as well as to the left anterior descending (LAD) artery unless the diagonal is very proximal, in which case the RA is used or occasionally the distal end of the ITA is used as a short Y-graft from the ITA. The pedicle of the ITA is opened longitudinally from the distal end to within 1–2 cm of the T-anastomosis to expose the artery when sequential grafting is planned. Occasionally when the left ITA will not reach the distal LAD artery, the ITA is grafted to the circumflex vessel(s) and the RA is grafted to the LAD (and the diagonal if needed) and brought over the acute margin of the heart to the posterior descending artery. In this instance, it may be helpful to add length to the RA by making the T-anastomosis a little more distal on the ITA depending on the length of ITA needed for lateral wall anastomosis. The ITA side-to-side anastomoses are usually in parallel and occasionally crossing and the ITA pedicle is always tacked to the epicardium proximal and distal to each anastomosis. Occasionally the ITA is grafted to two diagonals or the LAD may be grafted at two sites.

After each anastomosis, hemostasis is checked by removing the RA or ITA bulldog. This maneuver frequently restores contractile activity to part or most of the heart, depending on the stage of the operation, which is abolished by the next infusion of cardioplegia. At the end the heart is reperfused via the T-graft and grafts inspected before removing the cross clamp.

34.3

Harvest Complications

In a personal experience with 1,360 patients and an institutional experience with an additional 850 patients we have not recognized hand ischemia. One patient has had median nerve injury manifest by weakness and palmar sensory loss which I believe is secondary to excessive use of electrocautery to control retrograde bleeding from the distal end of muscular branches of the RA. When bleeding of this nature occurs and the branch cannot be clipped it is necessary to use low current electrocautery applied to the offending vessel and not indiscriminately to the muscle, which may cause injury to the median nerve.

Sensory disturbances due to trauma to the superficial radial nerve and thumb weakness were present in 11% of patients early after operation. At 1–4 years, 9% of patients had persistent symptoms with thumb weakness in 2.8%, dorsal sensory disturbance of the thumb

in 6.6%, and palmar sensory symptoms limited to the base of the thumb in 5.3% [9].

Forearm healing is unusually good and the incidence of significant infection is less than 1%. Evacuation of wound hematoma was required in three instances. Hand and forearm edema respond well to elevation.

We have not considered less invasive harvesting because of the need for the full length of the RA and concern over excessive trauma to the RA when exposure is not optimal.

34.4

Hypoperfusion

Arterial conduits are associated with hypoperfusion, most commonly due to spasm, but also due to intimal flaps or dissection of the ITA [10, 11]. With the latter, flow may be maintained until protamine is given, at which time the ITA will frequently thrombose.

In the first decade of ITA use, there was concern that the small size of arterial conduits (relative to saphenous vein) would not provide adequate flow. With increasing experience, it became apparent that the ITA provides adequate flow, even when grafted sequentially to the diagonal artery and the LAD or when used as the only left-sided conduits for left main disease [12]. The advent of Y and T grafting again raised the issue of the flow capacity of these configurations. However, flow measurements intraoperatively have demonstrated an RA T-graft flow reserve of 1.6 based on free flow and completion flow [13]. Five days postoperatively RA T-graft flow reserve was 1.5 with adenosine stimulation and fell to 1.3 when atrial pacing at 85% of maximum predicted heart rate was added [14]. These values are similar to those obtained 1 week postoperatively for the ITA and RA T-graft in which flow reserve with adenosine vasodilatation was 1.8 and increased to 2.5 at 6 months [15], which is consistent with conduit remodeling [16].

Intraoperative treatment of conduit harvest spasm is necessary. I have primarily used intraluminal papaverine and occasionally we add topical papaverine in saline during harvesting. Others have used intravenous nitroglycerin [17], verapamil [18], diltiazem [1, 2], nitroprusside and phenoxybenzamine [19]. I have not used diltiazem, which was touted as necessary for success of the RA [1, 2], but does not influence long term patency [20]. The RA has a more muscular media than the other arterial conduits and contracts more vigorously to potassium chloride [21], but has endothelial function similar to the ITA [21], which persists after grafting [20, 22]. We have not avoided vasopressors to support adequate perfusion pressure in the perioperative interval [23].

I have not recognized hypoperfusion postoperatively. Intraoperatively, I have had three patients with hypoperfusion, which was recognized by transonic flow measurement in one patient with no flow in the proximal ITA, reversal of flow in the distal ITA, and antegrade flow in the RA due to dissection of the proximal ITA with thrombosis after protamine. A vein graft was placed to the proximal RA and because the T-anastomosis was intact, the distal ITA was perfused. The second patient was having a reoperation and after giving protamine, deteriorated with findings of thrombus and cardiac fat in the side-to-side anastomosis of the ITA to the diagonal artery. Partial take-down of the anastomosis allowed removal of the obstruction with restoration of flow and return of cardiac function to its baseline level. The third patient was also having a reoperation with a free right ITA attached to the aorta and the RA attached to it. Just prior to closure of the incision, manipulation of the aortic hood of the ITA caused visible spasm of the ITA and cardiac collapse. This was treated with recannulation and cardiopulmonary bypass, topical papaverine to the ITA, and insertion of an intra-aortic balloon pump. The patient recovered uneventfully and without a supplemental vein graft.

34.5 Results

Although we have used the RA since October 1993, we have only intermediate term follow-up to 7 years at this time. In the first 909 patients having a primary RA T-graft, the mean age was 60 with 20% age 70 or greater. Triple vessel disease was present in 73%, female gender in 28%, diabetes mellitus in 27%, peripheral vascular disease in 11%, cerebral vascular disease in 10% and chronic obstructive pulmonary disease in 6%. The ejection fraction was less than 35% in 11% [24].

There were seven (0.8%) deaths within 30 days of operation. The incidence of perioperative Q-wave infarction was 3.3%, low cardiac output 2.7%, stroke 2.2%, reoperation for bleeding 3.8% and deep sternal infection 0.8%. Postoperative follow-up was 1–88 months (mean 35.4 months) and was 95% complete. Actuarial survival at 5 years is 90%, freedom from infarction 94%, freedom from catheterization 83% and freedom from reintervention (angioplasty or reoperation) 93%.

These results are similar to those reported for patients having one or two ITA grafts with additional vein grafts [25]. Our patients had a similar mean age, but more patients age 70 or greater, more females, and more diabetics, but our patients were operated on at a later time. Our outcomes are also similar to those reported for bilateral ITA and RA grafting [26].

34.6 Conduit Patency

Patency of the RA from the aorta was 83% at 5 years in the first series [2]. It has since improved to 91.6% at 105 months [20]. When used as a Y-graft from the left ITA, patency was 93.8% at 48 months [27]. Patency was similar for RA grafts arising from the aorta or from the in situ left ITA (Y- or T-graft) [27, 28]. Radial artery patency declines as the severity of coronary stenosis decreases with a minimal stenosis of 70% required for adequate patency [20, 27–29].

Our strategy from 1993 until 2001 was to use the radial artery without regard to the degree of coronary stenosis. Review of our angiographic data revealed decreasing RA patency with decreasing coronary stenosis [29]. Consequently, since 2001, the RA has not been used if the coronary stenosis is less than 70% and we have tried to fine-tune this by applying the 70% limit to smaller coronaries and for larger coronaries, using 80% as the minimal stenosis. This relates to the fact that measured cross sectional area is larger than the visually estimated degree of stenosis and this difference becomes greater as vessel diameter increases.

Our overall patency for aortocoronary and T-grafted RA has been 75% and 70% respectively ($p = ns$) [28]. Our patency for the RA to the LAD or proximal circumflex system with 90% or greater stenosis has been equal to that for the left ITA to the same targets at 4 years [29]. We believe our lesser patency for the RA is due to its liberal use without regard to the severity of coronary stenosis and its routine use for the right coronary system [28, 29].

If the RA is patent at 5 years, it is likely to remain patent as there are no indications of atherosclerotic change to 10 years and endothelial function remains good [20]. Angiography of two RA T-grafts at 10 years indicates healthy conduits.

34.7 Conclusions

The RA is eminently useful because of its size, length, handling qualities, freedom from dissection, and simultaneous harvest with other conduits. Harvest complications have been limited to injury to the superficial radial nerve in 9%. When used as a T-graft, complete revascularization can be achieved in most patients with two conduits. Potential drawbacks are spasm, which is adequately treated with intraluminal papaverine, and competitive coronary flow causing a loss of patency if the coronary stenosis is less than 70–80%. Hypoperfusion has been rare and secondary to mechanical problems, but not conduit spasm or intrinsic inadequacy of the T-graft.

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Arterial Grafting in Reoperative Coronary Artery Bypass Surgery

Role of Internal Thoracic Artery Grafts in Reoperative Coronary Artery Bypass Surgery

J.F. SABIK III, B.W. LYTLE

35.1

Introduction

Coronary reoperations account for 15–20% of all isolated surgical myocardial revascularizations [1]. Progression of coronary atherosclerosis and saphenous vein graft stenosis result in recurrent ischemia and the need for coronary reoperation in 20% of patients 15 years after primary coronary surgery [2]. Patients undergoing coronary reoperations often have patent internal thoracic grafts or internal thoracic artery grafting during their reoperation [3]. In this chapter, (1) the perioperative risk associated with internal thoracic artery grafting at reoperation, (2) the perioperative risk associated with patent internal thoracic artery grafts at reoperation, and (3) the long-term effects of internal thoracic artery grafts on survival after reoperation will be reviewed.

35.2

Perioperative Risk of Internal Thoracic Artery Grafting at Reoperation

Observational studies of primary coronary artery bypass surgery have demonstrated the superiority of internal thoracic artery grafting over saphenous vein grafting on both survival and freedom from recurrent ischemia and coronary reintervention [4–6]. These findings have prompted surgeons to extend the usage of internal thoracic artery grafting to reoperative coronary surgery. To examine the perioperative risk of internal thoracic artery grafting at reoperation, we reviewed the results of 1,663 consecutive patients who underwent a first reoperation for isolated coronary artery disease at the Cleveland Clinic Foundation from 1988 to 1991 [7]. One thousand and fourteen patients received at least one internal thoracic artery graft at reoperation. Of the 1,088 patients who did not have internal thoracic artery grafting at their primary coronary revascularization, 799 (73%) received at least one internal thoracic artery graft and 126 (12%) bilateral internal thoracic artery grafts. Of the 560 patients who had single internal thoracic artery grafting at their first op-

eration, 215 (38%) received a second internal thoracic artery graft at reoperation. Graft selection was at the discretion of the operating surgeon, and patients who did not have internal thoracic artery grafting at reoperation or have one from their primary operation were a higher risk group of patients than those who had a prior internal thoracic artery graft or received one at reoperation. Patients who did not receive or have a prior internal thoracic artery graft were more likely female ($P < .001$), >70 years old ($P < .001$), to have a history of congestive heart failure ($P = .017$), and to undergo an emergency operation ($P < .001$).

Hospital mortality for all 1,663 reoperative patients was 3.7%. Internal thoracic artery grafting at reoperation did not increase hospital mortality. Single and bilateral internal thoracic artery grafting at reoperation in patients without prior internal thoracic artery grafting were associated with very low hospital mortality, 2.4% (16/673), and 1.6% (2/126), respectively, and the use of a second internal thoracic artery graft in patients with a prior internal thoracic artery graft was also associated with a low hospital mortality of only 1.9%. Multivariable analysis identified no internal thoracic artery grafting at either the primary or reoperative coronary revascularization ($P < .0001$) as being associated with increased hospital mortality. Congestive heart failure ($P < .0001$), emergency surgery ($P = .01$), advanced age ($P = .018$), and female gender ($P = .029$) were also found by multivariate analysis to be associated with increased hospital mortality. In addition, no association was found by multivariate analysis between postoperative morbidity and the number of internal thoracic artery grafts received at the primary or reoperative coronary surgery.

Although this observational study suggests that internal thoracic artery grafting at reoperation decreases perioperative mortality, the biases in patient selection for internal thoracic artery grafting were so profound, it is doubtful that they were completely eliminated by multivariable analysis. The patients who received internal thoracic artery grafting at reoperation were a lower risk group of patients, and therefore they would be expected to have lower hospital mortality.

However, since the selection criteria of patients for internal thoracic artery grafting was very broad in this

study, it does appear that the majority of patients undergoing reoperation can have internal thoracic artery grafting without increasing surgical mortality. In this study, three-quarters of the patients who did not have internal thoracic artery grafting at their primary operation received it at their reoperation, and almost 40% of patients who had prior internal thoracic artery grafting received a second internal thoracic artery graft at their reoperation. Both these revascularization strategies were associated with very low operative risk. In addition to the very low hospital mortality with internal thoracic artery grafting at reoperation, there was no increase in morbidity. Sternal wound complications were uncommon. Overall, the sternal wound complications occurred in 1.4% of patients. Only 1.6% of patients who had bilateral internal thoracic artery grafting at reoperation, and 0.9% of patients who had staged bilateral internal thoracic artery grafting (one at primary operation, one at reoperation), had a wound complication. These findings suggest that internal thoracic artery grafting does not increase the perioperative risk of coronary reoperations, and they can be used safely in the majority of patients undergoing reoperation.

Others have similarly found that internal thoracic artery grafting at reoperation can be performed without increasing hospital risk. He and colleagues reviewed the results of 622 patients who underwent coronary reoperation [8]. At reoperation, 258 had saphenous vein grafting alone and 364 had internal thoracic artery grafting with or without additional saphenous vein grafting. Hospital mortality was similar between patients with and without internal thoracic artery grafting, 9.7% versus 13.2% ($P=.2$), respectively. In addition, multivariate analysis did not find an association between internal thoracic artery grafting and hospital mortality.

The study by Lytle also suggested that bilateral internal thoracic artery grafting can also be performed safely in reoperative patients. The hospital mortality was only 1.6% in the patients who underwent bilateral internal thoracic artery grafting at reoperation. However, this was a group of relatively low risk reoperative patients. To evaluate the risk of bilateral internal thoracic artery grafting at reoperation, Galbut and colleagues compared the outcomes of 88 patients who underwent reoperative coronary surgery with bilateral internal thoracic artery grafting to 88 computer matched patients who underwent primary coronary surgery with bilateral internal thoracic artery grafting [9]. The patients were matched for sex, age, left ventricular function, angina classification, and left main coronary artery disease. Hospital mortality was similar in the reoperative and primary patients, 6.8% versus 3.4% ($P=NS$), respectively. No significant difference was found in reoperation for bleeding (5.7% vs 4.5%, $P=NS$), sternal wound infection (3.4% vs 2.3%,

$P=NS$), myocardial infarction (8.0% vs 2.3%, $P=NS$), or stroke (3.4% vs 1.1%, $P=NS$) between the two groups. However, more reoperative patients had respiratory failure, 13.6% versus 3.4% ($P<.015$), respectively. The authors concluded that bilateral internal thoracic artery grafting can be performed with similar mortality at reoperation as at primary surgery. The increased respiratory morbidity observed in reoperative patients they believed was the result of longer operating and cardiopulmonary bypass times, and the increased need for blood and colloid transfusions.

Although the risk of reoperation does not appear to be increased with internal thoracic artery grafting, should an internal thoracic artery graft be used to replace an old saphenous vein graft? Most patients presenting for coronary reoperation have atherosclerotic saphenous vein grafts [3]. Because of the excellent long term patency and improved survival and freedom from cardiac events associated with internal thoracic artery grafting and the risk of atheroembolism from old vein grafts during reoperation, it is tempting to ligate and replace an old, atherosclerotic saphenous vein graft with an internal thoracic artery [10, 11]. However, doing this can result in catastrophic hypoperfusion, because the blood flow initially through an internal thoracic artery graft may not be adequate to meet the myocardial requirements [12–16].

To evaluate the efficacy of the internal thoracic artery as a replacement graft for old saphenous vein grafts at reoperation, Navia and colleagues at the Cleveland Clinic Foundation reviewed their revascularization strategies in 387 consecutive patients who underwent reoperation from 1985 to 1990 with stenotic saphenous vein grafts to totally occluded left anterior descending coronary arteries [13]. The patients were divided into four groups by revascularization strategy. Group I consisted of 155 patients who had replacement of the old saphenous vein graft with a new saphenous vein graft, group II, 90 patients who had the old saphenous vein graft left intact with internal thoracic artery grafting of the left anterior descending, group III, 37 patients who had ligation of the old saphenous vein graft with internal thoracic artery grafting to the left anterior descending and saphenous vein grafting to a diagonal, and group IV, 104 patients who had ligation of the old saphenous vein graft and internal thoracic artery grafting to the left anterior descending. Hospital mortality was greatest in group IV (7.9% for group IV vs 2.1% for groups I–III, $P=.01$), and multivariate analysis identified internal thoracic artery grafting alone to be associated with increased operative mortality ($P=.001$). Hypoperfusion in the distribution of the left anterior descending was present in 19% of patients, all of whom were in group IV. Multivariable analysis identified ligation of the old saphenous vein and replacing it with only an internal thoracic artery graft (revascularization

strategy group IV) as associated with hypoperfusion. Hypoperfusion was treated in 11 patients with either additional saphenous vein grafting to the left anterior descending (6 patients) or reconstruction of the previously ligated saphenous vein grafts (5 patients), and all but one (9%) of these 11 patients survived. In the remaining eight patients, hypoperfusion was treated with intra-aortic balloon pumping, and five (63%) died ($P = .01$).

These observations from Navia and colleagues strongly suggest that old saphenous vein grafts should not be ligated and replaced by internal thoracic artery grafts alone. The two revascularization strategies to best avoid hypoperfusion both involve supplementing internal thoracic artery grafting with saphenous vein grafting. Either the old saphenous vein graft can be left intact and internal thoracic artery grafting be performed, or the old saphenous vein graft can be ligated and, in addition to internal thoracic artery grafting, saphenous vein grafting of the left anterior descending or diagonal is also performed. Both these revascularization strategies have theoretical disadvantages. In the former strategy, there is a potential risk of atheroembolism from the old saphenous vein graft. The latter strategy decreases the risk of atheroembolism by ligating the old saphenous vein graft. Although leaving the old saphenous vein graft in place has the potential for atheroembolism and myocardial injury, observational studies where this has been done with internal thoracic artery grafting have not demonstrated an increased risk of myocardial injury [13, 17]. In the study by Navia and colleagues, myocardial infarctions occurred in only 1.1% of patients when the old saphenous vein graft was left in place [13]. Similar findings were also found by Galbut and colleagues [17]. Both revascularization strategies have the potential disadvantage of competitive flow from the saphenous vein graft resulting in the internal thoracic artery becoming atretic, and non-functional [10, 11]. Although angiographic, atretic, "string-sign," internal thoracic artery grafts have been reported to later dilate when competitive flow is decreased, it is doubtful this will occur in all cases [18–20].

How should an occluded left anterior descending coronary artery whose blood supply is dependent on an old, atherosclerotic vein graft be bypassed at reoperation? If the patient is elderly, replacing the old vein graft with a new saphenous vein graft is probably sufficient, because elderly patients will probably not live long enough to derive the long-term clinical benefits of internal thoracic artery grafting. In younger patients, with expected good long-term survival, an internal thoracic artery graft should probably be used to graft the left anterior descending. This should be supplemented by either leaving the old vein graft intact, or by replacing the old graft with a new saphenous vein graft to the left anterior descending or diagonal.

There are practical advantages of using internal thoracic artery grafts at reoperation. First, they are usually available and of good quality. Second, when used in-situ, they do not require a proximal anastomosis. This can be beneficial if there is extensive scarring and limited access to the ascending aorta.

Observational studies demonstrate that most patients undergoing coronary reoperation are candidates for internal thoracic artery grafting. However, there are some patients with extensive vascular disease where internal thoracic artery grafting may be contraindicated. They include patients with radiation induced atherosclerosis and extensive brachiocephalic atherosclerosis. In patients with prior mediastinal radiation, the internal thoracic arteries were also radiated, and therefore are likely to develop radiation induced atherosclerosis that would render them inappropriate as bypass conduits. In addition, sternal wound healing in patients with prior mediastinal radiation can be problematic, and we prefer not to decrease the blood supply to the sternum by harvesting the internal thoracic arteries. Patients with extensive brachiocephalic disease, particularly of the proximal subclavian, should not have in-situ internal thoracic artery grafting. Using an in-situ internal thoracic artery graft in cases of proximal subclavian stenosis may result in inadequate blood flow in the arterial graft, or worse, blood flow reversal in the in-situ internal thoracic artery graft, the subclavian steal phenomenon.

35.3

Impact of Patent Internal Thoracic Artery Grafts on Perioperative Risk

Coronary reoperations are technically more challenging than primary operations. Most patients undergoing reoperative coronary surgery have areas of their myocardium dependent on atherosclerotic saphenous vein grafts or patent in situ internal thoracic artery grafts. Studies have demonstrated that atherosclerotic vein grafts increase the mortality of reoperative surgery, most likely due to atheroembolism [21]. There has been concern that patent, in-situ internal thoracic artery grafts may also increase the risk of reoperation due to the technical difficulties of managing them during reoperation.

To determine whether patent internal thoracic artery grafts increased the risk of reoperation, we reviewed the results of 1,663 patients undergoing isolated coronary reoperation at the Cleveland Clinic Foundation from 1988 to 1991 [7]. Five hundred and seventy-five patients had prior internal thoracic artery grafting; 560 single and 15 bilateral. Four hundred and eighty-nine patients had patent internal thoracic artery grafts at reoperation. Despite the technical difficulties of re-

operation in patients with patent internal thoracic artery grafts, they were not at greater risk. Hospital mortality was 3.7% (62/1,663) for all reoperative patients and 3.6% (20/560) for patients with prior internal thoracic artery grafting. Damage to patent internal thoracic artery grafts occurred in 3.7% of cases.

Others have similarly found no increase in the perioperative risk of patients with prior internal thoracic artery grafting at coronary reoperation [22–24]. Coltharp and colleagues reviewed the hospital outcomes in 410 consecutive coronary reoperative patients [22]. Three-hundred and thirteen patients had received only saphenous vein grafts at their primary operation, and 97 had at least one internal thoracic artery graft at their first coronary revascularization. There was no difference in hospital mortality (3.1% vs 5.8%, $P=NS$) or overall morbidity (7.2% vs 11.5%, $P=NS$) between patients with and without prior internal thoracic artery grafting. Multivariate analysis did not identify prior internal thoracic artery grafting to be associated with hospital mortality or morbidity.

Christenson and colleagues similarly reviewed the hospital outcomes of 189 consecutive patients undergoing coronary reoperation [23]. There were 42 patients with prior internal thoracic artery grafting and 147 with only prior vein grafts. Hospital mortality (0% vs 4.8%, $P<.05$) appeared to be lower in patients with prior internal thoracic artery grafts. Overall morbidity was similar.

Cameron and colleagues followed 743 patients who underwent primary coronary artery bypass surgery [24]. Fifty-nine of these patients underwent coronary reoperation, 22 patients with a patent left internal thoracic artery graft, and 37 with an occluded or no internal thoracic artery graft. There were no hospital deaths or myocardial infarctions in the 22 patients who underwent reoperation with patent internal thoracic artery grafts; whereas the hospital mortality was 5.4% and myocardial infarctions occurred in 8.1% of the patients without a patent internal thoracic artery graft.

Despite the increased technical difficulties of reoperating on patients with prior internal thoracic artery grafting, these observational studies demonstrate that these technical difficulties can be neutralized by good surgical technique. What are the technical challenges of reoperating on patients with patent internal thoracic artery grafts and how can they be managed? The first challenge is preventing injury to the patent internal thoracic artery graft during sternal reentry and mediastinal dissection, and the second, myocardial protection.

To determine the occurrence of internal thoracic artery graft injury during reoperation and its effect on hospital outcome, Gillinov and colleagues at the Cleveland Clinic Foundation reviewed their experience in patients undergoing coronary reoperations with patent

in-situ internal thoracic artery grafts to the left anterior descending [25]. From 1986 to 1997, 655 patients underwent reoperation with patent left internal thoracic artery grafts to the left anterior descending. In 35 (5.3%) of these patients the internal thoracic artery graft to the left anterior descending was injured. Twenty were injured on initial opening or dissection, and 15 after cardiopulmonary bypass had been established. In 26 of these patients the preoperative chest X-ray was available for review, and in 17 (65%) the internal thoracic artery graft was adherent to the underside of the sternum. Strategies to restore left anterior descending blood flow included saphenous vein grafting (28 patients), anastomoses of left internal thoracic artery stump to other arterial graft (4 patients), primary left internal thoracic artery repair (3 patients), anastomoses of left internal thoracic artery to aorta (1 patient), and left internal thoracic artery repair by right internal thoracic artery interposition graft (1 patient). In patients who sustained an internal thoracic graft injury, hospital mortality was 8.6% (3/35) and myocardial infarctions occurred in 40% (14/35). In all three patients who died, the cause of death was cardiac failure, and their autopsies revealed either thrombosis or stenosis of the graft to the left anterior descending. Hospital mortality was 3% in the 620 patients who did not suffer an injury to the patent internal thoracic artery graft. Others investigators have reported injury to patent internal thoracic artery grafts in 15–40% of patients undergoing coronary reoperation, with mortality as high as 50% [26, 27].

Injury to a patent internal thoracic artery graft at reoperation can be catastrophic. The likelihood of this occurring at sternal reentry can be significantly decreased by positioning the internal thoracic artery graft away from the sternum at the primary operation. To do this, we routinely make a vertical slit in the left sided pericardium just lateral to the pulmonary artery. The internal thoracic artery is then routed through this opening in the pericardium under the left lung, away from the midline and sternum. If the pericardium is not incised, the in-situ internal thoracic artery graft is pushed medial and anterior by the pericardium and expanding left lung. This can result in the internal thoracic artery being adherent to the underside of the sternum, increasing the likelihood of it being injured on sternal reentry or when dissecting the mediastinum from the underside of the anterior left chest. When the internal thoracic artery is placed under the left lung, it cannot be injured on sternal reentry, and its dissection is easily accomplished. Others methods of protecting an in-situ internal thoracic artery from injury at reoperation have been described. They include the use of a polytetrafluoroethylene graft to cover the left internal thoracic artery pedicle, pericardial flap to cover the graft, and routing the left internal

thoracic artery through a posterior opening in the pericardium [28–30].

When a patient undergoing a reoperation has a patent in-situ internal thoracic artery graft, preoperative assessment must include determination of its location in the mediastinum. The metallic clips used to occlude the side branches of the internal thoracic artery graft may often be seen on the chest X-ray, and these clips often can be used to adequately identify the location of the internal thoracic artery graft. If its location cannot be determined by reviewing the preoperative chest X-ray, then coronary angiography or contrast-enhanced computerized tomography should be obtained to locate it.

If the internal thoracic artery graft is near the midline and sternum, there is a good chance that it will be injured on sternal reentry. This can result in bleeding, myocardial ischemia, and hemodynamic collapse. It is therefore prudent to be prepared for urgent peripheral cannulation and cardiopulmonary bypass when preoperative studies suggest that the internal thoracic artery graft is adherent to the underside of the sternum. This will maintain hemodynamic stability while the heart is being dissected if the internal thoracic artery graft is injured. Some surgeons suggest peripheral cannulation and institution of cardiopulmonary bypass prior to sternal reentry. The rationale for this approach is that any injury occurring to patent grafts or the heart is better tolerated and more easily controlled if cardiopulmonary bypass is already begun. We use this approach on occasion, when injury to a patent graft or heart appears unavoidable.

If a patent internal thoracic artery graft to the left anterior descending is injured, it must be replaced or repaired, and the adequacy of the new or repaired graft to the left anterior descending must be certain. In the Cleveland Clinic report, although 40% of the patients who had an injury to their internal thoracic artery graft sustained a myocardial infarction, the three patients who died all had ineffective revascularization of the left anterior descending demonstrated at autopsy [25].

Patent in-situ internal thoracic artery grafts to totally occluded coronary arteries present challenges in myocardial protection. Since antegrade cardioplegia will not reach these areas, additional myocardial protection strategies must be used. To protect areas supplied by in-situ arterial grafts, systemic hypothermia and leaving the graft unclamped may be used. Although this technique is effective, it requires additional cardiopulmonary bypass time for cooling and warming. We find that intermittent, cold, retrograde cardioplegia is very useful and effective in patients undergoing reoperations with patent in-situ arterial grafts to occluded coronary arteries. The in-situ internal thoracic artery graft is identified and dissected and an atraumatic clamp is placed across it during myocardial ischemia. Retrograde cardioplegia is administered

through a cannula placed in the coronary sinus.

There are also theoretical reasons as to why patients with prior internal thoracic artery grafting may be at lower risk at reoperation. First of all, because of selection bias, patients with prior internal thoracic artery grafting are probably a lower risk group of patients than those who had all saphenous vein grafting at their primary operation. Second, since internal thoracic artery grafts have excellent long-term patency, it is more likely that patients with prior internal thoracic artery grafting to the left anterior descending will have preserved anterior left ventricular wall function. Observational studies by Coltharp and Christenson support this assumption [22, 23]. In 110 reoperative coronary patients, Coltharp and colleagues compared their ventricular function at reoperation to their ventricular function obtained prior to their primary coronary operation [22]. There were 56 patients who had internal thoracic artery grafting at their primary operation and 54 who had all saphenous vein grafting. Patients with prior internal thoracic artery grafting were more likely to have preserved left ventricular function at their reoperation than those with all saphenous vein grafting. Fifty percent of patients with internal thoracic artery grafting at their primary operation had improved or stable left ventricular function at reoperation, as compared to only 21% of patients who received all saphenous vein grafts ($P=.003$). Christenson and colleagues also found that left ventricular function was more likely to improve or remain stable from the primary to reoperative coronary operation if an internal thoracic artery graft was performed at the first operation [23]. They found in 60% of patients with prior internal thoracic artery grafting, left ventricular function was improved at reoperation, as compared to only 3% in patients with only saphenous vein grafts at their primary operation.

An additional explanation as to why patients with prior internal thoracic artery grafting may have better outcomes at coronary reoperation is that atherosclerotic embolization does not occur with patent internal thoracic artery grafts, as it does with patent, atherosclerotic saphenous vein grafts. Atherosclerotic saphenous vein grafts have been associated with increased operative mortality and morbidity in patients undergoing coronary reoperation [21].

35.4

Internal Thoracic Artery Grafts and Survival after Coronary Reoperation

Internal thoracic artery grafting of the left anterior descending coronary artery at primary coronary surgery has been demonstrated in observational studies to improve long-term survival and decrease recurrent ischemic events and the need for coronary reintervention as

compared to saphenous vein grafting [6]. These clinical benefits of internal thoracic artery grafts are due to their excellent long term patency [10, 11]. Do patients undergoing coronary reoperation derive the same benefit from internal thoracic artery grafting as patients undergoing primary surgery? Although much has been reported in observational studies of the benefits of internal thoracic artery grafting after primary revascularization, there are only a few observational reports evaluating its influence on survival and freedom from recurrent ischemia after coronary reoperation [9, 31–33]. There are no randomized studies evaluating the long term effectiveness of internal thoracic grafting at reoperation.

To examine the influence of internal thoracic artery grafting on the long term results of coronary reoperation, Dougenis and Brown reviewed the late outcomes of 153 reoperative coronary patients [31]. Single or bilateral internal thoracic artery grafting with or without additional saphenous vein grafting was performed at reoperation in 103 patients and saphenous vein grafting alone was performed in 50 patients. The two groups had similar demographic characteristics. Hospital mortality (5.6% vs 10%, $P > .05$) and morbidity were not significantly different in patients with and without internal thoracic artery grafting. However, freedom from recurrent angina and event-free survival was better in patients who had internal thoracic artery grafting at reoperation. Freedom from recurrent angina at 5 and 10 years was 86% in patients with internal thoracic artery grafting, and 56% and 25% in patients with only saphenous vein grafting. Event-free survival at 5 and 10 years was 81% for patients with internal thoracic artery grafting and 52% and 20% for patients with only saphenous vein grafts. There was a trend for improved survival in patients with internal thoracic artery grafting versus those with only saphenous vein grafting, 95% and 88% versus 85% and 71% at 5 and 10 years, respectively.

Loop and colleagues at the Cleveland Clinic Foundation also evaluated the effect of internal thoracic artery grafting at reoperation on survival [32]. They reviewed the results of 2,509 consecutive reoperative patients. Internal thoracic artery grafting at either the primary or reoperative revascularization was found by multivariate analysis to be associated with improved long term survival. Ten year survival was 72.6% in patients with internal thoracic artery grafting, and only 65.5% in patients with only saphenous vein grafting ($P = .004$).

Others, however, have not identified a survival benefit of internal thoracic artery grafting at reoperation. Weintraub and colleagues from Emory reviewed the late results of 2,030 patients who underwent reoperative coronary bypass surgery, and multivariable analysis did not find that internal thoracic artery grafting at reoperation increased late survival [33].

Logic would dictate that using better bypass grafts, grafts with better patency would improve the late results of coronary revascularization. Therefore, survival should be better after coronary reoperation when internal thoracic artery grafts are used to bypass the left anterior descending. Few observational studies have addressed this issue, and there is not as much evidence supporting internal thoracic artery grafting over saphenous vein grafting at reoperation as there is for primary revascularization.

35.5 Conclusions

Coronary reoperations can be performed safely with internal thoracic artery grafts. There does not appear to be any increased perioperative risk in patients undergoing reoperation who have had prior internal thoracic artery grafting, or in patients having single or bilateral internal thoracic artery grafting at reoperation. Some observational studies demonstrate a decreased hospital risk in patients undergoing reoperative coronary surgery who have had prior internal thoracic artery grafting. This may be due to the excellent long term patency of internal thoracic artery grafts and how this preserves ventricular function. There is also some evidence that internal thoracic artery grafting at reoperation improves long term survival as compared to a reoperative strategy of only saphenous vein grafting.

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Quality Control of Arterial Grafting: Early Detection of Graft Patency and Flow

Flow Capacity of Arterial Grafts: Internal Thoracic Artery, Gastroepiploic Artery and Other Grafts 36

M. OCHI

The superior patency rate of the left internal thoracic artery (LITA) in coronary artery bypass grafting (CABG) is well known. The use of the internal thoracic artery (ITA), including a LITA-LAD anastomosis, has improved the long-term survival of patients [1]. In addition, the right gastroepiploic artery (GEA) is now widely used as a graft for the coronary artery and the indication, as well as the operative technique, has been established [2–4].

These in situ arterial grafts are used either as an independent graft to a single coronary artery or as a sequential graft to revascularize more than two coronary arteries. They are also used as a composite graft in which a free graft is attached to the side wall of the in situ graft to revascularize multiple coronary arteries.

When an in situ arterial graft is used as an independent graft to a single coronary artery, the most important and perhaps the only concern to surgeons is flow competition between the graft and the grafted coronary artery. Two major factors are related to this phenomenon, i.e., flow capacity of the graft and the degree of stenosis of the coronary artery.

When the in situ graft is used as a sequential graft or a composite graft to revascularize multiple coronary arteries, competitive flow phenomenon may be a more serious concern.

A free arterial graft such as the radial artery is used either as an aortocoronary bypass conduit or as a branch of a composite graft in combination with the in situ arterial graft.

In either situation, it is the aorta or the in situ arterial graft that generates the blood flow regulating the flow capacity of the free radial artery. Therefore, in this chapter, the flow capacity of the in situ arterial grafts, i.e., the internal thoracic arteries and the right gastroepiploic artery, will mainly be discussed.

36.1

Internal Thoracic Arteries

Since the diameter of the ITA is smaller than that of the saphenous vein or even the radial artery, it must be appreciated that if the coronary lesion is mild (<75%),

ITA flow will be reduced, while saphenous vein graft (SVG) flow may not be affected by competitive flow. However, to expand the usage of the prime quality graft, the ITA is used as either an independent graft or a sequential or composite graft. There has always been concern regarding the adequacy of the flow capacity of the ITA.

36.2

Studies of Flow Reserve of the ITA

Several studies have reported on the postoperative flow of the ITA with or without a comparison to that of the vein graft. Schmidt et al. reported isoproterenol-induced flow responses in the ITA and vein grafts using an injection of radioactive xenon-133 into the coronary artery or graft [5]. They demonstrated that the ITA could produce the same flow response to the increased flow demand as do vein grafts. Johnson et al. reported the results of a comparison of the ITA and vein grafts using exercise thallium-201 scintigraphy within 8 weeks of operation, revealing that the ITA provided excellent coronary flow at peak myocardial demand and compared favorably to the vein grafts [6]. Gurne et al. reported an evaluation of flow reserve of the ITA assessed by a Doppler guidewire in the early (8 ± 2 days) and late (19 ± 15 months) periods after operation, revealing that ITA flow reserve was significantly lower in the early period but normalized over time [7]. This difference appeared to be the result of injury to the microvasculature during operation.

Another study by Doppler guidewire at rest and during hyperemia, induced by intravenous infusion of dipyridamole, demonstrated that the flow reserve of the ITA was significantly reduced soon after operation (1 month) but improved late postoperatively [8].

Takemura et al. studied ITA function during exercise postoperatively by transthoracic Doppler echography [9]. They showed that the diameter of the ITA increased significantly postoperatively, especially when the ITA was anastomosed to an LAD with more than 90% stenosis.

These studies on flow reserve of the ITA are consistent with serial angiographic evidence of ITA enlarge-

ment over time [10]. Further, Kitamura et al. demonstrated the growth potential of the ITA in patients with Kawasaki coronary disease undergoing a LITA-LAD grafting in the course of their physical growth [11].

36.3

Effect of Competitive Flow on the ITA and Remodeling

Serial angiographic studies have demonstrated remodeling of the ITA in relation to the severity of stenosis of a grafted coronary artery. This phenomenon has been recognized as a response to flow demand leading to an appropriate inner diameter of the artery.

The “string sign” is defined as a thinning phenomenon of the ITA on postoperative angiograms with no demonstrable flow of the contrast material into the recipient coronary artery resulting from flow competition between the ITA and the coronary artery. Thinning of the ITA itself, however, is thought to be a physiological adaptation under a no flow situation, and the ITA may function properly later as a graft when the native coronary flow decreases [12]. In other words, the ITA grafts have flow adaptability responding to the flow demand of the coronary artery [13]. These observations and theoretical explanations are supported by an experimental study using an animal model [14]. Furthermore, a recent angiographic study of a large volume of patients on the influence of competitive flow on the long term patency of the ITA support the idea that the ITAs are able to autoregulate their size and blood flow in response to demand [15].

Despite this fact, it is important to know that the substantial blood flow of the ITA is apparently less than that of a vein graft used as an aortocoronary bypass conduit, and thus the ITA is more prone to be involved in flow competition against the recipient coronary artery. In fact, series of angiograms have revealed that, during a medium-term postoperative follow-up, stenosis in the recipient coronary artery affects arterial graft patency [16]. Especially, competitive flow between the graft and the coronary arteries is an essential problem when the ITA is used as a sequential or a composite graft to revascularize multiple vessels.

36.4

Capability of ITA to Respond to Flow Demand

To expand the usage of the ITAs, sequential grafting or composite T- or Y-grafting has been utilized. One of the major concerns, however, on performing these revascularization techniques is the capability of the ITA to respond to increased flow demand compared to its single isolated use.

Sequential grafting of the ITA was begun in the early 1980s [17,18], and since then the reported angiographic results have been excellent. However, there are only a few reports on studies of flow reserve of the ITA in sequential grafting. Hodgson et al. reported sequential ITA graft flow reserve using contrast-induced hyperemia demonstrated by a digital subtraction angiographic technique after surgery [19]. They demonstrated that sequential ITA grafts provided flow reserve to both proximal and distal myocardial zones. Hence, concern regarding the adequacy of flow reserve should not limit the use of sequential ITA grafts.

Tector et al. reported a large series using the composite ITA graft technique and demonstrated excellent results [20]. Since then, reports on this grafting technique with acceptable graft patency have been accumulating. In addition, several studies have been reported regarding the flow capacity of the composite left ITA that generates blood flow to all grafted coronary arteries.

Wendler et al. studied flow dynamics in the left ITA main stem using a Doppler guidewire [21]. They measured blood flow in the proximal left ITA at baseline and after injection of adenosine and calculated coronary flow reserve (CFR). They revealed that after 6 months in combination with an increased maximum flow, a significant elevation of the CFR was observed, and that baseline flow in the left ITA main stem was higher after T grafting than flow rates in single ITA grafts. They concluded that the flow reserve of the proximal left ITA is adequate for multiple coronary anastomoses.

Royse et al. studied blood flow in composite grafts measuring blood flow intraoperatively by the transit-time Doppler technique [22]. They confirmed that the construction of composite grafts resulted in a significant increase in flow through the left ITA. They concluded that total arterial revascularization, using a composite graft, provided a 2.3-fold reserve of blood flow to the coronary vascular bed through the grafts.

We studied the adequacy of flow capacity of the bilateral ITA T-graft by dobutamine stress echocardiography (DSE) 6 months after operation in 40 patients with patent T-grafts revascularizing the entire left coronary system [23]. No patient exhibited ischemic wall motion abnormality in DSE in the anteroapical, lateral, or posterolateral region of the heart where the T-graft revascularized. Thus, we concluded the left ITA main stem, forming a T-graft configuration with the free RITA, has an adequate flow reserve to supply at least the entire left coronary system with sufficient blood.

Sakaguchi et al. studied regional myocardial blood flow using positron emission tomography at rest and after dipyridamole infusion to compare the adequacy of left ITA blood flow when the ITA was used as either an independent graft or a Y-graft [24]. They concluded

that the arterial composite Y-graft was not as effective as independent grafts for improving coronary flow reserve soon after coronary artery bypass grafting. However, they stated that the clinical importance of this difference was unclear and that the coronary flow reserve might still be sufficient for revascularization of the left coronary system. Finally, they cautioned that the indication for the Y graft should be carefully reviewed, especially in the case of a small left ITA.

36.5

Effect of Skeletonization on the Flow Capacity of the ITA

Several studies have reported the effect of free flow in the skeletonized ITA [25, 26]. Choi et al. demonstrated that skeletonization itself increases free flow as efficiently as intraluminal papaverine injection does for the pedicled ITA. Wendler et al. reported that more increased free flow was obtained after injection of papaverine into the skeletonized ITA rather than into the pedicled ITA. Takami et al. [27] demonstrated that skeletonization is sufficient and papaverine injection is not necessary to increase ITA graft flow.

In fact, the skeletonized ITA is longer and can reach even to the distal coronary arteries [28]. Once freed from the constraining action of the thoracic fascia and surrounding tissue, the ITA has a superior free flow. To date, however, no data is available to prove the increased flow capacity of the skeletonized ITA in the long-term postoperative period.

36.6

Right Gastroepiploic Artery

Since the first clinical application of the right gastroepiploic artery (GEA) as a graft to the coronary arteries in 1987 by Suma et al. [2] and Pym et al. [3], favorable results have been reported with good angiographic patency comparable to that of the ITA [29–32]. In the decade following these results, however, reports on the GEA have been concentrated on the angiographic findings, i.e. competitive flow. As mentioned previously, competitive flow is an equally important problem in the ITA and not peculiar to the GEA [16]. However, the GEA seems to become involved in flow competition more frequently than the ITA.

In 1993, Mills et al. were quick to emphasize that the use of the GEA should be avoided in a setting with possible competition of flow [33]. Voutilainen et al. reported that among five cases in which the GEA could not be visualized in postoperative angiograms, in only one case was the proximal stenosis of the recipient coronary artery more than 70% of its diameter [34]. They

stated clearly that they considered competitive flow from the bypassed coronary artery itself could be the reason for the poor function of the GEA in their noncritically stenosed cases. Uchida et al. reported their angiographic findings of the GEA, revealing that GEA grafted to coronary arteries in an infarcted area and to coronary arteries with severe stenosis (>90%) tended to be GEA dominant [35]. They stated that flow competition depended on three factors: the viability of the revascularized area, the degree of proximal stenosis and the location of the stenosis. Albertini et al. also emphasized in their large series that they avoided the use of the GEA for a dominant right coronary artery, or for a right coronary artery with only a moderate stenosis [36]. Considering the fact that competitive flow has a great influence on the patency of the arterial grafts [16], current reports on the late patency of the GEA of 80.5% at 5 years by Suma et al. [37] may be partly attributed to flow competition.

Apart from the angiographic findings, there is some evidence that can be interpreted as a caveat to be cautious when using the GEA: silent myocardial ischemia can occur in the GEA-grafted area under some stress conditions while the GEA is angiographically widely patent [38, 39]. Dominancy on the angiogram is one thing and the flow reserve of the GEA is another. Based on these observations, one can consider that the flow capacity of the GEA is different from that of the ITA and is limited to some extent.

36.7

Pressure Characteristics of GEA

The GEA is the third branch of the abdominal aorta, while the ITA is the second branch of the proximal aortic arch. This difference in anatomic location arguably influences the pattern of the blood supply to the coronary artery where the blood flow is diastolic-dominant.

Tedoriya et al. studied pressure characteristics in arterial grafts [40]. They observed that the diastolic pressure was significantly lower in the GEA than in both the ascending aorta and the ITA, while the systolic pressure was similar in the three. They stated that the diastolic pressure gradient across the anastomosis was the important driving pressure for diastolic graft flow and concluded that arterial grafts originating from a systolic-dominant circulation far away from the heart have a limited ability to supply blood to the coronary circulation.

36.8

Adequate Size of the GEA as a Graft

Size is another determinant of flow capacity of the GEA. There have been several reports on the free flow rate

and the diameter of the GEA measured intraoperatively [33, 41, 42]. A large luminal diameter correlated with better flow rates. However, no data is available on what is the appropriate diameter of the GEA as a graft to the coronary artery. Furthermore, none of the previous reports has demonstrated the adequacy of the flow capacity of the GEA under stress conditions in the postoperative period.

We conducted angiographic and echocardiographic studies on the flow capacity of the GEA in 30 patients who had undergone CABG using both the ITA and the GEA [39]. The luminal diameter of the arterial grafts was measured from postoperative angiograms. The adequacy of the myocardial blood supply from the arterial grafts was evaluated by dobutamine stress echocardiography (DSE). All arterial grafts were proven to be patent and appeared normal in all patients. The luminal diameter of the ITAs ranged from 1.4 to 3.1 mm (2.3 ± 0.4 mm) and that of the GEA from 1.5 to 4.5 mm (2.9 ± 0.7 mm), the latter being significantly larger than the former ($p < 0.005$). In the DSE, no patients exhibited new wall motion abnormalities in the anteroapical to lateral region where the ITAs were grafted. On the contrary, a new wall motion abnormality during the DSE was identified in 14 patients in the inferoposterior region where the GEA was anastomosed. Of these patients, nine had no residual nongrafted vessels in the inferoposterior region, whereas five had residual nongrafted vessels in the inferoposterior region

(Table 36.1). The luminal diameter and angiographic status of the GEA in each group are shown in Table 36.2.

Table 36.1. Groups of patients according to the presence of ischemic change in the DSE and residual nongrafted vessels in the GEA-grafted region. (Reprinted from *Annals of Thoracic Surgery*, vol 71: Ochi M, Bessho R, Saji Y, et al.: Sequential grafting of the right gastroepiploic artery in coronary artery bypass surgery, p 1206. Copyright 2001, with permission from the Society of Thoracic Surgeons)

Variables	Group I	Group II	Group III
Patients	16	9	5
Ischemic change in the DSE	(-)	(+)	(+)
Residual nongrafted vessels	(-)	(-)	(+)

DSE dobutamine stress echocardiography, GEA gastroepiploic artery

Table 36.2. The luminal diameter and angiographic status of the GEA in each group. (Reprinted from *Annals of Thoracic Surgery*, vol 71: Ochi M, Bessho R, Saji Y, et al.: Sequential grafting of the right gastroepiploic artery in coronary artery bypass surgery, p 1206. Copyright 2001, with permission from the Society of Thoracic Surgeons)

Variables	Group I	Group II	Group III
Luminal diameter (mm)	3.1	2.2	3.6
Angiographic status			
Dominant GEA	13	6	4
Balanced	3	2	1
Dominant coronary		1	



Fig. 36.1. Angiogram of triple sequential grafting of the gastroepiploic artery (GEA) taken 1 year postoperatively. The GEA was anastomosed to the posterior descending and atrioventricular branches of the right coronary artery and the ramus intermedius branch (arrow) of the left coronary artery. (Reprinted from *Annals of Thoracic Surgery*, vol 71: Ochi M, Bessho R, Saji Y, et al.: Sequential grafting of the right gastroepiploic artery in coronary artery bypass surgery, p 1206. Copyright 2001, with permission from the Society of Thoracic Surgeons)

All patients in group III exhibited satisfactory angiographic results and had GEAs with a luminal diameter greater than 3 mm. The presence of residual non-grafted vessels in the right coronary system, however, made it difficult to determine the adequacy of the flow reserve of the GEA. Accordingly, patients in groups I and II were analyzed for predictors of the ischemic change in the DSE. Multivariate logistic regression analysis identified that the luminal diameter of the GEA was a major independent predictor for the ischemic change. Further, the receiver operator characteristic curve showed that a luminal diameter of the GEA of greater than 2.6 mm had a sensitivity of 70% and a specificity of 78.0% for nonischemic change in the GEA-anastomosed region.

The major determinant of the flow capacity of the GEA is its luminal diameter. From our observation of sequentially used long GEA grafts (Fig. 36.1), as long as the luminal diameter of the GEA is large enough, the length of the GEA graft may not influence its flow reserve [43].

However, there may be other factors that influence the flow capacity of the GEA as a graft. Further study such as measurement of changes in the flow velocity of the GEA under stress conditions using a Doppler guidewire or transcutaneous Doppler echography may provide a solution.

The flow capacity of the GEA differs from that of the ITA especially under maximal stress conditions. The GEA should not be used routinely in the same way as the ITA.

36.9

Effect of Skeletonization on the Flow Capacity of the GEA

Recently, several reports have advocated the advantage of skeletonization of the GEA using an ultrasonic scalpel [44]. Theoretically, removal of constraining surrounding tissue makes the GEA longer and wider. To date, however, no data is available regarding the effect of skeletonization on the flow capacity of the GEA either intraoperatively or postoperatively. Further study is necessary.

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Intraoperative Graft Evaluation in Coronary Artery Bypass Grafting Using a 15-MHz High-Frequency Linear Transducer: Maintaining the Comprehensive Quality of Coronary Surgery 37

H. NAKAJIMA, M. KOMEDA

As the emergence of novel devices, such as the drug eluting stent (DES), has advanced percutaneous coronary intervention (PCI), so coronary artery bypass grafting (CABG) has increasingly become a procedure used for older and critically ill patients. Consequently, complications related to the cardiopulmonary bypass procedure, including cerebrovascular accidents, renal failures, and infection due to a compromised immune system, have become important issues for which solutions are required.

In order to avoid these complications, surgeons tend to choose off-pump CABG (OPCAB) for serious cases. Nonetheless, even with the latest heart positioner and stabilizer models, it is not easy to completely restrain movement as a result of heartbeat. Moreover, bleeding from a coronary artery makes it difficult to detect the edge of the arteriotomy and anastomosis is often technically demanding. To maintain a high graft patency of OPCAB compared to PCI, intraoperative graft evaluation is recommended. When OPCAB is performed, routine assessment of the coronary artery, grafts, and anastomosis aims to attain perfection using a 15-MHz high-frequency linear transducer (high-frequency echo probe). Therefore, we describe this technique for evaluating grafts and anastomoses in order to maintain the quality of coronary surgery.

37.1

Routine Evaluation of Graft, Artery and Anastomosis

37.1.1

Echography System with a 15-MHz Linear Transducer

Echographic assessment is conducted utilizing a 15-6L UltraBand High-Frequency Linear Transducer (Model 21390A with HP SONOS 5500 imaging system, Agilent Technologies, Andover, MA). To obtain a better image, a transparent, 5 mm-thick echo-pad (SONAR-AID, Geistlich Pharma AG, Wolhusen, Switzerland) is applied to the epicardium.

37.1.2

Coronary Artery to Be Anastomosed

Even though preoperative coronary angiography shows a normal artery, sometimes a sclerotic plaque after coronary incision is encountered, making the anastomosis complicated. A plaque on the anterior surface can be detected by cautious palpation; however, the high-frequency echo probe can easily reveal a plaque even on the posterior side, and by scanning the coronary artery distally and proximally the best anastomotic site can be identified.

37.1.3

Arterial Graft

Surgeons do feel concerned about the quality of arterial graft harvested by an inexperienced surgeon when a poor free flow is observed on the graft. One of the causes of a reduced flow is arterial spasm, which can be released by injection of a vasodilator, such as papaverine. In contrast to functional stenosis, another cause of low flow in arterial graft is an organic lesion (e.g., hematoma, dissection of arterial wall) resulting from traumatic manipulation, which might be fatal. The high-frequency echo probe securely demonstrates this organic damage to identify an intact portion of the artery for ultimate use as a free graft. For educational purposes, the inexperienced surgeon should obtain feedback information regarding the injured graft to improve his skill.

37.1.4

Anastomotic Site

When a graft is properly anastomosed to the coronary artery, a short axis image with high-frequency echo probe shows the typical “snowman” figure (Fig. 37.1a), reflecting the precise configuration of the vascular lumen of anastomosis. By scanning the anastomotic lumen from heel to toe, it is confirmed that there is no suspicion of narrowing or distortion of the lumen. The velocity of graft flow is then measured by pulse wave Doppler method and flow rate is calculated from the diameter of the graft. When stenosis is absent in the anas-

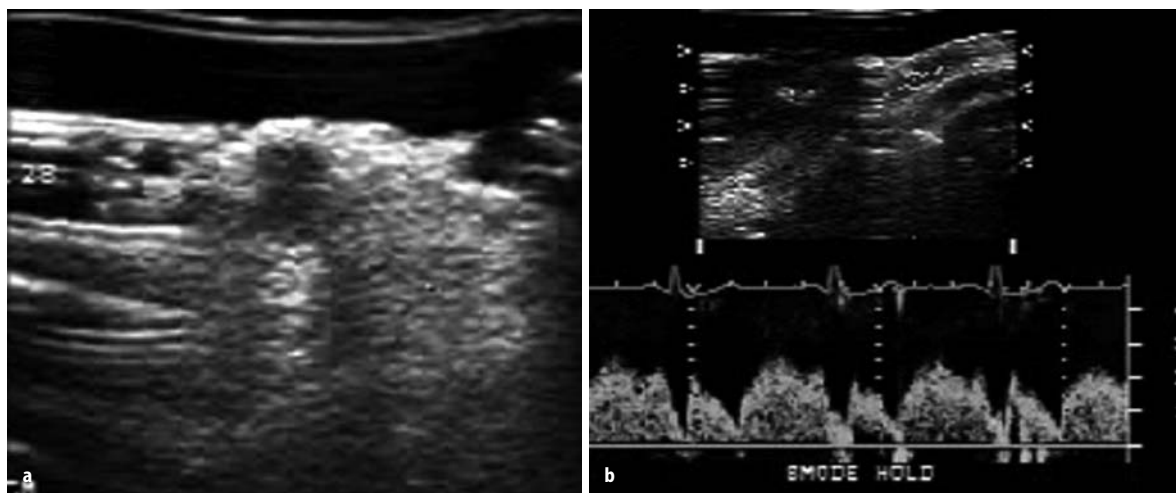


Fig. 37.1. **a** High-frequency echo probe shows the typical “snowman” figure with a proper anastomosis. **b** Diastolic phase dominant flow pattern indicates good patency of the graft

tomosis, the flow in the diastolic phase predominates in the flow pattern of the spectrum (Fig. 37.1b). After end-arterectomy, the stump of the resected intima can be checked using a longitudinal image of the coronary artery to determine whether it produces any stenotic lesions or not.

37.1.5

Ascending Aorta

As recent inventions of aortic connectors, such as the Passport or Heartstring, have broadened the choice of grafts for OPCAB, an intact wall must be confirmed when the graft is anastomosed to the aortic root to prevent plaque embolism. The echo probe is applied to the surface of the ascending aorta. The area where there is no atheromatous plaque and where wall thickness is less than 3 mm is determined. In the case of on-pump CABG, high-frequency echo is also useful for determining the aortic cross-clamp site.

37.2

Troubleshooting with Anastomosis in OPCAB

Revascularization of coronary artery when the heart is beating is technically more demanding than when it is under cardiac arrest. The former condition runs certain risks of causing anastomotic failure. To maintain the quality of anastomosis in OPCAB, it is very important to determine graft failure intraoperatively and to perform a prompt repair. The high-frequency echo is efficient in discovering graft failure. The following are examples of graft failure identified by high-frequency echo.

37.2.1

Case 1: Anastomotic Stenosis

The saphenous vein graft (SVG) was anastomosed to the left circumflex artery. High-frequency echo assessment of graft revealed a reduced peak flow velocity below 10 cm/s, a systolic phase-dominant flow pattern, and a compressed lumen. The anastomosis was revised and signs of patent graft (the triad) were then confirmed such as the “snowman” figure, a diastolic phase-dominant flow pattern, and a peak flow velocity over 30 cm/s. Angiography at the time of discharge showed patent SVG.

37.2.2

Case 2: Supra-anastomotic Stenosis

The left internal thoracic artery (ITA) was anastomosed to the left anterior descending artery (LAD). Immediately after the procedure, echo demonstrated the triad of patent graft. However, an hour after revascularization, graft flow deteriorated to the systolic-dominant pattern. On close inspection, supra-anastomotic stenosis caused by distortion of the LITA due to residual connective tissue on the adventitial surface was found. Resection of the residual connective tissue relieved the stenosis. Echographic findings of the flow pattern were normal thereafter.

37.3

Revascularization of Intramuscular Coronary Artery in OPCAB

Coronary artery occasionally runs deep under the fat tissue and myocardium. It is hard to detect and expose such an intramuscular coronary artery. Some surgeons

warn that it is not suitable for OPCAB and should not be chased too far [1]. For instance, in certain patients with cerebrovascular disease, cardiopulmonary bypass should be avoided. By making the best use of high-frequency echo probe, the intramuscular coronary artery has been identified and revascularized under beating conditions in such patients [2].

In this section, visualization and exposure of the intramyocardial coronary artery with a 15-MHz high-frequency linear transducer is first described. Then the clinical outcome of OPCAB involving this artery using the same method, without sacrificing the quality of the anastomosis, is reviewed

37.3.1

How to Detect an Intramyocardial Coronary Artery

When the distal portion of the target artery can be identified superficially, as is often the case, the echo probe is applied to the distal portion and the artery is traced from distal to proximal target. If the target artery has a branch, of which the distal end is seen, the branch is traced upstream. In the case where the artery has no branch or a distal superficial portion, a luminal structure in the area where the target artery is supposed to be located according to coronary angiography is searched for. To differentiate an artery from a vein, it would be useful to check the flow direction and pattern by Doppler method.

After identifying the target artery and the anastomotic site, a suction-type heart stabilizer is applied to the epicardium so that the anastomotic site is located just between the two arms of the stabilizer. The depth of the target artery from the epicardium is measured to fix the surgeon's aim (Fig. 37.2a). Fat and myocardial tissues are dissected toward the artery using a No. 15 surgical blade. For hemostasis of arterioles or venous

branches, a bipolar rather than a monopolar electrical coagulator is used as the latter sometimes induces ventricular fibrillation. Since a stabilizer often slips and slides subtly to the side due to the heartbeat, the target artery should be repeatedly aimed at using an echo probe during the dissection. Special attention to the right ventricular cavity should be given to prevent perforation. Eventually, the white arterial wall surrounded by the reddish myocardium is reached (Fig. 37.2b). This technique of identifying the coronary artery can also be applied to conventional CABG with intramuscular artery and to redo coronary surgery.

The procedure for anastomosis is generally similar to that for ordinary OPCAB. However, the plane of anastomosis from the stabilizer is deeper so that the coronary artery is stabilized less and the anastomosis is technically more demanding (Fig. 37.2c). The graft might be kinked just above the anastomosis, which is done at the bottom of the excavated myocardium. Thus, the course of the graft should be carefully designed so as not to result in distortion.

37.3.2

Operative Results of OPCAB with Intramuscular Coronary Artery

The clinical outcome and graft function in patients who underwent OPCAB with intramuscular coronary artery are compared with those undergoing OPCAB without intramuscular artery.

From March 2002 to April 2004, 11 patients underwent OPCAB including intramuscular LAD (group I) in our institute. Meanwhile, 32 patients underwent OPCAB without intramuscular coronary artery (group II) during the same period. The 15-MHz high-frequency linear transducer was used to identify the intramuscular artery and to evaluate the graft function. In group I,

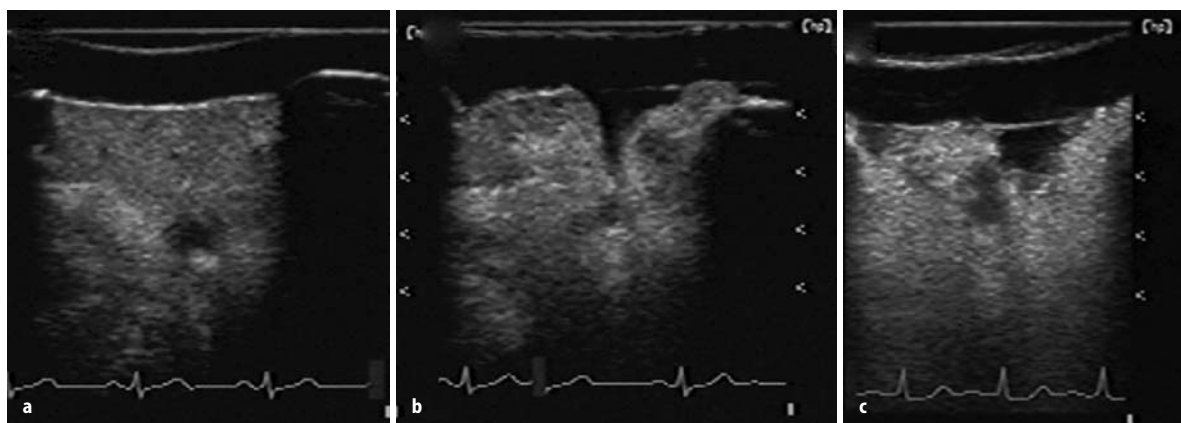


Fig. 37.2. **a** The target coronary artery at a depth of 5 mm from the epicardium is detected under fat and myocardial tissues. **b** The intramuscular coronary artery is exposed using a high-frequency echo. **c** At the bottom of the excavated myocardium, the properly anastomosed graft shows the “snowman” figure

there were nine males and two females; mean age was 69.6 ± 10.1 years. The left ITA was used as a graft for intramuscular LAD in nine patients and the right ITA in two patients. The reason for off-pump CABG was the previous cerebrovascular accident (CVA) in three patients, one each with chronic obstructive pulmonary disease (COPD) and CVA + COPD, and old age in six patients. The depth of the LAD from the epicardial surface was 6.4 ± 1.0 mm. The LAD exposure and anastomosis under the off-pump beating condition were successful in all 11 patients. The mean flow velocity in ITA was 27.4 ± 8.32 cm/s, and flow rate was 38.7 ± 25.5 ml/min. The spectrum of pulse wave Doppler showed the diastolic dominant pattern in all patients. Group II consisted of 29 males and 3 females; mean age was 69.7 ± 9.3 years. The left ITA was anastomosed to LAD in 27 cases and the right ITA in 5 cases. The mean flow velocity in ITA was 25.2 ± 9.45 cm/s, and flow rate was 25.7 ± 9.91 ml/min. A single patient in group II manifested a mean flow velocity below 6 cm/s and a compressed lumen of anastomosis by high-frequency echo. After anastomotic revision, the echo showed a mean velocity of over 20 cm/s and the typical "snowman" profile. The patent ITA was also confirmed by graft angiography 3 weeks after the surgery. No early or hospital deaths were noted in either group. Mediastinitis occurred in one patient of group I. In group II, reexploration for bleeding was necessary in two patients, and another two suffered from respiratory failure due to pneumonia. According to the postoperative angiography performed 3 weeks after surgery, the ITA to the LAD was patent in all 11 patients of group I, as well as the ITA in 13 patients of group II who underwent graft angiography in our institute (100% patency in both groups I and II).

To maintain high graft patency even in OPCAB, in which anastomotic technique is more challenging, several methods have been advocated for intraoperative assessment of graft patency. However, there is no unanimously accepted method. The transit-time flowmetry [3, 4] assesses flow rate and flow pattern conveniently but does not provide any visual image of graft flow. Although novel imaging methods, such as thermal coronary angiography [5] and fluorescent imaging [6, 7], allow visualization of graft flow in the operating room, a coronary artery under epicardial fat tissue or myocardium is detected as a stenosis. No quantitative information of graft flow is offered. The methods are not even cost-effective so that they are not easily accessible for surgeons.

The epicardial Doppler ultrasound technique has been used for more than 15 years [8–10]; however, with a 15-MHz high-frequency transducer, more precise imaging of vessel structure can be offered for coronary revascularization [2]. As the main body of the echo system is equipment usually found in the operating room for transesophageal echography, only the transducer needs to be purchased. The precise visualization of the anatomical shape of anastomosis is the greatest advantage of the high-frequency echo system over the other methods, which enables identification of the intramyocardial artery as described above. Although assessment of anastomosis on the lateral wall is sometimes difficult due to there being limited space for the transducer, the graft flow can be measured in all areas. With the development of new transducers, all anastomoses will be accessible in the near future. In conclusion, we believe the 15-MHz high-frequency echo system is the best method for intraoperative graft evaluation for maintaining a high patency in coronary surgery.

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Role of Venous Grafts in Arterial Grafting

Role of Venous Grafts in Combination with Arterial Grafting

G.-W. HE

38.1 Introduction

Since the first successful coronary artery bypass grafting (CABG) was performed using a saphenous vein graft at the Cleveland Clinic, the saphenous vein has become widely used as a coronary artery bypass graft [1]. From 1968, the internal mammary artery (IMA) became more widely applied as new surgical techniques evolved. Green [2] and Favaloro [3, 4] used a combination of single and bilateral IMA grafting, alone and in combination with saphenous vein grafting (SVG).

However, the patency rates of SVG in the early reports were unsatisfactory. The occlusion rate of SVG in the first year is 10~26% [5, 6]. By 10 years, 50% of grafts are occluded [7–9] and of the grafts still patent, 50% show marked atherosclerotic changes [7].

In contrast, in an early study, the patency of the IMA within 5 years of operation was 97% with only 2% occlusion and 2% stenosis, compared to the patency rate of 82%, 5% stenosis or irregular, and 13% occlusion in SVG [9]. These reports confirmed the superior patency of arterial grafting and promoted the search for arterial conduits other than the IMA.

Most recent reports from large series continuously support the superiority of IMA grafting. A report by Tatoulis and colleagues in Melbourne [10] has clearly shown in 2,127 arterial to coronary conduits over 15 years a LIMA patency at 5 years of 98%, 95% at 10 years, and 88% at 15 years.

On the other hand, the average number of grafts in a patient is 3~4. Although the LIMA has been established as the first choice of the graft for coronary artery, other arterial grafts such as the right IMA, the gastroepiploic artery (GEA), the inferior epigastric artery (IEA), and the radial artery (RA) are routinely used by fewer surgeons. This means that SVG is still widely used in combination with arterial grafts. Recognizing the lower patency of SVG compared to arterial grafts, surgeons are more cautious with the protection of the SVG during harvesting and in the careful choice of the target vessel. A number of techniques have been developed to protect the graft particularly the endothelium of the graft [11]. With these improved techniques, the paten-

cy rate for SVG has been reported to be better than that reported previously. Further, with the most important coronary branch – the LAD grafted by LIMA, the SVG is often grafted to other branches. Under such circumstances, the patient's survival is improved [12]. The role of SVG in the current practice of CABG should therefore be updated.

38.2 Recent Reports on the Long-Term Patency of SVG

Recent studies in the last 5 years have reported that graft occlusion is nearly twofold higher in vein grafts [13]. Brueck and associates [14] reported that the average occlusion/stenosis rates of saphenous vein and LIMA grafts were 43.1% and 14.1%, respectively. In a multivariate analysis, Moderato and colleagues [15] identified saphenous vein grafts as independent predictors for graft occlusion and angina recurrence. Knatterud and associates [16] concluded that patients who had substantial progression of atherosclerosis in vein grafts are at an increased risk for subsequent coronary events and suggested that angiographic changes in vein grafts are appropriate surrogate measures for clinical outcomes.

On the other hand, compared to 30 years ago, the patency of SVG has been improved over the past few decades. In a report by the group of Buxton [17], in a series of total of 1,339 patients with a mean age of 59 years, the mean period from operation to reangiogram was 99 months. The saphenous vein was grafted to the left anterior descending artery in 557 (15%), to the diagonal artery in 669 (18%), to the obtuse marginal artery in 1,300 (35%), to the right coronary artery in 409 (11%), and to the posterior descending artery in 780 (21%) cases. Graft failure was defined as $\geq 80\%$ stenosis. They found that during the course of the study, 2,266 (61%) grafts were patent, and 1,449 (39%) had failed. The patient variables that significantly reduced graft patency were younger age and an ejection fraction $< 30\%$. Operative variables associated with reduced graft patency were small coronary artery diame-

ter, large conduit diameter, and the coronary artery grafted (lowest patency in the right coronary artery and maximum patency in the left anterior descending artery territory). The interval from operation to repeat angiogram (with 78% patent at 1 year, 78% at 5 years, 60% at 10 years, and 50% at 15 years) and the year in which the operation was performed (more recent operations had better patency) significantly affected graft patency. Importantly, they indicated that SVG patency improved over the course of the study. The best results were obtained in older patients with good left ventricular function. Large-caliber arteries on the left system, when grafted with a small-diameter vein, were associated with the best outcome [17].

A new and interesting topic with regard to the patency of the SVG is the comparison between SVG and alternative arterial grafts because results showing that the IMA, particularly the LIMA, is superior to the SVG have been well known for many years now. In a recent study, Buxton and colleagues [18] compared the RA with the SVG in an older group ($n=153$, ≥ 70 years), reporting angiographic and clinical outcome results during the first 5 years. Graft patency estimates were as follows: 0.86 in 24 RAs versus 0.95 in 22 SVGs. Cardiac event-free survival estimates were as follows: 0.84 for RA versus 0.89 for SVG. The 5-year interim results do not support the hypothesis that the RA has superior patency to or is associated with fewer clinical events than free right IMA or SVG [18].

In my own experience, in an angiographic study on mid-term patency of RA grafts in Chinese patients, we studied the patency of IMA, RA, and SVG [11]. There were 131 patients who underwent elective CABG by a single surgeon (myself) [19]. The operative mortality was 1.5% (2/131). There were 109 male and 22 female patients aged 61.5 ± 8.5 years. The average number of grafts was 3.1 per patient. The RA was grafted to left anterior descending (LAD, 33 patients), diagonal (22), intermediate (20), obtuse marginal (OM)1 (30), OM2 (9), right coronary or posterior descending artery (RCA/PDA, 16), or left ventricular branches (1). LIMA was mainly grafted to LAD (86), and SV to obtuse marginal (OM, 83) or right coronary artery (RCA)/posterior descending artery (PDA) (60). Seventy-eight patients (59.5%) had recatheterization at the postoperative day of 210.9 ± 64.3 (42 ~ 532 days). In these patients, the patency was 92% for the LIMA (46/54), 88.4% for the RA (61/69), and 92.3% (84/91) for the SV, respectively ($p=0.67$), and there were no significant differences between any two of these groups (Fisher's exact test: $p=0.28 \sim 0.59$). This study gives evidence that at least at mid-term, the SVG has a comparable patency to RA.

A factor that is thought to be related to the graft patency is diabetes. Schwartz and associates [20] studied the influence of diabetes on the graft patency. Patients with diabetes are more likely than those without to have

small (<1.5 mm) grafted distal vessels (29% vs 22%) and vessels of poor quality (9% vs 6%). On follow-up angiography, 89% of IMA grafts were free of stenoses $\geq 50\%$ among patients with diabetes versus 85% among patients without diabetes. For vein grafts, the corresponding percentages were 71% versus 75% ($p=0.40$). After statistical adjustment, diabetes was unrelated to having a graft stenosis $\geq 50\%$. The authors conclude that despite diabetic patients having smaller distal vessels and vessels judged to be of poorer quality, diabetes does not appear to adversely affect patency of IMA or vein grafts over an average of 4 years follow-up. Previously observed differences in survival between CABG-treated patients with and without diabetes may be largely a result of differential risk of mortality from noncardiac causes.

In comparison to the use of composite arterial grafts using either bilateral IMA or a single IMA and RA, Legare and associates [21] found that use of composite arterial grafting may be associated with an increase in risk-adjusted patient morbidity when compared with a conventional coronary artery bypass grafting with IMA and SVG.

Finally, when the SVG is used for CABG in the aortic dissection patients, the patency rate of vein grafts anastomosed proximally to prosthetic grafts of the ascending aorta and distally to the native coronary arteries is similar to that of conventional CABG using saphenous vein grafts [22].

In summary, the long-term patency of SVG has been confirmed to be inferior to that of IMA grafting even in recent reports. However, the patency of SVG in the last decades has been improved due to technological evolution and other factors. The SVG can still be used as a safe graft, with comparable patency to alternative arterial grafts, or composite arterial grafting.

38.3

Methods to Improve SVG Patency

The major causes for the lower patency of the SVG compared to IMA may involve a few factors. First, as a free graft, the disruption of the vasa vasorum of the venous wall causes ischemia of the vein. This is an unavoidable cause. Second, the SVG almost inevitably goes into vasospasm when taken from the leg due to surgical stimulation. The spastic vein requires distension as the normal procedure to overcome vasospasm and to check leaking from side branches. The distension pressure, which is not normally monitored, may easily go up to 500 mm Hg without the surgeon being aware of it [11], and this high pressure distention has been demonstrated as being damaging to both the endothelium and the smooth muscle of the vein. The damage of the vein causes late occlusion of the graft. This factor becomes

more important during minimally invasive harvesting of the saphenous vein because more surgical manipulation may be involved. In undistended saphenous vein segments isolated from patients undergoing minimally invasive surgical and open techniques of harvesting, there was no acetylcholine-mediated endothelium-dependent relaxation in the minimally invasive surgery group but it exists in the vein taken by the open technique. Therefore harvesting of the saphenous vein through multiple small incisions might result in endothelial dysfunction, possibly caused by traction injury [23].

In order to improve SVG patency, it is essential to perform CABG using the SVG in such a way that the vein structure can be better preserved. In particular, the distension procedure should be improved. This is feasible by gentle manipulation of the vein when it is taken in order to minimize the surgical damage to the vein. Further, the use of proper vasodilators on the vein may improve the preservation of the vein. For example, a mixed VG (verapamil-nitroglycerin) solution used for arterial grafts can also be used to prevent venous spasm, reducing the distension pressure and therefore preserving the endothelium and smooth muscle of the vein [11].

Souza and associates [24] compared the patency of the SVG that was harvested by three different methods. With the conventional method, the vein was stripped, distended, and stored in saline; with the intermediate group, the vein was stripped, local application of papaverine was used instead of distention, and the vessel was then stored in heparinized blood. In the no-touch group, the vein was harvested with the surrounding tissue, not distended, and stored in heparinized blood. The vein graft patency at an average of 18 months was 88.9%, 86.2%, and 95.4%, respectively, and they concluded that preservation of the surrounding tissue of the saphenous vein using this no-touch technique abolishes venospasm intraoperatively and plays an important role in maintaining vein graft function and patency.

Another important factor in the SVG occlusion is anastomosis technique. A perfect anastomosis may improve the patency.

Other technical points are also worth taking into account. For example, in diffuse coronary artery disease, the arteriotomy can be treated by extending over the plaques, with graft patency rates comparable to those of bypass grafts onto less diseased segments [25].

There are new technical innovations including the use of the St. Jude Medical connector. The angiographic patency ranges from 86% [26] to 100% [27]. However, further long-term studies are required to confirm the safety of the St. Jude Medical connector with regard to endothelial function and restenosis.

In addition, fibrin glue effectively prevents overdistension and preserves some distensibility in the high-

pressure range in both the upper and lower leg saphenous vein. This might provide a basis for clinical application of perivenous support [28].

Finally, the major reason for the difference in patency between the SVG and IMA may be the structure differences between arteries and veins. Change of the venous structure to arterial structure by using gene therapy may be the approach of the future. This will be discussed in separate chapters.

38.4

Use of SVG in Combination with Arterial Grafts

Nowadays, it is rare that the SVG is used alone. It is almost always used in combination with arterial grafting; preferably, it is used for those territories that are not grafted with arterial grafts. There is large variation among surgeons as to the target vessel for the vein graft. However, it is almost unanimously accepted that the LIMA is grafted onto the LAD. Therefore, the SVG is grafted onto either the diagonal, obtuse marginal (or ramus marginalis), or RCA, depending on the use of the second arterial graft by the surgeon.

38.5

Use of SVG in Minimally Invasive CABG

Use of the SVG in minimally invasive CABG involves two issues – minimally invasive harvesting of the vein and use of SVG in minimally invasive CABG such as on beating heart. As mentioned above, the preservation of the endothelium of the SVG in minimally invasive harvesting is particularly important due to the usually greater manipulation of the vein during this procedure.

In off-pump coronary artery bypass grafting (OP-CAB), the quality of surgical revascularization, which showed favorable initial results, has been frequently questioned. In a recent study [29], with a mean period of angiography of 50.1 ± 22.6 months (range, 22–83 months), the occlusion rate for SVG was 19.4% at anastomosis and the rate of stenosis at the anastomotic site was 8.3%. This of course needs further investigation.

38.6

Surgical Strategy and Technique for the Use of SVG

38.6.1

Selection of Conduits

The choice of conduit largely depends on factors discussed in other chapters of this book, whereas this chapter focuses on the use of SVG. As the LIMA is al-

most always grafted onto the LAD, the rest of the targeting vessels are subjected to the surgeon's preference as to what conduit is selected. When the RA or GEA is selected to be grafted to the diagonal, or RCA, the SVG may be grafted to the obtuse marginal artery. Under other circumstances, the SVG may be grafted to the diagonal or RCA.

38.6.2

Harvesting of SVG

The open technique of harvesting the SVG was the standard method for many years until the minimally invasive technique became popular. An endoscopic harvesting method is popular in the developed countries, particularly in the United States. The method is described in detail in another chapter. The method only requires one small incision on the leg. However, there are two points that should be kept in mind. First, as mentioned before, the manipulation on the vein is usually more than with the open technique so that particular attention should be paid to the protection of the vein; second, this method is costly because it uses a disposable device. An economic and safe way to take the SVG is by using multiple small incisions on the leg under a reusable lighting retractor or without any specific equipment as in our practice. We only use a long thyroid retractor to expose the vein by multiple incisions and this economical method works well. The vein is usually exposed and vasodilator solutions such as verapamil-nitroglycerin (VG) solution may be used topically to prevent vasospasm. The side branches are identified and tied by 0 silk. The required vein is taken out and gently distended by heparinized Ringer's or VG solution. The side branches are checked and tied again if necessary. Metal clips may be used to reinforce the tie of the branch. The vein is stored in the above solution for later use. Careful hemostasis is performed in the leg wound, which is then closed by layers. A drain may be needed if oozing is significant.

38.6.3

Myocardial Preservation

In conventional CABG, blood cardioplegia is always the choice and details are given in a separate chapter in this book. In OPCAB, although there is no requirement, it may become necessary to convert into conventional CABG in a small number of patients in whom cardioplegia has become necessary.

38.6.4

Left Ventricular Venting

In order to prevent left ventricular distention and to provide a bloodless field during the distal anastomosis,

left ventricular venting is always used in conventional CABG in our practice.

Although many methods of left ventricular venting have been described including venting through the apex, the left atrium, pulmonary artery, or aorta, we hold that the effective and simple way is by venting the left atrium through the right superior pulmonary vein.

38.6.5

Operative Technique

In conventional CABG, the operative technique follows the methods which have matured over the past few decades and are well documented in a number of textbooks. The heart is arrested and the distal anastomosis is performed first. The sequence for anastomosis is usually RCA-OM-ramus marginalis-diagonal, and LAD. In our practice, the vein graft is used for anywhere but the LAD. The RA graft is preferably used for either the diagonal or ramus marginalis. We perform the SVG grafting first, usually for one or two coronary branches, for example, RCA and then OM. The RA is then grafted to the ramus marginalis or diagonal. Finally, the LIMA is grafted to LAD. The heart is then deaired and the cross clamp is released. When the heart is resuscitated, a side-bite clamp is placed on the aorta and a 4-mm punch is used to make holes for the SVG and a 3.5-mm punch is used for the RA anastomosis. All the grafts are anastomosed to the aorta directly and separately. When the anastomoses are completed, the grafts are deaired and the side-bite clamp is released. Cardiopulmonary bypass is then ceased and the heart is decannulated.

A usual technique for the distal anastomosis of a vein graft to the OM is described below.

The heart is retracted by hand, with the apex toward the patient's right shoulder. The epicardium is incised and the artery is exposed. If the OM is submyocardial, the location is usually indicated by a groove in the myocardial surface with a light streak [30]. The artery can either be seen or palpated by finger at the atrioventricular groove before it goes into the myocardium, and this helps to identify the submyocardial artery.

Once the artery is allocated, the epicardium is incised with a No. 15 blade to fully expose the front of the artery. A diamond knife is then used to make a longitudinal incision on the front wall. The length of the incision is important and should be adequate for the size of the prepared SVG. A 7-0 Prolene stitch is taken through the vein first, from outside (Fig. 38.1) with the other end tagged, through the artery from inside (Fig. 38.2) and continuously running in this way. After a few loops, the vein is lowered into place and the suture line is continuous to the toe of the vein, around the toe, and towards the heel of the vein at the left side, and tied with the other end to complete the anastomosis.

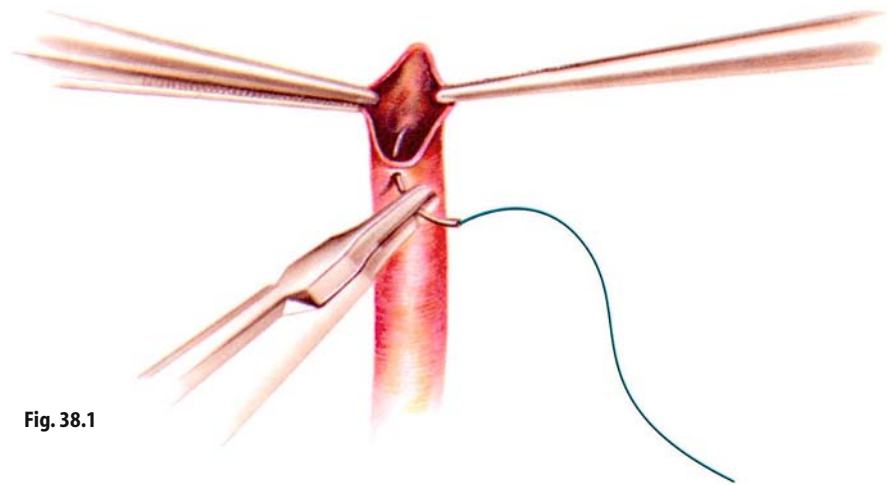


Fig. 38.1

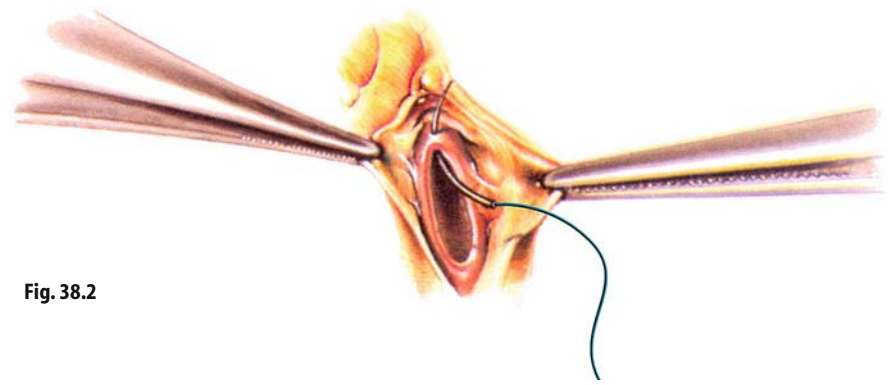


Fig. 38.2

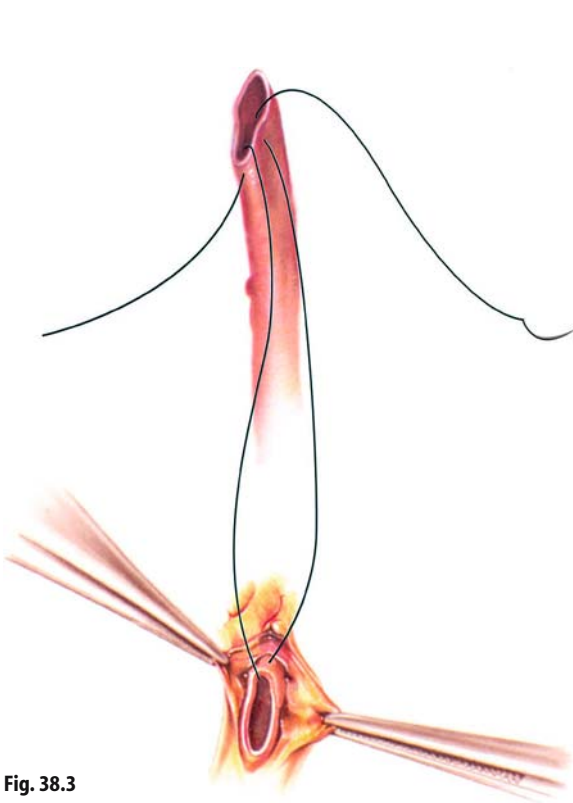


Fig. 38.3

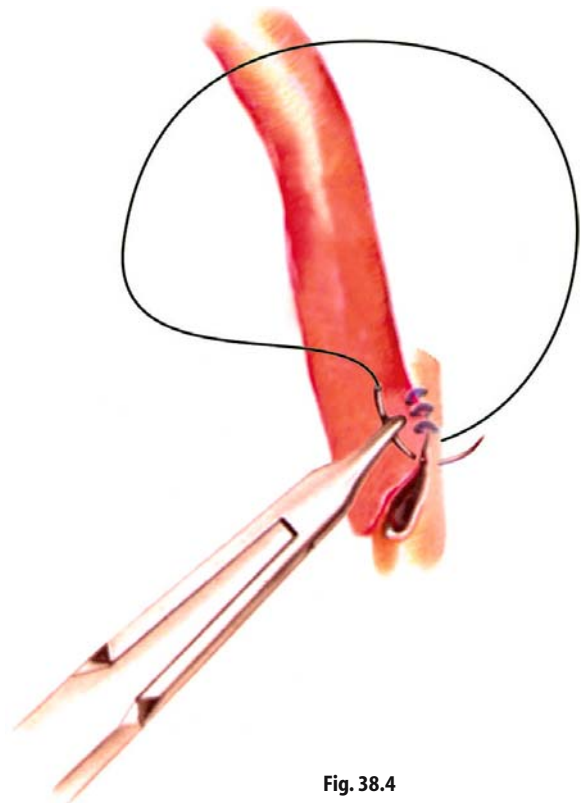


Fig. 38.4

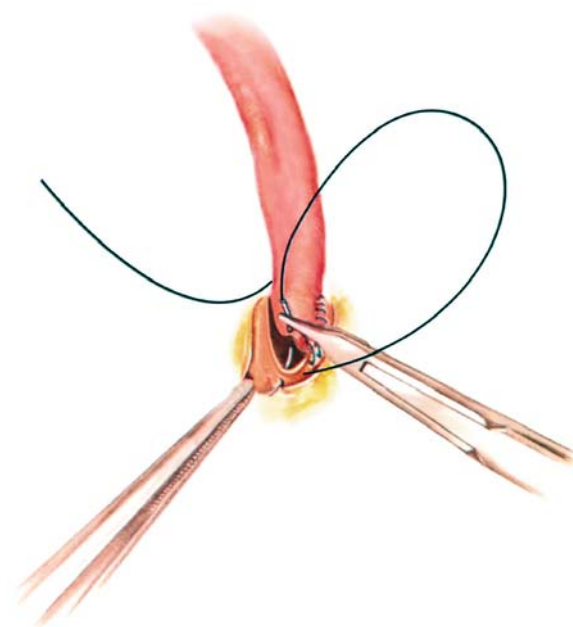


Fig. 38.5

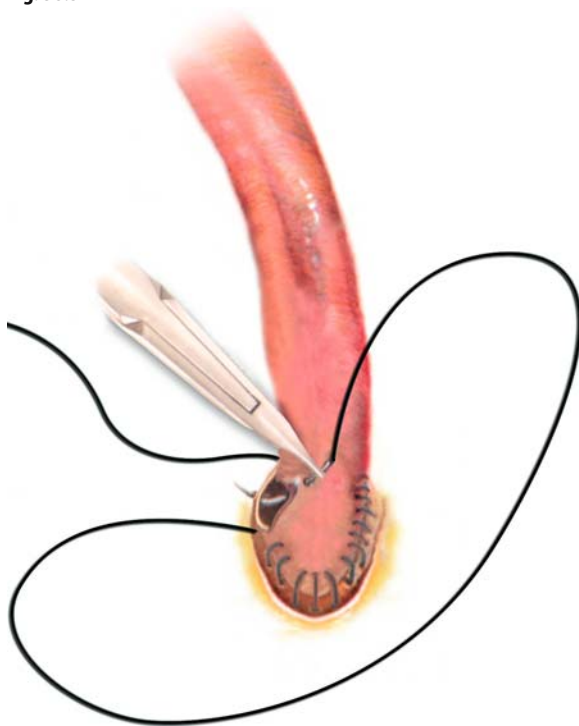


Fig. 38.6

After the anastomosis for all free grafts, the LIMA is grafted to the LAD. The technique is described in the other chapters.

The proximal anastomosis between the SVG and the ascending aorta follows the usual practice with a side-bite clamp on. 6-0 Prolene is used for the anastomosis. We prefer a separate anastomosis for each free graft, either for the SVG, or for the RA.

Acknowledgement. The artistic work in preparation of figures by Miss Maggie Wong is gratefully acknowledged.

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39 Minimally Invasive Saphenous Vein Harvesting for Coronary Artery Bypass Grafting

M.S. SLATER

39.1 Introduction

Despite the steadily increasing use of arterial grafts, the greater saphenous vein remains the most commonly used conduit for coronary artery bypass grafting (CABG). Utilized sporadically in the late 1950s and early 1960s, saphenous vein use for coronary artery bypass grafting increased exponentially in the 1970s and 1980s.

Patency rates following coronary bypass grafting using saphenous vein have been reported to be 78 %, 65 %, and 57 % at 1, 5, and 10 years respectively [1]. The saphenous vein has been proven versatile, has provided reliable results, and remains central to the conduct of surgical revascularization of the heart.

Traditionally, the greater saphenous vein has been harvested via a continuous or near continuous incision on the medial aspect of the lower extremity [2]. This approach is attractive in several ways as it provides excellent exposure, is rapid, does not require specialized equipment, and can be carried out by team members with basic surgical skills such as physician's assistants and surgical trainees. Unfortunately, complications such as wound infections and seromas are frequently associated with the long incisions required for the open technique. Wound infection rates from 14 % to 26 % have been reported [3–5] and overall complication rates as high as 43 % have been described [6]. Co-morbidities such as obesity, peripheral vascular disease, and diabetes are all associated with increased wound complication rates and are prevalent in this patient population. The high rate of complications associated with lower extremity vein harvest incisions is not unexpected given the debilitated, aging population of patients currently undergoing coronary artery bypass surgery.

The highly varied rates of complications reported in studies of saphenous vein harvest may be explained by differing definitions of complications, duration and quality of follow-up, and variations in patient population and surgical technique. Because the majority of complications related to lower extremity harvest incisions develop after hospital discharge, studies without

Table 39.1. Complications related to saphenous vein harvest

Infection
Superficial
Deep
Hematoma
Seroma
Lymphedema
Delayed mobility
Deep venous thrombosis (DVT)
Neurological
Pain
Numbness

formal follow-up often underestimate wound complications. The high complication rate associated with saphenous vein harvest and the growing trend to less invasive surgical techniques has motivated cardiac surgical teams to explore ways of minimizing the morbidity associated with traditional saphenous vein harvest. Endoscopic vein harvest was reported by Lumsden in 1994 [7] and has slowly gained acceptance in the practice of cardiac surgery. This chapter will outline the techniques, benefits, and limitations of minimally invasive vein harvest techniques for use in coronary artery bypass surgery (Table 39.1).

39.2 Minimally Invasive Techniques for Saphenous Vein Harvest

Although a myriad of techniques for the less invasive harvesting of saphenous veins have been proposed [8], most approaches can be divided into endoscopic and non-endoscopic techniques. Non-endoscopic techniques utilize a series of smaller incisions over the length of the saphenous vein. Exposure may be facilitated by lighted retractors, some designed specifically for this purpose such as the SaflITE retractor system (Genzyme Surgical Products, Cambridge, MA, USA) [9]. Additionally, anchored retractor arms have been employed to facilitate vein harvest.

Non-endoscopic techniques offer several advantages compared to both conventional and endoscopic approaches. Non-endoscopic techniques require little if any specialized equipment and are therefore associated with minimal start-up costs. Personnel familiar with standard surgical techniques can be taught to harvest saphenous vein utilizing the open technique. Compared to traditional techniques, significant reductions in wound complications have been reported using more minimally invasive techniques [4, 5, 10–12]. This reduction in wound complications has been primarily attributed to the reduction in incision length and the preservation of skin bridges.

Endoscopic vein harvest techniques take advantage of the technological developments and surgical skills that have emerged from the rapidly evolving field of laparoscopic surgery and apply them to vein harvest. Although several commercially available systems exist they share several similarities. A small incision is made and the saphenous vein is located. The camera system is introduced and a working space is created, most commonly with the insufflation of CO₂. The vein is then dissected free, side-branches are divided either with clips, bipolar electrocautery (or alternative energy source), and the vein is extracted.

Endoscopic vein harvest offers the potential to dramatically reduce incision length and thereby provide superior cosmetic results; often the entire saphenous vein can be harvested with only a single 2-cm incision near the knee and puncture incisions near the groin and ankle. Marked reductions in both incisional pain and wound complications have been reported and patient satisfaction is high with this technique [5, 10, 13].

In addition to reductions in wound complications, minimally invasive saphenous vein harvest techniques have been associated with more rapid mobilization of patients and decreased length of hospital stay [14]. Patel and colleagues conducted a prospective non-randomized study comparing open and endoscopic vein harvest in a cohort of 200 patients undergoing coronary artery bypass grafting. They were able to demonstrate a reduction in mean days to ambulation from 2.3 to 1.4 days ($p < 0.05$) and a corresponding reduction in length of stay from 4.8 to 3.3 days ($p < 0.05$).

Reductions in leg pain [11, 15] and improved cosmetic outcomes have been reported using minimally invasive approaches to saphenous vein harvest. Kiaii was able to demonstrate a statistically significant reduction in leg discomfort at discharge but this difference was no longer significant at 6 weeks. A similar improvement in cosmesis was noted at discharge, but again lost significance at 6 weeks [5].

Two meta-analyses by Athanasiou and colleagues have demonstrated reductions in both infectious and non-infectious complications by using minimally invasive techniques of saphenous vein harvest. They ana-

Table 39.2. Minimally invasive vein harvesting techniques

Non-endoscopic (direct visualization)
“Skip” incisions
Lighted retractor systems
Self-retaining retractor systems
Endoscopic
Insufflation techniques (CO ₂)
Non-insufflation techniques

lyzed 14 prospective randomized trials of vein harvest between 1962 and 2002. They found that compared to conventional open techniques, minimally invasive vein harvest was associated with an odds ratio of 0.22 (CI 0.14–0.34) with regard to wound infections and an odds ratio of 0.24 (CI 0.16–0.38) with regard to non-infectious wound complications. The authors suggest that the use of minimally invasive techniques of saphenous vein harvest for coronary artery bypass surgery offer the potential to reduce both infectious and non-infectious lower extremity complications significantly [8, 13]. Additionally, the authors propose that cost savings are possible with the use of minimally invasive harvest techniques. The cost savings derived from the expected reductions in length of stay and a reduction in complications requiring additional treatment (Table 39.2).

39.3

Limitations of Endoscopic Vein Harvest

Endoscopic vein harvest has several drawbacks; it represents an entirely new technique compared with traditional harvest and has a significant learning curve. Various authors have estimated that between 5 and 30 cases are required to gain proficiency [14, 15]. Some authors have reported longer harvest times with endoscopic technique but this has not been a consistent finding. Additionally, the learning curve associated with minimally invasive techniques, especially endoscopic techniques, is considerable. However, the time-savings associated with closing the small incisions used with the endoscopic technique have resulted in shorter overall harvest/closure times in some studies [15]. It is important to realize that time spent by the entire surgical team waiting for conduit is not directly comparable to the time spent closing lower extremity incisions while other components of the operation proceed in parallel. Overall, once the learning curve has been overcome, endoscopic vein harvest does not interfere with the conduct of coronary revascularization.

Equipment for endoscopic vein harvest is expensive; laparoscopic cameras, monitors, and insufflators are required and disposable equipment costs can be high. The placement of the requisite endoscopic equipment

into the operating theater can require rearrangement of the existing operative setup. Some costs can be defrayed if endoscopic equipment is already available. However, it is important that endoscopic equipment is readily available for use by the cardiac surgery team. This often requires equipment that is dedicated to the cardiac surgery team.

39.3.1

Vein Quality

Because visualization is not direct and tactile feedback is limited with minimally invasive vein harvesting techniques (particularly endoscopic techniques), concerns relative to vein quality have emerged. Obviously, conduit quality cannot be compromised in coronary artery bypass grafting if excellent outcomes are to be maintained. Studies assessing the quality of vein harvested by non-endoscopic minimally invasive techniques have demonstrated equivalence; Black and colleagues evaluated the effects of minimally invasive vein harvest (Saf-LITE lighted retractor system) on endothelial and smooth muscle harvest. They were unable to demonstrate any differences in either smooth muscle or endothelial function between veins harvested traditionally and those harvested with the minimally invasive technique [16]. Crouch and colleagues studied segments of saphenous vein harvested by both traditional and endoscopic techniques. They were also unable to demonstrate any adverse effect of endoscopic harvest from a histological perspective. Other authors have confirmed these results [5] and it appears that minimally invasive vein harvest does not result in increased histological injury to the saphenous vein [3].

Studies evaluating the durability of saphenous vein harvested endoscopically for coronary artery bypass grafting have also been encouraging [17]. In a prospective, randomized study, Perrault and colleagues demonstrated equivalent vein graft patency rates of 85.2% and 84.4% using open and endoscopic techniques respectively. Additionally, significant stenosis (>50%) was seen in 3.7% of the veins harvested with the open technique and 0% of veins harvested endoscopically [18]. This study utilized angiographic follow-up a mean of 3 months after surgery to assess patency. To date studies have been unable to demonstrate inferior vein quality associated with minimally invasive vein harvest techniques.

39.3.2

Harvest Time

Time required to harvest vein by endoscopic techniques has been reported to be prolonged relative to traditional open techniques. The differential in harvest times is somewhat offset by the reduction in closing

time associated with minimally invasive techniques, particularly endoscopic approaches [10]. Some authors have even reported *faster* harvest times utilizing the endoscopic technique [5] while others have reported essentially identical total operative times with both techniques [4, 15].

39.3.3

Carbon Dioxide Toxicity

The use of CO₂ insufflation can produce elevated levels of CO₂ in the bloodstream [19], which can be problematic in patients with impaired pulmonary and cardiovascular function. The safety of CO₂ insufflation has been extensively researched in relation to laparoscopic abdominal procedures. Pneumoperitoneum with CO₂ has been documented to decrease venous return, increase end-tidal CO₂ (ETCO₂), and adversely effect cardiac hemodynamics.

The effects of CO₂ insufflation in the lower extremity during minimally invasive saphenous vein harvest have not been well studied. Patients undergoing CABG differ from those patients undergoing laparoscopic procedures in several important ways that affect both the accumulation and sequelae of CO₂ insufflation. First, patients undergoing cardiovascular procedures often have decreased ventricular performance. Although the direct compressive effects of pneumoperitoneum are absent in this instance, CO₂ absorption from the leg occurs and the anesthesia team must anticipate the effects of elevated PaCO₂. Additionally, saphenous vein harvest is often undertaken simultaneously with IMA harvest, which is often facilitated by the lowering of ventilation volumes. This decrease in ventilation can accelerate the rise in PaCO₂ and must be monitored with either ETCO₂ devices or frequent blood gases.

Despite the above observations and the potential adverse effects of increased PaCO₂ during saphenous vein harvest, we have not observed any morbidity directly attributable to high PaCO₂ levels. End tidal CO₂ monitoring is routinely used at our institution. When PaCO₂ levels are noted to be increasing, either ventilation volumes are restored or endoscopic saphenous vein harvest is briefly postponed and the tunnel deflated.

39.3.4

Lower Extremity Hematoma

Hematoma in the vein harvest tunnel represents an additional area of potential concern. The combination of indirect visualization, anticoagulation, and a large potential space created by dissection in the thigh can all contribute to the formation of hematomas. Although we observed hematomas early in our experience, we have subsequently avoided this complication with two simple modifications to the vein harvest technique.

First, the legs are wrapped with elastic bandages at the conclusion of vein harvesting. Second, closure of the vein harvest incisions is deferred until anticoagulation is reversed. After closure the legs are again wrapped with elastic compression bandages.

39.3.5

Cost

Cost has been another criticism of endoscopic vein harvest. The initial investment in endoscopic equipment, disposables, training and the increase in operative time during the “learning curve” all reflect early “up-front” costs. However, the reduction in lower extremity wound complications actually results in a net *decrease* in hospital costs overall. Illig and colleagues were able to demonstrate a cost savings of \$1,200 per procedure during hospitalization and this figure rose to \$2,200 per procedure overall when the cost of readmission for leg wound infection was included [20]. The cost savings in this instance were attributed to shorter length of stay, decreased rates of wound infections, and a reduction in the need for readmission. Decreased length of stay has been reported by others [14] and the potential to reduce overall costs has been projected in both meta-analyses conducted by Athanasiou and colleagues [8, 13].

39.4

Evolution and Technique of Endoscopic Technique at Our Institution

At our institution we have used the VasoView (Guidant Co., Indianapolis, IN, USA) endoscopic vein harvesting system for the last 5 years. We transitioned from traditional open technique to skip incisions and briefly used a lighted retractor system (SaphLITE) before electing to move to a completely endoscopic system. We currently attempt endoscopic vein harvest on all patients undergoing CABG in whom we anticipate using saphenous vein grafts. We convert to open technique when the saphenous vein is unable to be located at the knee, the vein is too small or is a “dual system” or the quality is difficult to assess endoscopically. We rarely convert to open technique because of patient size (obesity) and have in fact observed the greatest benefit in the patients with large lower extremities and those with lower extremity vascular disease (both arterial and venous). In diabetic patients with advanced lower extremity arterial vascular disease and those with venous stasis ulcers we often perform endoscopic vein harvest on both thighs rather than instrumenting the lower extremity below the knee. The need to harvest vein far below the knee has become uncommon as we frequently employ arterial conduits (predominantly LIMA and radial ar-

tery) for coronary revascularization. With this approach usually only two remaining coronary targets require saphenous vein to be harvested and this is easily accomplished utilizing vein harvested from the thigh.

As in all surgical techniques, patient positioning is critical. We have found it useful to place rolled towels behind the knees to facilitate exposure and aid in locating the saphenous vein medial to the knee. Video monitor position is also critical, especially as the transition to endoscopic technique is being made. It is important that the individual harvesting the saphenous vein endoscopically does not “work against themselves” and has both the monitor and the operative field in front of them.

To help locate the saphenous vein near the knee we frequently utilize either preoperative vein mapping or a small portable ultrasound machine in the operating room just prior to surgery. This technique allows for precise placement of incisions directly over the vein. Ultrasound visualization by either method also provides a rough estimate of vein size and quality and helps to determine which leg to harvest from. Modification of the operative setup and changes in patient orientation within the operative suite may be required to facilitate endoscopic vein harvest. Endoscopic procedures are equipment dependent and endoscopic vein harvest is no exception. Cameras, monitors, lighting, and insufflators all must work well to facilitate timely recovery of undamaged vein. Poor visualization will result in frustration and injury to the conduit. We have elected to purchase and maintain a equipment set dedicated to endoscopic vein harvest and this has proven to be a worthwhile investment.

We do not administer the complete “pump dose” of heparin until the vein has been extracted from the harvest tunnel. Initially, we used no heparin during endoscopic vein harvest but noted small amounts of clot in the vein after extraction and subsequently now administer 5,000 units of heparin prior to CO₂ insufflation. CO₂ insufflation is maintained at 10–14 mmHg and end-tidal CO₂ monitoring is carried out on all cases. Since our transition to endoscopic vein harvest we have observed a dramatic reduction in both infectious and non-infectious lower extremity complications.

39.5

Conclusion

Traditional saphenous vein harvest through long lower extremity incisions has been associated with significant morbidity. Multiple studies have demonstrated a reduction in wound complications when minimally invasive vein harvest techniques are used and the safety of this technique has been confirmed. Histological analysis has failed to demonstrate an increase in vein

Table 39.3. Comparison of vein harvest techniques

Technique	Learning curve	Ease	Equipment cost	Speed	Wound complications	Vein quality	Patient satisfaction
Traditional (open)	None	Easy	Low	Rapid	High	Good	Low
Skip incisions	Small	Intermediate	Low	Intermediate	?	Good	Intermediate
Minimally invasive, non-endoscopic	Significant	Intermediate	Intermediate	Slow initially, equivalent to open after learning curve	Low	Good	High
Minimally invasive, endoscopic	Significant	Difficult, significant learning curve	High	Slow initially, equivalent to open after learning curve	Low	Good	High

injury with endoscopic technique and outcome studies have produced equivalent patency rates for saphenous veins harvested by traditional and endoscopic techniques. Additionally, patient satisfaction is high, post-operative pain scores are reduced, and costs may be reduced with this technique. Although a commitment of both time and money is required to transition to more minimally invasive techniques for saphenous vein harvest, the end result is improved clinical outcomes (Table 39.3).

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Novel Strategies for the Prevention of Vein Graft Failure

S. WAN, A.P.C. YIM, G.D. ANGELINI, J.Y. JEREMY

40.1 Introduction

Autologous saphenous vein continues to be the most widely used conduit for coronary artery bypass grafting (CABG) worldwide. However, early vein graft failure due to thrombosis occurs in as many as 18% of cases within the first postoperative week [1, 2]. Up to 50% of the patients may require reoperation by 10 years after CABG to alleviate symptoms and treat graft occlusion [1, 2]. Vein graft thickening (increased medial thickening and neointima formation) is the main cause of late failure [3], a process mediated by the proliferation and migration of vascular smooth muscle cells (Fig. 40.1). Superimposed on neointima formation is atherogenesis, which ultimately leads to plaque rupture and graft occlusion [1, 2]. Apart from lipid lowering therapy [4], no intervention has hitherto proved clinically effective in preventing late vein graft failure [5]. This clearly constitutes a major clinical and economic problem that needs to be urgently resolved.

The pathophysiology of vein graft failure is complex, involving disparate factors that include adhesion of

platelets and leukocytes, rheological forces, metalloproteinase expression, proliferation and migration of vascular smooth muscle cells, neointima formation and oxidative stress. In this chapter, we will briefly summarize the diverse etiology of vein graft disease and then consider novel approaches to prevent late vein graft failure which include external sheaths, the endothelin-1_A (ET_A) receptor antagonists, nitric oxide (NO) donating aspirin, cytostatic drugs and antioxidants.

40.2 Mechanisms Underlying Neointima Formation, Graft Thickening and Atherogenesis

Implantation of saphenous veins for bypass surgery results in removal of the endothelium and immediate adhesion of platelets and leukocytes, which precipitate not only acute thrombosis but also trigger neointima formation [6] (Fig. 40.2). Endothelial removal also results in the loss of vasculoprotective systems that prevent inflammation and thrombosis, these principally being NO and prostacyclin [7, 8]. NO and prostacyclin

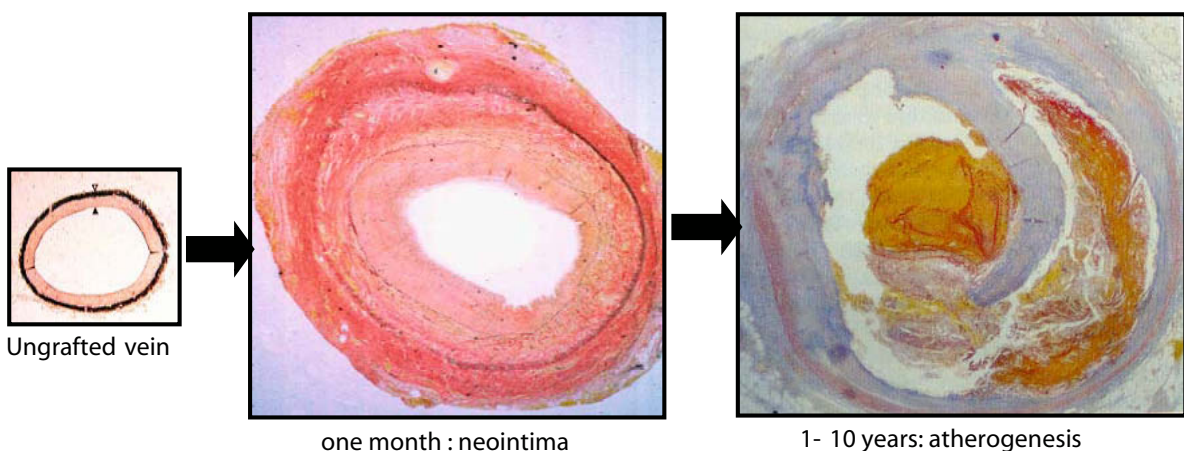


Fig. 40.1. Saphenous vein graft disease. Within 1 month after implantation, the saphenous vein graft has thickened markedly and a new layer of cells, the neointima, has formed. This process involves the proliferation and migration of vascular smooth muscle cells, the expression of peptide growth factors, remodeling by metalloproteinases and deposition of matrix proteins. The neointima renders the graft susceptible to atherogenesis, macrophages infiltrating this layer to develop into the foam cell and then a plaque, such that as many as 50% of grafts may occlude within 10 years after the procedure (see Fig. 40.2)

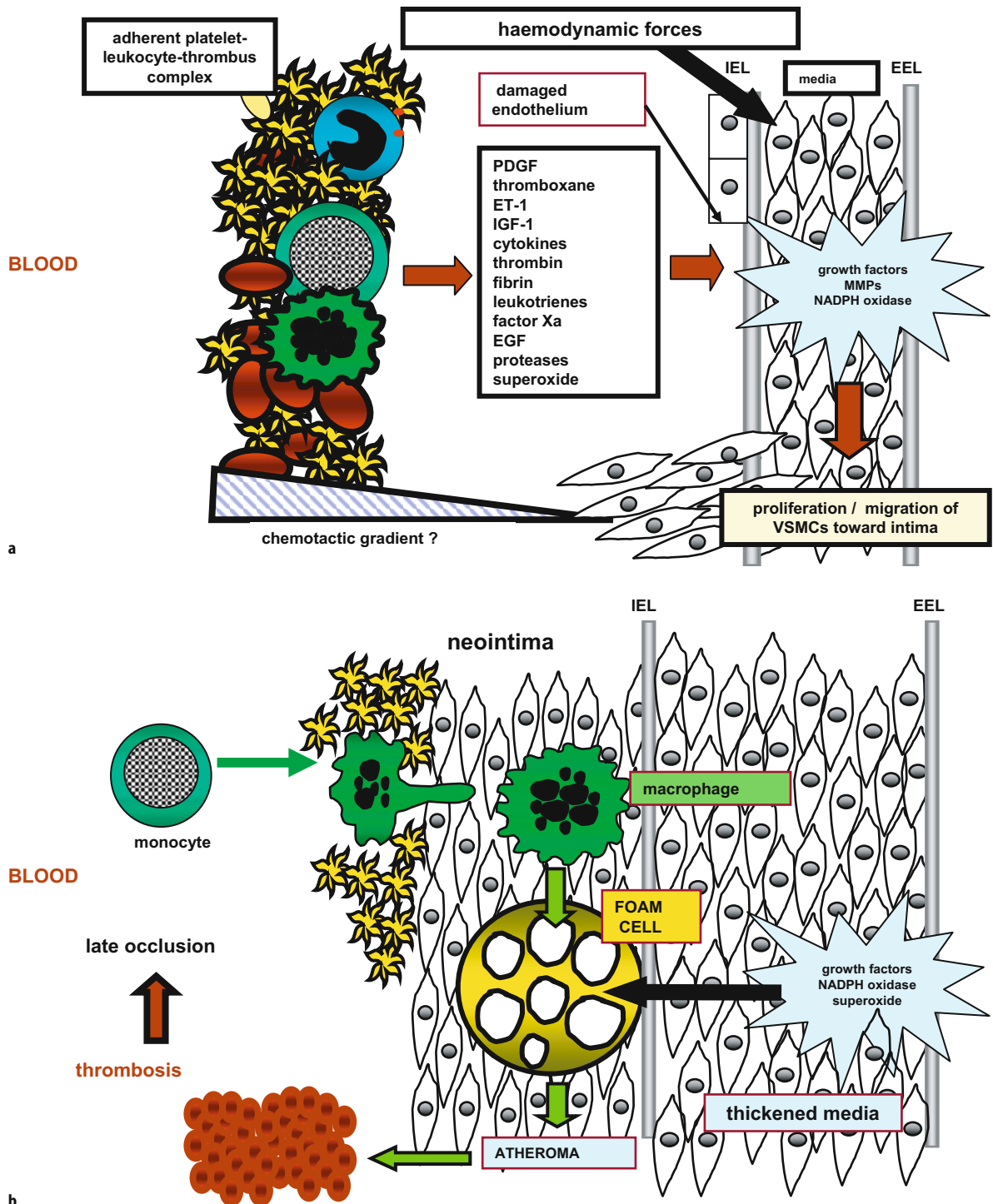


Fig. 40.2. Principal events leading to neointima formation and late vein graft failure. **a** Early triggers for neointima formation are immediate denudation of the endothelium resulting in adhesion of blood cells which release a battery of factors triggering the events that lead to the proliferation and migration of vascular smooth muscle cells. These include the endogenous expression of peptide growth factors, metalloproteinase activation and oxidative stress. Hemodynamic forces also promote the process simultaneously. **b** Once the neointima has formed, monocytes infiltrate the layer and become resident macrophages, the progenitor of the foam cell. This in turn is the epicenter of the atherosclerotic plaques, which ultimately result in late vein graft failure

inhibit blood cell adhesion, vascular smooth muscle cell proliferation and migration, metalloproteinase expression, proteoglycan synthesis, tissue plasminogen activator release and cholesterol metabolism [7, 8]. The NO-cGMP and prostacyclin-cAMP axes at the medial level are also impaired in vein grafts [9, 10]. Endothelial cells proliferate and migrate to “reline” vein grafts, complete coverage occurring within 1–2 weeks [11]. It has been suggested that the accelerated reendothelialization in vein grafts can reduce both thrombogenicity and neointima formation [12].

The adhesion of leukocytes to vascular cells, each other and platelets is mediated principally by the selectins, intracellular adhesion molecule, and vascular endothelial cell adhesion molecule [6]. In turn, a causal link between adhesion molecule expression and neointima formation has been demonstrated [13]. Vein graft surgery is associated with an increased expression of adhesion molecules [13]. Monocyte adhesion is another early event [13]. Monocytes then infiltrate the neointima and become resident macrophages which become the foam cells, the epicenter of an atherosclerotic plaque, a process that results ultimately in vein graft failure [13].

Following implantation, the vein graft is immediately subjected to arterial pressure, increased wall tension, shear stress and pulsatile blood flow [14]. These are all associated with an increase in the expression of growth factors, adhesion molecule expression and proliferation. The process of vein graft remodeling also intrinsically alters intragraft hemodynamics. The asymmetric hyperplasia of the graft may also promote aberrant and chaotic blood flow patterns which in turn promote platelet and leukocyte adhesion, thrombosis and graft hyperplasia [13].

Peptide growth factors are expressed in vein grafts and include ET-1, platelet derived growth factor, and fibroblast growth factor promoting the proliferation and migration of vascular smooth muscle cells [13], all of which are induced in vein grafts by hemodynamic forces, platelet and leukocyte release substances [13]. Vascular smooth muscle cells are surrounded and embedded in the extracellular matrix proteins, such as collagens and elastin, which act as a scaffold for cell and tissue architecture [15] and exert an inhibitory influence on vascular smooth muscle cell proliferation *in situ* [15]. In vein grafts, the extracellular matrix protein is “dissolved” by metalloproteinases, which allows vascular smooth muscle cells to migrate to the intima to form the neointima [15]. Upregulation and activation of certain metalloproteinases has been implicated in negative vein graft remodeling [15].

Superoxide (O_2^-) derived from NADPH oxidase is an important pathological component of vein graft pathobiology [16, 17]. O_2^- promotes vascular smooth muscle cell proliferation and migration and upregulates metal-

loproteinases [16, 17]. O_2^- also reacts with NO (reducing NO bioavailability), which is itself associated with vein graft disease [16, 17]. NADPH oxidase is rapidly expressed in vein grafts, which in turn is upregulated by platelet and leukocyte release substances [18–20].

Hypoxia appears to play a key role in mediating vein graft disease. Surgical removal of the saphenous vein, *ipso facto*, results in a loss of continuity of the vasa vasorum, a microvessel complex that infiltrates and oxygenates large blood vessels which in turn would result in hypoxia of the tissue [21–23]. Since the vein graft thickens rapidly, the graft is probably subject to an increase in oxygen demand which may also increase hypoxia. Hypoxia promotes O_2^- formation via activation of NADPH oxidase, xanthine oxidase and mitochondrial respiratory chain [16, 17] and rapidly induces the expression of NADPH oxidase and an increase in O_2^- formation in pulmonary arteries [24].

40.3

External Dacron Stents and Biodegradable Sheaths

In a porcine model, placement of a porous, non-restrictive, external, polyester Dacron stent around saphenous vein-carotid interposition graft significantly reduced neointima formation and total wall thickness at both 1 and 6 months after implantation [25, 26]. In order for the external polyester stent to prevent neointimal thickening, it had to be loose-fitting [27, 28] and macroporous [29]. Tight-fitting external stents may even exacerbate neointima formation or graft thickening [26]. With the loose-fitting polyester stent, the space between the graft and the stent becomes organized into a cell-rich “neoadventitia”, abundant with microvessels following entrapment of fibrin rich exudates (Fig. 40.3). Loose fitting PTFE (microporous) stents not only promote neointimal and medial thickening, but also prevent microvessel formation [29]. Porosity may be crucial since it allows the microvessels that form in the neoadventitia to connect with the vasculature outside the stent, allowing a fully integrated blood flow to the graft.

Since the external Dacron stent blocks neointima formation in vein grafts within the first month after implantation, long-term support with a prosthetic sheath may not be necessary. One possible means of avoiding these complications is to employ an absorbable external sheath that remains intact for at least 1 month and then is subsequently biodegraded. We therefore studied an external polyglactin (Vicryl, Vascutek Ltd.) sheath which matched the structure and dimension of the original polyester Dacron external stent. Polyglactin is hydrolyzed by macrophages between 60 and 90 days [26]. The polyglactin sheath reduced porcine

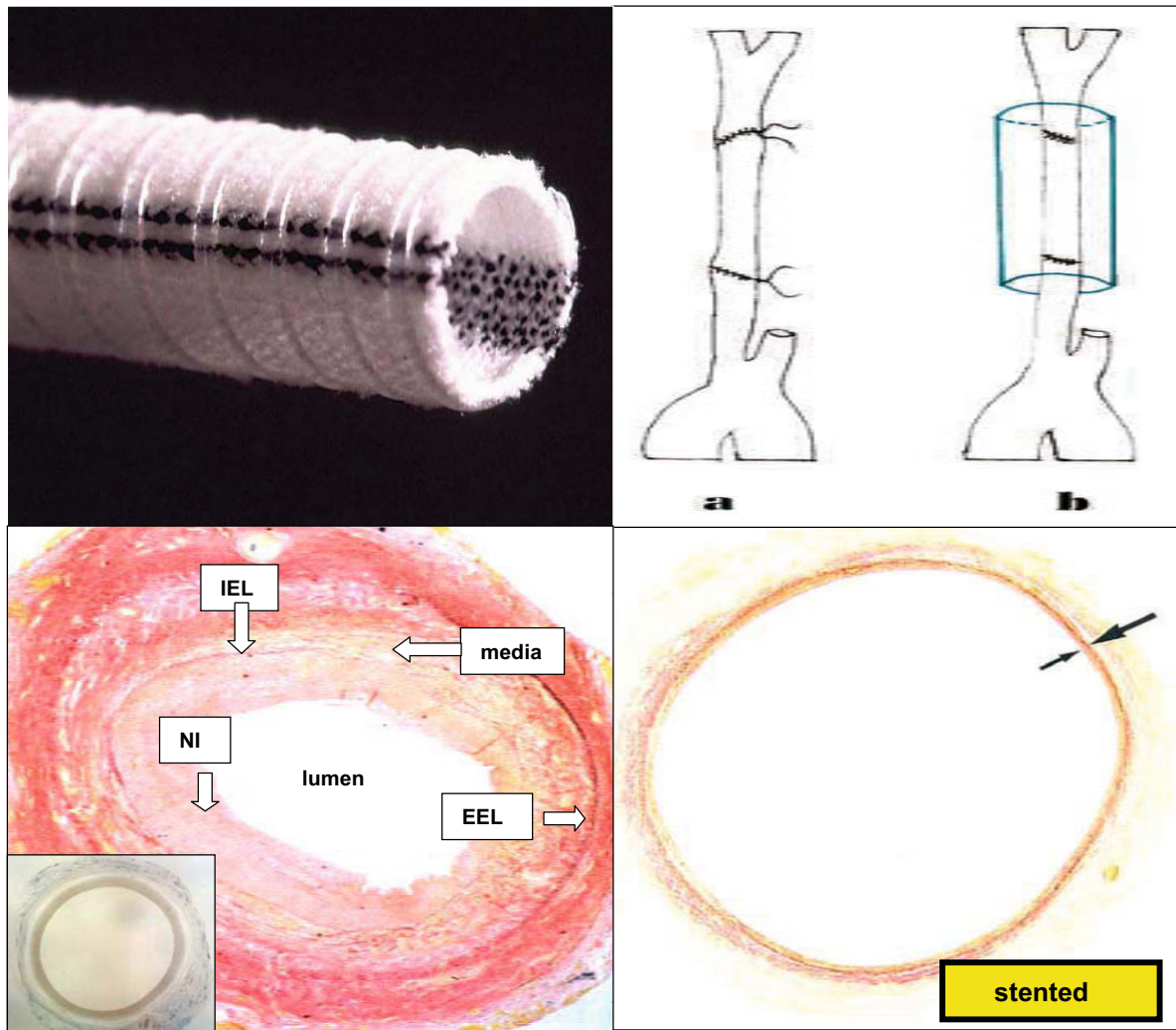


Fig. 40.3. Effect of the external Dacron stent. A loose fitting Dacron sheath or stent (*upper left panel*) was placed around a saphenous vein into a carotid artery interposition graft (*upper right panel*). After 1 month, the graft was excised and studied histologically. As shown (*lower left panel*), there is a marked increase in graft size and neointima formation (the layer between the internal elastic lamina, IEL, and the lumen) compared to the original ungrafted saphenous vein (*inset*). It is this thickening that is the basis of vein graft failure. The graft fitted with the external stent, however, shows a profound reduction of graft thickening (*small arrow* IEL, *large arrow* external elastic lamina, EEL) and a complete inhibition of the neointima

vein graft thickening at 1 month [30], which persisted for 6 months [31]. One clear feature of the vein grafts fitted with the polyglactin sheath was the presence of a microvessel rich adventitia, indicating the main mode of action of the sheath is to promote angiogenesis and therefore prevention of graft hypoxia. We therefore concluded that external polyglactin sheath allows for adaptation of the vein graft to arterial conditions while at the same time preventing the “overshoot” of intra-graft vascular smooth muscle cell proliferation and migration. The long-term presence of the sheath may not be necessary to prevent graft thickening and late failure, which may constitute a distinct advantage over the Dacron stent.

40.4

Endothelin-1_A Antagonists

Endothelin-1 (ET-1) is involved in every facet of vein graft disease [32–34], which can be summarized as follows: (1) ET-1 is released in large amounts by adherent blood cells; (2) ET-1 promotes growth factor expression, matrix deposition and oxidative stress; (3) the saphenous vein contains high levels of ET_A receptors that are expressed in the neointima following graft implantation; (4) ET-1 synthesis is rapidly upregulated by all those factors associated with vein graft disease, including peptide growth factors, hypoxia and hemodynamic forces; and (5) early and later atherogenic events, in-

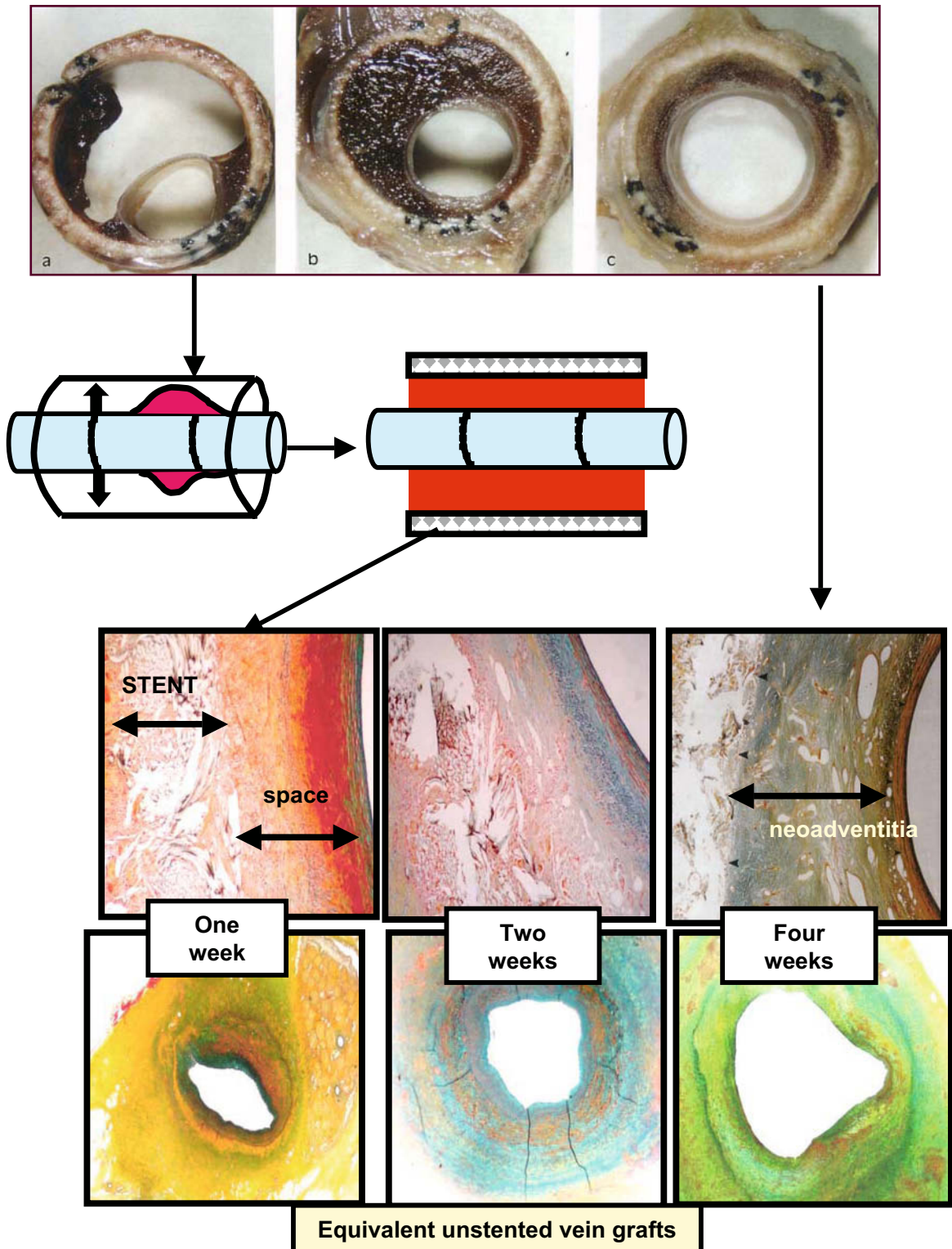


Fig. 40.4. Time course of events that occur with a loose-fitting external Dacron stent on porcine vein grafts: **a** 1 day after, **b** 1 week after, **c** 1 month after implantation. From **a** it can be seen that the stent is loosely fitting. By 1 week after implantation (**b**), however, the space between the graft and the stent has filled with fibrin rich exudates. By 1 month (**c**), this area has organized into a “neoadventitia” that is rich in microvessels. We suggest that the fibrin rich exudate that forms in the space between the graft and the stent promotes the formation of new microvessels that in turn oxygenates the graft, thereby preventing hypoxia-induced pathogenesis, including cell proliferation

cluding monocyte adhesion, are mediated by ET-1. In turn, a recent study has demonstrated that a specific ET_A antagonist is an extremely potent inhibitor of neointima formation and vein graft thickening in an experimental model and blocks each of the above listed events [35]. Other potential benefits of ET_A blockade in patients following CABG include a reduction in early thrombosis due to the relief of vein graft spasm, improved compliance in distal run-off coronary arteries, improved functional recovery of hibernating myocardium, a reduction in postoperative arrhythmias and attenuation of renal dysfunction [13]. As such, clinical studies on ET_A receptor antagonist in patients undergoing CABG are clearly warranted.

40.5

Nitroaspirin

Aspirin has been the most widely investigated drug in CABG patients [36]. Although aspirin reduces the incidence of vein graft thrombosis in both the short and long term, it has no effect on late vein graft failure [36]. Because of its beneficial effects, however, aspirin is routinely administered to patients following CABG and continued indefinitely thereafter [36]. The relative lack of effect on eventual outcome has been ascribed to a lack of effects on vascular smooth muscle cell proliferation and minimal effects on the adhesion and release reactions of platelets and leukocytes [6, 37]. Another major drawback of aspirin is the promotion of gastric erosion and ulceration over the long term [38].

In contrast to aspirin, NO is a potent inhibitor of platelet and leukocyte adhesion and the release of mitogens dilates saphenous vein and inhibits neointima formation [8]. It was suggested, therefore, that the co-administration of an NO donor may compensate for the limitations of aspirin [5]. A novel drug type that intrinsically fulfills these pharmacological criteria is the NO-releasing aspirins (NO-aspirin) [39], which inhibit the proliferation of vascular smooth muscle cells and relax isolated human saphenous vein in vitro [39].

We therefore studied the effect of oral administration of the NO-aspirin (NCX 4016) on neointima formation in saphenous vein-carotid artery interposition grafts 1 month after surgery in the pig compared to aspirin alone or the NO donor, SIN-1 [40]. NCX 4016, at 10 mg, 30 mg and 60 mg/kg, once daily, had a potent inhibitory effect on neointimal thickening. Both aspirin alone (60 mg/kg) and SIN-1 alone (1 mg/kg) also inhibited neointimal thickness and neointimal area, although they were less potent than NCX 4016. At 30 mg/kg/day aspirin had no effect. These data indicate that NCX 4016 confers not only the beneficial properties of aspirin alone but the additional positive effects of NO in inhibiting neointima formation. Taken together, the

repertoire of properties displayed by NCX 4016 (inhibition of neointima thickening, antithrombotic, antiatherogenic effects and gastroprotection) render them potentially useful in treating both early and late vein graft failure and, therefore, the application of these adducts in patients undergoing CABG should be further validated.

40.6

Antioxidant Therapy

Oxidative stress, in particular the upregulation of NADPH oxidase and superoxide formation, appears to play a key role in promoting vein graft disease [16, 17]. The risk factors associated with increased incidence of graft failure (diabetes mellitus, hyperhomocysteinemia, hypercholesterolemia and smoking) all promote intravascular oxidative stress [16, 17]. It would seem logical, therefore, that the administration of antioxidants may be effective in preventing vein graft disease. Possible antioxidants include the vitamins C, D and E, probucol, flavanoids and folic acid. In 87,245 female patients followed for 8 years and in 39,910 men followed for 4 years, significant inverse associations were found between cardiac events and vitamin E intake [41, 42]. In the CHAOS trial, there was a significant 75% reduction in non-fatal myocardial infarction in cardiac patients taking vitamin E [43]. However, this latter observation was not supported by subsequent trials [44–47]. Although the results of randomized clinical trials do not support the use of vitamin E for treating atherogenesis, it has been suggested that antioxidant therapy is likely to be clinically useful at the initial stage of atherosclerosis and over many years of treatment [49]. It is proposed, furthermore, that given the etiology of vein graft disease (early inflammation and superimposed atherogenesis) the administration of antioxidant adjuvant regimes may prove particularly effective in patients undergoing CABG and other cardiac surgical procedures, including heart transplantation [46]. Another point to take into account is that any given antioxidant may not impact at the tissue level. As was stressed above, intragraft oxidative stress is mediated principally by an upregulation of NADPH oxidase expression and as such antioxidants such as vitamin C and E may simply not be potent enough to exert an impact on the expression of pro-oxidant enzymes. However, in a series of recent studies, we found that a number of important drugs are potent inhibitors of NADPH oxidase expression. These include NO donors and nitroaspirin [19], iloprost, a prostacylin analogue [20] and sildenafil, a type 5 phosphodiesterase inhibitor [50]. These drugs may therefore be effective in preventing vein graft failure through suppression of oxidant stress.

Surgery also promotes fundamental metabolic changes that may augment oxidative stress. For example, we found a striking increase in plasma levels of homocysteine, copper and ceruloplasmin CP that persisted for up to 6 weeks after surgery [51]. This change could not be ascribed to an acute phase response, since C-reactive protein was elevated for only days [51]. These changes could contribute to vein graft disease since homocysteine and copper interact to produce superoxide and O_2^- promotes all the pathological components of vein graft disease (i.e., platelet and leukocyte adhesion, thrombosis, vascular smooth muscle cell proliferation and neointima formation). It also follows that the administration of homocysteine-lowering regimes such as folic acid and the B vitamins or the administration of a copper chelator may prove useful in CABG patients. Indeed, we recently found that the administration of penicillamine, a copper chelator, was an extremely potent inhibitor of vein graft thickening in the pig [52].

40.7

Concluding Remarks

It is clear that there are several possible strategies available for preventing late vein graft failure, which include the placement of external stents or sheaths, as well as the more conventional pharmacological approach. With regard to the Dacron external stent, clinical trials are currently underway to test the device in patients undergoing CABG, the results of which should be available soon. In preclinical studies, drugs including an ET_A antagonist, NO-aspirin and a copper chelator have all proved extremely promising. It is important, therefore, to endeavor clinical trials with these drugs in order to solve a hitherto intractable clinical problem which has enormous economic and human consequences.

Acknowledgements. This work was supported by the Hong Kong Research Grant Council Earmarked Grant (CUHK 4133/01M) and, in part, by the British Heart Foundation.

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Gene Therapy for Vein Graft Disease

D.G. CABLE, H.V. SCHAFF

The durability of coronary artery bypass grafting is intrinsically dependent upon the patency of the graft. The long term patency of arterial grafts, in particular internal mammary grafts, has been clearly defined by multiple groups to be greater than 90% at 10–20 years following construction. This has been fully addressed in Chaps. 13 and 14. Moreover, a recent randomized trial between radial artery and saphenous vein grafts demonstrated the superiority of radial artery conduits at 1 year [1]. However, certain clinical scenarios require the use of venous grafts. The intrinsic limitations of saphenous vein bypass grafts and the subsequent acceptance of these imperfections guide our clinical decisions in a fundamental fashion. To address these shortcomings in saphenous vein grafts, a growing body of research has endeavored to improve the function of saphenous veins in an attempt to ultimately increase patency rates and durability of the surgical revascularization.

41.1 Gene Therapy

There are several reviews published which have dealt with recombinant gene fundamentals [2–5]. The composition of a gene, the various methods of how a gene can be inserted into a cell, and the mechanism by which a cell expresses the gene are handled by these reviews. Rather than reiteration of these central principles, this discussion will primarily focus on how gene therapy may impact on saphenous vein graft disease. However, it is reasonable, prior to reviewing the literature, to note the methods by which new genetic information can be inserted into a cell, or a saphenous vein designed for coronary bypass grafting.

Several methods have been utilized to enhance cellular uptake of recombinant genes. Caution must be entertained in the review of this topic as many of the methods will not be clinically applicable; several methods will remain confined to the laboratory. Insertion of recombinant genes can be classified as chemical facilitators, electroporation, direct microinjection, liposomal delivery, and viral vectors. Chemical facilitators

employ precipitators to place the exogenous DNA in close proximity to the cell membrane, typically utilizing calcium phosphate or DEAE-dextran precipitation. Baseline endocytic uptake of the exogenous gene or increase in endocytic activity by rendering the membrane more “fluid” are two mechanistic explanations for calcium phosphate precipitation. However, chemical facilitators can only be used in tissue culture secondary to technical considerations. Electroporation involves the direct application of an electric current to cells to impart transfer of the exogenous gene across cell membranes. Efficacious currents often approach 500 V and are associated with cell mortality approaching 50% in suspension cultures. Microinjection involves the direct injection of recombinant genes into the cytoplasm or nucleus under high-power magnification. As with chemical facilitators, these methods of gene transfer will not reach clinical applicability in the treatment of cardiovascular disease secondary to the inherent graft injury associated with their application.

The current methods of gene transfer which have clinical potential are liposomal delivery and viral vectors. Liposomal gene therapy utilizes lipids as carriers for the recombinant gene until incorporation into the cell. Liposomes can further be subclassified as either cationic liposomes or anionic, pH-sensitive liposomes. Cationic liposomes are positively charged lipids, and a co-lipid, which form microvesicles that can spontaneously condense with DNA. Internalization of the gene into the cell as an endosome is favored by the positive lipid charge in a process called endocytosis.

Viral vectors utilize adenoviruses, adeno-associated viruses, or retroviruses for gene delivery. An adenovirus is a double-stranded, linear DNA virus that produces the characteristic common “cold” as well as influenza, pharyngitis, conjunctivitis, and pneumonia. There are 42 serotypes of adenovirus that are capable of infecting human tissue. In particular, serotype 5, responsible for the common cold, is frequently used for the generation of adenoviral vectors in recombinant gene technology. The infective cycle of adenovirus comprises two distinct phases, the early phase and the late phase. Correspondingly, the genes for virus propagation, and thus continuation of an infection, require

the early transcriptional genes. The E1 genes render the infected cell capable of rapid viral DNA and protein synthesis. The E2 genes encode for DNA replication proteins. The E3 genes function to counter cell defense mechanisms and are particularly important in gene therapy as they may prolong expression. The E3 genes attempt to negate tumor necrosis factor (TNF) and prevent the membrane expression of MHC class I to reduce presentation of viral proteins for a cell-mediated immunologic response. The E4 genes regulate the transition between early and late cycles. The currently used adenoviral vectors are constructed by the insertion of the recombinant gene desired into the E1a or E1b region of the virus genome. In this manner, the virus is rendered replication-defective at the same time the gene is inserted. In other words, the virus could not replicate in unaltered human tissue, and affords a measure of biologic safety to gene therapy.

Adeno-associated virus (AAV) is a small, nonautonomous virus composed of linear single-stranded DNA. AAV is described as nonautonomous because it requires concomitant infection with adenovirus to replicate. Though AAV is known to be widespread in the population, no association with a pathologic process is currently known. The genome of AAV is extremely simple, comprising only two genes. The rep gene encodes for a family of proteins involved in replication and integration. The cap gene encodes for a family of three viral structural proteins. At each end of the genome, terminal repeats (TR) are present. As a consequence of the simple genomic structure of AAV, vectors based on AAV are extremely simple, composed of the recombinant gene flanked on both sides by viral TR sequences. The only constraint in generation of the vector is the length of the recombinant gene; it must be less than 4,680 base pairs, the length of the viral genome.

Retroviruses are a large class of enveloped viruses that consist of single-stranded RNA as the viral genome and, consequently, require a reverse transcriptase to generate DNA copies of the RNA genome after viral infection of a cell. The prototypical retrovirus encodes at least three genes: *gag*, encoding for a group of core proteins; *pol*, encoding for a reverse transcriptase; and *env*, encoding for the viral envelope protein. The genome is flanked on both sides by long terminal repeats (LTR) and contains a packaging signal. A retroviral vector can be composed of the recombinant gene of interest, the packaging signal, and flanking LTR sequences. This will theoretically render the retroviral vector replication-defective as the genes encoding for viral core, envelope, and reverse transcriptase are absent. Retroviral vectors are capable of integrating within the human chromosome in dividing cells, thereby imparting long-term expression of the recombinant gene. However, retroviral vectors have expressed low efficiency rates in vascular tissue, on the order of 0.1–1.0% arterial cells to which exposed.

41.2

Saphenous Vein Graft Disease

The application of gene therapeutics to a given disease is predicated upon an understanding of the pathophysiology and natural history of the process. The simplicity of this statement masks the intrinsic complexity of the task, for even single gene defects have been difficult to approach. Cystic fibrosis is a clear example. A multifactorial disease process such as vein graft disease markedly increases the number of variables that must be considered in order to develop a rational approach for gene therapy.

Several publications have reviewed important aspects of saphenous vein graft disease [6, 7], and Table 41.1 outlines fundamental aspects of the problem. It is reasonable, prior to reviewing the literature, to note some of the pathophysiologic aspects of vein graft disease.

Saphenous vein grafts (SVG) used in coronary artery bypass grafting fail due to thrombosis, neointimal hyperplasia, and/or progressive atherosclerosis. The patency of a grafted conduit is a function of intrinsic conduit properties and the environment in which it is placed. Hydraulics teaches that flow within a graft is dependent upon three variables, the inflow source, resistance of the graft, and the outflow vascular bed. The former two are rarely at issue as SVG grafts most commonly arise from the aortic root and are larger than the targeted coronary artery. Therefore, the resistance in the distal coronary artery is most commonly the flow limiting variable.

The graft blood flow at time of implantation correlates with subsequent SVG patency. Chesebro found that 34% of SVG would occlude within 1 month of surgery if the intraoperative graft flow was ≤ 40 ml/min [8]. If intraoperative SVG flow was 41–80 ml/min, the

Table 41.1. Variables associated with vein graft occlusion

Technical errors
Distal anastomosis complication (intimal flap, purse-string)
Proximal anastomosis complication
Improper graft length (redundant kink, tension)
Vein graft stasis
Coronary artery < 1.5 mm
Small vessel disease, poor distal runoff, high runoff resistance
Endarterectomy required (surrogate of distal poor runoff)
Competitive flow (graft to subcritical lesion < 70% stenosis)
Vascular bed – bypass to coronary artery other than left anterior descending coronary artery
Endothelial injury
Harvest trauma
High distention pressure during harvesting
High arterial perfusion pressure
Risk factors of smoking, diabetes, end-stage renal disease, and hyperlipidemia

occlusion rate dropped to 18%, and SVG flows greater than 81 ml/min were associated with only a 6% occlusion rate. The importance of initial SVG flow, and the implication of target vessel runoff, was equally important in predicting late graft patency. Chesebro demonstrated that 46% of SVG occluded within 1 year if the intraoperative graft flow was ≤ 40 ml/min but only 15% of SVG occluded if the flow was greater than 81 ml/min [9].

The early studies on antiplatelet therapy, as is now the current standard of care, demonstrated that SVG patency is highly dependent on the target vessel [8, 9]. If the targeted vessel was either the left anterior descending or left circumflex artery, only 6% of SVG occluded within 1 year of implant. The occlusion rate was 2.3 greater when the target vessel was the right coronary artery. A similar finding was reported from the Cleveland Clinic, noting right coronary SVG had a two-fold increase in occlusion compared to those used for the left anterior descending coronary artery [10]. The Veterans Administration Cooperative Study reported a SVG to the right coronary artery was associated with a 2.2 greater occlusion rate compared to left anterior descending coronary artery SVG, despite antiplatelet therapy [11].

Additionally, SVG patency is dependent on coronary artery lumen [8, 9, 11], number of distal anastomoses performed (i.e., sequential graft) [8, 9, 12], and whether an endarterectomy [8, 9, 12] was performed at the time of grafting.

Thrombosis remains the most common mode of graft failure early, and is promoted by low velocity of flow with stasis of blood within the graft. Many of the predictive variables (coronary artery size, coronary artery targeted, need for endarterectomy) that impact on outflow resistance cannot be addressed by gene therapy. However, molecular techniques can target thrombogenicity in the perioperative period. It is also likely that altering this early thrombogenicity may impact upon subsequent graft disease.

Development of intimal hyperplasia in SVG may be a compensatory response of the graft wall to the increasing hemodynamic pressures of the arterial circulation and a mitogenic response to endothelial damage and subsequent platelet aggregation. There is evidence that subsequent development of SVG atherosclerosis may be dependent upon the degree of intimal hyperplasia.

41.3

Vein Graft Gene Therapy

41.3.1

Reporter Gene Experiments

Gene therapy is dependent not only on the vector utilized but also the gene insert, and the subsequent expression of the gene differs importantly between vasculature beds. Therefore, a body of literature is dedicated to determining the susceptibility of differing methods to insert genes whose only function is to demonstrate that they were successfully inserted. Tsutsui et al. found that β -galactosidase, essentially a nonfunctioning but easily identified gene, was expressed differently following adenoviral transfer in canine basilar, coronary, and femoral arteries [13]. Several studies have been performed to see if human SVG can express reporter genes such as β -galactosidase following various transfer methods (Table 41.2), including use of an adenoviral vector [14]. Imagawa et al. utilized a liposomal method to transfer β -galactosidase to human SVG [15]. However, there is preliminary evidence that human SVG express this reporter gene to a lesser degree than paired human internal mammary or radial arteries (unpublished data, DG Cable and HV Schaff).

Various animal models of vein graft disease have also been studied in reporter gene trials. Kupfer et al. evaluated β -galactosidase expression 3 and 7 days following transfer in rabbit jugular veins [16]. Channon et al. performed adenoviral-mediated β -galactosidase transfer to rabbit jugular veins [17]. Chikada and Jones optimized adenoviral-mediated β -galactosidase transfer to rabbit jugular vein grafts by the addition of dimethylsulfoxide and hyaluronidase [18].

Certain limitations have been identified in these laboratory models which have clinical relevance. Gene transfer efficiency to atherosclerotic vessels was significantly decreased in a rabbit model [19]. Not all studies have come to the same conclusion though. Human atherosclerotic coronary arteries demonstrated similar efficiency of adenoviral-mediated gene transfer of the reporter gene human placental alkaline phosphatase compared to controls [20]. It has been demonstrated that gene transfer may be less efficient after graft implantation. The transfer rates in veins were decreased when performed 3 days after implantation compared to transfer at the time of graft construction [17]. There-

Table 41.2. Reporter gene transfer to human coronary bypass grafts

Author	Tissue	Transfer method	Reporter gene
Cable (1997)	Human saphenous vein	Adenoviral	β -Galactosidase
Cable (1999)	Human saphenous vein	Adenoviral	β -Galactosidase
Cable (1999)	Human radial artery	Adenoviral	β -Galactosidase
Imagawa (1996)	Human saphenous vein	Liposomal	β -Galactosidase
Reckhter (1998)	Human saphenous vein, human internal mammary artery	Adenoviral	Placental alkaline phosphatase

fore, while it is currently feasible to genetically manipulate vein grafts at the time of surgery, clinical application to vein grafts at a later date may be impaired.

In addition to the method of gene transfer, another factor that may impact on subsequent gene expression is the promoter utilized. Most of the experiments in vein grafts have used either the cytomegalovirus immediate early promoter (CMV-IEP) or Rous sarcoma virus long terminal repeat (RSV-LTR) promoters. It is difficult to directly compare the effectiveness of these two promoters as the studies have other confounding variables. For instance, in studies of gene transfer to rabbit jugular veins, Channon et al. [17] used a higher titer of CMV promoter than Chikadain and Jones [21] did in their RSV studies. What is known is that the promoters behave differently, as Champion et al., in a murine lung model, demonstrated that CMV promoted β -galactosidase peaked at 1 day but RSV promotion peaked at 5 days [22]. Further, Champion reported that CMV expression decayed over a 7- to 14-day course while RSV expression lasted for 21–28 days.

The titer, or amount, of virus used for the gene transfer has also been found to influence subsequent gene expression. In canine coronary artery bypass grafts, the titer of adenovirus vector used influenced the amount of β -galactosidase subsequently produced [23]. Vein segments from each animal were exposed to an adenoviral vector encoding β -galactosidase, at titers of 2.5×10^9 or 5×10^9 pfu/ml, for 1 h [24]. Control segments were exposed to diluent alone in an identical manner. Aortocoronary anastomoses were then performed to the left anterior descending or circumflex arteries, and the dogs sacrificed 3 days later. Quantitative β -galactosidase ELISA demonstrated a dose-dependent increase in gene expression, in comparison to the control vessels, such that the highest titer of virus produced 12.0 ± 2.7 mg β -galactosidase/mg total protein.

The lower titer of virus produced half this level of gene product while undetectable levels were noted in vehicle controls.

Reckhter et al. noted that human saphenous veins and internal mammary arteries were able to express human placental alkaline phosphatase following adenoviral gene transfer [20]. Vessels were exposed for 3 h to a titer of 2×10^9 pfu/ml, following optimization studies in rabbit aortas. Luminal endothelial cells predominantly expressed the transgene in immunohistochemical studies.

We have evaluated the titer response in human coronary bypass grafts (D.G. Cable and H.V. Schaff, unpublished data) by quantifying the amount of β -galactosidase produced in common venous and arterial conduits. Human saphenous veins were exposed to either vehicle control or an adenovirus encoding *E. coli* β -galactosidase (10^7 – 10^{10} pfu/ml). In control veins, β -galac-

Table 41.3. Candidate genes for vein graft disease

Category of action	Gene
Anticoagulant	Hirudin
	Thrombomodulin
	Tissue plasminogen activator (r-TPA)
Endothelial vasoactive substances	Cyclooxygenase-1 (COX-1)
	Endothelial nitric oxide synthase
	Inducible nitric oxide synthase
Inhibitors of neointimal hyperplasia	Retinoblastoma protein
	Soluble vascular cell adhesion molecule (VCAM)
	β -Adrenergic receptor kinase (β ARK _{CT})
	Tissue inhibitors of metalloproteinases (TIMP-1, -2, -3)
	Elafin
	Senescent cell-derived inhibitor gene-1 (<i>sdi-1</i>)
Antisense gene therapy	Basic fibroblast growth factor (anti-bFGF)
	E2F decoy

Author	Tissue	Transfer	Gene
Bai (1998)	Rabbit vein	Liposomal	Senescent cell-derived inhibitor gene-1
Cable (1997)	Human saphenous vein	Adenoviral	eNOS
Cable (1999)	Human saphenous vein	Adenoviral	eNOS
Chen (1994)	Human saphenous vein	Adenoviral	VCAM
George (1998)	Human saphenous vein	Adenoviral	TIMI-1
George (1998)	Human saphenous vein	Adenoviral	TIMI-2
George (2000)	Human saphenous vein	Adenoviral	TIMI-3
Hagen (1998)	Rabbit vein graft	Adenoviral	β -Adrenergic receptor kinase
Kibbe (1999)	Porcine vein	Adenoviral	iNOS
Mann (1995)	Rabbit jugular vein	Oligonucleotide	Cell division cycle 2 kinase
Matsumoto (1998)	Canine peripheral vein	Liposomal	eNOS
O'Blenes (2000)	Rabbit jugular vein		Elafin
Petrofski (2004)	Canine vein	Adenoviral	β ARK
Schwartz (1999)	Rabbit jugular vein graft	Adenoviral	Retinoblastoma protein

Table 41.4. Gene transfer to vein grafts

tosidase was undetectable, and a clear titer response was noted to increasing concentrations of the viral vector. An interesting finding of these experiments was that human radial arteries expressed a hundredfold greater expression of β -galactosidase than saphenous veins despite the same viral titers, suggesting that venous grafts may be more resistant to gene therapeutics than arterial grafts. Human internal mammary arteries were quite susceptible to adenoviral gene transfer and did not demonstrate a marked titer response. This differential susceptibility also crosses species. In separate experiments, we found that canine veins expressed twofold greater β -galactosidase levels than human saphenous veins, and the maximal titer response in canine was 10^9 pfu/ml compared to 10^{10} pfu/ml in human veins.

Several conclusions can be drawn by these investigations. First, genes can be inserted in veins, and the genes will produce a recognizable outcome, in these cases a protein which can be readily stained. Second, many variables have been identified which will be important for clinical application, including viral titer, exposure duration, promoter, and tissue targets. Third, the duration of action may be limited based upon the above variables. While the latter may at first glance suggest a critical limitation, review of the pathophysiology of SVG disease suggests that actions taken in the first month following surgery may have direct implications on the long term durability of the graft.

41.4

Candidate Genes

Thus far we have examined the methods of gene transfer, the pathophysiology of SVG disease, and studies performed to optimize or define the appropriate conditions by which SVG gene therapy can be successfully applied. It is now reasonable to evaluate the literature regarding therapeutic gene insertion. The subsequent discussion will be divided according to the method of action.

41.4.1

Anticoagulants

A natural anticoagulant produced by leeches, hirudin, blocks the anion-binding site responsible for thrombin-fibrinogen interaction and platelet receptors, and for the active site responsible for protease activity. Hirudin produces this at an extremely low concentration, micromolar, and therefore may provide anticoagulation of SVG with endothelial release. Dichek and associates have utilized both adenoviral and retroviral vectors to transfer a hirudin gene into vessels [25, 26]. These series of experiments further defined that pro-

duction of active hirudin resulted in a significant reduction in neointimal hyperplasia in a rat carotid angioplasty model. Since the half-life of hirudin is so short, selective anticoagulation of a SVG could occur while the systemic coagulation system is unaffected.

Another potent anticoagulant is endothelial thrombomodulin which binds thrombin and subsequently converts protein C to its active form. Waugh and colleagues in a rabbit model of arterial injury reported thrombomodulin gene transfer significantly decreased intravascular thrombosis [27]. In addition, the infiltration of leukocytes was significantly reduced. However, this model did not demonstrate a significant reduction in neointimal formation following thrombomodulin gene transfer. Tabuchi et al. demonstrated that thrombomodulin gene transfer to rat inferior vena cava reduced the thrombogenicity after simulated arterial circulation [28].

Tissue plasminogen activator (r-TPA) is an exogenous stimulator of the fibrinolytic system, catalyzing the conversion of the inactive plasminogen to active plasmin. Plasmin is a nonspecific proteolytic enzyme that catalyzes the degradation of fibrin, fibrinogen, prothrombin, factor V, and factor VIII. As the circulation contains a large concentration of plasmin inhibitor to neutralize its effect, the action of plasmin is relatively specific to fibrin clots. Retroviral gene transfer of TPA to venous endothelial cells has been subsequently seeded onto synthetic grafts [29]. While these experiments were not applied directly to SVG, it raises yet another interesting prospect of selective anticoagulation of vein grafts via gene therapeutics.

41.4.2

Endothelial Vasoactive Substances

The endothelium produces three factors which causes vasodilatation, collectively known as endothelium-dependent relaxing factors. They include prostacyclin, nitric oxide, and endothelium-derived hyperpolarizing factor (EDHF). Because the latter substance remains to be defined chemically, it is not a candidate, at present, for experimental gene therapeutics to vein graft disease.

Prostacyclin causes vascular relaxation and inhibition of platelet aggregation, and is synergistic with nitric oxide. Prostacyclin has not been specifically reported in venous grafts to date. However, Zoldhelyi et al. [30] used adenoviral vectors to transfer cyclooxygenase-1 (COX-1) to porcine carotid arteries which had been denuded of endothelium; 54% of control vessels occluded while none of the treated vessels following COX-1 transfer were occluded. Furthermore, cyclic flow changes, a surrogate of nonocclusive platelet aggregation, was significantly reduced (441 events over 10 days in controls versus none after COX-1 transfer).

Prostacyclin production was increased fourfold following gene transfer.

Nitric oxide is also an endogenous endothelial product that not only produces vasodilation but also inhibition of platelet aggregation, decreased smooth muscle cell proliferation, and attenuation of leukocyte adhesion. While prostacyclin gene therapy has not been described in SVG, there are studies of nitric oxide augmentation in venous tissue. Cable and colleagues demonstrated a tenfold increase in stimulated nitrite production, a stable metabolite of nitric oxide, in human SVG after transfer of endothelial nitric oxide synthase [14]. This was associated with a twofold increase in relaxation in organ chambers and luminal release of nitric oxide in superfusion bioassay.

The reduction of intimal hyperplasia in extended organ culture of paired human SVG was demonstrated following endothelial nitric oxide gene transfer [31]. Human SVG and internal mammary arteries were mounted in organ culture and incubated for 0, 4, 7, 10, and 14 days. Following staining by Verhoeff-van Gieson, the intima/media (I/M) ratio was averaged over the entire length of each specimen using an image analysis system. The model was validated as the SVG produced progressive increases in the I/M ratio while the arterial samples demonstrated no significant change,

similar to the documented clinical outcomes. Paired human SVG were then exposed to either phosphate-buffered saline with 0.1% albumin (dilution vehicle, PBSA) alone, recombinant adenovirus encoding *E. coli* β -galactosidase (Ad.CMVLacZ, 10^9 pfu/ml), or adenovirus encoding bovine endothelial nitric oxide synthase (Ad.CMVeNOS, 10^9 pfu/ml). Following 14 days of organ culture, the I/M ratio was noted to be significantly reduced in Ad.CMVeNOS veins compared to vehicle and viral controls (Fig. 41.1).

Matsumoto et al. utilized a liposomal transfer of bovine endothelial nitric oxide synthase in a canine vein graft model of poor-runoff [32]. After 4 weeks, nitric oxide synthase gene transfer was associated with significantly reduced intimal thickness (90 μ m) compared to both vehicle and vector (193 μ m) controls. These experiments are of particular interest because the investigators attempted to duplicate the clinical situation of poor runoff and low graft flow. Matsumoto was able to demonstrate not only graft patency but also a reduction in neointimal hyperplasia.

While inducible nitric oxide synthase (iNOS) is not generally associated with normal endothelium, the product of this enzyme also produces nitric oxide and may produce greater quantities than endothelial isoform. Kibbe et al. demonstrated that porcine internal

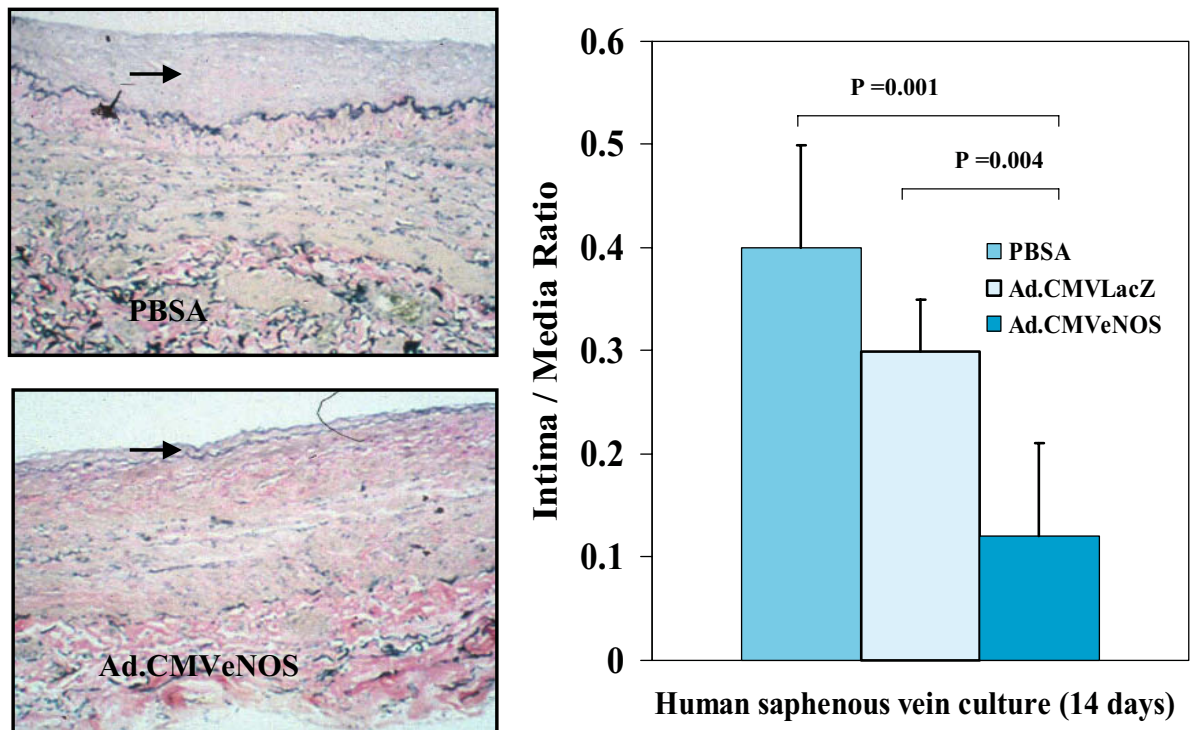


Fig. 41.1. Human saphenous veins were exposed to control saline (PBSA), reporter gene (Ad.CMVLacZ), or endothelial nitric oxide synthase gene transfer (Ad.CMVeNOS), and then maintained in organ culture for 14 days. The neointima (arrow) was significantly greater in controls (PBSA, upper left) than following endothelial nitric oxide synthase gene transfer (Ad.CMVeNOS, lower left)

jugular vein grafts would functionally express iNOS, and nitric oxide production was augmented if vein grafts were exposed concomitantly to an adenovirus encoding for guanosine triphosphate cyclohydrolase, the rate-limiting enzyme in the production of tetrahydrobiopterin, a cofactor of NOS [33].

41.4.3

Inhibitors of Neointimal Hyperplasia

The above noted studies attempted to impact upon SVG disease by reducing thrombogenicity or endothelial dysfunction. There are a number of studies, though, that attempt to inhibit neointimal hyperplasia directly. Platelet aggregation in nonocclusive thrombi releases mitogenic factors that stimulate neointimal hyperplasia, and these factors have been examined by several groups.

Retinoblastoma protein, in the unphosphorylated state, is cytostatic by means of transcription factor E2F and Elf-1 inactivation. Schwartz et al. demonstrated a 22% reduction in neointimal formation of rabbit jugular vein grafts following adenoviral-mediated gene transfer of unphosphorylatable retinoblastoma protein [34].

Several mitogenic factors are released by leukocytes which are important in neointimal hyperplasia. Secretion of a soluble vascular cell adhesion molecule (VCAM-1) may inhibit mononuclear cell binding by competitive inhibition of cell-surface bound VCAM. While functional expression following adenoviral-mediated transfer to porcine jugular and human SVG was demonstrated by Chen et al., no analysis of intimal hyperplasia was performed [35].

Some mitogenic factors utilize a G-protein signaling pathway; inhibition of G-protein subunits with β -adrenergic receptor kinase (β ARK_{CT}) may inhibit neointimal hyperplasia. Hagen and associates have demonstrated a 37% reduction in rabbit vein graft neointimal hyperplasia following gene transfer of β ARK_{CT} [36, 37]. Coronary artery bypass grafting was performed in dogs by Petrofski and colleagues, and β ARK_{CT} was transferred to SVG in two canines [38]. While Northern analysis demonstrated transgene expression, the effect on neointimal hyperplasia could be determined due to the small numbers.

Smooth muscle cell migration is considered to be fundamental to initiation of neointimal hyperplasia of SVG, and is dependent on activation of matrix-degrading metalloproteinases. Four isoforms of endogenous tissue inhibitors of metalloproteinases (TIMP) have been identified, three of which have been cloned. A series of experiments transferring TIMP-1 [39], TIMP-2 [40], or TIMP-3 [41] to human SVG has been described by George and associates. After extended organ culture of 14 days, neointimal hyperplasia was significantly re-

duced, 79% with TIMP-1, 79% with TIMP-2 and 84% with TIMP-3 transfer. This model was also associated with decreased smooth muscle cell migration, gelatinolytic activity, and apoptosis. However, these results should be interpreted cautiously. While TIMP-2 gene transfer inhibited neointimal formation in human SVG in organ culture, no significant effect was noted in porcine jugular vein grafts.

Elafin is a naturally occurring inhibitor of serine elastases found in human skin. The serine elastases may be critical to the proliferation and migration of smooth muscle cells which cause neointimal hyperplasia. Liposomes were used by O'Blencs et al. to transfer elafin to jugular vein grafts in rabbits [42]. Neointimal hyperplasia was reduced by 50% at 4 weeks following elafin gene transfer. The importance of this study was the subsequent demonstration that early results had implications on late graft disease. When the rabbits were fed a cholesterol-rich diet, elafin gene transfer was associated with a 40% reduction in atherosclerotic plaque formation.

The tumor suppressor p53 is mediated by human senescent cell-derived inhibitor gene-1 (*sdi-1*). Bai et al. demonstrated a 70% inhibition of neointimal formation in rabbit vein grafts after 2 weeks [43]. Also of note, the phenotypic modulation of the predominant smooth muscle cell type, favoring adult type versus embryonic, was found following *sdi-1* gene transfer. The *p53* gene itself has been transferred to human SVG by Wan et al., and shown to not only increase apoptosis but also to reduce the thickening of the neointima [44].

41.4.4

Antisense Gene Transfer

The studies described previously have inserted genes which directly produce a result secondary to production of a functional protein. An alternative strategy is to insert a gene which prevents the natural production of a cell product. Rather than augmenting the production of a cell product (i.e., nitric oxide), or producing something which the SVG does not naturally produce (i.e., hirudin), antisense technology inhibits the production of a normally produced product.

Basic fibroblast growth factor stimulates smooth muscle cell proliferation, and vascular injury upregulates the expression of the receptors on smooth muscle cells which potentiates the effect. Golden and colleagues have used adenoviral-mediated transfer of a gene antisense to basic fibroblast growth factor (bFGF) to inhibit vein graft neointimal hyperplasia [45]. Following gene transfer with antisense bFGF, the mean vein graft wall thickness was greater while the luminal cross-sectional area was unchanged and, thus, tangential wall stress was significantly decreased. This same group demonstrated reduced neointimal hyperplasia

in arterial angioplasty models with similar methods of antisense strategy [46, 47].

Cyclin-dependent kinase 2 (cdk2) belongs to a family of kinases which are key regulatory components that coordinate numerous events in the cell cycle, controlling DNA replication and transcription. Morishita and colleagues used liposomes to deliver a single dose of cdk2 kinase antisense oligonucleotides to injured rat carotid arteries [48]. Significant reduction in neointimal hyperplasia was noted. Mann et al. used similar technology in rabbit jugular vein grafts [49], and demonstrated preserved endothelial function of rabbit vein grafts [50].

Transcription factor E2F regulates a dozen cell-cycle genes. Mann and colleagues have used an antisense oligonucleotide to block this transcription factor. A clinical trial was performed in 41 patients undergoing peripheral bypass surgery [51]. Organ culture demonstrated that transfection efficacy was 89% following pressurization to 300 mmHg for 10 min. At a median follow-up of 53 weeks, E2F decoy vein grafts had reduced rates of high-grade obstructions on ultrasonography.

E2F decoy therapy has been further defined in animal models. Rabbit jugular vein grafts demonstrated a significant reduction in neointimal hyperplasia at 6 weeks and 6 months [52]. In addition, the same group has demonstrated that while smooth muscle cell proliferation was attenuated with E2F decoy therapy, it did not inhibit endothelial healing following injury [53].

The PREVENT IV trial has recently been published in which 3014 CABG patients were randomized to have SVG treated with placebo or Edifoligide, an E2F decoy [54]. No difference in vein graft patency at one-year was found. No difference in cardiac events was noted. In addition, an angiographic marker or neointimal hyperplasia, mean graft diameter by quantitative angiography, was not different between E2F decoy and placebo SVG.

41.5

Future Directions

Gene therapy has enormous potential to apply localized therapy to an individual vein graft while leaving the remaining circulatory system undisturbed. Imagine a SVG that is fully anticoagulated while the systemic circulation is unaffected, and one can appreciate the potential of gene therapy. In addition to affecting thrombosis and hyperplastic response within the graft, gene therapy of vein grafts may also provide an opportunity to modulate vascular function in the grafted territory, providing a "downstream effect." The paracrine action of some transgene products, such as the anticoagulants and endothelium-derived relaxing factors,

may have beneficial effects on distal native vessels and might inhibit or retard progression of coronary artery atherosclerosis and prevent coronary spasm.

Unfortunately, despite the early hype, there has been little real success following the first clinical trial in gene therapy with adenosine deaminase-deficient patients on 14 September 1990. The death of a patient during a U.S. adenoviral clinical trial certainly raised questions regarding the safety and efficacy of human gene therapy [55]. The only trial reported to date for vein graft disease following coronary artery bypass grafting found that gene transfer of a decoy oligonucleotide was not more effective than placebo [54].

The method of gene delivery, method of gene transfer, inflammatory response to either the vector or the transgene proper, safety of gene transfer in the specific anatomic location targeted, duration of expression, ability to repeatedly dose, and viable clinical endpoints all need to be addressed. As mentioned previously, there are also important issues of appropriate promoters for the transgene, inducibility of promoters, and appropriate transgene selection.

41.6

Conclusion

In conclusion, much work has focused on the principles of gene transfer, optimization of methods, and candidate genes. Specifically for human saphenous veins, nitric oxide synthase and TIMI have been most fully evaluated. Gene transfer of nitric oxide synthase has been demonstrated to increase nitric oxide production and reduce neointimal hyperplasia in human SVG.

E2F decoy oligodeoxynucleotide has been used in humans undergoing coronary artery bypass grafting, but no significant difference was observed in graft patency, neointimal hyperplasia, or myocardial infarctions.

Acknowledgements. This study was supported by The Mayo Foundation.

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Minimally Invasive Techniques in Arterial Grafting

Minimally Invasive Coronary Artery Bypass Surgery and the Role of Arterial Conduits

M.J. MACK

Conventional coronary artery bypass surgery (CABG) has been performed routinely since the late 1960s utilizing initially cardiopulmonary bypass (CPB) and subsequently ischemic cardioplegic arrest to create the optimal operative conditions of a still heart and a bloodless field. Although the early and late outcomes were generally good, significant perioperative morbidity and mortality exists. An operative mortality of approximately 3%, a stroke rate of 1.5–2.0%, and a perioperative myocardial infarction rate of 1–2% along with the invasiveness of the procedure led to the search for alternatives to improve perioperative outcomes and make the procedure less invasive. These efforts began in earnest in the mid-1990s with initiatives to perform limited access incisions thereby avoiding a median sternotomy or performing surgery on a beating heart thereby eliminating the effects of CPB, or both. Limited access arrested heart surgery, termed port access, utilized femoral artery cannulation with endo-balloon aortic occlusion and typically a single bypass utilizing the left internal mammary artery (LIMA) to the left anterior descending (LAD) was performed. The MIDCAB (minimally invasive direct coronary artery bypass) procedure used the same limited access left anterior thoracotomy incision and direct harvest of the internal mammary artery through this incision, yet performed the anastomosis on a beating heart without cardioplegic arrest or CPB using a local stabilization device. The third approach, off-pump coronary artery bypass (OPCAB), still employed the median sternotomy incision but multivessel CABG was able to be performed on a beating heart using stabilization devices and subsequently suction exposure devices. A fourth approach, the hybrid procedure, combined limited access CABG on a beating heart, a form of the MIDCAB procedure, to bypass the left anterior descending with a left internal mammary artery with the remainder of multivessel disease being treated by percutaneous coronary intervention (PCI). For a multitude of reasons, which will be discussed below, minimally invasive CABG to a large degree has evolved to the OPCAB procedure, which is performed in approximately 25% of all CABG procedures. Despite a plethora of evidence in the peer reviewed literature attesting to the benefits of the OPCAB

procedure, significant disagreement persists regarding its overall efficacy, benefit, and graft patency. The role of each of these procedures and the use and outcomes of arterial grafts with them will be discussed.

42.1 MIDCAB Procedure

MIDCAB was initially described by Benetti [1] in 1995. That procedure utilized a LIMA harvested through a limited access incision under direct vision, and using a localized stabilization device an anastomosis was performed to the LAD. An extensive experience was gained worldwide using the MIDCAB procedure with excellent early and mid-term angiographic results (Table 42.1). Six-month angiographic follow-up by Drenth [2] demonstrated a 96% anastomotic patency. Early angiographic results in 62 anastomoses by Jatene [3] demonstrated angiographic patency in 96.8% with an early mortality of 1.6%. Vassiliades [4] demonstrated graft patency of 98.3% (60/61 grafts) at an average of 6 months postoperatively. Biglioli [5] demonstrated early angiographic patency of 96.8% in 64 patients with a 25-month survival of 100% and myocardial infarction free survival of 98.4%. Diegler [6] reported results of 618 MIDCAB procedures with a 30-day mortality of 0.6%, perioperative myocardial infarction rate of 1.6%, and a 6-month graft patency of 97%. Fraund [7] reported the outcomes of 206 MIDCAB procedures, which demonstrated superior results compared to 256 patients undergoing PCI at an average of 3.4 years postoperatively.

Table 42.1. Angiographic outcomes of LIMA to LAD with MIDCAB

Author	Grafts (n)	Time period	Patency %	Reference
Drenth	51	6 months	96%	[2]
Jatene	120	Discharge	96.8%	[3]
Vassilades	61	6 months	98.3%	[4]
Biglioli	64	Discharge	96.8%	[5]
Diegeler	618	6 months	97%	[6]
Olveira	115	Discharge	98.1%	[8]

Despite these excellent results utilizing the LIMA to the LAD by a limited access approach, this procedure has fallen largely into disuse [9]. The reasons for this include the success of PCI, particularly using drug-eluting stents (DES) for single vessel disease. It is unusual at the present time for de novo single vessel disease of the LAD to be referred for surgical intervention without previous PCI. The few limited applications at the present time are in patients with recurrent restenosis of the LAD after DES.

A second reason for lack of widespread use of the MIDCAB procedure is the morbidity associated with the procedure. Many surgeons have questioned whether the morbidity of a limited anterior thoracotomy with rib spreading incision is any less morbid or painful than a median sternotomy incision. Indeed because of this, numerous surgical modifications have been made to limit the morbidity of the procedure. Those include the use of thoracoscopic internal mammary artery (IMA) harvest with or without robotics, and the use of robotics, and/or anastomotic connectors to perform the anastomosis [10]. All of these techniques will be discussed below under "Facilitating Technology."

The MIDCAB procedure also has isolated application for limited access bypass of single vessel disease elsewhere besides the LAD. A limited left lateral thoracotomy incision for bypass of branches of the circumflex vessel as well as limited right anterior thoracotomy incision for bypass of the main right coronary artery (RCA) are occasionally used procedures. Utilization of a limited access subxiphoid approach to bypass branches of the RCA using a right gastric epipleural artery underwent limited clinical application. Its use at the current time is rare.

42.2 Minimally Invasive CAB (Port Access)

The port access approach employs a limited access incision, usually a left anterior fourth interspace thoracotomy, for single vessel disease or a third interspace thoracotomy for multivessel disease. The procedure is performed on CPB under ischemic cardioplegic arrest. Access for CPB is obtained through percutaneous cannulation of the femoral artery and vein and use of an endoballoon placed through the femoral arterial cannula into the ascending aorta for both aortic clamping and cardioplegia delivery. Because of the paucity of surgical single vessel disease as well as the ability to perform the same operation on a beating heart, the port access approach is rarely used for coronary artery disease at the present time and is utilized mostly for minimally invasive mitral valve surgery. Enabling technologies including robotics have been used to facilitate multivessel CAB, but its use is limited to centers with a specific interest in this area.

42.3 Off-Pump Coronary Artery Bypass Grafting (OPCAB)

The most widely employed application of minimally invasive surgical techniques for coronary revascularization is the OPCAB procedure, which is performed through a full median sternotomy incision, but without CPB. Over 2,500 peer review articles are now in publication, the overwhelming majority of which show a benefit in either all patients or in high-risk selected subgroups. The primary benefits of the off-pump technique are related to the elimination of CPB and its attendant incitement of the systemic inflammatory response. The second benefit of the off-pump technique is the need for minimization of manipulation of the ascending aorta. Neurologic injury associated with coronary revascularization is related as much to manipulation of the atherosclerotic ascending aorta as it is to the use of the heart-lung machine. Additional techniques to minimize manipulation of the ascending aorta including epiaortic scanning to detect atherosclerotic disease of the ascending aorta, use of T-grafts or Y-grafts with multiple arterial grafting to avoid the ascending aorta altogether, or the placement of grafts on the ascending aorta with clampless techniques all serve to enhance the beneficial effects of off-pump surgery in avoiding diffuse and focal neurologic complications.

The techniques of beating heart surgery are now well described. The technical aspects include a wide opening of the pericardium and techniques to minimize compression and distortion of the right ventricular cavity. Adverse hemodynamic consequences associated with cardiac manipulation are mainly due to compression and distortion of the right ventricle. The use of apical suction exposure devices on the apex for access to the left-sided vessels and on the acute margin of the heart for access to the RCA and its branches facilitates the procedure (Fig. 42.1). Suction stabilization devices for immobilization of the target coronary artery have become routine. Adjunctive devices including intracoronary shunts and misted carbon dioxide blowers significantly facilitate execution of the arterial conduit coronary artery anastomosis under optimal conditions. The use of multiple arterial conduits and total arterial revascularization can be performed routinely off-pump as well as on-pump. We find that anastomosis of the LIMA to the LAD performed first is preferable (Fig. 42.2). The exception to this is when there is total occlusion of the right coronary artery. In those instances placement of a right internal mammary artery (RIMA) to the RCA before revascularization of the LAD is preferable to avoid ischemia to two regional distributions. It is our preference to routinely use the LIMA to the LAD, the RIMA to the RCA, and the radial artery to the circumflex system (Fig. 42.3). If a diagonal vessel is

Fig. 42.1. Apical suction device to distract heart for exposure to all surfaces while minimizing hemodynamic compromise

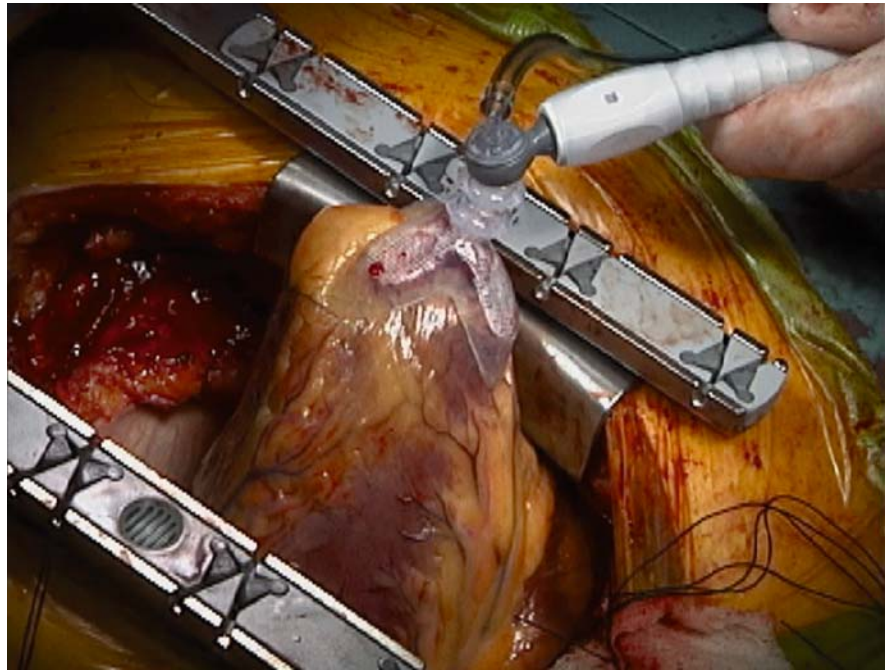
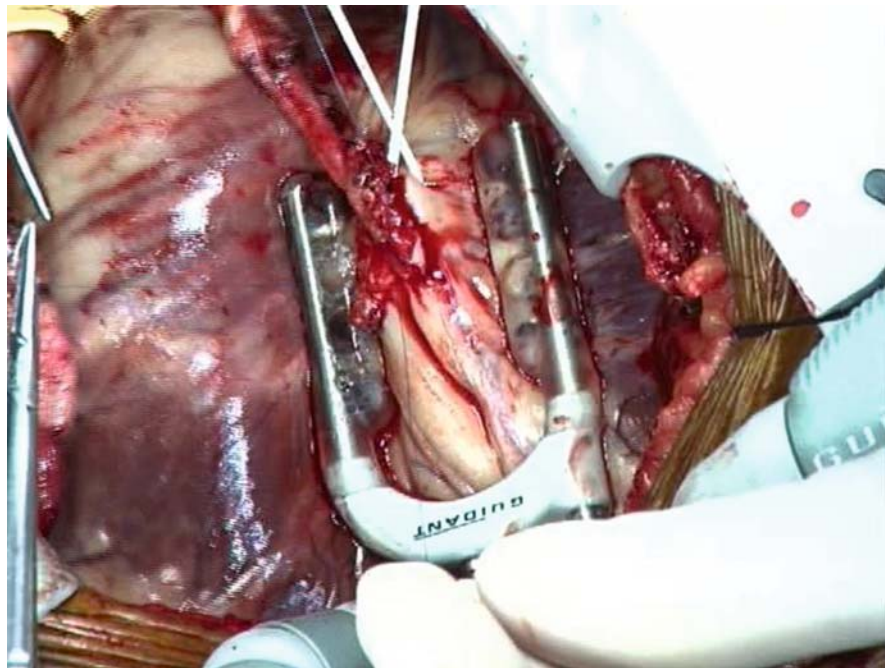


Fig. 42.2. LIMA to LAD anastomosis with suction stabilizer in place



in need of grafting, a sequential arterial anastomosis with the LIMA to the LAD and diagonal branch is feasible. In a similar manner, multiple obtuse marginal branches of the circumflex coronary artery can be bypassed sequentially with the left radial artery. It has become our preference to perform a T-graft with the left radial artery placed as a T anastomosis to the LIMA (Fig. 42.4). If there is concern about adequacy of flow

through the LIMA the radial artery can be brought as a graft directly off of the ascending aorta.

Concerns about radial artery graft patency exist. What has become apparent is that radial artery patency is compromised when a non-critically diseased vessel is bypassed. It is therefore our practice to use the radial artery to target vessels that have a minimum of 80% occlusion. Depending upon the anatomy therefore, if the

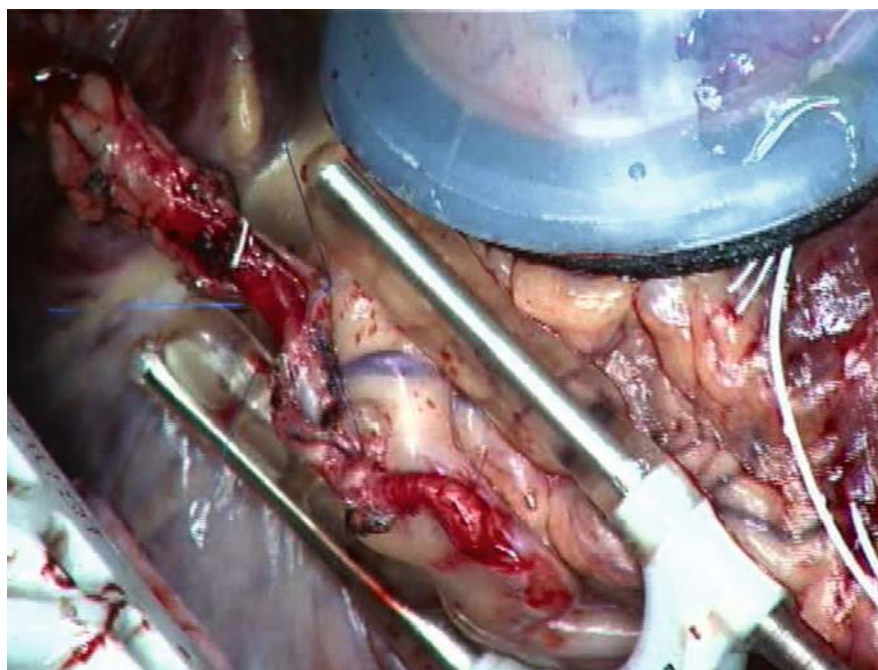


Fig. 42.3. RIMA to RCA anastomosis with suction stabilizer in place



Fig. 42.4. LIMA to radial artery T-graft

RCA is totally occluded we place the radial artery to the RCA and then bring the RIMA as a T-graft off of the LIMA to the circumflex system rather than as an in situ graft to the RCA.

42.3.1

Outcomes of Arterial Revascularization in OPCAB

Numerous reports exist in the literature regarding the safety and benefit of off-pump total arterial revascularization. Pandey reported 360 patients who underwent off-pump coronary surgery with complete arterial revascularization and matched them to a similar number of patients undergoing complete arterial revascularization on CPB [11]. They found no difference in in-hospital mortality; however, the off-pump patients were less

likely to develop sternal wound infections (2.5% vs. 5.8%, $p=0.03$), significantly lower blood loss (675 ml vs. 780 ml, $p\leq 0.001$), red blood cell transfusion (8.6% vs. 38.9%, $p<0.001$), enzyme rise (13 vs. 23 units/l, $p\leq 0.001$), inotrope support (11.9% vs. 28.9%, $p\leq 0.001$), and ventilation time (5 h vs. 8 h, $p\leq 0.001$). Intensive care unit (ICU) and hospital stay were also significantly lower in the off-pump patients. Mariani studied 569 multivessel CABG patients who underwent total arterial revascularization by the off-pump approach [12]. In-hospital mortality was 2.3%. Survival at 36 months was 95.6% and freedom from cardiac related events was 91.6%. They concluded that total arterial OPCAB had safe outcomes and low cardiac related events at follow-up even for patients in a moderate- to high-risk profile. Singh reported a prospective study of 803 patients undergoing total arterial revascularization on a beating heart [13]. Single vessel disease was present in 9% of patients, double vessel disease in 25%, and triple vessel disease in 66%. Grafting was routinely performed using both LIMA and RIMA as well as the radial artery. There were 2,661 grafts placed with a mean of 3.31 grafts/patient. Operative mortality was 0.5%. There were no postoperative strokes. Blood transfusion was not required in 69% of patients and the mean hospital stay was 5.6 days. Overall graft patency in the 25% of patients on whom angiography was carried out before discharge was 98.6%. Muneretto prospectively enrolled 176 patients undergoing total arterial revascularization into on-pump and off-pump groups [14]. They found mean number of anastomoses was similar in both groups (2.8% vs. 2.7%). They con-

cluded that off-pump surgery could be successfully used for arterial grafting without compromising the completeness of revascularization. They also found the avoidance of CPB significantly decreased the mechanical ventilation support and length of ICU and postoperative stay. All other outcomes were equal early and mid-term.

Concern has been raised regarding graft patency in off-pump surgery in relationship to on-pump surgery. In addition to the above outcomes, the PRAGUE-IV trial reported 400 patients randomized to off-pump versus on-pump [15]. One-year follow-up angiography was performed in 255 patients. Although saphenous vein graft patency was poor in both groups (59% on-pump vs. 49% off-pump), arterial graft patency was 91% in both groups. They concluded that the patency of arterial CABG done on a beating heart was excellent and equal to grafts performed on-pump.

42.4

Multivessel Off-Pump Limited Access Surgery

Although as mentioned under the MIDCAB procedure arterial revascularization through a limited access approach has been limited for the most part to single vessel bypass, a few centers are performing multivessel total arterial revascularization through a left thoracotomy. Srivastava reported 200 patients undergoing what he termed “ThoraCAB” [16]. Through a 5-6 incision over the 4th or 5th left intercostal space the procedure is performed. An average of 2.9 grafts/patient were performed with one death (0.5%), two conversions to CPB (1%), and no strokes. Singh reported 27 patients undergoing multivessel total arterial revascularization via an anterolateral thoracotomy [17]. An average of 3.2 grafts/patient were performed with no operative mortality and no conversions to CPB and excellent graft patency.

42.5

Hybrid Procedure

The hybrid procedure or “integrated coronary revascularization strategy” evolved in the mid-1990s in an attempt to effectively treat patients with multivessel disease while lowering procedure related morbidity by combining minimal access coronary surgery with percutaneous techniques. As initially conceived, it was heralded as innovative representing the best of interventional cardiology and minimally invasive cardiac surgery. There have been a total of ten series representing just under 300 patients in the medical literature describing this integrated approach [18–27]. Although immediate LIMA graft patency has ranged from 92% to

100%, the Achilles heel has been repeat revascularization necessitated by stented PCI vessels. It has been speculated that in the era of DES the hybrid approach combining a LIMA to the LAD with DES to other coronary vessels may now be a more viable option. Further issues regarding the integration of the two approaches include the logistics of performing two procedures in one patient preferably during one hospital stay and the need for treatment of all patients with DES with clopidogrel postoperatively. In addition, the recent increased aggressiveness with the use of DES in multivessel disease would appear to limit the hybrid approach to a small niche of patients who are high risk for both PCI and conventional multivessel bypass surgery by a median sternotomy. In a limited number of these patients with ostial or bifurcation or complex left main disease who are elderly with significant comorbidities, the hybrid approach combining a LIMA to the LAD with DES may be a viable option [28]. Our use of the integrated approach has been for the most part limited to patients in need of reoperative procedures or having previous chest wall radiation.

42.6

Facilitating Technology for Minimally Invasive Arterial Grafting

A wide variety of new technology has become available for facilitating minimally invasive cardiac surgery and thus the use of arterial grafting. Those include robotics, anastomotic connectors, clampless proximal anastomotic techniques, intraoperative imaging systems, and finally techniques of clampless anastomoses.

42.6.1

Robotics

Robotics was introduced into cardiac surgery in order to enhance precision movement in a closed chest environment (Fig. 42.5). Robotics has been used both for thoracoscopic IMA harvest and for precision suturing of the IMA coronary artery anastomosis [29–36]. Although the IMA can be harvested by non-robotic thoracoscopic approaches, robotics appears to be safe and technically facilitates endoscopic conduit harvest. Stahl reported 54 patients from four institutions using endoscopic IMA harvest with either a voice activated system or a telemanipulation system [33]. Bonatti performed 50 procedures with the DaVinci system including endoscopic IMA harvest in 19 patients, robotic assisted suturing of the LIMA to the LAD in 15 patients, and totally endoscopic coronary bypass on an arrested heart in 15 patients [32]. Bolotin described safe harvest of 18 internal thoracic skeletonized internal mammary arteries in the animal model [34]. Finally, Subramanian re-



Fig. 42.5. Robotic system for totally endoscopic artery bypass

ported on 30 patients who underwent off-pump minimally invasive multivessel bypass with the internal mammary arteries harvested with robotic telemanipulation [35]. The use of the robot for arterial CABG remains in the feasibility arena at the present time with only a few centers pursuing this approach.

42.6.2 Anastomotic Connectors

Endoscopic suturing of arterial coronary anastomoses even with robotic enhanced precision remains problematic. In order to facilitate this aspect of the procedure anastomotic connectors were introduced to eliminate the need for suturing endoscopically. Although at least eight different anastomotic connectors, most of them for proximal anastomoses, were introduced, due to financial and regulatory issues only one anastomotic connector, the C-Port Distal Anastomosis System (Cardica, Inc., Redwood City, CA), remains a viable option at the present time in the U.S. Extensive preclinical and clinical studies had been performed with a set of magnetic couplers for coronary arterial grafting (Ventrica, Medtronic, Inc., Minneapolis, MN). On early and 6-month angiographic follow-up patency was excellent [37, 38]. Despite promising clinical results, however, this technology was voluntarily withdrawn from the clinical arena. The C-Port system, which performs an automated stapled anastomosis, has performed well in initial clinical trials. Numerous arterial anastomoses

have been performed in clinical models with 6-month graft patency exceeding 90%. This device has now been approved for use outside the United States and is awaiting regulatory approval at this time. If such a device proves as beneficial as its early trials limited access arterial grafting may be facilitated.

42.6.3 Intraoperative Imaging

A shortcoming of CABG surgery has been the inability to easily perform coronary angiography to demonstrate intraoperative patency of arterial anastomoses. Recently intraoperative imaging has been introduced using an infrared fluorescence imaging system (SPY Intra-Operative Imaging System, Novadaq Technologies, Inc., Mississauga, Ontario, Canada). There have been a limited number of reports in the literature demonstrating good correlation of this imaging system with conventional postoperative dye angiography [39, 40]. If this early experience bears out with broader use, this intraoperative imaging system may enhance arterial graft patency.

42.6.4 Clampless Proximal Anastomosis

Manipulation of the atherosclerotic ascending aorta can be a cause of stroke even in off-pump surgery. In order to minimize this potential complication, a clamp-

less proximal anastomosis has been performed [41, 42]. We routinely perform epiaortic scanning in all patients in which a proximal anastomosis is anticipated. If disease is present then the Heartstring II Proximal Seal System device (Guidant Co., Indianapolis, IN) is used to place the radial artery directly off the ascending aorta in a clampless fashion.

In summary, all arterial grafting can be routinely performed using minimally invasive techniques. Extensive experience exists with total arterial revascularization by off-pump techniques and it appears that the results in terms of graft patency are equal to on-pump all arterial revascularization, yet with less mortality and morbidity. Although excellent results have been demonstrated with limited access arterial grafting, due to the limited number of patients with single vessel disease being referred for surgery it has become a niche procedure. Multivessel limited access grafting with all arterial grafts remains in the feasibility stage at the present time awaiting perfection of techniques using robotics and anastomotic connectors.

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Off-Pump Coronary Artery Bypass Grafting Using Arterial Grafts

E. BUFFOLO, L.R. GEROLA

Coronary surgery started with arterial grafts, and in 1951 Vineberg et al. used the original concept of internal thoracic artery implantation to treat coronary insufficiency [1]. In 1961, Goetz et al. performed the first direct myocardial revascularization, both experimentally and clinically, using the right internal thoracic artery anastomosis to the right coronary artery without extracorporeal circulation [2]. Some years later, Kolesov [3] clinically used the left internal thoracic artery (LITA) anastomosis to the left descending coronary artery without extracorporeal circulation through a left thoracotomy using mechanical sutures in some patients.

In 1968, Green et al. [4] presented an experimental study using the left internal thoracic artery directly anastomosed to the left descending coronary artery in dogs; and at the end of the paper they reported a successful clinical application in one patient. At the same time, Green et al. utilized sternotomy and microscopic and optical devices to perform mammary-coronary artery anastomoses.

Notwithstanding this progress in coronary artery bypass grafting, it was only after the saphenous vein was used, a method developed by Favaloro et al. [5], that surgical myocardial revascularization made a great impact and became a real alternative in the treatment of coronary insufficiency.

For many years, the saphenous vein graft was considered the graft of choice for use in the operation because it was easily harvested from the legs and easier to perform anastomoses with than the internal thoracic artery.

Only in the 1980s did Loop et al. [6] and others [7, 8] demonstrate the superiority of the internal thoracic artery over the saphenous vein along with the clinical benefits, especially long-term results. It was more than 10 years before the internal thoracic artery was regarded as the ideal graft.

During this period, the use of cardiopulmonary bypass was considered necessary to perform aortocoronary bypass grafts, and a generation of surgeons learned to perform operations with this technique. Nevertheless, Buffolo et al. [9] in 1981 in Brazil and almost at the same time Benetti [10] in Argentina per-

formed the first consecutive series the result of which was to recommend myocardial revascularization without cardiopulmonary bypass.

During subsequent years they presented evidence to support this method and demonstrated the benefits of performing the operation without extracorporeal circulation [11–17].

Only in the mid-1990s did cardiovascular surgeons recognize the value of this technique, with the development of the concept of the minimally invasive operation. Minimally invasive direct coronary artery bypass (MIDCAB) was performed without cardiopulmonary bypass through a small left thoracotomy.

Like arterial grafts, the operation without the need for extracorporeal circulation proved advantageous for many years and can be considered a real advance in the surgical treatment of coronary insufficiency.

Our experience started in 1981 and during the past 23 years we have performed 3,804 operations without cardiopulmonary bypass. This represents 30.3% of the total myocardial revascularization operations performed at our institution. At the beginning this figure was around 20% with application to anastomoses in the left anterior descending artery, diagonal artery and right coronary artery.

Nowadays, we have increased the indications with the development of stabilizers and techniques to expose the left marginal artery, and in the past 2 years we have reached an application rate of almost 50%.

During this time, many surgeons have asked us: how, when and why perform myocardial revascularization without cardiopulmonary bypass? What is the role of arterial grafts in this operation? The following sections will try to answer these questions.

43.1

Extracorporeal Circulation

First of all, it is important emphasize that extracorporeal circulation has represented the most important advance in cardiac operations and it is the basis of all development in this area. On the other hand, cardiopulmonary bypass is not free from complications and, in

most cases, is the cause of organ damage, either transient or permanent.

During cardiopulmonary bypass many humoral or cellular alterations occur that promote an inflammatory reaction which leads to liberation of complements [18], cytokines [19, 20] (TNF) or vasoplegic syndrome [21]. The inflammatory response leads to capillary permeability, sequestration of neutrophils and microembolism. These alterations may cause respiratory insufficiency, renal failure, low cardiac output and other disorders in different organs.

The technical procedure of cardiopulmonary bypass can be responsible for some lesions. Transesophageal echocardiography and transcranial Doppler studies showed that cerebral embolization occurs in 100% of patients at the time of cannulation, aortic clamping and declamping [22, 23]. We have also shown a decreased incidence of postoperative complications in elderly patients where cardiopulmonary bypass was not used, especially those related to the central nervous system [24].

43.2

When Can Myocardial Revascularization Without Extracorporeal Circulation Be Performed?

We need to consider two aspects: (1) the angiogram characteristics and (2) the clinical situation. Initially we believed that patients with one or two vessel disease, that is lesions involving the left anterior descending artery (LAD) and/or the diagonal and right coronary artery, were ideal candidates.

Recently, there have been two important contributions toward expanding the use of the off-pump technique: (1) maneuvers to expose the marginal and posterior arteries and (2) the development of stabilizers that promote a "regional cardiac arrest," decreasing cardiac motion and creating good conditions under which to perform an ideal anastomosis.

The use of mechanical stabilizers has become fundamental and represents a better way to perform off-pump operations, making this procedure safe, effective and reproducible for different groups [25–27]. Calafiore [28] demonstrated, from angiograms, a superior early left internal thoracic artery patency using stabilizers.

The second important advance was made by Lima [29], who proposed maneuvers for the presentation of the marginal branches with less hemodynamic imbalance. Using a stitch positioned strategically between the inferior vena cava and the inferior left pulmonary vein, the traction of this stitch brings the heart outside of the chest with the apex upward, a true "ectopia cordis." Some modifications to the operation table, and combination with the other maneuvers, determine the appropriate exposure of the left marginal artery.

These major advances, access to marginal branches

and stabilizers, produce conditions for off-pump coronary artery bypass grafts to be applied for all kinds of patients and for complete myocardial revascularization to be performed.

When we think about preoperative clinical conditions we should consider some situations in which operation without cardiopulmonary bypass represents a good alternative, e.g., angioplasty failures, the elderly, reoperations, patients with poor left ventricular function, poor clinical conditions, Jehovah's Witnesses, ascending aortic calcification, chronic obstructive pulmonary disease, renal failure and other clinical co-morbidities.

In fact, these patients with severe clinical co-morbidities represent the ideal application for this approach, and we can say that: "*the worse the patient the better the outcome.*"

Recently we randomized 160 patients with good left ventricular function and without major clinical morbidities; 80 operations were performed using extracorporeal circulation and cardioplegic arrest and the other 80 were operated on using the off-pump technique. No difference was observed regarding postoperative complications, necessity for blood transfusion, bleeding, neurologic complications, hospital and intensive unit stay, time of operation, intubation time and the possibility for extubation in the operating theater [30].

Another important aspect is with regard to patients with severe left ventricular dysfunction. In these patients we have two alternatives for performing coronary artery bypass, first, using the off-pump procedure and, second, using assisted extracorporeal circulation without cardioplegic arrest. The real benefit for this subgroup should be studied through clinical randomized trials. We analyzed the patients individually and chose one of these two alternatives.

43.3

Arterial Grafts and Off-Pump Myocardial Revascularization

The off-pump procedure does not limit the use of arterial grafts. Our initial experience was that patients with one vessel disease in the left anterior descending artery (LAD) were a better indication for the off-pump technique using the left internal thoracic artery to LAD. In fact, we need to choose the arterial graft based on the target coronary artery and not according to whether the procedure will be done on- or off-pump.

For LAD, nobody doubts that the left internal thoracic artery is the graft of choice; in our experience, the left internal thoracic artery is used in 100% of patients with isolated lesions in the LAD.

Other arterial grafts such as right internal thoracic artery, radial artery, epigastric artery and gastroepiploic artery are the most frequently used.

For the marginal coronary artery we have used the radial artery composite with left internal thoracic artery. This creates a total arterial revascularization of the left coronary artery and better long-term left ventricular protection. On the other hand, when we use the right internal thoracic artery through the transverse sinus we still prefer to do it on-pump.

The diagonal artery is a secondary system and to use a saphenous vein is a good alternative, but in some young patients we have used an epigastric artery composite with left internal thoracic artery, or a sequential anastomosis using the left internal thoracic artery.

The right coronary artery is the artery to receive the gastroepiploic artery graft, but it is important to define when to do it. The right coronary system is important, many patients having occluded right coronary artery and continuing with normal left ventricular function. When the right coronary artery is a dominant coronary artery giving posterior ventricular branches after the crux cordis, in young patients with normal ventricular function, then we should use an arterial graft.

Another important characteristic of arterial grafts is that of expanding the concept of minimally invasive surgery, with the idea of “no-touch aortic.” This concept is based on the fact that even aortic lateral clamping in the off-pump technique can pose a risk of cerebral embolization.

When we used two internal thoracic arteries and a radial artery composite or pedicle gastroepiploic artery, this operative strategy reduced the possibility of neurological damage due to any necessary manipulation of the aortic.

Kobayashi et al. [31] reported total arterial off-pump coronary revascularization with only the internal thoracic artery and composite radial artery grafts. They used this approach in 257 patients with a mean age of 66.1 years and 3.28 grafts per patient, one operative death (0.4%) due to cerebral hemorrhage and two episodes of stroke (0.8%) during postoperative angiography. Perioperative myocardial infarction occurred in 12 patients (4.7%), sternal dehiscence in 5 (1.9%). Early postoperative angiography revealed a 97.8% graft patency of internal thoracic arteries and a 97.9% graft patency of the radial artery.

Hirose et al. [32] operated on 48 patients using bilateral internal thoracic arteries and the gastroepiploic artery in the elderly (mean age 74.5 ± 9.9 years) using the off-pump procedure. There was no hospital mortality and stroke was observed in two patients. During the follow-up period of 2.3 ± 1.2 years, no deaths, angina recurrence or coronary interventions were observed.

During these 23 years of experience using the off-pump technique we started using 15% of arterial grafts and nowadays 94.7% of patients receive at least one arterial graft. The types of arterial grafts used during this period are shown in Table 43.1.

Table 43.1. Types of arterial graft

Type of arterial graft	Number	%
LITA	3233	95.3
RITA	67	2.0
Radial	128	3.9
Gastroepiploic	16	0.4
Composite epigastric grafts	8	0.2

43.4

Operative Technique

We describe this procedure as performed through sternotomy. Prior to surgery, the angiograms are reviewed and the number of grafts planned. Although a perfusionist is always present in the operation room, the cardiopulmonary bypass circuit is not set up. After a 12–14 cm limited skin incision, a full median sternotomy is performed. The LITA is harvested avoiding opening the left pleura. Simultaneously, other conduits (saphenous vein, epigastric, gastroepiploic and radial arteries) are harvested. Heparin (2 mg/kg) is administered a few minutes prior to occlusion of the coronary artery. The artery to be treated is controlled with a piece of silicone tube in a segment where there is no plaque. We need to avoid the possibility of lesion in the coronary artery in the place when the artery is snared, and this is achieved with a special and delicate type of silicone that we have used since our experimental study in cadavers. In this study we observed a positive relationship between the degree of coronary arteriosclerosis and the degree of lesion. In this way, we learned that snaring is safe if it is done in a segment with no or mild arteriosclerosis of the coronary artery.

When we started our experience, we used 5 mg of verapamil, which was given intravenously in order to decrease arterial pressure, heart rate and oxygen consumption. Now, with the development of stabilizers and the experience of many years we no longer administer drugs. The blood flow can be interrupted for periods of up to 17 min without myocardial damage.

The right coronary artery represents a particularly difficult problem, because there is the possibility of bradycardia, atrioventricular block and hypotension during occlusion. In this artery, we consider an important and safe strategy to be the use of intracoronary shunt as developed by Rivetti et al. [33].

For each coronary artery there is a specific exposure maneuver. For LAD anastomosis the heart is elevated with a sponge placed dorsolaterally in the pericardium and suture retraction of the pericardium anterior to the phrenic nerve. For right coronary artery, we have used the Trendelenburg position and traction at the marginal border of the right ventricle. The left marginal artery and other branches of the posterior wall of the heart represent the last challenge, which was performed by

Lima et al. [29], through a stitch positioned strategically between the inferior vena cava and the inferior left pulmonary vein; the traction of this stitch brings the heart outside of the chest with the apex upward, a true “ectopia cordis.” Some modifications to the operation table determine the appropriate exposure with which to perform a safety anastomosis. Nowadays, suction devices such as the “Starfish” placed in the heart apex obtain the same result as Lima’s stitch.

All distal anastomoses are performed with a 7-0 running Prolene suture and using stabilizers. Proximal anastomoses are performed in the ascending aorta via lateral clamping. At the end of the anastomoses, protamine is administered and the mediastinum is closed leaving behind a chest drain.

Patients are transferred to an ICU for 1 day and are usually discharged on the fifth postoperative day. Now the majority of cases proceed extubated to the ICU.

43.5 Clinical Experience

Our experience started in 1981, and up to and including February 2004 we have operated on 3,804 patients, 3,723 through limited sternotomy and 80 through a left small thoracotomy and in one case using robotic technology. This number clearly expresses our preference.

Although the LAST (left anterior small thoracotomy) procedure represents an advance, the concept of the minimally invasive operation involves the absence of cardiopulmonary bypass, and not only minimal incision.

From 1981 to February 2004, our institution performed 12,553 myocardial revascularizations, 3,804 of them (30.3%) off-pump. In the last 5 years, we have increased that application rate up to 51.1% as shown in Table 43.2.

Two thousand seven hundred and eighty-one patients (73.1%) were male and 1,023 (26.9%) were female. Ages varied from 20 to 90 years (mean 62.0 ± 12 years). Preoperative clinical conditions were: chronic coronary insufficiency, 2,709 (71.2%); angioplasty failure (acute or chronic), 374 (9.8%); reoperations, 290 (7.6%); unstable angina, 208 (5.4%); after thrombolysis, 104 (2.7%); acute evolving myocardial

Table 43.3. The main coronary arteries grafted using the off-pump technique

Grafted coronary artery	Number	%
Left anterior descending	3266	87.4
Right coronary artery	2089	54.9
Diagonal artery	917	24.1
Marginal – circumflex	667	17.5
Descending posterior	218	5.7
Ventricular posterior	214	5.6

infarction, 74 (1.9%); and cardiogenic shock with intra-aortic balloon, 24 (0.6%).

Regarding the number of bypass grafts, 28.6% of the patients received one graft, 50.5% two grafts and 20.8% received three or more grafts. The mean number of grafts per patient was 1.9. The main coronary arteries grafted off-pump are shown in Table 43.3.

The hospital mortality was 1.9% (75 patients) and the main causes were: low cardiac output, 13 patients (0.3%); perioperative myocardial infarction, 14 (0.3%); and sudden death, eight patients (0.21%). Other causes were observed with a lower incidence, such as arrhythmias, infections, pulmonary embolism and insufficiency.

Regarding arterial grafts, we started using 15% of arterial grafts and especially LITA to LAD. At that time (1981–1985), the advantages of the LITA on late survival were not as clear as today.

During the past few years, 94.7% of patients received at least one arterial graft, and in young patients with good ventricular function the use of LITA to LAD is around 100%.

We used 7,371 grafts in 3,804 patients. The LITA was the most important graft used (3,323 patients). Other arterial grafts were used without cardiopulmonary bypass: right internal thoracic artery (67 patients), radial artery (128 patients), inferior epigastric artery (8 patients), gastroepiploic artery (16) and bovine mammary artery (2 patients).

The off-pump technique represents a real advance in cardiac surgery and it is established as the alternative to performing myocardial revascularization with the same security as the conventional operation with extracorporeal circulation and cardiac arrest.

On the other hand, it is important emphasize that the off-pump procedure is not for all patients and to reach 100% patients operated on using this technique is not our goal.

Several studies have documented a better off-pump application rate in patients with severe clinical co-morbidities [34], such as renal dysfunction, the elderly [35–37], reoperation, and chronic pulmonary disease [38] patients. In addition, some randomized studies have failed to prove the superiority of off-pump versus on-pump myocardial revascularization in patients with good clinical conditions [30, 39, 40].

Table 43.2. Applicability of off-pump technique in recent years

Year	% Off-pump
1999	42.0
2000	43.3
2001	49.2
2002	51.1
2003	46.3
23 years	30.3

Like all procedures and techniques developed during the evolution of cardiac operations, off-pump myocardial revascularization has its own indications and applicability; most importantly for us is that it can be used to perform better myocardial revascularizations with safety in our patients.

The off-pump procedure is one more technique that all surgeons should learn and perform in order to offer another alternative for treatment of patients under different clinical conditions. The best choice of method for performing myocardial revascularization should be looked at for each patient and we must consider the risk, benefits and necessity for complete myocardial revascularization.

Sometimes, in patients with severe preoperative comorbidities, for whom cardiopulmonary bypass could represent a high risk of organic damage, we can perform a physiologic myocardial revascularization, treating only ischemic areas, identified by functional tests such as nuclear perfusion.

Finally, we would like to say that on-pump and off-pump approaches are not methods competing with each other. Surgeons should choose between the two techniques based on their own experience, preoperative clinical conditions and angiography. After all these factors have been analyzed we must then choose the most safe and effective technique for each patient.

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Comparison of the Effect of On-Pump and Off-Pump Coronary Artery Bypass Grafting on Neurological Events

Y. ABU-OMAR, D.P. TAGGART

44.1 Introduction

Cerebral injury has been a recognized complication of cardiac surgery since the 1950s [1] and is still the most significant and disabling complication of coronary artery bypass grafting (CABG). Although cerebral injury also occurs after major non-cardiac surgical procedures [2], it is more common and severe after operations using cardiopulmonary bypass (CPB), supporting the potentially deleterious effects of extracorporeal circulation. Over the last decade, improvements in anaesthetic and surgical techniques, as well as in postoperative management, have resulted in a reduction in mortality following CABG. This, however, has not been paralleled by a reduction in cerebral injury, as patients with a higher risk profile increasingly constitute the surgical population.

Cerebral injury can be broadly classified, in decreasing order of severity but increasing incidence, as stroke, delirium (encephalopathy) and neurocognitive dysfunction. The aetiology of postoperative cerebral injury is multifactorial. Stroke is largely caused by embolic debris during aortic manipulation while delirium and neurocognitive dysfunction are more closely linked with the use and conduct of CPB. CPB has three main pathophysiological mechanisms: gaseous and solid cerebral microembolization, intraoperative hypotension and/or hypoperfusion and the systemic inflammatory response syndrome [3]. Intraoperative cerebral microembolization is probably the most important mechanism [4, 5]. Brown and colleagues demonstrated large numbers of lipid microemboli in the brains of patients who died after cardiac surgery and whose numbers correlated with the duration of CPB [5]. Recently we have confirmed the occurrence of both gaseous and particulate cerebral microemboli during CPB and that both are substantially reduced with off-pump CABG [6].

This chapter explores current concepts of the incidence, pathophysiology and prevention of cerebral injury in on-pump and off-pump surgery.

44.2 Stroke

Major cerebral injury such as stroke affects 3% of patients undergoing CABG [7] and up to 8–11% of those undergoing open-cardiac procedures [8]. The functional and economic impact of stroke is considerable: it is associated with a tenfold increase in mortality and substantial increases in the length of hospitalization and in the use of intermediate- or long-term care facilities [3]. The risk of perioperative stroke increases with advancing age, the presence of concomitant cardiovascular risk factors [9] and the female gender [10, 11]. Embolization from the atheromatous aorta is the single most important aetiological factor for stroke and arises from intraoperative manipulation of the aorta with cannulation for cardiopulmonary bypass, application and removal of the aortic cross-clamp and the use of side-clamps for anastomosis of the proximal end of the graft to the aorta [3]. Atherosclerosis of the ascending aorta and aortic arch is therefore the strongest predictor of perioperative stroke [7, 12–14].

44.2.1 Off-Pump

Although there have been no large scale randomized trials of stroke in on-pump and off-pump surgery several large observational studies have reported a reduction in cerebral injury with off-pump surgery [15–20]. In the largest single report from the STS Database, comparing over 100,000 on-pump and 11,000 off-pump patients, the hazard ratio for stroke with the latter was 0.6 [15]. In a study of almost 68,000 patients Racz and colleagues reported a reduction in the rate of perioperative stroke from 2% in the on-pump group to 1.6% in the off-pump group [16]. Likewise, in an analysis of over 17,000 patients Mack's group reported a reduction in stroke from 2.1% in the on-pump group to 1.4% in the off-pump [17].

Other studies have highlighted the importance of avoiding or minimizing intraoperative manipulation of the aorta in addition to the avoidance of CPB. In a study by Calafiore, patients were divided into two groups: the

first group underwent conventional CABG using CPB with or without aortic side-clamping, and the second underwent off-pump CABG with or without aortic side-clamping. The rate of postoperative stroke in the on-pump group with and without aortic side-clamping was 2.3% and 1.2% respectively [18]. In the off-pump group, the rate of stroke was 0.2% in the group without any aortic manipulation compared to 1.1% in those where a side-clamp was used.

The importance of avoiding any aortic manipulation has also been reported by others. Kim and colleagues reported a 0% stroke rate in 222 patients undergoing off-pump CABG with a “no-touch” aortic technique [19] while Lev-Ran et al. reported a marked reduction in the rate of stroke and mortality with avoidance of aortic manipulation in a study of 160 consecutive off-pump CABG patients older than 75 years [20].

44.3

Delirium

Delirium is characterized by acute global impairment of cognitive function, reduced level of consciousness, attention abnormalities, increased or decreased psychomotor activity and disordered sleep-wake cycle [21]. While this form of brain injury has not been studied as extensively as postoperative stroke, its importance is highlighted in four prospective studies [7, 8, 22, 23]. It affects 3–8% of patients and results in a fivefold increase in mortality and prolonged hospital stay [24].

44.3.1

Off-Pump

The largest study of delirium in off-pump surgery has recently been reported by the Leipzig group. They described a cohort of 16,000 cardiac surgical patients undergoing CABG with and without CPB over a 5-year period [23]. The incidence of delirium was 8% in patients undergoing conventional CABG with CPB compared to 2% in the off-pump group. This study identified numerous pre- and intraoperative (but not postoperative) predictors of postoperative delirium including cerebrovascular disease, peripheral vascular disease, atrial fibrillation, diabetes mellitus, impaired left ventricular function, urgent operation, intraoperative haemofiltration, prolonged operation and high transfusion requirements. Furthermore, off-pump surgery and younger patient age conferred a protective effect against postoperative delirium. While this was not a randomized trial, it provides incremental evidence of the potential neuroprotective effects of off-pump surgery.

44.4

Cognitive Impairment

While postoperative stroke is a well-defined entity following cardiac surgery using clinical and radiological criteria, cognitive impairment is less well-defined and its detection is mainly dependent on detailed neuropsychological assessment. It is far more common than postoperative stroke or delirium and affects up to 50% of patients in the early postoperative period and persists in up to half of those at 6 months [25–27]. More importantly its occurrence early after cardiac surgery is closely associated with later progression of cognitive decline and impaired quality of life [28, 29].

Neuropsychological testing is currently regarded as the ‘gold standard’ for quantifying postoperative cognitive impairment [30]. However, it has several limitations: it is time-consuming and laborious for both patient and examiner and is influenced by learning effects and regression toward the mean with repeated testing [30, 31]. It follows that neuropsychological testing may have too much ‘noise’ to be able to detect subtle changes in cognitive function with adequate sensitivity, particularly in lower risk groups [24]. These limitations are highlighted by the variability in the incidence of neuropsychological impairment reported in different studies [25, 26, 32, 33].

44.4.1

Off-Pump

The evidence that off-pump CABG reduces cognitive dysfunction is conflicting with reports of marked [33], modest [26] or no benefits [25]. In the first prospective trial assessing cognitive dysfunction following on-pump and off-pump surgery, we reported similar rates of cognitive decline in both groups [25]. Similar observations were noted in a randomized trial by van Dijk and colleagues [26]. The limitations of these studies include the small sample size, rendering them underpowered to detect a statistical difference, and the use of a young low-risk population who are at least risk of such deficits. In contrast, a recent study by Zamvar and colleagues reported a marked reduction in postoperative cognitive dysfunction with off-pump surgery (27% vs. 63%) [33]. The fact that the latter study included well-matched groups receiving the same number of grafts, as well as having complete early and late follow-up, may explain the discrepancy with the results from other trials. As suggested earlier, failure to consistently demonstrate significant improvement in cognitive dysfunction with off-pump surgery may be due to the high signal-to-noise ratio inherent in neuropsychological testing and which may hide subtle but real differences [24].

On the other hand, several reports have shown a significant reduction in microembolization with avoid-

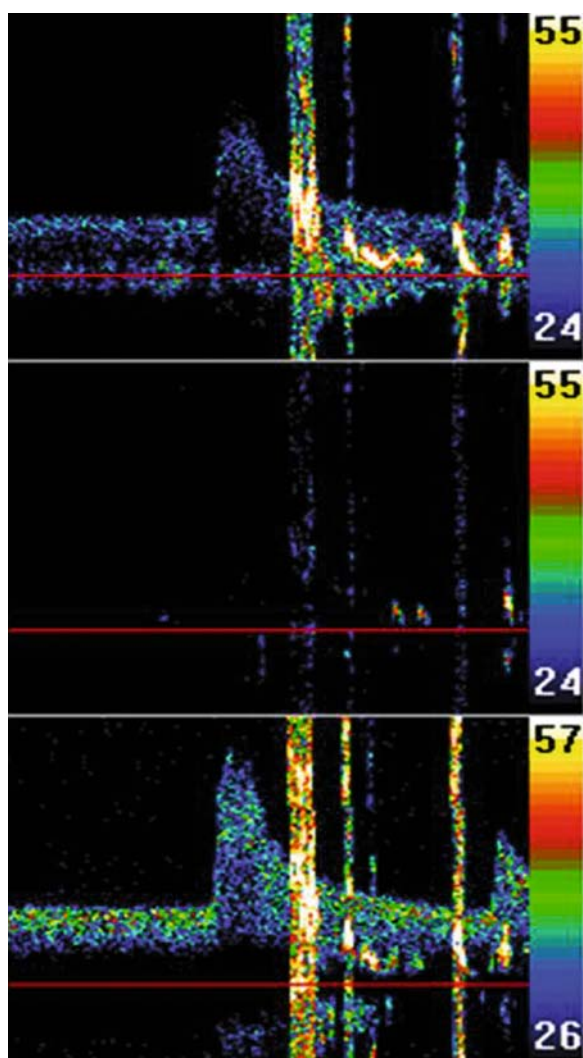


Fig. 44.1. High intensity transient signals (HITS), representing microemboli, identified using multirange multifrequency transcranial Doppler. These occurred with aortic side-clamping. The *top and bottom traces* represent the 2.0- and 2.5-MHz middle cerebral artery gates, respectively. The *middle trace* represents the 2.0-MHz reference gate used for automatic artefact rejection [6]

ance of CPB [6, 34, 35]. In a study of 100 patients undergoing cardiac surgery using CPB, Pugsley and colleagues reported a significant reduction in microembolization with use of a 40- μ m arterial line filter which resulted in a reduced incidence of postoperative neuropsychological deficit [4]. Work from our own group has recently confirmed and expanded these observations. Using a new generation multirange multifrequency Doppler that combines online artefact rejection and automatic discrimination between gas and solid microemboli, we showed a significant reduction in the total number of microemboli detected with off-pump surgery (Fig. 44.1). In addition, we demonstrated a signifi-

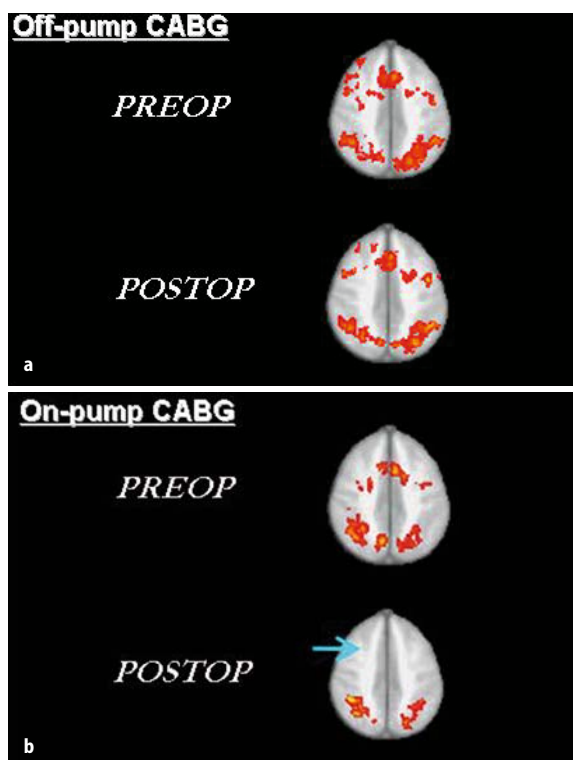


Fig. 44.2a, b. Functional MRI activation images during performance of a cognitive verbal memory task. This demonstrates no postoperative difference in the activation pattern in patients undergoing off-pump surgery. There was, however, a significant reduction in activation in the frontal regions postoperatively in the on-pump group (arrow)

cant reduction in the proportion of solid microemboli in the off-pump group from 22% to 12% [6]. We have also reported significant adverse changes in postoperative cerebral function as measured using functional magnetic resonance imaging (fMRI) that correlated with the degree of intraoperative gas and solid microembolization [36]. More recent work from our group demonstrated a significant reduction in postoperative cerebral activity, as defined by fMRI of the brain during performance of a verbal memory task, with on-pump but not off-pump surgery (Fig. 44.2).

As microembolization can be minimized with complete avoidance of aortic manipulation, total arterial revascularization using composite grafts has the potential of significantly reducing the incidence of neurocognitive injury.

44.5 Conclusions

Potential prevention of neurological morbidity following cardiac surgery can be achieved with modifications of the operative technique. A reduction in both stroke

and microembolization with off-pump surgery can be further enhanced with complete avoidance of aortic manipulation. This 'no-touch aortic technique' can be achieved with total arterial revascularization, using bilateral internal thoracic artery and composite radial artery grafts and carries the additional benefit of graft longevity and prolonged survival [37]. The benefits of off-pump surgery are most likely to be seen in older patients with other risk factors for neurological morbidity. As these patients represent an ever increasing proportion of the surgical population, the challenge of prevention of brain injury following cardiac surgery will remain an important issue.

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45 Closed-Chest Cardiopulmonary Bypass and Cardioplegia for Coronary Artery Bypass Surgery: History and Development

J.I. FANN, T.A. BURDON

45.1 Introduction

Video-assisted endoscopic surgery has become the standard approach for a variety of general and thoracic surgical disorders. Advances that enable closed-chest cardiopulmonary bypass and methods of cardioplegia delivery, as well as the recent progress in robotics using endoscopic technology, have furthered the concept and investigation of closed-chest surgery through incisions that are no larger than that required for placement of instrumentation [1–33].

Notwithstanding these developments, challenges remain in defining the patient population, optimal means of exposure, and considerations unique to cardiac surgery, such as the need for cardiopulmonary bypass and myocardial protection. Additionally, established success with coronary artery bypass without cardiopulmonary bypass utilizing novel stabilizers and retraction devices has encouraged some surgeons to pursue off-pump coronary artery bypass grafting in combination with robotic technology [17, 23, 26–33].

This chapter presents the history and development of a closed chest approach to cardiac surgery focusing on coronary artery bypass grafting using an endovascular system that achieves cardiopulmonary bypass and cardioplegic arrest. Additionally, the contribution of robotic technology to the field of closed chest surgery is discussed.

45.2 History and Development

Although cardiopulmonary bypass was utilized for the vast majority of coronary revascularization procedures in the previous 3 decades, the cardiac surgery community witnessed a resurgence of off-pump coronary artery bypass grafting in the 1990s [34–49]. Improvements in mechanical stabilization devices, recognition of adverse effects of cardiopulmonary bypass, increased patient comorbidities, and medical economic concerns resulted in the development of and refinements in off-pump coronary artery bypass via either

minithoracotomy or median sternotomy. Concerns related to off-pump coronary revascularization include accurate suture placement at the distal anastomosis, maintenance of adequate hemodynamics, and minimizing myocardial injury. Enabling technology for this approach consists of devices that provide a stable anastomosis site by compressing the myocardium adjacent to the artery or immobilizing the myocardium with suction achieved with a remote vacuum source. Off-pump coronary artery bypass via a median sternotomy has become the more popular approach than the limited thoracotomy approach, mainly as a result of the ease and familiarity of internal mammary artery mobilization, target vessel identification and exposure and the increased ability to achieve complete revascularization.

In 1993, Peters described the concept of closed-chest cardiac surgery by using a unique endovascular aortic balloon catheter that provides aortic occlusion, cardioplegia delivery, and aortic root venting during femoral-femoral cardiopulmonary bypass [1]. This design formed the basis for the less invasive cardiopulmonary bypass system developed by Heartport, Inc., a company that was later acquired by Cardioversions, Inc. (Ethicon, Somerville, NJ). The intent of this technology was to provide a platform to treat a variety of cardiac disorders by permitting the surgeon to achieve an arrested and decompressed heart in a closed-chest fashion, so that smaller incisions and possibly endoscopic surgery may be performed [2–7].

The Heartport or port-access system is catheter-based and designed to accomplish cardiopulmonary bypass and cardioplegic arrest based on principles developed for conventional cardiopulmonary bypass (Fig. 45.1). The venous drainage is achieved by the 22 or 25-Fr cannula introduced through the femoral vein. The smaller 22-Fr cannula may be placed directly or percutaneously using the Seldinger technique. Drainage is augmented using vacuum-assisted venous drainage or a centrifugal venous drainage pump. Arterial inflow is through a dual-armed, 19, 21 or 23-Fr femoral arterial cannula introduced via a surgical cutdown. One arm of the cannula is connected to the arterial line of the cardiopulmonary bypass circuit, and the other serves as a conduit for introducing the endovascular

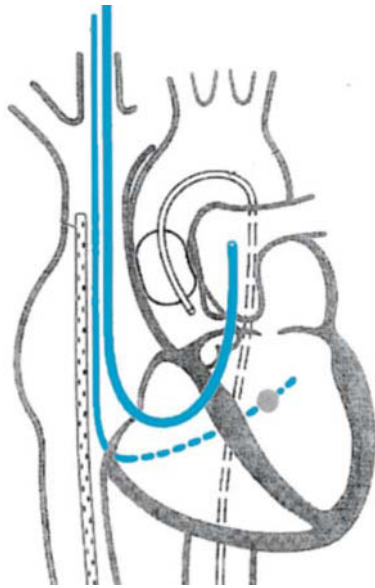


Fig. 45.1. Port-access cardiopulmonary bypass system. The pulmonary vent and coronary sinus catheter are placed percutaneously. The endoaortic clamp is passed through the side port of the femoral arterial cannula and directed into the ascending aorta using echocardiographic and fluoroscopic guidance. The venous drainage is achieved with a venous cannula directed from the femoral vein into the right atrium. (Reproduced with permission. Siegel et al. Monitoring considerations for port-access cardiac surgery. *Circulation* 1997; 96:562–568)

aortic occlusion catheter, or “endoaortic clamp,” which is a 10.5-Fr balloon-tipped catheter that performs four functions (Fig. 45.2). The endoaortic clamp, which is inserted into the arterial return cannula and advanced to the ascending aorta over a guidewire, is designed to achieve aortic occlusion just distal to the coronary ostia, deliver antegrade cardioplegia, vent blood from the aortic root, and monitor aortic root pressure. Cardioplegia solution is delivered through the central lumen, which also acts as an aortic root vent after cardioplegia delivery; a separate smaller lumen serves as an aortic root pressure monitor. Retrograde cardioplegia is achieved through a 9-Fr percutaneously placed catheter with a balloon tip in order to occlude the coronary sinus and permit coronary sinus pressure measurement. This catheter passes through an 11-Fr right internal jugular vein introducer sheath and is directed into the coronary sinus. An additional catheter is the 8.3-Fr pulmonary artery vent catheter that passes through a 9-Fr internal jugular vein introducer sheath and floated into the main pulmonary artery. Transesophageal echocardiography and fluoroscopy are used to guide placement of these catheters [13, 14]. Transesophageal echocardiography is later used to monitor catheter position during the procedure. Adequate endoaortic occlusion of the ascending aorta is also evaluated by comparing simultaneous measurements of aortic root and

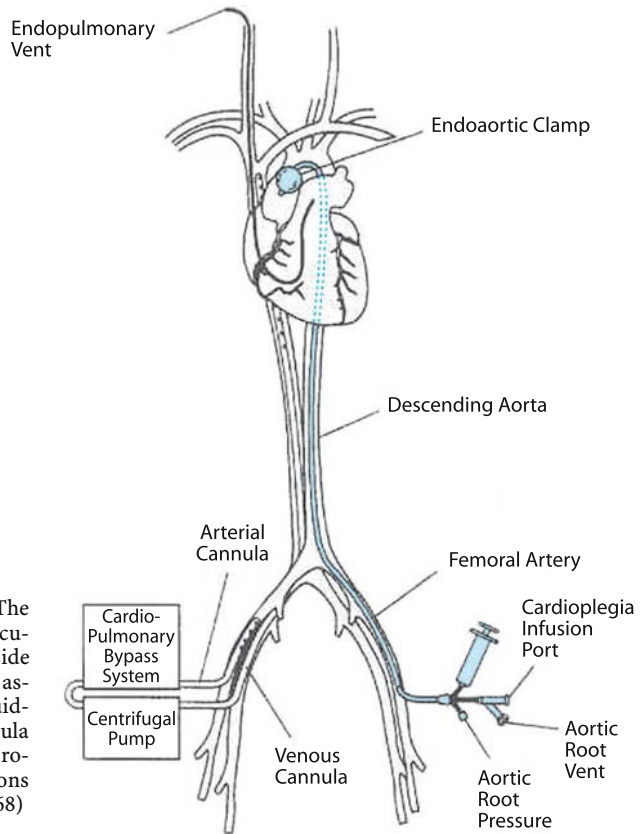


Fig. 45.2. The endoaortic occlusion balloon catheter with three lumens. One lumen is used to inflate the balloon and occlude the aorta. The second lumen is used to measure the aortic root pressure. The third lumen is used to deliver antegrade cardioplegia and also serves as an aortic root vent. (Reproduced with permission. Fann et al. Port-access cardiac operations with cardioplegic arrest. *Ann Thorac Surg* 1997; 63:35–39)

radial artery pressures. Right radial artery pressure is monitored to detect any potential migration of the balloon causing obstruction of the brachiocephalic artery.

Schwartz et al. experimentally evaluated the effectiveness of the port-access cardiopulmonary bypass in achieving myocardial protection during endoaortic clamping [7]. Parameters assessed included end-diastolic stroke work, preload recruitable stroke work, stroke work end-diastolic length relationship, maximal elastance and myocardial temperature. No differences were found in indexes of left ventricular contractility in animals supported with port-access approach and those undergoing conventional cardiopulmonary bypass. Peters et al. investigated the efficacy of port-access cardiopulmonary bypass with cardioplegic arrest in 54 dogs during cardiac procedures [4]. The mean cardiopulmonary bypass time was 111 min and the cardiac arrest time was 66 min. Closed-chest cardiopulmonary bypass with adequate myocardial protection was safely and reproducibly instituted as evidenced by no change in preoperative and postoperative cardiac

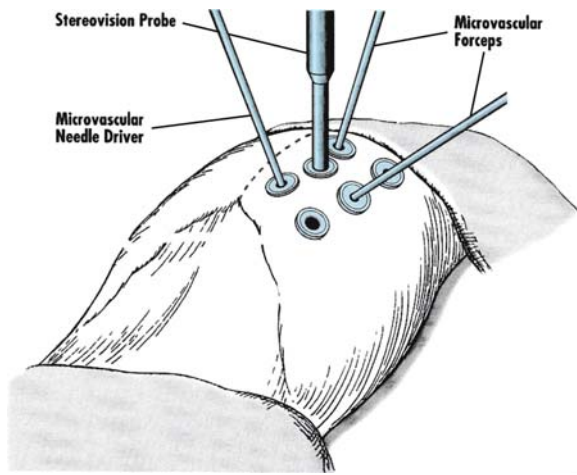


Fig. 45.3. Thoracoscopic coronary artery bypass grafting in the canine model. The probe providing stereoscopic vision is shown with five additional ports for placement of microvascular instruments for coronary anastomosis. (Reproduced with permission. Stevens et al. Port-access coronary artery bypass grafting: A proposed surgical method. *J Thorac Cardiovascular Surg* 1996; 111:567–573)

outputs. Stevens et al. assessed port-access coronary revascularization in the experimental setting [2, 3]. After harvesting the internal mammary artery graft thoracoscopically, port-access cardiopulmonary bypass and cardioplegic arrest were achieved; the internal mammary artery to coronary artery anastomosis was performed in a still and bloodless field with the aid of an operating microscope inserted through a separate port (Fig. 45.3). The mean aortic clamp time was 61 min, and the mean cardiopulmonary bypass time was 104 min. The early patency rate of the internal mammary artery graft was 93%.

Clinically, patient selection for port-access cardiac surgery is generally similar to that for conventional cardiopulmonary bypass; importantly, there are some specific considerations. The vascular system should be evaluated to determine whether the patient's vasculature will permit introduction and placement of the canulae and catheters. The severity of aortic atherosclerosis needs to be assessed. Dilation of the ascending aorta may limit the ability to achieve appropriate balloon occlusion with the endoaortic clamp catheter. Potential contraindications to this technique include significant peripheral vascular disease or diffusely diseased aorta, which increases the risk of femoral arterial cannulation and passage of the endoaortic clamp. Aortic insufficiency is not an absolute contraindication to port-access surgery, since the heart may be arrested with retrograde cardioplegia; in these cases, the central lumen of the endoaortic clamp can be used as an aortic root vent during the procedure. Various tests may be used preoperatively to evaluate the patient's cardiovascular anatomy, including chest X-ray, aortography, iliofemoral arteriog-

raphy, vascular magnetic resonance imaging methods, vascular ultrasound, and echocardiography.

In the initial ten patients who underwent port-access coronary revascularization in late 1995 and early 1996, Reitz et al. reported no early mortality [5]. In three patients, internal mammary artery harvesting was performed entirely using thoracoscopic guidance. Three patients required conversion to open procedure due to early thrombosis of the graft, kinking of the internal mammary pedicle at the pericardial edge, or trauma to the distal internal mammary artery during dissection. Because of technical difficulties associated with the use of multiple thoracic ports, the limited anterior thoracotomy approach was utilized in seven patients. In the seven patients who did not require conversion to an open procedure, the mean hospital stay ranged from 2–6 days. At follow-up, all patients are alive, and nine of ten patients have functioning grafts. In an early series of 32 port-access coronary artery bypass grafting procedures, Ribakove et al. reported 98% overall graft patency and 100% patency of left internal mammary-to-left anterior descending grafts prior to discharge [10]. In another early series of 42 patients undergoing port-access coronary bypass grafting, Reichensperner et al. reported a graft patency of 100% in the first ten patients evaluated with intraoperative angiography [15]. One patient was converted to sternotomy because of a severely atherosclerotic internal mammary artery that could not be used. There was one death due to complications associated with retrograde aortic dissection. A case of right iliac artery dissection required the placement of a femoral-femoral cross-over bypass graft.

From a multi-institutional registry, Galloway et al. reported the outcome of 583 patients who underwent intended port-access coronary artery bypass grafting procedures from 1997 through 1998 [9]. The conversion rate was 5%. In this experience, 48% were single-vessel coronary artery bypass grafting, 31% double-vessel, and 21% triple-vessel. The operative mortality rate was 1%, the myocardial infarction rate 1% and the stroke rate 2%. The incidence of new-onset postoperative atrial fibrillation was 5%. In a smaller study, Grossi et al. found that of the 302 patients who underwent isolated port access coronary artery bypass grafting, 25% had single vessel bypass, 36% double bypass, and 73% triple bypass [11]. The operative mortality in this series was 1%. Compared to the risk matched morbidity rates from STS database, complications rates for the port-access coronary bypass patients were lower. The risk for atrial fibrillation in this series was also significantly lower at 13% [11]. Groh et al. reported their experience with 229 consecutive patients who underwent port-access coronary artery bypass grafting from 1996 to 1998 [12]. The observed mortality was 0.9%. Postoperative complications were compared with a matched cohort of

patients undergoing conventional coronary artery bypass. Complications of stroke and perioperative myocardial infarction were not significantly different between the two groups. Reoperation for bleeding was more likely in the port-access group, while infections were more frequent in the sternotomy group. The length of hospital stay postoperatively was shorter and the need for transfusion was less frequent for the port-access patients. Atrial fibrillation was observed in 14.4% of port-access cases and 16.6% of conventional cases [12]. Grossi et al. compared postoperative pain, stress response, and functional recovery in 14 patients undergoing port-access coronary artery bypass grafting and 15 undergoing coronary artery bypass grafting via standard sternotomy [16]. There were no differences between the two groups in preoperative comorbidities, although the mean age was greater in the sternotomy group. In those undergoing port-access surgery, norepinephrine levels were lower, pulmonary function parameters were better, and the pain was less in the early postoperative period. The port-access cohort also had less muscle soreness, shortness of breath, and fatigue at 1, 2, 4, and 8 weeks postoperatively. In a prospective randomized trial comparing port-access coronary artery bypass grafting via a minithoracotomy to the conventional approach in 40 patients, Dogan et al. reported no hospital mortality in either group. There was one case of retrograde aortic dissection, which was successfully treated [8]. Although there was no difference in troponin T and CK-MB, total CK and myoglobin was higher in the port-access group, which is not surprising given the incision extending through the muscles of the chest wall. S-100B was elevated in the port-access group but neuron-specific enolase levels were not different. Both groups did not display any significant difference in neuropsychological testing. Though prolonged operating and cardiopulmonary bypass times with significantly higher S-100B concentrations were observed in the port-access group, equivalent myocardial and cerebral protection and similar whole-body inflammatory response were found [8].

Because of the facility of most surgeons with the conventional approach to coronary artery bypass grafting and the improved technology and success with the off-pump approach, the port-access coronary artery revascularization is used less often in the current environment. Nonetheless, with continued interest in less or minimally invasive surgery using smaller incisions and ports and robotic technology, the port-access cardiopulmonary bypass system has been found to provide a platform for innovative approaches to a variety of cardiac disorders.

45.3

Closed-Chest Cardiac Surgery and Robotics

During the development of port-access cardiopulmonary bypass system and in the early clinical experience, it was found that sutured anastomoses performed endoscopically were difficult because of limited mobility of the instruments and the confined access between the chest wall and the target coronary arteries [2, 5]. Manipulating endoscopic instruments through fixed entry points, surgeons have to reverse hand motions (because of fulcrum effects), and instrument drag requires higher manipulation forces, leading to less precision and greater muscle fatigue [20, 24, 26, 30, 32, 33]. Also, previous attempts with the endoscopic approach were hampered by the lack of three-dimensional visualization. Thus, a completely endoscopic coronary artery bypass procedure awaited technological refinements in visualization and instrumentation. Recent advances in computer-enhanced telemanipulation systems and three-dimensional visualization have provided the next step in the evolution of closed chest coronary artery bypass surgery [17–33]. In spite of the progress and increased surgical experience with robotic technology at certain centers, operative safety, speed of recovery, level of discomfort, procedural cost, and long term operative quality (particularly, with respect to graft patency) have not been fully defined.

The robotic system that is currently used in the clinical setting is the daVinci system (Intuitive Surgical, Mountain View, CA), which consists of a master console that connects to a surgical “manipulator” with two instrument arms and a central arm to guide the video-scope (Fig. 45.4) [23, 26, 32, 33]. The surgeon manipulates two “master” handles at the console. The position and orientation of the hands on the handles trigger highly sensitive motion sensors that translate the hand movements to the end of the instrument located remotely, or in this case within the thoracic cavity. The surgical manipulators provide three degrees of freedom (pitch, yaw, and insertion) and provide motion coupling to the exchangeable surgical instruments. These instruments provide another three degrees of freedom by means of a mechanical wrist for a total of six degrees of freedom. The system provides motion scaling, tremor filtering, and the possibility to disconnect the slave from the master thereby enhancing precision and providing optimal hand-eye alignment and favorable ergonomics. With the assistance of three-dimensional visualization system, the surgeon can manipulate handles through an interface in a fashion that is analogous to the use of traditional surgical instruments.

Experimentally, in isolated porcine hearts and using a microsurgical robotic system (Zeus Robotic Microsurgical System acquired by Intuitive Surgical), Stephenson et al. evaluated the ability to perform endo-

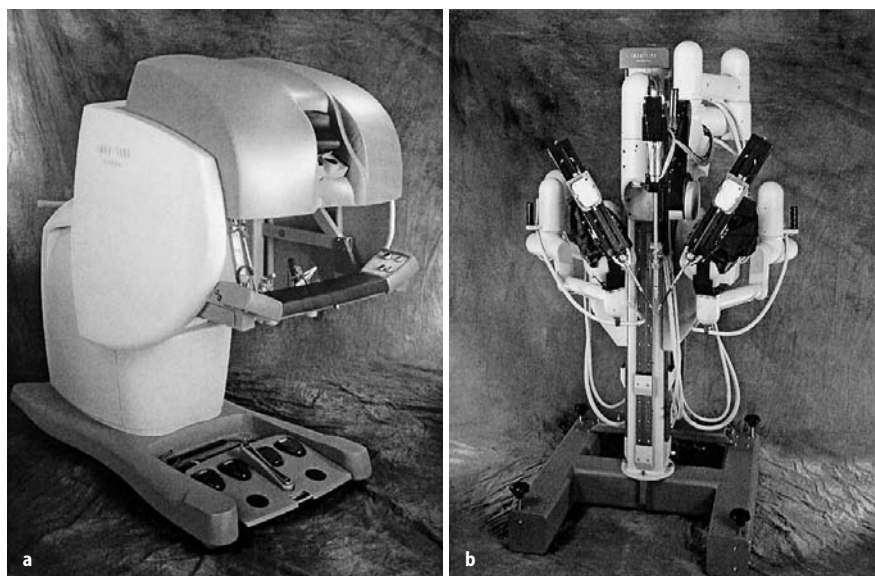
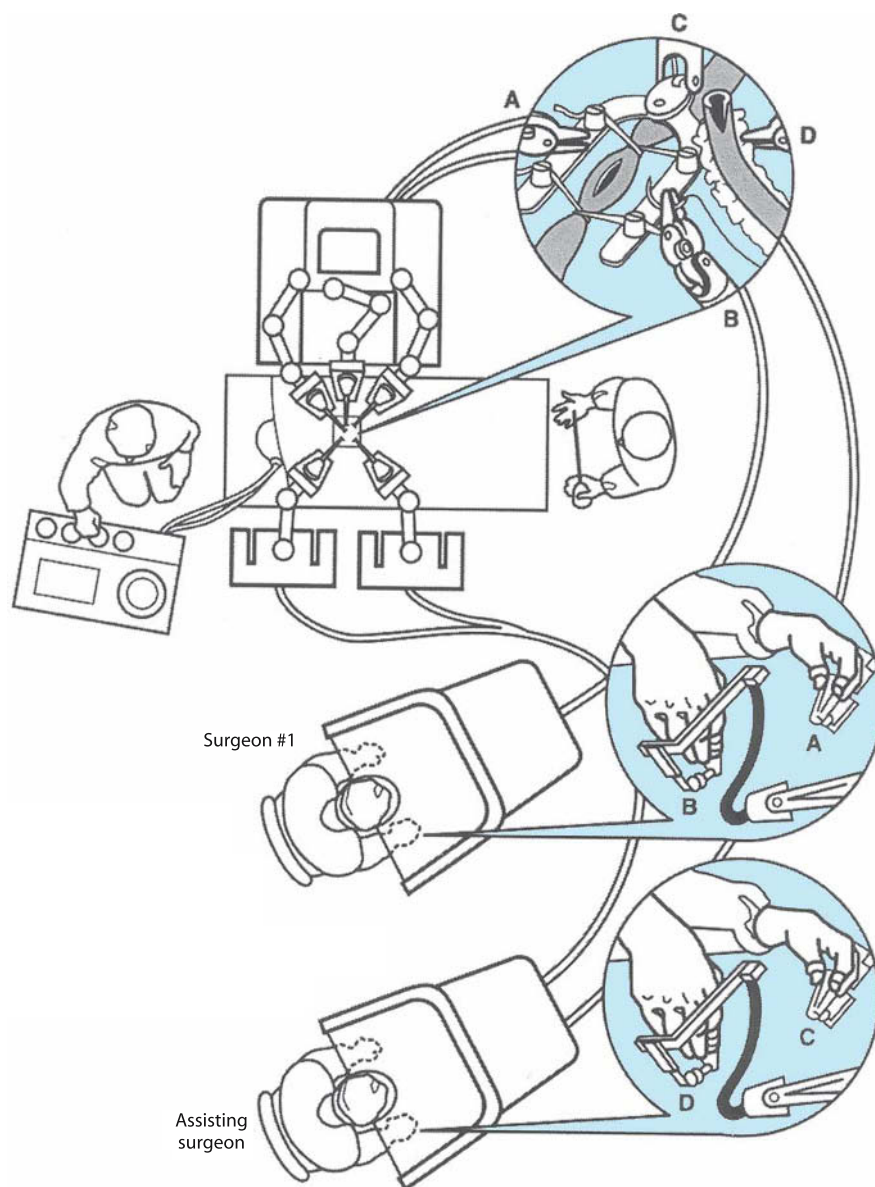


Fig. 45.4. The da Vinci surgical robotic system **a** is the surgeon's console. In **b** is the patient side cart with the surgical manipulators. (Reproduced with permission. Falk et al. Influence of three-dimensional vision on surgical telemanipulator performance. *Surg Endoscopy* 2001; 15:1282–1288)

scopic anastomoses to the left anterior descending artery [18]. The technological advantages using robotics, including increased precision with instrumentation, motion scaling and tremor elimination, and the ability to operate in a confined environment, may help to overcome some of the obstacles observed in early attempts at minimally invasive or closed-chest coronary artery bypass grafting. Particularly important is appropriate port placement and orientation relative to the left anterior descending artery. In a closed chest environment and using the da Vinci robotic technology, Falk et al. experimentally evaluated the ability to harvest the internal mammary artery and perform beating heart coronary artery bypass in the canine model. The approach was successfully employed in seven of ten animals [24]. In three animals, the procedure could not be completed because of ventricular arrhythmia, left atrial laceration, and right ventricular outflow obstruction. They found that coronary artery anastomoses are technically feasible and within acceptable time limits using robotic instrumentation. In May 1998, Mohr, Falk and their colleagues at Leipzig harvested the internal mammary artery with the da Vinci system and performed the first clinical coronary artery bypass grafting through a small left anterior thoracotomy incision [20]. The flow of the procedure was compromised by the lack of active assisting personnel. Additionally, there is a distinct learning curve associated with not only the use of the system, but also the experience of working in an endoscopic environment. Loulmet et al. at the Broussais Hospital reported the first clinical experience with total endoscopic coronary artery bypass grafting on an arrested heart using the da Vinci robotic system and cardiopulmonary bypass achieved with the port-access system [22]. In two patients, the entire operation, in-

cluding the internal mammary artery takedown and anastomosis, was performed endoscopically using the robotically assisted instrumentation. Patients were well at 6 months follow-up. Falk et al. reported their experience with 32 patients undergoing thoracoscopic internal mammary artery harvest followed by coronary artery bypass grafting via a small anterior minithoracotomy using the da Vinci robotic system [23]. In 18 patients, the entire operation was performed successfully using the robotic system to takedown of internal mammary artery and perform the distal anastomoses on an arrested heart with the port access cardiopulmonary bypass system. In four patients, the closed chest approach was attempted but was converted to a minithoracotomy for various technical reasons. In an extension of their experience, Mohr et al. presented their series of 131 patients who underwent computer-enhanced robotic coronary artery bypass grafting [30]. Using the da Vinci system, 79 of 81 patients underwent successful takedown of the internal mammary artery followed by minimally invasive direct coronary artery bypass grafting with a graft patency of 96%. Total endoscopic coronary artery bypass grafting with an arrested heart was successfully completed in 22 of 27 patients with a 95% graft patency at 3 month follow-up. In two of eight patients, closed-chest endoscopic coronary artery bypass on a beating heart was successfully performed. They concluded that total endoscopic coronary bypass is feasible on the arrested heart but does not offer a major benefit over the minimally invasive direct approach at this time because cardiopulmonary bypass is still required [30]. Using the da Vinci robotic system, Dogan et al. described their experience of 45 patients (37 single-vessel and 8 two-vessel) who underwent total endoscopic coronary artery bypass operations on the arrest-

Fig. 45.5. Schematic illustration of setup for endoscopic beating heart coronary artery bypass grafting using two consoles and five manipulator arms. The surgeon at the primary console manipulates two instruments and navigates the scope, whereas the assisting surgeon directs the stabilizer and an assisting tool from a second console. *A* left tool (primary surgeon), *B* right tool (primary surgeon), *C* stabilizer (left hand assisting surgeon), *D* assisting tool (right hand assisting surgeon). (Reproduced with permission. Falk et al. Endoscopic computer-enhanced beating heart coronary artery bypass grafting. *Ann Thorac Surg* 2000; 70:2029–2033)



ed heart with the port-access system [31]. The initial conversion rate was 22% and dropped to 5% in the last 20 patients. The first 22 patients had documented graft patency on discharge. However, procedural time was relatively long because of technical and monitoring issues associated with endoscopic surgery and the use of the endoaortic occlusion technique. Kappert et al. at Dresden reported their experience of 143 patients who underwent computer-enhanced coronary artery bypass grafting [29]. In this series, 13 patients underwent total endoscopic coronary artery bypass on an arrested heart, with the majority of the remainder undergoing a portion of the operation (in particular, internal mammary artery takedown) using robotic assistance followed by a variation of minimally direct coronary ar-

tery bypass grafting [29]. The patients in the endoscopic coronary artery bypass grafting group were operated upon via a three or four point stab incision using the daVinci system for internal mammary artery takedown and for performance of anastomoses.

Currently, robotic technology for closed-chest cardiac surgery continues to advance with increased surgical experience. Using port-access cardiopulmonary bypass with cardioplegic arrest has permitted some groups to successfully perform total endoscopic coronary artery bypass grafting. What has been emphasized by investigators in this exciting field relates to the learning curve, patient selection and positioning, placement of instrumentation ports, whether to use port access cardiopulmonary bypass as opposed to an

off-pump approach, orientation of the internal mammary graft and techniques to facilitate the distal anastomosis [23, 26, 29, 32, 33]. These important concerns are being clinically investigated and need to be resolved prior to general adoption of such technology.

45.4

Conclusions

Advances in videoscopic and endovascular techniques have provided the groundwork for the port-access technique for cardiac surgery. This peripherally based catheter system effectively achieves cardiopulmonary bypass, endovascular aortic occlusion, cardioplegia delivery, and left ventricular decompression. The development of this technology has facilitated and provided the basis for a closed chest approach to cardiac surgery. Robotic technology has contributed to the ability to perform closed chest procedures by providing the surgeon with more natural and precise movements in a confined space. While conventional sternotomy provides a reliable approach to most cardiac disorders, the goals of less invasive and perhaps a closed chest approach are to provide a safe and effective operation with less patient trauma and pain, shorter hospitalization and more rapid recovery. Continued technical advances in the field of minimally invasive cardiac surgery and robotic systems will facilitate the conduct of more diverse cardiac procedures in a safe and effective fashion with optimal outcomes.

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Subject Index

- AAV, *see* adeno-associated virus
- abdominal aorta 225
- acetylcholine 18, 25, 65, 246
- adeno-associated virus (AAV) 312
- adenosine 42, 263, 280
- thallium 215
 - triphosphate 52
- adenovirus 311
- gene transfer 314
- adipositas 113, 114, 198
- α -adrenoceptor antagonist 41
- adventitia 40, 100, 131, 141, 159, 255, 256, 262
- albumin 316
- Allen test 152, 158, 171
- amrinone 40
- anaerobic metabolism 51
- anaerobiosis 56
- anastomosis 3, 56, 81, 89, 101, 113, 119, 132, 140, 142, 154, 169, 171, 181, 187, 193, 196, 203, 205, 208, 220, 223, 227, 233, 239, 243, 244, 249, 253, 255, 262, 271, 279, 281, 285, 288, 293, 313, 323, 328, 331, 337, 342, 345
- diagonal 135
 - end-to-end 102
 - end-to-side 102
 - sequential 101
 - side-to-side 102, 256
 - stenosis 209
 - Y-shaped 134
- anemia 119
- aneurysmectomy 92
- angina 55, 75, 89, 109, 121, 137, 166, 173, 203, 220, 221, 231, 259, 270, 333, 334
- pectoris 73, 75, 121, 220
 - recurrence 121, 123, 291
- angiogenesis 306
- angiography 181, 252, 282
- postoperative 206
- angioplasty 231, 256, 264, 332
- angiotensin
- II 18, 25
 - receptor antagonist 84
- ante-aortic cross arrangement 132
- antebrachialis fascia 153, 171, 172
- antegrade cardioplegia 57
- anterior interosseous artery 227
- anterolateral thoracotomy 75, 327
- anticoagulant 315
- antihypertensive drug 42
- antioxidant therapy 308
- antispastic
- drug 151, 159
 - therapy 34, 39, 84, 159
- aorta 3, 57, 60, 65, 89, 102, 141, 142, 154, 169, 205, 209, 217, 225, 254, 272, 279, 294, 337
- abdominal 225
 - ascending 141, 159, 172, 239, 250, 255, 271, 286, 324
 - clamping 51, 53, 54, 142
 - – cross clamp 101, 103, 256, 337
 - descending 220
 - thoracic 141
 - unclamping 51
- aortocoronary
- bypass 89, 215
 - – conduit 279
 - graft 181, 246
- aortotomy 102
- aponeurosis 204
- aprotinin 115
- arachidonic acid 17
- arginine vasopressin 18, 25
- arrhythmia 334, 346
- arteriae nervorum 227
- arterial
- anastomoses 250
 - angioblasty 318
 - conduit 3, 24, 43, 74, 81, 91, 101, 113, 151, 165, 174, 181, 182, 193, 199, 223, 230, 233, 238, 248, 261, 324
 - graft 17, 18, 20, 25, 28, 31, 39, 51, 81, 113, 133, 141, 154, 156, 203, 217, 218, 243, 271, 285, 291, 293, 298, 311, 323, 331
 - reconstruction 91, 92
 - revascularization 56, 130, 151, 171, 175, 181, 191, 261, 280, 324, 326
- arteriosclerosis 105, 237, 333
- obliterans 237
- arteriotomy 101, 103, 135, 188
- ascending aorta 159, 172, 234, 239, 250, 255, 271, 286, 323, 334
- ascorbate 67
- aspartate 53
- aspirin 308
- asystole 51, 56
- atheroembolism 270, 271
- atherogenesis 308
- atheroma 146
- atherosclerosis 3, 11, 13, 27, 33, 82, 93, 113, 130, 153, 167, 169, 182, 203, 204, 221, 238, 253, 256, 269, 271, 291, 312, 313, 337, 344
- embolization 260, 273
 - lesion 225
 - obstructive 254
 - plaque 22, 161, 205, 305, 317
 - stenosis 183
- ATP-sensitive K⁺ (K_{ATP}) channel 17
- atrial fibrillation 257, 345
- atrioventricular block 333
- axillary artery 153
- axillobifemoral artery bypass graft 215
- Balfour retractor 184
- balloon angioplasty 73, 74
- basilic vein 215
- Beck II procedure 89
- benzothiazepine 157, 162
- beta-blocker 158, 191
- beta-receptor agonist 41
- bilateral
- IEA 209
 - internal mammary artery 243
 - internal thoracic artery (BITA) 97, 113, 115, 130, 144, 194, 209, 259, 261, 264
 - – coronary bypass 140
 - – grafting 109, 270
- BITA, *see* bilateral internal thoracic artery
- blood
- cardioplegia 52
 - transfusion 332
- brachial artery 153, 227
- brachiocephalic
- artery 343
 - disease 271
 - vein 3, 100
- bradycardia 333
- bradykinin 21, 27, 64
- Buerger's disease 228
- bypass graft 182
- CABG, *see* coronary artery bypass graft
- cadaver vein 215
- calcification 153
- calcium 17
- antagonist 34, 39, 40, 81, 84, 156–158, 161, 162
 - channel 19
 - – blocker 165, 171, 175, 191, 209, 246

- influx 52, 66
- calcium-activated K⁺ (Kca) channel 17
- cAMP, *see* cyclic 3',5'-adenosine monophosphate
- candidate gene 315
- cannulation 220
- cardiac
 - arrest 51, 67, 332
 - contractility 40
 - disorder 345
 - dysfunction 51
 - failure 272
 - hypertrophy 117
 - protection 68
- cardiogenic shock 55, 101, 103, 334
- cardioplegia 51, 53, 59, 63, 65, 131, 142, 172, 255, 262, 273, 294, 342
 - antegrade 58
 - oxygenated 55
 - pressure 57
 - retrograde 57, 58, 343
- cardioplegic
 - arrest 103, 348
 - delivery 57
 - protection 51
- cardiopulmonary bypass (CPB) 63, 74, 9, 101, 105, 133, 141, 176, 199, 220, 234, 238, 239, 243, 255, 262, 270, 285, 294, 323, 331, 337, 342
 - closed-chest 342
- cariporide 67
- catastrophic hypoperfusion 270
- catheterization 152, 165
- celiotomy 217
- cerebral
 - embolization 333
 - microembolization 337
- cerebrovascular accident (CVA) 288
- CFS, *see* coronary flow reserve
- cGMP, *see* cyclic 3',5'-guanosine monophosphate
- chemical facilitator 311
- chronic
 - hemodialysis 153
 - obstructive lung disease 257
 - obstructive pulmonary disease (COPD) 264, 288
- circumflex 109, 135, 239
 - coronary artery 92, 100, 325
- citrate phosphate dextrose (CPD) 53
- clip application 131
- closed-chest cardiopulmonary bypass 342
- CO₂ insufflation 300
- cognitive dysfunction 338
- colateral circulation 89
- comorbidity 108, 342
- composite
 - anastomosis 136
 - arterial graft 83, 210
- conduit
 - artery 28, 32
 - remodeling 253, 263
- congenital disorder 113
- congestive heart failure 269
- conjunctivitis 311
- contractility 25, 33
 - contraindications 82, 101, 106, 113, 152, 166, 181, 209, 344
 - COPD, *see* chronic obstructive pulmonary disease
 - copper 309
 - coronary
 - anastomosis 165, 186
 - angiography 89, 153, 172, 285
 - arteriogram 92
 - arteriography 91
 - artery 11, 26, 31, 84, 91
 - bypass 167, 218, 345
 - bypass graft (CABG) 24, 26, 31, 39, 63, 73, 81, 90, 101, 105, 113, 130, 156, 158, 171, 193, 208, 215, 216, 219, 223, 227, 234, 253, 279, 281, 285, 291, 298, 303, 311, 323, 337
 - disease 161
 - off pump 255
 - stenosis 73
 - bypass 154
 - surgery 113, 124, 165, 183
 - circulation 63, 134
 - disease 157, 166
 - endarterectomy 90
 - flow reserve (CFS) 280
 - grafting 82
 - lesion 279
 - revascularization 51, 93, 171, 196, 269, 272, 288, 301, 333
 - spasm 42
 - stenosis 44, 56, 81, 92, 264
 - stenting 74, 76
 - venous ligation 89
 - corticotropin-releasing factor (CRF) 20, 27
 - Cox model 138
 - COX, *see* cyclooxygenase
 - CPB, *see* cardiopulmonary bypass
 - CPD, *see* citrate phosphate dextrose
 - C-Port system 328
 - creatinine phosphate 54
 - CRF, *see* corticotropin-releasing factor
 - cross clamp 263
 - interval 60
 - cross-sectional luminal area 5
 - cruciate anastomosis 233
 - crystalloid solution 52
 - cubital fossa 227
 - CVA, *see* cerebrovascular accident
 - cyclic 3',5'-adenosine monophosphate (cAMP) 17
 - cyclic 3',5'-guanosine monophosphate (cGMP) 17
 - cyclooxygenase (COX) 17
 - 1 (COX-1) 315
 - cystic fibrosis 312
 - cytokine 332
 - cytomegalovirus 314
 - deep fascia 228
 - deferoxamine 67
 - delirium 338
 - DES, *see* drug eluting stent
 - descending aorta 220
 - diabetes 106, 113, 114, 137, 138, 228, 230, 244, 252, 257, 258, 292, 298
 - dysfunction 117
 - mellitus 74, 137, 153, 171, 264, 308
 - dihydropyridine 157, 158, 162
 - diltiazem 40, 161, 165, 172, 221, 263
 - disuse atrophy 106
 - dobutamine 41
 - stress echocardiography (DSE) 282
 - donor heart 55
 - dopamine 42
 - receptor agonist 41
 - Doppler ultrasound 152, 153, 228
 - drug eluting stent (DES) 75, 285, 324
 - duodenum 181
 - dysesthesia 166
 - echocardiography 282
 - EDCF, *see* endothelium-derived contracting factor
 - edema 56
 - EDHF, *see* endothelium-derived hyperpolarizing factor
 - EDRF, *see* endothelium derived relaxing factor
 - EET_{11,12}, *see* epoxyeicosatrienoic acid_{11,12}
 - elastic
 - lamellae 4, 5, 10, 12, 24, 25, 100, 200
 - lamina 82, 105, 204, 223
 - elastin 12
 - electrocardiographic (ECG) stress testing 123
 - electrocautery 185, 193, 204, 263
 - electrolyte solution 161
 - electroporation 311
 - enalaprilat 42
 - endarterectomy 90, 91
 - endoaortic clamp 343
 - endocytosis 311
 - endoscopy 299, 301
 - coronary artery bypass grafting 346
 - technique 300
 - endothelial
 - dysfunction 293
 - function 22, 32, 39, 63, 157, 263, 318
 - thrombomodulin 315
 - endothelin 18, 25, 31
 - 1_A antagonist 306
 - endothelium 19, 20, 21, 27, 63, 156, 182, 291, 292, 303, 315
 - endothelium-dependent
 - hyperpolarization 27, 66
 - relaxation 17, 27, 33, 63, 66, 159, 293, 315
 - endothelium-derived
 - contracting factor (EDCF) 17, 25
 - hyperpolarizing factor (EDHF) 17, 63, 315
 - EDHF-mediated hyperpolarization 33
 - EDHF-mediated relaxation 33
 - relaxing factor (EDRF) 17, 24, 32, 63, 106, 160, 225
 - stimuli 20
 - vasoactive substance 17
 - endothelium-smooth muscle interaction 21, 63

- epicardium 287, 294
 epigastric artery 206, 332
 epoxyeicosatrienoic acid_{11,12}
 (EET_{11,12}) 66
 erythrocyte 52
 E-selectin 64
 event-free survival 122
 extracorporeal circulation 52, 53, 331
- fasciotomy 102
 femoral artery 233, 323
 fenoldopam 42
 fibrin glue 293
 fibroblast growth factor 194, 317
 fibrosis 140
 flexor retinaculum 227
 fMRI, *see* functional magnetic resonance imaging
 forearm artery 227, 228
 free graft 83
 functional magnetic resonance imaging (fMRI) 339
- β -galactosidase 313–315
 G protein 317
 gastric epiploic artery 324
 gastroduodenal artery 7, 181
 gastroepiploic
 – artery (GEA) 3, 7, 8, 13, 20, 31, 40, 59, 81, 91, 113, 131, 171, 174, 181, 184, 215, 216, 218, 236, 238, 239, 279, 281, 291, 332
 – graft 183, 333
 – pedicle 187
 GEA, *see* gastroepiploic artery
 gene therapy 311, 313, 316
 glutamate 53
 glyceryl trinitrate (GTN) 40
 graft
 – composite in situ 103
 – construction 313
 – disease 151, 168, 194
 – extension 101
 – failure 210, 256, 257, 286, 303
 – hyperplasia 305
 – in situ 99, 238, 245, 273, 279, 326
 – occlusion 22, 82, 93, 161, 205, 208, 303, 318
 – patency 1, 105, 125, 143, 145, 167, 168, 280, 288, 292, 293, 313, 323, 326, 344
 – thrombosis 90, 209
 GTN, *see* glyceryl trinitrate
- hand ischemia 151
 Harmonic Scalpel 185, 187, 190, 196, 197, 200, 261
 heart stabilizer 287
 hematoma 132, 186, 208, 219, 263, 300
 hemisternotomy 184
 hemoclip 142, 159, 243
 hemodialysis 171
 hemodynamic 12, 188, 300, 305, 342
 hemostasis 131, 132, 142, 187–189, 199, 225, 263, 287, 294
 heparin 132, 158, 172, 187, 199, 261, 293, 301, 333
 hernia 208
- high-energy phosphate 56
 high-frequency
 – echo probe 285
 – linear transducer 285
 histamine 18, 25
 histidinetryptophan-ketoglutarate (HTK) solution 65
 homocysteine 309
 hybrid procedure 327
 hydralazine 42
 5-hydroxytryptamine 18, 25
 hypercholesterolemia 308
 hyperemia 279
 hyperhomocysteinemia 308
 hyperkalemia 53, 64–66
 hyperlipidemia 113
 hyperplasia 305
 hyperpolarization 19, 66
 hypertension 113, 257
 hypocalcemia 52, 66
 hypomagnesemia 66
 hypoperfusion 117, 209, 246, 256, 263, 264, 271
 – catastrophic 270
 hypotension 333
 hypothermia 53, 64, 67, 172, 191, 273
 hypothyroidism 257
 hypovolemia 119, 191
 hypoxia 204, 305, 306
- IABP, *see* intra-aortic balloon pump
 ICA, *see* intercostal artery
 IEA, *see* inferior epigastric artery
 IMA, *see* internal mammary artery
 in situ graft 99, 238, 245, 273, 279, 326
 incisional hernia 208
 inferior
 – epigastric artery (IEA) 3, 8, 13, 24, 31, 40, 93, 113, 156, 193, 203, 204, 208, 215, 218, 236, 243, 248, 252, 291, 334
 – gastric artery 236
 – mesenteric artery 24, 81, 223
 – pulmonary vein 239
 influenza 311
 infusion pressure 64
 innominate artery 3
 inositol trisphosphate (IP3) 41
 in-stent restenosis 73, 76
 insulin 138
 intercostal artery (ICA) 3, 10, 24, 28, 73, 81, 82, 91, 97, 238
 – graft 239
 internal
 – hyperplasia 168
 – iliac 224
 – mammary artery (IMA) 3, 4, 9, 13, 20, 24, 39, 81, 151, 152, 156, 169, 215, 216, 223, 238, 239, 243, 248, 291, 315, 344, 346
 – elastic 12
 – grafting 59, 138, 174, 219, 221
 – pudendal artery 224
 – thoracic artery (ITA) 18, 24, 31, 89, 97, 105, 130, 165, 182, 193, 208, 223, 230, 234, 244, 253, 254
 – bilateral grafting 101, 131
 – contraindications 106
 – grafting 107–109, 119, 125, 135, 269
 – kinking 135
 – malfunction 118
 – skeletonized technique 131
 – thoracic vein 100, 254
 interosseous artery 227, 230
 intestinal peptide 25
 intima 153, 159, 217, 238, 254–256, 305
 intimal hyperplasia 4, 6, 7, 14, 82, 94, 105, 146, 171, 174, 253, 313, 316
 intra-aortic balloon pump (IABP) 115, 191, 215, 258
 intracellular calcium 19
 intramuscular coronary artery 287
 intravascular
 – microthrombosis 64
 – pressure 57
 IP3, *see* inositol trisphosphate
 ischemia 14, 52, 54, 105, 117, 119, 143, 230, 231, 263, 292, 324
 – hand 151
 – heart disease 94
 – medullar 239
 – reperfusion 63, 65
 ischemia-reperfusion injury 64, 66
 isoproterenol 27
 ITA, *see* internal thoracic artery
- Kaplan-Meier method 34, 143
 Kawasaki disease 113
- labetalol 42
 LAD, *see* left anterior descending artery
 L-arginin 65
 LAST, *see* left anterior small thoracotomy
 lateral
 – circumflex coronary artery 239
 – circumflex femoral artery (LFCA) 24, 81, 233
 latissimus dorsi muscle 219, 220
 LCA, *see* left colic branch
 LDL, *see* low-density lipoprotein
 left
 – anterior coronary artery 105
 – anterior descending artery (LAD) 29, 31, 74, 81, 89, 113, 132, 140, 182, 208, 216, 223, 226, 239, 243, 253, 256, 263, 270, 286, 292, 323, 332, 346
 – anterior small thoracotomy (*see* LAST) 93, 334
 – colic artery 223
 – colic branch (LCA) 223
 – internal mammary artery (LIMA) 171, 218, 323
 – internal thoracic artery (LITA) 74, 97, 113, 203, 279, 286, 331
 – main disease 263
 – main stenosis 171
 – phrenic nerve 99
 – thoracotomy 219
 – ventricular venting 294
 leg pain 299
 length-tension curve 39
 less invasive surgical technique 103
 leukocyte 305, 308, 316

- leukocyte-endothelium adherence 64
- LFCA, *see* lateral circumflex femoral artery
- LIMA, *see* left internal mammary artery
- limb artery 31
- liposomal delivery 311
- liposome 311
- LITA, *see* left internal thoracic artery
- long terminal repeats (LTR) 312
- long-term
 - patency 13, 22, 24, 27, 31, 33, 51, 81, 82, 91, 105, 125, 130, 146, 156, 160, 183, 203, 238, 253, 273, 274, 292, 311
 - survival 113
- low-density lipoprotein (*see* LDL) 82
- LTR, *see* long terminal repeats
- L-type calcium channel, *see* voltage-operated calcium channel
- lymphatic drainage 12, 140
- lymphedema 140
- lymphatic drainage 144

- mainstem disease 113
- media 238, 254, 255
- medial calcification 83
- median artery 227
- mediastinitis 115, 137, 219, 288
- mediastinum 273
- medullar ischemia 239
- membrane stabilization 52, 66
- metal clip 294
- metalloproteinase 305
- methoxamine 18, 25, 26
- microemboli 339
- microinjection 311
- MIDCAB, *see* minimally invasive direct coronary artery bypass
- middle rectal artery 224
- milrinone 40, 84
- minimally invasive
 - direct coronary artery bypass (MIDCAB) 93, 219, 323, 331
 - technique 298
- minithoracotomy 345
- mitogenic factor 317
- monocyte 305
- morbidity 125, 252, 269, 272, 273
- mortality 89, 115, 114, 125, 137, 160, 165, 199, 203, 208, 243, 252, 257, 269, 270, 272, 273, 292, 323, 334, 338
- multivessel
 - disease 73–75, 113
 - revascularization 108
- muscular
 - fiber 203
 - tunica media 245
- musculophrenic artery 3, 5, 205, 239
- myocardial
 - arterial revascularization 135
 - dysfunction 52
 - edema 52, 54
 - fibrosis 51
 - function 63
 - Q wave 172
 - infarction 54, 74, 81, 109, 113, 115, 117, 120, 121, 131, 165, 166, 173, 174, 203, 208, 230, 237, 245, 249, 257, 259, 270, 271–273, 308, 323, 333, 334, 344
 - injury 271
 - ischemia 113, 143, 165, 226, 273, 281
 - muscle 124
 - necrosis 61
 - protection 51, 57, 101
 - revascularization 3, 105, 110, 130, 140, 176, 193, 203, 208, 233, 243, 248, 250, 269, 331
- myocardium 57, 63, 82, 181, 287, 294, 342
- ischemia 253
- myoglobin 345

- Na⁺/K⁺
 - ATPase 17
 - pump 54
- neoadventitia 305
- neointima 305, 306, 308
- neointimal
 - formation 303
 - hyperplasia 312, 317, 318
 - proliferation 73
- neurocognitive injury 339
- nicardipine 42, 158, 159
- nicorandil 42
- nifedipine 40, 43
- nitrite 65
- nitrate 43, 65
- nitric oxide (NO) 17, 19, 24, 32, 40, 63, 161, 162, 253, 303, 315, 316
 - synthase (NOS) 17
- nitroaspirin 308
- nitroglycerin 39, 42, 156–158, 160, 187, 191, 209, 263, 293
- nitroprusside 263
- nitrovasodilator 40, 84
- NO, *see* nitric oxide
- non-endoscopic technique 299
- norepinephrine 25, 26, 31, 41
- normothermia 54
- NOS, *see* nitric oxide synthase

- obesity 298
- obtuse marginal (OM) branch 243
- off-pump 75, 93
 - coronary artery bypass (OPCAB) 103, 140, 196, 216, 255, 323
 - – grafting 172, 285, 293, 342
 - grafting 188
 - surgery 338
- omentum 181, 199
- on-pump 75, 93
- OPCAB, *see* off pump coronary artery bypass
- organ
 - bath 39
 - preservation solution 63
- oxidative stress 64, 308, 309
- oxygen 55
- oxyhemoglobin 66

- paclitaxel 75
- pancreas 181
- pancreaticoduodenal artery 7
- pancreatitis 182, 217

- papaverine 39, 43, 59, 84, 98, 130, 132, 141, 151, 156, 159–162, 199, 204, 219, 225, 229, 230, 234, 243, 246, 254, 255, 261–263, 281, 285
 - hydrochloride 193
- paresthesia 166
- patency rate 132, 156, 175, 193, 209, 235, 250, 264, 279, 291, 300
- patent ductus arteriosus (PDA) 83
- PCI, *see* percutaneous coronary intervention
- PDA, *see* patent ductus arteriosus, posterior descending artery
- PDE inhibitor 84
- pedicle graft 83
- percutaneous
 - coronary intervention (PCI) 73, 109, 285, 323
 - transluminal coronary angioplasty (PTCA) 74, 114, 166
- pericardiophrenic artery 100
- pericardiectomy 238
- pericarditis 89
- pericardium 3, 89, 98, 119, 132, 143, 187, 205, 220, 256, 262, 272, 324
- perioperative spasm 184
- peripheral
 - bypass surgery 318
 - vascular disease (PVD) 74, 115, 137, 171, 175, 208, 209, 215, 257, 264, 298, 311
- PGI₂ 161
- pharyngitis 311
- phenoxybenzamine 41, 263
- phenylalkylamine 157, 162
- phenylephrine 18, 25
- phosphodiesterase inhibitor 40
- phospholipase A₂ 17
- phrenic nerve
 - lesion 117, 118
 - paralysis 117
- pleura 97, 131, 132, 143, 239
- pneumonia 311
- pneumoperitoneum 300
- Poiseuille's law 224
- polyglactin 305, 306
- polytetrafluoroethylene graft 272
- port access 324, 347
 - coronary bypass grafting 344
- posterior descending artery (PDA) 132, 135, 143, 188, 194, 243, 249, 262, 291
- potassium 53, 60, 67
 - (K⁺) channel 17
 - – opener 41, 65, 84
 - ion 18, 25
- primary anastomotic stenosis 81, 194, 196
- procaine 66
- proliferation 12, 157, 303, 305, 317
- prostacyclin 17, 19, 63, 105, 303, 315
- prostaglandin F_{2a} 18, 25
- prostanoid 25
- protamine 208
- P-selectin 64
- PTCA, *see* percutaneous transluminal coronary angioplasty

- pulmonary
 – complication 115
 – embolism 257, 334
 – hypertension 12, 60
 pulsatile stress 12
 PVD, *see* peripheral vascular disease
- RA, *see* radial artery
- radial artery (RA) 3, 9, 14, 24, 31, 59,
 113, 141, 151, 156, 165, 171, 193, 210,
 215, 218, 227, 233, 236, 238, 243, 246,
 248, 259, 261, 279, 291, 311, 324, 332,
 343
 – calcification 153
 – graft
 – – angiographic studies 175
 – – Y graft 167
- Raynaud's disease 171
- RCA, *see* right coronary artery
- RE CAB, *see* totally endoscopic coronary
 artery bypass
- recatheterization 124, 292
- reconstruction 101
- rectus femoris muscle 234
- recurrent
 – angina 121, 174, 176, 274
 – ischemia 105, 269
 – restenosis 324
- reintervention 105, 122, 130, 249, 253,
 264, 269, 273
- renal
 – dysfunction 74, 308
 – failure 113, 257, 285
- reoxygenation 59
- perfusate 59
- reperfusion injury 59
- restenosis 75, 76, 293
- re sternotomy 97, 132
- resuscitation 51, 54
- rethoracotomy 115, 116
- retrograde cardioplegia 56
- retrovirus 312
- revascularization 75, 100, 103, 105,
 113, 119, 131, 140, 154, 171, 174, 182,
 253, 270, 274, 280, 286, 293, 298, 311,
 326, 342
- RGEA, *see* right gastroepiploic artery
- right
 – axilla 220
 – coronary artery (RCA) 132
 – gastroepiploic artery (RGEA) 193,
 196, 243, 245
 – internal mammary artery (RIMA)
 218, 324
 – internal thoracic artery (RITA) 81,
 97, 113, 140
 – – anastomosis 331
- RIMA, *see* right internal mammary
 artery
- RITA, *see* right internal thoracic artery
- robotics 326, 345, 346
 – da Vinci system 347
- r-TPA, *see* tissue plasminogen activator
- SA, *see* sigmoid branch
- saphenous vein (SV) 3, 20, 24, 40, 74,
 92, 93, 101, 105, 113, 123, 140, 152,
 161, 168, 171, 176, 182, 193, 196, 203,
 205, 208, 215, 218, 234, 243, 256, 259,
 269, 286, 291, 298, 303, 311, 331
 – graft 105, 107, 108, 130, 190, 218,
 230, 235, 270, 271, 274, 279
- semilunar fold of Douglas 8
- semi-skeletonization 98
- sequential graft 135, 172, 190, 199,
 249, 253, 255, 263, 279, 280
- serotonin 64, 246
- sigmoid branch (SA) 221
- single vessel disease 75
- sirolimus 75
- SITA 115
- skeletonization 13, 34, 81, 98, 135,
 146, 153, 156, 172, 174, 184, 194, 196,
 198, 225, 243, 244, 254, 256, 261, 281,
 283
- skeletonized artery 130, 132
- small vessel disease 114
- smooth muscle 20, 21, 26, 42, 100, 146
- snowman figure 286, 288
- sodium nitroprusside 40, 42
- sodium-hydrogen ion exchange (NHE)
 inhibitor 67
- somatic artery 28, 31
- spasm 83, 106, 151, 156, 165, 171, 172,
 193, 21, 209, 231, 245, 253, 263, 285
- spasmogen 18, 25
- splanchnic artery 28, 31, 33
- spleen 216
- splenectomy 182, 217
- splenic artery 24, 81, 181, 215, 216
- St. Thomas' Hospital cardioplegia 65
- St. Thomas solution 52
- stenosis 101, 106, 114, 143, 146, 152,
 153, 156, 168, 176, 194, 225, 231, 234,
 245, 252, 256, 264, 272, 279, 280, 281,
 285, 291, 318
 – anastomotic 209
 – vertebral artery 29
- stent 73, 257, 305
- sternal
 – dehiscence 244, 256
 – wound infection 92, 115, 117, 125,
 137, 138, 166, 244, 258, 264, 270
- sternotomy 142, 184, 197, 215,
 219–221, 228, 254, 324, 342
 – incision 131
- sternum 130
- string sign 209, 280
- stroke 117, 118, 137, 253, 270, 333,
 337, 338, 343
- Student's t-test 143
- subclavian
 – artery 3, 114, 153, 255
 – stenosis 117, 133, 256
 – vein 254, 261
- subscapular artery 24, 28, 81, 218, 220
- substance P 65
- superior
 – epigastric artery 3
 – rectal artery 226
 – rectal (hemorrhoidal) branch 221
- SV, *see* saphenous vein
- Swan-Ganz catheter 143
- systemic hypertension 12
- systolic pressure 281
- T anastomosis 134, 261
- T graft 100, 101, 102, 136, 140, 181,
 190, 232, 253, 255, 257, 263, 280, 324
- Takayasu's disease 216
- thoracic
 – aorta 141
 – artery graft 269
- thoracotomy 221
 – anterolateral 75
 – left 221
- thromboangiitis 228
- thromboembolism 14
- thrombosis 41, 105, 146, 153, 168,
 210, 215, 257, 263, 264, 272, 303, 312,
 313, 344
- thromboxane A₂ 18, 25
- thoracodorsal artery 218
- thyroidectomy 89
- TIMP, *see* tissue inhibitors of metallo-
 proteinase
- tissue
 – acidosis 59
 – inhibitors of metalloproteinase
 (TIMP) 317
 – plasminogen activator (r-TPA) 315
- TNF, *see* tumor necrosis factor
- topical cooling 60
- totally endoscopic coronary artery
 bypass (TE CAB) 93
- trauma 146, 188, 228, 263
- triglyceride 82
- troponin T 345
- tumor necrosis factor (TNF) 312
- TxA₂ antagonist 41, 84
- ulnar
 – artery (UA) 9, 24, 81, 227, 261
 – – agenesis 152
 – nerve 228, 231
- ultrasound 301
- University of Wisconsin (UW) solu-
 tion 65
- unstable angina 113
- valve replacement 92, 140
- vasa vasorum 6, 100, 174, 244, 256,
 292
- vascular
 – cell adhesion molecule (*see* VCAM-1)
 317
 – endothelial growth factor 27, 42
 – endothelium 17
 – pathology 12
 – tone 19, 21
- vasoconstriction 19–21, 40–42, 191
- vasoconstrictor 25, 31
- vasodilatation 19
- vasodilator 39, 156, 253, 285, 293
- vasoplegic syndrome 332
- vasopressin 40
- vasospasm 18, 21, 25, 29, 32, 33, 39,
 40, 84, 159, 162, 253, 292
- VCAM-1, *see* vascular cell adhesion
 molecule
- vein/venous graft 11, 31, 58, 59, 113,
 122, 165, 264, 279, 311
 – patency 124
 – spasm 308

- venous
 - conduit 3
 - drainage 144
- ventricular
 - aneurysm 140
 - dysfunction 58, 121, 165, 259, 332
 - function 114
 - hypertrophy 54, 60, 113
 - septal defect (VSD) 52
- verapamil 39, 40, 157, 158, 160, 161, 187, 263, 293
- vessel
 - disease 107
 - revascularization 76
- videoscopic thoracoscopy 239
- viral vector 311
- visceral peritoneum 186
- visualization 345
- voltage-dependent Ca^{2+} -channel
 - L-type 41
 - T-type 41
- voltage-operated calcium channel (*see* L-type calcium channel) 161
- VSD, *see* ventricular septal defect
- wall trauma 132, 146
- wound infection 298
- Y-graft 100–102, 117, 133, 135, 140, 146, 172, 181, 190, 209, 220, 221, 226, 230, 232, 235, 243, 261, 263, 280, 324