Cancer Treatment and Research 174
Series Editor: Steven T. Rosen

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Multidisciplinary Care of the Head and Neck Cancer Patient

Indexed in
PubMed/Medline

Springer

Cancer Treatment and Research

Volume 174

Series editor

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More information about this series at http://www.springer.com/series/5808

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Multidisciplinary Care of the Head and Neck Cancer Patient

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ISSN 0927-3042 ISSN 2509-8497 (electronic)
Cancer Treatment and Research
ISBN 978-3-319-65420-1 ISBN 978-3-319-65421-8 (eBook)
https://doi.org/10.1007/978-3-319-65421-8

Library of Congress Control Number: 2017958027

Printed on acid-free paper

This Springer imprint is published by the registered company Springer International Publishing AG part of Springer Nature
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Head and neck oncology requires a well-orchestrated ensemble of subdisciplines that collectively enhance patient care. The wealth of fields that intersect within head and neck cancer is extraordinary compared to most disease sites. When in synchrony, the multidisciplinary approach can confer a dramatic improvement in patient experience, quality of life, and survival. The challenge for the busy provider is to embrace the team approach, supporting patient access to the most up-to-date science and technology.

The multidisciplinary approach allows for the cross cultivation of knowledge, performance improvement opportunities, and system-wide operational efficiencies. The surgeon learns about radiation contouring, the radiation oncologist learns about drug therapies, and the medical oncologist learns about surgical considerations. Just as important is the integration of necessary supportive services and rehabilitative care that often makes the difference in whether a treatment plan is properly executed or falls short. The team input broadens our scope, tailors our approach, and raises the bar on what should be considered the standard of care.

From the beginning, the head and neck teams at City of Hope and Cedars-Sinai have been built with this interdisciplinary concept in mind. Our mutual philosophy has been to provide multifaceted treatment driven by guidelines and patient goals of care rather than personal experience or institutional dogma. This volume is intended to help educate the reader about the integrated facets of head and neck care, with a spotlight on ancillary disciplines. It should be clear that the passion and skill that they provide are crucial to the care of the patient, both during treatment and afterward in survivorship.

A cancer diagnosis can be overwhelming. Head and neck cancer patients are particularly vulnerable as the cancer itself and the treatments prescribed can impact self-image, mental and physical stamina, and daily functions. Although each patient's experience with diagnosis, treatment, and recovery may be different, there are common challenges in the head and neck cancer journey, as illustrated in our patient perspective. This journey and others humanize the efforts described in the

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following chapters in ways beyond the written word. We hope that you will enjoy reading this book as much as we have enjoyed assembling it.

Los Angeles, USA — Allen S. Ho
Duarte, USA — Ellie Maghami

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Head and Neck Cancer—The Patient Perspective

1

Sally Lapiduss and Francesca Bartoccini

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Abstract

The following chapter details diagnosis, treatment, and aftermath from a head and neck cancer patient's point of view. It illustrates the potential daily challenges of undergoing treatment while coping with the diagnosis of cancer. The toxicities of treatment and recovery from them are described to better inform treating physicians, as well as counsel future patients on the preparation needed for a successful outcome. We acknowledge each patient has a unique story to tell. This is one patient's story.

Keywords

Survivorship · Head and neck cancer · Patient perspective
Chemoradiation toxicity · Quality of life

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_1

1.1 Introduction

In the hopes of giving doctors and other caregivers some insight into what their throat cancer patients go through, I have tried to record the facts of my case, the treatments I went through, and the emotional toll it took on my family and me. Since my recovery, several people about to embark on the same treatment asked me to please "tell them EVERYTHING!" They wanted to know what might and did go wrong for me. I realized knowing the possibilities helps patients be less fearful when things the doctors may not have mentioned start happening. Obviously, it's impossible to know EVERYTHING, and each patient is different, but having some idea of what to expect is intellectually and emotionally very helpful.

Doctors know the treatments they have prescribed for their patients, and the many possible outcomes. They may see us once a day (radiation oncologist) or once a week (medical oncologist), or even once every several weeks (supervising surgeon) as we go through the protocols. During that time, however, they may lose sight of the myriad things that go on the other 23 hours of their patient's day. Having lived through this ordeal and come out the other side 100% cancer free, I feel lucky and grateful, and I am happy to share my thoughts about the experience with you all.

1.2 Cancer Diagnosis

On Memorial Day weekend, 2015, I was diagnosed with a tumor on the base of my tongue. For months I had sometimes felt like a popcorn kernel was stuck under my tongue—but experienced no pain. Over time, I asked various doctors, including an ENT doctor, to examine me—but no one found anything. Finally, after my cat began draping himself around the front of my neck, sticking his snoot into my mouth, and even tapping with his paw at a spot on my neck, I became concerned. I pressed that spot, and felt a zap of pain that radiated up my neck. I called the doctor the next day.

My internist still saw and felt nothing, but given what I had described, (Sans the cat story) decided to send me for an MRI. That scan revealed the tumor. My internist immediately ordered a PET/CT and sent me to the head and neck surgeon, who also ordered a PET scan. The surgeon scoped my throat in his office, to visualize the tumor and try to get enough of the growth to make an exact diagnosis.

That was one of my first and more hellish medical experiences. Lots of gagging and lots of blood, but I got through it. Unfortunately, the clinic biopsy was non-diagnostic, so I underwent a formal biopsy under anesthesia in the hospital a week or so later. While still in recovery, the surgeon came to tell my wife that it was indeed cancer. A 2.9-cm midline base of tongue, (oropharyngeal) squamous, HPV-positive cell carcinoma, to be exact. Phew. That was a lot to digest (at least I didn't say "swallow!") and we went home quite shaken. Or my wife did, as I was

still pretty dopey from the drugs. Once the doctor called to explain what all those medical words above mean, the whole "cancer adventure" began in earnest.

The diagnosis left me rather numb. I remember being slightly relieved that there was actually something there, and that they had found it. At least now there was something specific to do something about. I bless that cat for making me listen to my body and return to the doctor, and I bless that doctor for taking me seriously and moving forward toward a diagnosis. Most of us know our bodies well, and rather than ignore something and hope for it to go away, I'd now tell anyone who felt there was really something wrong, to persevere and keep looking for the answer.

The good news, I was told by literally every clinician I encountered in those first couple of weeks, was that I was very lucky because I had one of the "best" possible cancers, one with a 95 % cure rate. The bad news, they all hastened to add, was this was also the cancer with one of the worst treatments. They said that because "killing" the tumor involves radiating the head, neck, tongue, palate, teeth, gums, salivary glands, taste buds, etc. … it can be a hellish proposition. You can lose the ability to swallow and eat. The skin on your neck gets very burned, as does the tissue on the inside of your mouth and throat. Sometimes a person undergoing this treatment needs a feeding tube. Also, the chemo drug used to make the cells more susceptible to the radiation (cisplatin), may sometimes have a deleterious effect on one's hearing. Yikes!

In anticipation of the treatment beginning, I met with a dental oncologist—(who knew?) who explained what some of the side effects (dry mouth, gum, tissue, enamel damage, etc.) could/would be. Again, a bit scary and daunting, but he and his nurse were helpful in trying to make me more comfortable as the weeks wore on. Much attention was paid to my not losing the ability to swallow, so I also began seeing a speech and swallow therapist. After an evaluation, she gave me a series of exercises to start and continue to do throughout and after my treatment. They proved to be invaluable.

I was also measured and fitted for a "mask" (Fig. 1.1), which covered the entire upper third of my body during my daily radiation treatments. I had to purchase upper and lower mouth guards to protect my teeth, gums, and dental work and visit my dentist to have a cleaning and to set up a dental baseline. My dentist is also a cancer survivor, so he was very empathetic and helpful.

Despite the fear of the treatment and the cancer itself, I think because I was given that positive prognosis immediately, I always felt the odds were on my side. It truly never entered my mind that I was going to be one of the five percent. I felt like I had to suit up and show up… and there was quite a lot to do to prepare for the treatment to come.

The surgeon explained he felt surgery was not the wise course to take as the position of the tumor, pretty much in the middle of the base of the tongue, meant it was between two major arteries and surgery would be too risky. Instead, he advised chemo and radiation as the most effective course of treatment.

Because I was over 65 years old, the chemo would be once a week, and it was a drug specifically targeted to make the tumor more susceptible to the radiation. The radiation would be Monday through Friday, for 7 weeks (which stretched into eight

Fig. 1.1 Mask during radiation treatments

and a half, for various reasons). We next met with our radiation oncologist and his knowledgeable, empathetic nurse. Later we met with the medical oncologist who would oversee the chemo. Over the months of treatment, and after, my wife and I would come to rely on him and his team of equally skilled and caring nurses, nurse practitioners, and nutritionists.

1.3 Treatment

Once it was decided that I was a candidate for radiation and chemo without surgery, my day-to-day care was basically handed over to the clinicians mentioned above. Everyone bolstered that "can do" attitude by never talking down to me, really listening to my assessment of my physical and emotional state, and always making me feel a part of the treatment. They also informed me about *most* of the possible negative effects. Oddly enough, after preaching all this positivity, I will also say that I would have liked to have been given more information, even the negatives, so I would have had a better sense of what to expect during the long months of treatment and recovery, and beyond.

Pain was definitely discussed, and I was told the doctors would do everything they could to lessen it. At first, topical preparations like Magic Mouthwash (an elixir of lidocaine, Mylanta, and diphenhydramine) worked a bit. But soon the pain from the radiation was intense, and I rather quickly worked my way up to a 50 mg fentanyl patch, with oxycodone added in as needed.

I was told early on that after several weeks of radiation treatment on my throat, I would have what could best be described as horrible sunburn… inside my mouth and throat. This would make swallowing difficult. That was quite the understatement!

I actually had a friend who had gone through this treatment the year before me and discovered that putting a few drops of liquid medical marijuana (specifically cannabis oil with no THC) under her tongue or brewing it in a tea, allowed her to numb her throat long enough to eat without pain so she could maintain an acceptable weight. We were happy that my oncologist supported our efforts in this direction, and after my first chemo treatment immediately provided us with the necessary paperwork. Unfortunately, despite two informative and amusing trips to medical pot dispensaries, none of it worked for me. It is important to note, however, that even with a similar diagnosis and treatment approach, each person's journey with this disease is different. What works for some, does nothing for others. I think it is important to try everything and see what works best for you.

My big problem was after only a week or two of radiation, I couldn't swallow at all. It was horribly painful. The meds all helped control the pain, but I just couldn't swallow anything—no water, and therefore no food or pills—and ended up having a G-tube surgically inserted very early in the process, which necessitated all sorts of other adjustments for us. I say "us" because I really went through all this with my wife. It became very important that all the doctors and nurse practitioners deal with her directly as my surrogate, and trust that the information she gave them was accurate.

At first, discombobulated by the mere fact of the diagnosis—then later because I was so weakened by treatments and the inability to eat, plus addled by all the pain medications—I desperately needed someone clearheaded to be with me throughout all this. I needed an advocate, and someone to help translate my feelings to the doctor. I lost my voice fairly early on, and although I used my iPad to communicate—it was

often frustrating and laborious. I would urge doctors to encourage their patients going through any kind of treatment like this to have a spouse, partner, or friend accompany them to all doctor appointments and treatments. They need to reach out to friends and family for help. They (and their spouse/partner/family) will need it.

I was very reluctant to do this at first. I didn't even want to tell friends and family that I had been diagnosed. But the fact of the matter was my wife had a full-time job and couldn't take me to every appointment. A friend turned us on to a wonderful website called LotsaHelpingHands.com, (there are others) which allows you to gather email addresses of friends and family, and then send them each a calendar, complete with dates, times, and locations the patient needs to get to, etc. People can simply go to the site to sign up to help and see what slots have already been filled by others. No muss, no fuss. We actually found that our friends and family were so grateful to be given a way to help, they thanked us for providing them with a means to lend a hand. It would have been terrific if one of our doctors or clinicians had mentioned this site/service, or ones like it to us. We stumbled upon it accidentally while trying to set up something similar on our own. It really made our lives much easier during this long ordeal.

Another thing I found very helpful was writing everything down. Questions I had for the doctors, their answers, how to take meds, eventually how to work the food pump, etc. At first, we had sheets of paper all over the house. Then my wife bought several spiral notebooks in which we began jotting down everything (Fig. 1.2). Once the treatments began in earnest, and there were so many medications to take and mouth and teeth preparations to do morning and night—we began dating each page and keeping track of the meds I took and when. Soon each day was recorded in detail… meds taken, pain levels, nutritional supplements, sleep, bowel movements, etc.. We would also jot down questions for the doctors. Having this notebook with me when I went to chemo or to a doctor's appointment proved invaluable. I could show them my questions and they could look at my pages to answer their questions about what had been going on with me at home.

In fact, on one follow-up appointment, the surgeon told us that the people who write things down tend to do well. He even asked to see the notebooks and we brought them to my next appointment. I think it would have been tremendously helpful if a doctor or nurse had suggested we do this at the beginning of treatment. So while the doctors prepared me somewhat for what was ahead, and dutifully answered my questions as they arose, here are a few more things I would have liked to have had more information about right from the get-go.

No one mentioned how severe the loss of the ability to make and swallow saliva would become. I know it is different for every person depending upon the facts of their individual case, and also how and where they are radiated. I was lucky not to have lost or (hopefully) have permanent damage done to my salivary glands. But… the amount of thick, ropey, heavy saliva constantly dripping into my mouth and down my throat, coupled with my inability to swallow, made for several months of horrible and almost constant coughing and spitting. We had plastic "spit buckets" (aka Tupperware wash basins lined with paper towels) stationed strategically

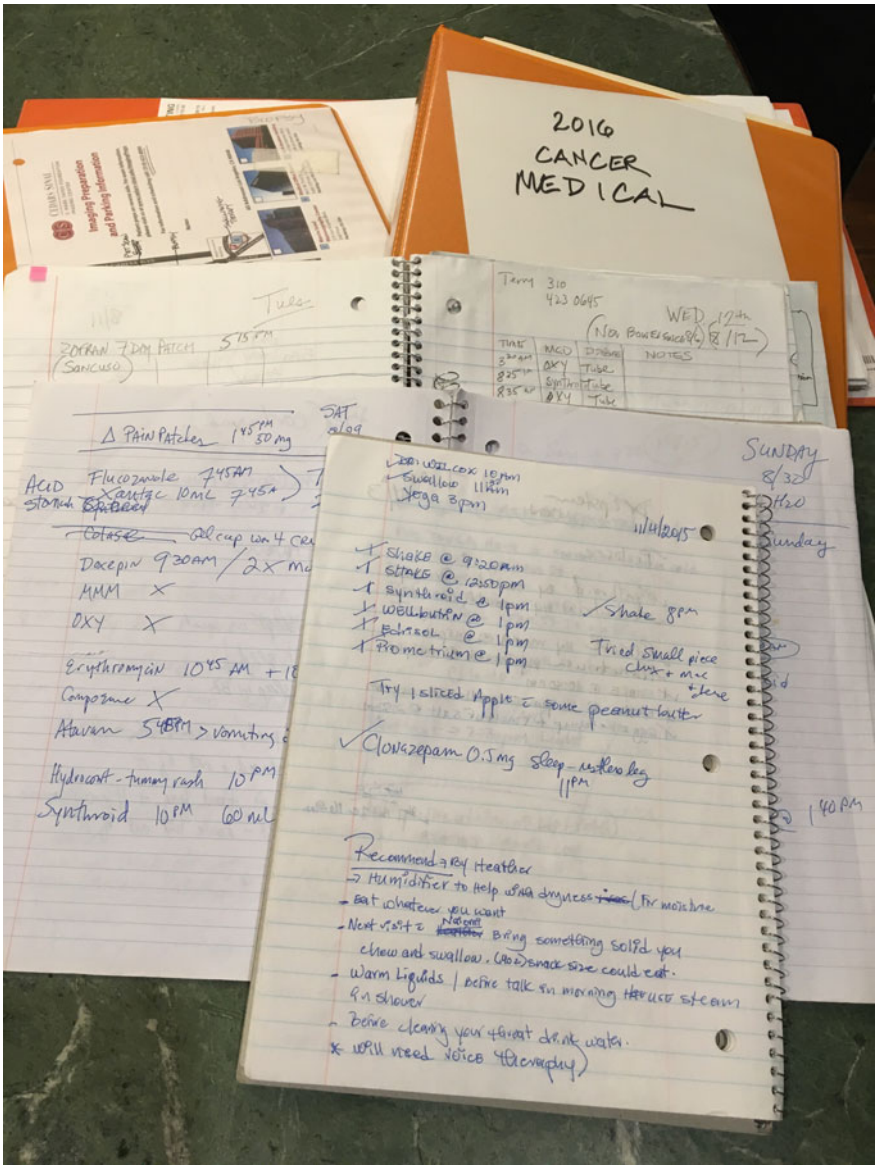

Fig. 1.2 Notebooks with questions during treatment

throughout our home. I took one with me in the car to and from treatments. Regular facial tissues irritated my lips, probably from the chemicals used in processing, but we found a type of toilet paper that did not irritate me.

The saliva and mucus production also made me constantly nauseous. If I had been told about all this beforehand—it might not have made a difference—but because I wasn't told—I spent an extremely anxious few days thinking something else was terribly wrong.

At the outset of this severe discomfort, my dental oncologist suggested I try Doxepin… but not for depression! I mixed the contents of one capsule into two teaspoons of water, swished it around in my mouth for a minute, then spit it out. For several days, this really helped to dry up the saliva and mucus, but then it abruptly stopped working. Weeks later I tried it again, and it worked again… for a few days, then ceased to make any difference. That happened a lot. I learned things might work for a few days, and then cease to be effective. Again, that would have been a useful bit of information to have going into all this.

This saliva/mucous combo platter was the agony I was sure would never end. I still have some thick saliva in my throat, and only a little saliva recovery in my mouth, but 1 year after the end of radiation treatments, it was much better. Now, almost 2 years past the treatments, it is still not at 100 present—but significantly improved. I did try several products from my dental oncologist, but none of them worked for me. Occasionally, Biotene spray would help. The problem was the products would give some moisture in my mouth, but increase the "gook" in my throat, which I hated the most. It was like a constant, horribly thick postnasal drip. I had to sleep sitting up a lot, too. Various smells also became intolerable, and overall, my olfactory sense became much more acute. Unfortunately, everything smelled bad! Perfume was a killer! This lasted for several weeks during treatment, then went away.

On a more serious note, I had never heard the word "lymphedema" until the day I looked in the mirror and thought I was developing a goiter. The front of my neck was incredibly swollen. Only then was I told that radiation can damage the lymph glands, causing fluid to collect in tissues under the skin, and that this is a chronic condition that may never resolve itself fully. Again, not really good news for me and my neck, but still something I wish I had been informed about pretreatment. In the moment, I had panicked because I had no knowledge that this could happen, let alone that it was so common. It might sound silly, but I thought my tumor might be growing back.

Once it happened to me, my radiation oncologist sent me to a lymphedema therapy specialist, (at a hefty cost that insurance would not fully cover), which proved to be very helpful. The sessions consisted mostly of a very specific neck massage, which attempts to open the lymph channels. They had me purchase a compression garment, which I still wore at night a year out, but not during the day. I probably should still be wearing it—but I don't. It is very uncomfortable. The lymphedema will probably not go away completely, but it has diminished, and the therapists taught me how to do the message myself, so I'm hopeful that its effects will continue to diminish.

Another particular problem I faced was dealing with my small and "rolling" veins. After various painful episodes during the hospital biopsy and PET scan (blood draws and nuclear med injections were extremely painful for me because of

how hard it is to find a good vein on my arms), I was told to get an implantable port. There were so many blood drawing sticks and pokes, that despite the pain I had for about 10 days after the port was put in, (it hurt like hell, then became merely irritating), ultimately it was a lifesaver.

Although doctors, of course, know what chemo and all these tests entail, I had no idea how many times my blood would be drawn and drugs (steroids, antinausea drugs, potassium, the chemo drug itself) would be pumped into me. Before the port was inserted, caregivers and I quickly learned to ask for an experienced person to take my blood. When someone knows what they're doing, it makes a world of difference to the patient. And although over the course of long months of treatment, drawing blood might seem like a little thing to a doctor, to the patient it can mean the difference between a good day and another very bad one.

One other salient patient point; I had a lot of pain and discomfort with both the port surgery and the post-surgery G-Tube insertion. I was repeatedly told neither was a big deal, but for me they were. And I'm sure I'm not alone. The port also hurt like hell coming out—but I could never have had that many injections and blood drawings without it. I just wish I had been told about the port option earlier on, and that when I went through these surgeries, my very real feelings of pain were not questioned, but acknowledged as such.

I was told my taste buds would get burned and things would begin to taste bad, or have no taste at all. It was more the former, as everything, even and especially water, tasted like rocket fuel (or what I imagine rocket fuel to taste like). For a while, I was able to drink sips of carbonated water, but then that too began to taste horrible.

As I said, I do know each patient is different, and perfect storm of complications—how quickly the radiation shut down my ability to swallow, coupled with my already lousy digestive system (acid reflux and pre-Barrett's)—made me incapable of keeping down much of the several different nutritional supplements prescribed to keep up my weight and energy. It also caused a great deal of acid pain in my chest, stomach, and throat.

Not being able to keep any of the liquid nutrition down meant it came up… by way of my radiated and very raw throat. I actually had only a few days of bad chemo nausea and vomiting—but many, many weeks of total nausea and vomiting because of the supplements. The whole process of having the G-tube inserted and then trying to function with it became my Achilles heel in all this.

Because I could not swallow at all, everything had to go through the G-tube, including all medication, either crushed or in liquid form… and it came back up a lot. At various times I was prescribed many things to try to keep the acid reflux, nausea, and nutritional supplements down, including; Zofran, Carafate, Compazine, Prilosec, Reglan, Milk of Magnesia, you name it**!** Because of my weight loss (86 lb total on a five-foot four-inch frame), which continued even after I completed chemo and radiation, I ended up needing IV fluids several times a week. I developed mouth sores and much worse, thrush. I was prescribed Fluconazole and a Nystatin rinse. Even after I tested negative for thrush, I still had a very thick, white coating on my

tongue and inside my mouth, which was very uncomfortable. My acupuncturist said it was a part of the saliva issue and would dissipate in time. It has.

I was throwing up about once or twice a week starting around 2 weeks before the end of treatment—and for some weeks after treatment. Since I wasn't eating, it was mostly violent retching with nothing but a little blood and some fluid brought up. It was very painful and felt like I was throwing up the lining of my throat.

I was told to drink as much water as I could manage, but dehydration was a big problem for me. Lack of water led to shaking, fainting, and extreme fatigue. I never knew how sick one could feel just from not drinking enough water.

I experienced anxiety at different levels. At one point, I couldn't watch any TV shows where anyone died, although CSI and crime shows had been my favorites. Instead, I watched DIY sports, and nature shows… and some comedy shows… if I could follow them. I had pretty rough bouts of being scared. I saw a shrink for this for one session and it helped. Ativan was a tremendous help for anxiety and sleep. I took it before bed and often during the day as well.

Speaking of trying to follow things… "Chemo Brain" is real, and another thing no one mentioned to me early on. During the months of treatment, it was very hard to focus. Today my memory is still a bit spotty, and I'm told this can go on for some time. People have gotten frustrated with me because it seemed like I wasn't paying attention, but it's the chemo. I just couldn't retain information. I'm much better now, and am even back to work, which was unthinkable several months ago.

1.4 Posttreatment Recovery

I had been told that the days after my radiation treatments ended might be the worst. A nurse explained that you "keep on cooking" while your body is also dealing with the greatest accumulation of all the chemo and radiation. This turned out to be true for me. (And it's a good example of getting negative information early on, which proved to be helpful). After my treatment ended, I had lost so much weight and was so weak; I spiked a fever and was hospitalized for 8 days. I remember going back to chemo for hydration and potassium, and feeling so sick and now really scared. Here I was, finished with all the hellish treatments, yet I felt like I was dying. One of the nurse practitioners realized what was going on with me; that I had hit the wall emotionally. She realized I had been sent home after my last radiation treatment and pronounced "healthy", but I was still sick… and in a way, having withdrawal from all the care and attention I had been getting while undergoing treatment. I hadn't even realized that, but once she said it I cried in recognition and relief.

Several hours later, I was admitted to the hospital with "failure to thrive" listed as a reason for my hospitalization. At one point, I'm told, I was on two antibiotics, plus all the other meds, and I was given a blood transfusion. I say, "I'm told" because I really remember very little of those 8 days. Finally, in the hospital, they hit on a nutritional supplement that—for the most part—stayed down and in my system. My fever dissipated, and I was sent back home with an electric stomach

pump to ensure the nutritional supplement would drip very, very slowly into my G-tube, 24/7. The tube would remain in place another few months as I healed.

My voice became very gravelly during the duration of treatment. Trying to talk or whisper was painful. Relying on the iPad was frustrating as the heavy-duty meds and chemo brain made me very slow to put thoughts together and use a keypad. We placed bells in every room so I could summon my wife or "sitter" for the day. Yes, dear reader, I needed a sitter. I could not really be left alone for several weeks because I was so addlepated, and could not be trusted to dispense my own meds—which had to be crushed, mixed with water, and poured into my G-Tube… or to keep a close eye on my temperamental nutrition pump.

It took several weeks and much exercise to regain most of my voice, but I still can't sing. (Before cancer I could sing. In fact, during my younger days I was an actress/singer). I used to sing all the time, so I really miss it. Using a humidifier, breathing in steam, and doing the exercises I was given and continue to do, have helped. I had a good speech/swallow therapist, and though I stopped seeing her months ago, I continue to do the exercises she taught me. They aim to open the swallowing muscle in your throat that radiation can shut down. Mine is opening again, though I still have a little "back up issue". Sometimes water feels like it's backing up and trying to get into my windpipe. I have to re-swallow to keep it going down.

At 1 year out, I still had to be careful with many things. I flossed religiously after meals and at night. Without saliva, everything got stuck in and around my teeth and above my gums. I also brushed with a concentrated prescription fluoride solution—SF 1.1% Gel—after the regular electric toothbrush cleaning. I didn't rinse my mouth after the fluoride, just spit and then trap the little bit left on my teeth under my mouth guard at night to further protect the teeth from decay. I was told to keep on top of this, as once again the radiation will keep on cooking, sometimes for years.

Because I kept up my regimen—now, 2 years later, I am greatly improved. I've recovered more saliva than anticipated; I have almost no swallowing issues.

My tumor was to the right middle of my tongue, so now I have some scar tissue on the right. Occasionally, if I don't chew food long enough, or if I try to swallow a big pill, it will get stuck on the right. I can easily cough it back up, chew and/or re-swallow on the left. The first time this happened, however, it terrified me and I thought I would choke to death. I have to drink water with every bite of food to form the necessary bolus so it can be swallowed. If I don't, little particles of food can get stuck in my throat and even get inhaled into my trachea. This happened once and scared the heck out of me, but now I drink water constantly. I never liked water before I had cancer. I hated the taste. But I'm ever so grateful for it now.

I drink a meal replacement protein drink every day. A month or two post-radiation, I could only get down a little scrambled egg and, oddly, pancakes with pure maple syrup. Soon I could do chicken vegetable soup, and things like turkey burgers and other protein crumbled into tomato soup. In fact, tomatoes, and anything tomato based (pasta sauce, soup, etc.) became my go-to food. As I said earlier—it's very different for each person. The rate at which tastes return and are

pleasurable again varies greatly. I would try something that would taste bad, but try it again a few weeks later to find it tasted good again. The list of foods I could eat comfortably grew over time. I would advise taking it slow, experimenting, and trying not to get too frustrated.

Two years after treatment, I can eat most things, although I still have trouble with sugar and sweets. All sugar tasted like bad chemicals in my mouth. Several months after treatment, I discovered one kind of dark chocolate that tasted good to me… and believe me, I had to try a lot of different types of dark chocolates before I found the one that worked. For a long time, rice, bread, and anything dry were untenable. All bread was horrible and tasted like paste except, for some reason, English muffins. Go figure! Now I can eat bread, especial if it's dipped in oil or sauce. Good-bye SIZE ZERO!

I had some burned skin on my neck, but all the doctors said I escaped remarkably unscathed compared to other patients. Early on my radiation oncology nurse recommended I use a natural lotion called Calendula. I used it two or three times a day on my neck and still try not to let my skin get too dry.

From the beginning of radiation to the end, my weight sank from 189 to 103 lbs. After my weight stabilized at 112 lbs, I was finally able to have the G-tube removed. I know it saved my life, but it was a pain to deal with. For instance, showering involved wrapping my mid-section in saran wrap and tape to keep the tube insertion area dry. Along with the clear plastic sleeve, I wore to keep the port dry, I was quite the bathing beauty! I was also thrilled to be done with the nutritional supplements and the constant hum of the electric pump. Now with my taste and swallow returned, my weight is at 130 lbs.

I would advise patients to take advantage of all the post-cancer and rehab treatments around them. I began to do restorative yoga, which was offered in the building where I went for my chemo treatments. It is a gentle, slow-moving form, which was very helpful in getting my strength back, and building up my energy and range of motion. The yoga made me stronger! I can't emphasize how even just a little non-strenuous exercise greatly improved my balance, fatigue energy, and concentration levels.

It seemed mostly to consist of lying on a mat and ever-so-slowly raising and lowering each extremity until I dozed off in class. But they encouraged that. It was like a meditation. I never thought I'd get my energy back, and I still have a day here and there of deep fatigue. But when I do, I surrender to it. I realize rest is very important. This is not the sort of thing you "power through", and I try to be gentle, kind, and patient with myself.

I was also told about a physical therapy rehab program offered free of charge by the hospital, and it has been a godsend. I had been walking a bit and wanted to go back to a gym, but was still too weak, and frankly too afraid I might hurt myself. In this program, I was evaluated by a doctor and then trained by professionals who slowly increased my regimen. Like the yoga, it's been incredible to see how little it takes to regain movement and strength.

Along with dealing with the physical aspects of recovery, there are emotional ones to contend with as well. When my first PET/CT scan showed that everything was all clear, I felt compelled to get rid of everything that reminded me of what I'd been through. I needed to purge myself of the cancer experience. I had no idea I would have this reaction. While going through treatment, I found it best to just accept it all and take each step as it came. I also had to recognize that many things (taste buds, saliva, aches, pains, etc.) would go away, but then come back again for a while. Recovery can be very frustrating, yet it helps to remember you're going in the right direction… toward wellness. Having and keeping a sense of humor is also very helpful.

Before I started treatment we went to Old Navy and I bought about six tee shirts, four pairs of stretchy pants, and some slip-on sneakers: my chemo clothes. I couldn't wait to give them all away. I kept my radiation mask thinking I'd use it in some cool art project… but after hanging it from a tree in our front yard last Halloween, I threw it away, too! I decided it was best to get rid of it all. I don't need to have any reminders.

I was also in the enviable position of being semi-retired. I had worked for years in the film business as an art director and production designer. I had segued from that to get my contractor's license and was now doing home remodels. I didn't work for a year during treatment and recovery, and came back slowly with one or two small design projects during the next six months after that. It was really all I felt I could handle because of the chemo brain effects. During this time I was very frustrated with my lack of focus and memory issues. The good news is that now at 2 years out, I feel that I am at 90% and getting better every day.

Since the cancer, I have given up the contracting part of the job—too much heavy lifting and stress—and now design home remodels, furnishing clients with plans and models.

I also have quite an impressive woodworking shop, filled with every tool and machine imaginable. I loved spending time building and repairing furniture, models for work, other people's mangled DIY projects… you name it. But early in my recovery, I told my wife to sell everything, since I believed I'd never again have the strength or the desire to work in my shop. Wisely, she didn't listen to me, and a few months later, one day out of the blue, those thoughts and feelings lifted and I found myself puttering away… then rebuilding several old chairs I had collected. In retrospect, I realized the pall lifted after my physical rehab had begun to take hold and the chemo brain had begun to lessen. Now I'm back at work for clients, and spending hours in my shop again.

We were very lucky that my wife's full-time job included great health insurance and sympathetic bosses and co-workers who allowed her ample time off to deal with my issues.

I know many others would not be so fortunate, and I again urge anyone dealing with this to put out the word amongst family and friends and allow them to help. It was an extremely welcomed gift when, after my hospitalization at the end of radiation and chemo, my brother offered to pay for a trained LPN/caregiver for a

few weeks. Having her there gave my wife the ability to be at work full time, and get a bit of a break from the 24/7 routine my medical needs demanded.

I do understand that perhaps you want to tell the patient only so much, and some of this posttreatment information can and should come… post treatment. Perhaps doctors tell us just as much as they think we need to know to get through the steps right in front of us. They don't want to overwhelm us. But a lot of what I experienced, even weeks after my hospitalization, was never mentioned or discussed. As I've said, things like being told by one nurse in oncology that I'd "keep cooking" after radiation treatments ended, proved very helpful. It allowed me to mentally prepare myself for the weeks ahead, and not expect to feel great a few days after the dreaded radiation dosing was done.

So on an individual basis, I think a doctor needs to make a judgment as to whether their specific patient can handle more. I would have liked to have been told more about what to expect upfront. In several instances, if I had been armed with that information, when it happened to me I would not have been so afraid that something else was wrong.

My hope is that some of the information in this chapter will allow doctors and caregivers to realize the daily minutia faced by their throat cancer patients, thus being better able to allay their fears, and arm them with creative ways to make their treatment more comfortable and effective. Doctors and caregivers need to keep in mind the patient's struggle continues outside the treatment rooms, and for many months after that. Any and all aid they can give them regarding what to expect down the road is very valuable and will be much appreciated.

I think because we met medical professionals on every level who were kind, empathetic, communicative, and worked in conjunction with each other and us—our experience was better than most. All those skills proved to be critically important in getting me through this nightmare. We were, of course, extremely trepidatious going into this, but all of the doctors, physician assistants, nurses, and med techs—with very few exceptions—were terrific. One year out from all this, I cannot overemphasize how much being surrounded by positive clinicians, family, and friends aids in one's recovery. Even when telling patients the unvarnished truth and the worse case scenario, if doctors can also be encouraging, and empower the patient with that optimism, it will go a long way toward affecting a positive outcome.

1.5 Epilogue

The silver lining in all this was discovering how truly empathetic and supportive friends, family, and people, in general, could be. Folks I met in chemo, in restorative yoga class, and physical therapy rehab… waiters and waitress who worked with me so I could find something to eat on their menus… even our once nameless neighborhood pharmacists—they all became members of Team

Francesca, pushing me steadily and patiently along the road to recovery. If they had faith in me, how could I not work hard to get through this ordeal?

Now, 2 years out, I am healthy and strong and cancer free. I am back up to 130 lb (Fig. 1.3), mostly regained muscle, since I am still a size 4. (Although I will forever cherish those 4 glorious months I was a Size 0!)

Fig. 1.3 Disease-free 2 years after completing treatment

I am so grateful to my wife, doctors, clinicians, family, and friends. I am even grateful for the experience of having had cancer, because I was allowed to come out the other side with a renewed appreciation for living every day to its fullest. I am working on a kitchen remodel and adding a second story to a client's home, traveling, eating welI, exercising, and about to celebrate my 70th birthday!

Sure, you're going to have bad days, even weeks, but I urge anyone going through this trial to stay strong, ask questions, accept help, and fight the disease with everything you have. In an unexpected way, post-cancer, we've been given the opportunity to appreciate and embrace life in a whole new way.

Physician Assistants and Nurse Practitioners in Head and Neck Surgery

2

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_2

Abstract

This chapter explores the role of advanced practice clinicians (APCs) and patient care coordinators in the head and neck cancer setting. APCs, which include physician assistants (PAs) and nurse practitioners (NPs), are licensed professional healthcare providers who diagnose and treat illnesses, order and interpret diagnostic tests, and prescribe pharmaceutical and non-pharmaceutical therapies. Although the training, education, and licensure differ between PAs and NPs, their roles are quite similar in head and neck surgery. They collaboratively participate in the medical and surgical management and coordination of head and neck cancer patients in a variety of settings including outpatient clinic, inpatient, and in the surgical suite. APCs can function autonomously in an outpatient clinic with the medical management of postoperative visits and new consults. In an inpatient setting, they perform daily inpatient rounds and manage patient care preoperatively and postoperatively. In head and neck surgery, registered nurses (RNs) usually function in the role of patient care coordinators. They serve as a liaison between the patient and all members of the multidisciplinary team. APCs and patient care coordinators work closely with medical oncologists, radiation oncologists, surgeons, and other allied health professionals to provide high-quality care and achieve optimal patient outcomes in the head and neck cancer setting.

Keywords

Head and neck · Cancer · Physician assistants · Nurse practitioners
Patient care coordinators · Registered nurses

2.1 Advanced Practice Clinicians Educational Background and Training

Advanced practice clinicians (APCs) are a subset of clinicians that include physician assistants (PAs) and nurse practitioners (NPs), each sharing a major role in the management and treatment of head and neck cancer patients. In order to practice in this specialty, APCs must undergo rigorous postgraduate-level training. PAs and NPs are licensed professional healthcare providers who diagnose and treat illnesses, order and interpret tests, and prescribe pharmaceutical and non-pharmaceutical therapies. APCs practice medicine and serve in both rural and urban communities nationwide in the United States (U.S.). Though each APC training program varies (Table 2.1), each licensed clinician can collaboratively participate in the management and coordination of the intricate medical care often required in a head and neck surgery practice.

Table 2.1 Comparison of background and training required of PAs and NPs

	Physician Assistant-Certified (PA-C)	Nurse Practitioner (NP or DNP)
Bachelor degree required?	Yes— any discipline	Yes— BSN or other undergraduate degrees
Postgraduate degree obtained?	Yes— MSPA	Yes— MSN or DNP
National board certification required?	Yes— PANCE	Yes— NCLEX-RN, specific population focus exam for NP certification
Recertification?	Reexamination every 10 years—PANRE	Option to recertify by continuing education and clinical practice hours or by examination every 5 years
Residency?	Optional, 1–2 years and specific to specialty	None
State licensure required?	Yes	Yes
CME required?	Yes	Yes
Ability to diagnose illness and prescribe medications?	Yes	Yes
Eligible to apply for DEA license?	Yes	Yes
Eligible to first assist in OR?	Yes	Yes—requires additional certification, RNFA
Requires supervising physician?	Yes—In-person oversight and chart co-sign requirements vary by state	Varies by state

2.1.1 Physician Assistants

PAs are certified at the national level and licensed in the state of their practice. They work with one or more supervising physicians (SPs) allowing them to extend the physician role in the operative, inpatient, and outpatient settings. The scope of practice of a head and neck surgical PA includes but is not limited to evaluation of patients in clinic, performing in-office procedures such as direct laryngoscopy, assisting in the operating room, making daily inpatient rounds, and seeing patients for long-term surveillance (Fig. 2.1). The average accredited PA program is approximately 27 months long and admission requirements generally include a bachelor's degree, completion of prerequisite courses similar to that of medical schools, and prior direct hands-on patient care experience [1]. PA programs are accredited by the Accreditation Review Commission on Education for the Physician Assistant (ARC-PA). The majority of PA programs award a master's degree and this will become the ARC-PA standard by 2020 [1].

PA education strongly emphasizes team-based care and the curriculum largely focuses on general or primary medicine. The first year of the curriculum is a didactic classroom-style education often taught by instructors with a Doctor of

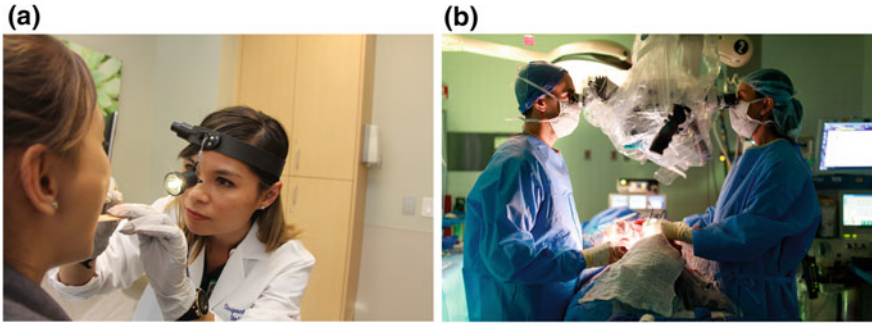

Fig. 2.1 The role of the advanced practice clinician encompasses both outpatient clinic visits and major inpatient surgeries. (a) Outpatient clinic evaluation and diagnostic workup of head and neck cancer patients. (b) Intra-operative arterial anastomosis of free flap during microvascular reconstruction

Medicine (MD), Doctor of Osteopathic Medicine (DO), Doctor of Philosophy (Ph.D.), PA or NP degree and focuses on basic sciences, laboratory medicine, behavioral sciences, clinical medicine, research methods, billing and coding, and clinical skills. The second year involves more than 2000 hours of clinical rotations in community clinics, private practices, and hospitals with physicians and licensed PAs in internal medicine, family medicine, pediatrics, emergency medicine, general surgery, and electives such as plastic surgery, dermatology, orthopedics, and cardiology [2]. Upon completion of an accredited PA program, PAs must pass a Physician Assistant National Certifying Exam (PANCE). A certified PA, denoted as a PA-C, must maintain continuous medical training education (100 hours every 2 years) throughout the course of their career. Once certified by the board, PAs may apply for their Drug Enforcement Agency (DEA) license and state-specific prescriptive license. To maintain certification, PAs are required to successfully complete a Physician Assistant National Recertifying Exam (PANRE) every 10 years.

As a rapidly growing profession, the number of PAs in the U.S. increased from 80,000 certified PAs in 2010 to over 100,000 certified PAs in 2015, as reported by the National Commission on Certification of Physician Assistants (NCCPA) [3]. The profession is projected to continue to increase 30% by 2024 [3]. PAs have the option to practice in primary care, as well as any specialty or subspecialty of medicine or surgery. Data from the 2016 American Academy of Physician Assistants (AAPA) Salary Survey showed 26.3% of PAs in clinical practice were working within surgical subspecialties, followed by 24.4% in primary care and the remaining 20% in emergency and internal medicine [2]. In 2015, less than 1% of PAs held principle clinical positions in otolaryngology [1]. A PA that elects to go into a specialty practice such as head and neck surgery will receive most of his or her specialty-specific training directly from one or more SPs in that clinical practice.

2.1.2 Nurse Practitioners and Advanced Practice Registered Nurses

NPs are registered nurses (RNs), who receive advanced education and training to provide health promotion and maintenance through the diagnosis and treatment of acute and chronic conditions [4]. There were over 222,000 NPs in the U.S. in 2015 with a growth projection of 244,000 NPs by 2025 [5]. A potential NP candidate begins his or her path by earning a Bachelor of Science in Nursing (BSN) or other undergraduate degrees. Certification is then obtained through the National Counsel Licensure Examination for Registered Nurses (NCLEX-RN) prior to practicing as an RN. It is recommended that the RN gain sufficient clinical experience before he or she applies for a graduate-level NP program. The curriculum of a typical 2-year program for NPs includes research, pathophysiology, pharmacology, advanced assessment, and management in health care with the integration of faculty-supervised clinical rotations of various specialties [6].

NPs must pass a national board-certifying exam in a specific population focus: acute care, family practice, women's health, pediatrics, adult-gerontology, neonatal, or psychiatric-mental health. NPs are licensed through state-specific boards for their initial RN certification and through a NP national certifying body, such as the American Academy of Nurse Practitioners (AANP) or American Nurses Credentialing Center (ANCC) [7]. After achieving board certification, NPs may apply for additional credentials at the state and federal level. The NP must achieve a minimum of 75 continuing medical education credits and clinical practice hours every 2 years to maintain certification and licensure. NPs are required to recertify every 5 years to be considered board certified by AANP, and may do so by either examination or by completion of at least 1,000 clinical practice hours and 100 hours of continuing education [8].

During their career path, a NP may develop an interest in a surgical subspecialty such as head and neck surgery. He or she may undergo additional training to assist in surgery as a Registered Nurse First Assistant (RNFA) [9]. First assistant training involves a minimum of 120 intra-operative first assistant hours through a formal post-basic RN education course [10]. One such example is the National Institute of First Assisting, Inc. (NIFA), which offers a course to train NPs to become RNFAs and in 2016, enrolled over 250 applicants [11]. A survey suggested that this increase is due to the desire of nurses to follow the patients through their perioperative experience, aid in reducing the surgeons' workload, and gain the ability to bill Medicare Medicaid [11].

In 2004, the American Association of Colleges of Nursing (AACN) recommended that the Doctor of Nursing Practice (DNP) degree become a new standard for the higher level of preparation for NPs by 2015. There are 303 DNP programs in the U.S. with an increase in the number of students from 21,995 to 25,289 between 2015 and 2016. During the same period, the number of DNP graduates increased from 4,100 to 4,855 [7]. Although there is a growing movement for NPs to earn a DNP degree, a Master of Science in Nursing (MSN) remains the minimum post-graduate degree requirement for a NP. At this time, no state boards of nursing have

made a requirement for a licensed NP to earn the DNP degree [12]. However, if a NP is interested in pursuing a DNP, he or she is required to have increased knowledge in his or her practice areas by completing projects that examine specific practices or outcomes via pilot study, consulting collaboration, or program evaluation.

2.2 Patient Care Coordinator

A patient care coordinator is a liaison between the patient and all members of the multidisciplinary head and neck team. In most head and neck practices the patient care coordinator is a senior-level RN. A head and neck team includes the oncologic surgeon(s), a reconstructive surgeon, a medical oncologist, a radiation oncologist, a pain management specialist, PAs and/or NPs, and a patient care coordinator. Additional team members can include a financial counselor, social worker, speech and language pathologist, dentist, and physical therapist. The patient care coordinator plays an integral role in the care of the head and neck patient from the time of their initial consultation extending to long-term surveillance.

The pathway from initial diagnosis to treatment and/or remission can be lengthy with variable adverse effects. The patient may experience depression, sequelae of radiation therapy and/or chemotherapy, wound healing issues or chronic pain. The patient care coordinator provides continuity for the patient, ensuring that he or she always has someone to call regarding his or her condition or any related issues.

2.2.1 Roles and Challenges for the Patient Care Coordinator

Implementation of the treatment plan in a timely manner is the key to improving the outcome for the patient. Once each multidisciplinary team member has provided feedback regarding the treatment plan and timeline, the patient care coordinator customizes a treatment plan schedule. Table 2.2 illustrates the timeline for a typical head and neck patient from week 1 to 16, highlighting the roles and challenges for the patient care coordinator.

The months leading to recovery can be arduous for head and neck patients, especially those who experience multiple adverse effects related to their diagnosis and treatment. Once the patient has completed relevant adjuvant therapies, the patient care coordinator checks in monthly for the first 6–12 months, depending on the needs of the patient. By this point, the patient care coordinator can ensure that the patient understands their long-term surveillance plan.

In addition to providing multidisciplinary continuity of care for the patient, the patient care coordinator educates and provides numerous resources. This includes group therapy referrals and community resources, and/or locating funding for specific procedures. The goal of the patient care coordinator is to ensure that the

Table 2.2 The role of the patient care coordinator and challenges encountered during a typical head and neck cancer treatment time course

Time interval	Treatment	Coordinator role	Coordinator challenges
Week 1	1. Initial consult 2. Biopsy if indicated 3. Relevant imaging and labs reviewed 4. Diagnosis 5. Prepare case history for head and neck tumor board	1. Obtain outside imaging and pathology reports 2. Schedule further imaging or biopsies if needed 3. Schedule pre-op appointment and testing 4. Notify team of any new test results 5. Schedule surgery and coordinate appointments for possible adjuvant therapy 6. Obtain insurance authorization 7. Referral to financial counselor if needed	1. Request of pathology slides from outside hospitals can take up to 2 weeks 2. Insurance authorization can take 5–7 days and is often required for imaging and surgical planning 3. Scheduling surgery in a timely manner, coordination with collaborating MDs or co-surgeons' schedules
Week 2–3	1. Patient undergoes surgery 2. Inpatient recovery and home treatment plan 3. Postsurgical head and neck tumor board presentation 4. Postsurgical pathology reviewed 5. Arrange for transportation to appointments if needed	1. Arrange for chemotherapy and/or radiation oncology consultation appointments if needed 2. Arrange dietitian consult 3. Provide feeding tube instructions and other dietary instructions if needed 4. Involve social worker to ensure appropriate support and smooth discharge from the hospital	1. Feeding tube formulas and supplies are frequently not delivered quickly enough for the patient to be discharged home
Week 4–6	1. Start radiation and/or chemotherapy treatment	1. Arrange dental visit and obtain dental clearance for radiation treatment, if needed	1. Ensure patient adherence to instructions and treatment plans

(continued)

Table 2.2 (continued)

Time interval	Treatment	Coordinator role	Coordinator challenges
Week 7–10	1. Onset of chemotherapy and radiation side effects	1. Patient education for treating chemotherapy and/or radiation side effects 2. Maintain communication between patient and oncologic teams 3. Arrange for wound care consult and home wound management as needed 4. Arrange for psychosocial support if needed 5. Pain management referral if needed 6. Arrange for a follow-up appointment with surgical team(s) 1–2 months after completion of adjuvant treatments	1. Maintain communication and encourage patient compliance regarding treatment plan and schedules
Week 11–13	1. Peak of chemotherapy and/or radiation side effects	1. Contact patient at least once weekly to check in. Address any physical and/or psychological symptoms 2. If additional support needed, contact appropriate teams or provide referrals 3. Maintain clear communication between patient and oncologic teams	1. Maintain communication with satellite offices that are providing follow up care

patient is well informed and receives the necessary support during their diagnosis and treatment.

2.3 Integration of Advanced Practice Clinicians

The role of APCs varies from practice to practice. However, the common foundation and goal of providing the highest standard of care to patients are of utmost importance. APCs have the scope of practice which is delegated to them by one or more of their SPs.

APCs play an important role in cancer survivorship, surveillance, prevention, identification, and management of side effects from head and neck cancer treatment. APCs care for head and neck cancer patients in various settings including the outpatient clinic, inpatient, and the surgical suite.

In the outpatient clinic, head and neck APCs can see patients in consultations as well as perform various procedures (Table 2.3) [13]. Although some are not specific to head and neck cancer care, they illustrate the APC breadth of expertise.

Head and neck surgery APCs are trained to diagnose head and neck cancers and provide the workup necessary to prepare a patient for treatment.

For example, a 40-year-old male patient may be seen for a right-sided neck mass without prior workup. On examination, a right tonsillar mass may be noted. During the office visit, head and neck APCs may perform a fiberoptic laryngoscopy to

Table 2.3 Common procedures performed by APCs in Otolaryngology–Head and Neck surgery [13]

Cerumen disimpaction	Removal of foreign body of ear
Flexible scope exam	Pre-Op H&P
Packs/splints removal	Nasal cautery
Removal of nasal foreign body	Rigid nasal endoscopy
Majority of practice's post-op visits	Mastoid cavity cleansing
Anterior nasal packing	Post-FESS debridement
Excision/biopsy skin lesion	Oral biopsy
Hospital rounds	Hospital consults
I&D of peritonsillar abscess	Fine needle aspirate
Removal of tube/TM patch	Posterior nasal packing
I&D of helical hematoma	Allergy testing
Tympanostomy	Tympanostomy & tube insertion
Stroboscopy	Transnasal esophagoscopy
Facial nerve monitoring in O.R.	Sialolithotomy
Audiometry	Gentamicin injection
Closed reduction nasal fracture	Packs/Splints removal
Nasal cautery	

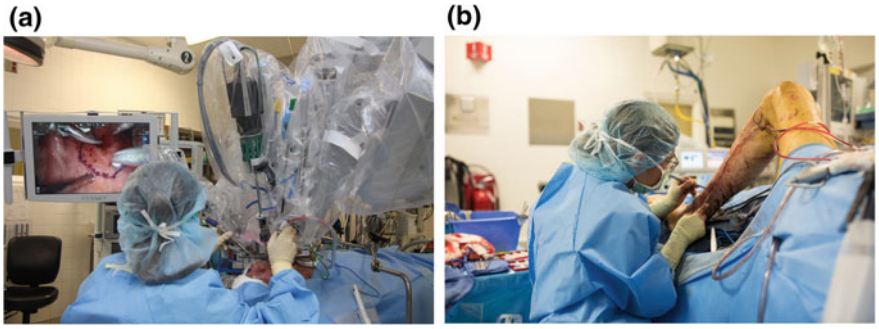

Fig. 2.2 Advanced Practice Clinician responsibilities in the operating room includes a wide range of first-assist responsibilities, including (a) facilitating resection during transoral robotic surgery (TORS) and (b) closure of free flap donor sites during microvascular reconstruction

assess the patient's airway, perform a biopsy of the tonsillar mass, perform a Fine Needle Aspiration biopsy of the neck mass, and order appropriate imaging to determine the extent of the patient's disease.

By completing the proper workup necessary to diagnose and treat head and neck cancer patients, APCs can expedite the patient's diagnosis and care. APCs can also counsel patients regarding smoking and alcohol cessation [14]. Once the patient completes treatment, APCs may be involved in clinical surveillance and assure that the patient's posttreatment side effects are managed properly.

In the surgical suite setting, APCs are first assistants to their SP. APCs assist in common otolaryngology surgeries such as thyroidectomies, parathyroidectomies, and Sistrunk procedures. APCs also participate in the large head and neck tumor resections and reconstruction which include segmental mandibulectomies, orbital exenterations, total maxillectomies, complex free and pedicle flap reconstruction, and transoral robotic surgery (Fig. 2.2) [14].

As first assistants, APCs work with the operating room team by directing and ensuring that proper instruments and supplies are available. APCs work alongside their SPs and can make skin incisions, raise skin flaps, tie vessels, dissect, place and secure tracheostomy tubes, harvest skin and/or nerve grafts, close skin incisions and place postoperative admission orders.

In the inpatient setting, APCs are responsible for daily inpatient rounds and providing postoperative care. This ranges from postoperative wound care, tracheostomy care, triaging postoperative complications, pulling drains, adjusting medications, ordering scans or labs and coordinating discharge planning [14]. Complications that APCs may recognize include surgical site infections, chyle leaks, hematomas, and nonviable flaps needing emergent reoperation.

For example, a 66-year-old female with anaplastic thyroid cancer status post total thyroidectomy, central neck dissection and bilateral modified radical neck dissections is noted to have a left Jackson-Pratt drain output that is copious with a milky discoloration. APCs would be able to recognize this finding and would alert

their SP to a possible chyle leak. APCs can then collect a sample of the drain output, send it to the lab for triglyceride evaluation, change the patient's diet to a low-fat/fat-free diet and consider the addition of medium chain triglycerides. If the drain output continues to increase in volume with these treatment changes, the SP may be notified and surgical ligation may be considered.

2.4 Challenges of Incorporating Advanced Practice Clinicians in Practice

This chapter has examined the vital role of APCs in a head and neck practice and ways in which they can care for and treat patients both in and out of the operating room. A medical practice or hospital that does not already utilize APCs may be wondering where and how to start the process of hiring a PA or NP to join their team. One of the first steps toward incorporating APCs in a head and neck practice is to understand and become familiar with state-specific laws and regulations regarding APC licensure. An APC's scope of practice is defined largely by the state and in part by the SP. For example, PAs in California must have a Delegation Services Agreement (DSA) signed by both the PA and SP that serves as a regulatory document outlining the medical services the PA may provide [15].

The next step is to evaluate the needs of the head and neck practice and determine what role the APC will have (e.g. primarily first assistant in the OR versus seeing patients for post-op visits, or both). This will help guide a SP during their search for an APC that will be a good fit for their practice. SPs may consider searching for APCs by networking with other surgeons who already utilize APCs and by providing a job listing on their hospital portal. There are also state-specific associations for PAs and NPs, as well as specialty organizations for APCs in surgery and surgical subspecialties, such as the American Association of Surgical Physician Assistants (AASPA). The Society of PAs in Otorhinolaryngology-Head and Neck Surgery (SPAO-HNS) maintains a year-round otolaryngology job listing for its PA and NP members. SPAO-HNS also hosts an annual conference attended by physicians, PAs and NPs who are already practicing or are interested in otolaryngology and head and neck surgery. Finally, though it is not required that PAs complete a residency or fellowship to practice in a surgical specialty, there are several surgical residency and fellowship programs in the U.S. that provide an additional 12 months of perioperative training and can serve as a beneficial resource [16].

As mentioned above, an APC's scope of practice is determined largely by the state. State regulations and statues for physicians are quite consistent across the U.S. [17]. However, regulations and statues for APCs vary from state to state. Understanding these regulations and statutes as well as the professional responsibility of having an APC in a head and neck practice will help to streamline the onboarding process.

SPs can be directly liable or vicariously liable for their supervision of APCs. Direct liability is often due to negligent supervision. Examples of negligent supervision include the SP not being accessible to the APCs for medical consultation, hiring an unfit APC, and/or exceeding the number of APCs that can be supervised by one SP. Vicarious liability is when a SP is liable for the actions of the APCs even if the SP themselves, did not perform such action. If it is found that the actions of the APCs can be prevented by the SP, the SP may be held vicariously liable [18].

By understanding the potential liability of having APCs in practice, strategies can be implemented to minimize the risk. One of the most important methods to prevent potential liability is to establish open communication between the SP and the APC. This can be in the form of frequent meetings to review cases or protocols, shadowing the SP in clinical practice, lectures on various head and neck diagnoses and quarterly reviews of the APCs work habit and knowledge fund [18].

Practices that are successful in incorporating APCs have protocols and policies to regulate the APC's activities. These protocols and policies may determine the type of patients that the APCs see, establish when referral to SPs are needed for a higher level of care and/or clarify the standard management of various head and neck diagnoses. Protocols and policies should be signed by both the SP and the APC to assure acknowledgment and understanding of the practice standards [17].

The use of an APC in a head and neck practice should be tailored to their strengths as clinicians. In some practices, NPs are utilized more in the inpatient setting while PAs may be of more value in the operating room, and RNs may find their niche in the clinic setting. Selecting an APC and developing goals for incorporating them into a head and neck surgery practice are important decisions for the SP.

The overwhelming majority of head and neck APCs acquire their experience from on-the-job training. Depending on the prior experience and/or training of an APC, there will be an abundance of clinical content for the APC to digest and apply into clinical, inpatient and operative settings. Experience in either general otolaryngology or another surgical subspecialty, such as oncologic surgery, reconstructive surgery, or facial plastic surgery are optimal backgrounds to transition into a head and neck practice. In the first weeks to months of training, learning the fundamentals of the physical exam, documenting otolaryngology review of systems, disease diagnosis, treatment plans, and surveillance should be highlighted.

An academic head and neck practice offers an enhanced learning environment for both residents and APCs. Educational meetings such as morbidity and mortality conferences, tumor board, national meetings, and even on-site surgical training allow APCs to learn side by side with the residents, and vice versa. As residents rotate on and off a head and neck service, the APCs can be a valuable resource for the residents for a range of skills from electronic medical record utilization, communicating SP preferences, and teaching surgical techniques.

Increasing responsibilities, educational requirement, and restricted hours may reduce the availability of residents in a busy head and neck practice [19]. Residents and APCs share the responsibility of patient care, which includes documentation,

discharge planning, prescription writing, home health and social work form completion, rounding, and OR case coverage. APCs can be a positive influence in an academic setting by working side by side with residents to decrease resident workload, provide safer patient care, and continuity for both the SPs and their patients.

The collaborative care that APCs provide help head and neck practices function more efficiently and generate additional revenue. Medicare and almost all commercial insurances cover both medical and surgical services provided by PA or NP [20]. Medicare reimburses services provided by a PA or NP at a uniform rate of 85% of the SP fee. Medicare does not require the MD to physically be available when an APC manages a patient, if the service is billed under the APC's name [21]. In a head and neck practice this is beneficial when an APC can bill for services such as in-office nasal laryngoscopy, FNA, excisional biopsies, established and new patient visits. Additionally, an APC can also bill 85% of the SP fee as the first assist in the operating room when there is no qualified resident or fellow available [22].

2.5 Conclusion

The role of APCs continues to expand, leveraging the physician's skills to focus on areas where they may be of greatest use. By partnering with others in health care, the versatility of APCs addresses needs in both inpatient, operative, and outpatient settings to collectively enhance outcomes and fulfill the evolving needs of health care in the twenty-first century.

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3 Role of the Speech-Language Pathologist (SLP) in the Head and Neck Cancer Team

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_3

Abstract

While treatments for head and neck cancer are aimed at curing patients from disease, they can have significant short- and long-term negative impacts on speech and swallowing functions. Research demonstrates that early and frequent involvement of Speech-Language Pathologists (SLPs) is beneficial to these functions and overall quality of life for head and neck cancer patients. Strategies and tools to optimize communication and safe swallowing are presented in this chapter.

Keywords

Dysphagia · Speech-language pathology · Laryngectomy
Voice · Speech · Feeding tube

3.1 Introduction

The restoration and rehabilitation of speech and swallowing disorders are crucial to optimize the quality of life after treatment of head and neck cancers. Treatment outcomes can be impacted by the quality of rehabilitation and a strong interdisciplinary team approach is essential [1]. Speech-language pathology plays a vital role in both the inpatient and outpatient settings. It is imperative for the SLP to meet the patient as early in the care process as possible (ideally in the multidisciplinary clinic) as this further facilitates patient compliance and ultimately improves short- and long-term outcomes for the patient [2].

Normal voice, speech, and swallowing functions require a series of precise coordinated movements of neuromuscular structures [3]. These functions can be impacted by the tumor itself or the treatments aimed at the tumor. The variable impact is to be expected based on any premorbid conditions, tumor location and size, mode of treatment, number of treatment modalities employed, expertise of the treatment team, and access to rehabilitative and supportive services. It is within the speech pathologist's scope of practice to evaluate speech and swallow function at baseline and through cancer treatment and prescribe rehabilitative interventions to maximally restore these functions after therapy.

3.2 Pre-habilitation

A diagnosis of cancer triggers intense emotions including, but not limited to, fear of the unknown as well as fear of future disfigurement, loss of function, and pain. Evidence has demonstrated that a multidisciplinary team approach starting at the time of diagnosis promotes improved outcomes [4].

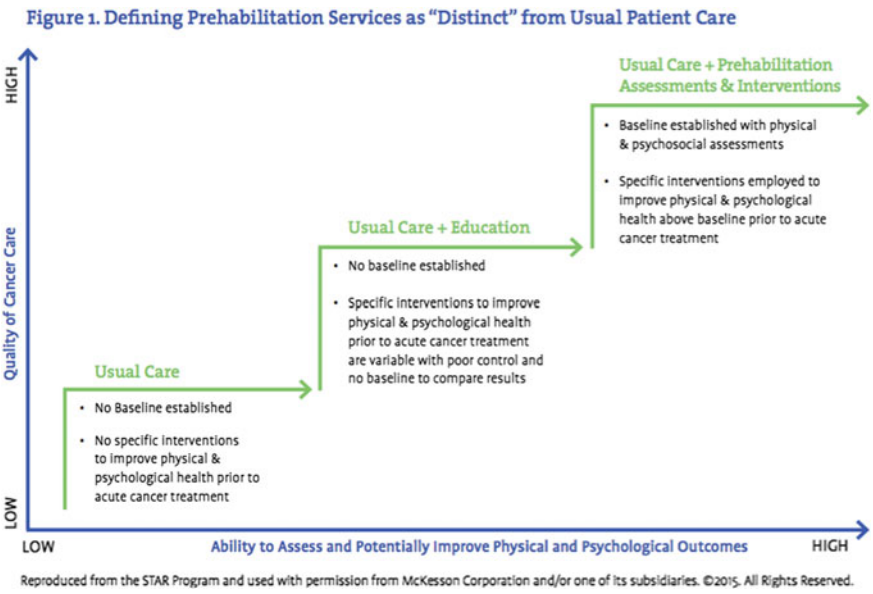

Fig. 3.1 Quality of life is significantly improved when pre-habilitation occurs along with establishment of baseline and usual care/education

Pre-habilitation is defined as "a process on the cancer continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment and includes physical and psychological assessments that establish a baseline functional level, identify impairments, and provide interventions that promote physical and psychological health to reduce the incidence and/or severity of future impairments" (Fig. 3.1) [5]. Patients benefit from a team to navigate their journey through cancer to recovery. Speech pathologists are an integral part of that team. A baseline of voice, speech, and swallowing function is often achieved by a myriad of studies including videostroboscopy, Modified Barium Swallow Studies (MBSS), and/or Fiberoptic Endoscopic Evaluation of Swallowing studies (FEES).

Beyond the baseline data, pre-habilitation sessions provide the patient and family with much-needed education regarding strategies to compensate for any current deficits (i.e., communication strategies, diet modifications, or aspiration precautions), as well as what to expect for recovery given their diagnosis. Speech and swallow exercises are often started immediately [6]. During these pre-habilitation evaluation and counseling sessions, post-treatment potential to regain speech, voice, and swallow function are reviewed as well as the importance of the patient's active participation in the treatment planning and program. The severity of baseline impairments may not always be self-perceived, as the frequency of subjective dysphagia before treatment has been reported as high as 59%. Patients with lower stage tumors have fewer complaints of swallowing, as do patients with oral cavity lesions [7]. Severity of baseline speech and swallow dysfunction is highly predictive of post-treatment functioning [8]. It is very important to consider

the patient's specific condition, coping style, access to therapy and rehabilitative preferences when developing the treatment plan. Pre-laryngectomy patients, for example, are shown an electrolarynx (their own device is ordered so it is ready for them during their acute hospitalization phase) and offered the opportunity whenever logistically possible to meet with another laryngectomee patient in order to get a more vivid understanding of what to expect following treatment. If pertinent for the pre-laryngectomy patient, esophageal speech and a tracheoesophageal puncture/prosthesis (TEP) are explained to the patient and family.

All of these discussions may help to ease anxiety and fear of the unknown and lead to improved outcomes [9]. The newly diagnosed head and neck cancer patient thus enters into the treatment phase of their care having had the necessary guidance and education to ease their experience during the acute phase of treatment. The use of pre-habilitation in cancer treatment results in the highest quality care for this population, as the newly diagnosed patient feels well supported in their treatment plan.

3.3 Rehabilitation

3.3.1 Dysphagia

Dysphagia is a common outcome post treatment. Instrumental swallowing evaluations, such as Modified Barium Swallow Studies (MBSS) conducted under fluoroscopy or Fiberoptic Endoscopic Evaluations of Swallowing (FEES) can be utilized to identify the presence of dysphagia. The SLP will determine if the individual is safe for oral intake or if alternative means of nutrition and hydration must to be considered. If the patient is deemed safe for consumption of PO, recommendations regarding diet type (e.g., regular, mechanically altered, minced, puree), and use of specific compensatory strategies (e.g., multiple swallows, breath hold, chin tuck) are often recommended (Table 3.1). A robust therapy program to improve dysphagia may include the use of specific swallowing maneuvers, changes in body posture, range of motion, use of biofeedback, and modification of diet consistencies [1]. Completing the aforementioned exercises on a routine basis may help to decrease long-term swallowing deficits that arise after treatment. The role of the speech pathologist is vital in order to ensure best outcomes.

Radiotherapy (RT) can result in significant swallowing difficulties during and/or following treatment. It is important to mention that head and neck cancer patients are frequently malnourished at the time of diagnosis and prior to the beginning of treatment. In addition, chemoradiation (CRT) causes or exacerbates symptoms, such as alteration or loss of taste, mucositis, xerostomia, fatigue, nausea, and vomiting, with consequent worsening of malnutrition. Moreover, it has been shown that during radiotherapy or CRT 55% of the patients may lose an additional 10% or more of body weight [10]. Clinicians must be mindful of the complications that arise while a patient is actively involved in radiation therapy, including xerostomia, mucositis, fibrosis, and neuropathy [1]. Severe effects of RT may be addressed with dysphagia exercise

Table 3.1 Swallow strategies

Maneuver	Indications	Rationale
Postural Changes		
Chin tuck	• Aspiration DURING swallow • Delayed onset pharyngeal swallow	Pushes Base of Tongue (BOT) to pharyngeal wall Moves epiglottis posteriorly
Chin tuck with resistance [21]	• Upper Esophageal Sphincter (UES) dysfunction • Reduced anterior and superior of the hyolaryngeal complex	Sit upright in chair, perform chin tuck against resistance (usually a ball); improves activation of suprahyoid muscles
Head turn (to weak side)	• Unilateral pharyngeal weakness	Directs bolus away from weak side by twisting pharynx
Head tilt (to strong side)	• Unilateral pharyngeal weakness	Directs bolus to strong side
Swallow Maneuvers		
Supraglottic swallow	• Reduced airway closure • Aspiration DURING swallow	Holding breath keeps the vocal cords closed
Supra-supraglottic swallow	• Reduced airway closure • Aspiration BEFORE and DURING swallow	Effortful breath hold tilts forward the arytenoids, which closes the laryngeal vestibule before/during swallow
Mendelsohn maneuver	• Decreased range/duration of hyolaryngeal elevation, CP opening, pharyngeal swallow coordination	Increased laryngeal elevation stretches open the cricopharyngeus (CP) Prolonged elevation keeps CP open longer
Effortful swallow	• Vallecular valleculae residue • Reduced BOT retraction	Swallow "hard"; excess effort should be clearly visible in neck during the swallow; increased effort increases posterior BOT movement
Jaw stretch	• Trismus • Masseter weakness	Open jaw to maximum extent and maintain position for 10 s; improves jaw ROM and mastication, facilitates good oral care
Masako	• Reduced BOT strength • Reduced pharyngeal constriction	Protrude tongue between teeth and swallow; strengthens pharyngeal constrictors to improve contraction
Shaker	• UES dysfunction • Reduced anterior and superior of the hyolaryngeal complex	Lie supine, raise chin to chest and maintain for 60 s; Improves opening UES, reduces pyriform sinus residue, strengthens the suprahyoid muscles
Behavioral Strategies		
Liquid wash	• Residue after swallow	Clear residue before next bolus attempted
Larger bolus	• Delayed triggering of swallow	Larger bolus is easier to sense for some patients
Multiple swallows	• Residue after swallow	Decrease aspiration by clearing residue before next bolus attempted

programs aimed at countering long-term adverse outcomes, such as dysphagia, aspiration, percutaneous endoscopic gastrostomy (PEG) dependence.

Multiple studies have demonstrated that implementation of swallowing exercises during CRT may help to preserve intra-treatment and posttreatment swallowing function in patients with advanced head and neck cancer [6]. Exercise programs developed by a speech-language pathologist target tongue range of motion (ROM), tongue strengthening, jaw and laryngeal ROM, which are required to preserve swallowing function. These exercises are utilized to maintain strength, coordination, and timing of the oral and pharyngeal phases of swallowing. For example, if a patient presents with impaired laryngeal elevation and reduced opening of the upper esophageal sphincter (UES), the SLP may recommend the "Shaker" exercise (Table 3.1). This particular exercise improves hyoid bone movement, thyrohyoid shortening, and opening of the esophageal sphincter in advanced head and neck cancer [6]. Patients are instructed by SLPs to complete the aforementioned exercise on a daily basis for maximum benefit.

However, if above interventions are unsuccessful there may be a need for enteral nutrition (EN) such as a nasogastric tube (NGT) or PEG to prevent weight loss, failure to thrive, aspiration, dehydration, and aspiration pneumonia. Swallow exercises should continue regardless. Muscles associated with laryngeal elevation, for example, undergo unused muscle atrophy leading to swallowing dysfunction [11]. Exercise programs recommended by the SLP are imperative to muscle strength, elasticity, and range of motion (Table 3.1). Literature suggests patients who continue to eat and complete a daily exercise regimen during CRT fare far better than those who do neither. Long-term swallowing outcomes have been shown to be best in patients who maintained both 100% PO throughout CRT and reported adherence to swallowing exercises, and uniformly worst in those who were NPO at the end of treatment and non-adherent to exercise (Figs. 3.2, 3.3 and 3.4).

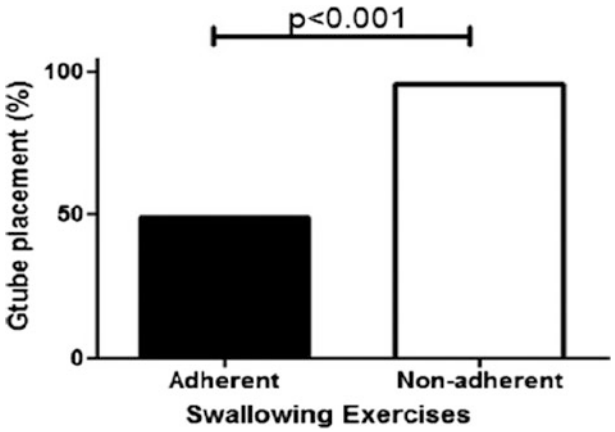

Fig. 3.2 PEG placement is significantly reduced in patients who report adherence to swallowing exercises

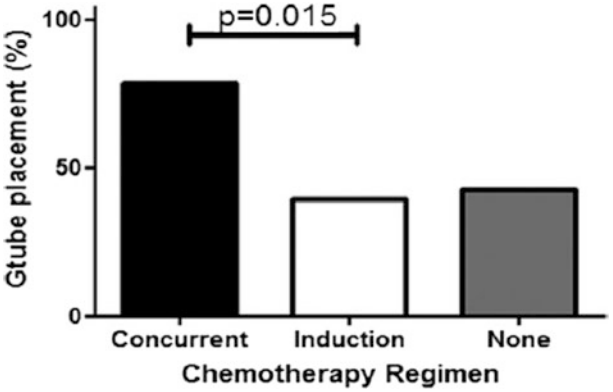

Fig. 3.3 PEG placement is significantly reduced in patients who do not receive concurrent chemoradiotherapy. Bhayani et al., Gastrostomy tube placement in patients with oropharyngeal carcinoma treated with radiotherapy or chemoradiotherapy: Factors affecting placement and dependence. *Head and Neck* 2012

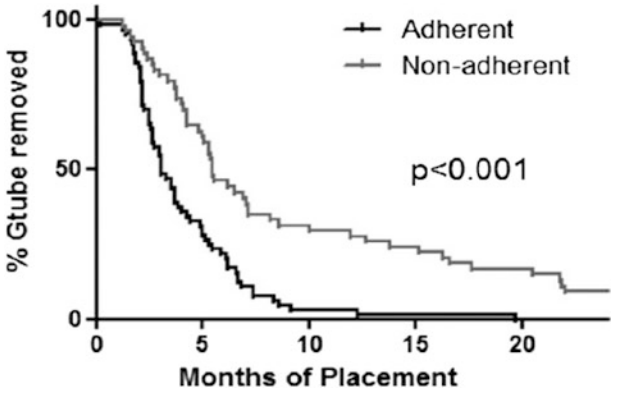

Fig. 3.4 Length of PEG dependence is decreased in patients who report adherence to swallowing exercise regimen. Bhayani et al., Gastrostomy tube placement in patients with oropharyngeal carcinoma treated with radiotherapy or chemoradiotherapy: Factors affecting placement and dependence. *Head and Neck* 2012

Individuals who complete this process often have the highest incidence of returning to a regular diet and shortest duration of gastrostomy dependence [12]. At one time, PEG placement was standard in all patients who were being treated for head and neck cancer. However, feeding tube placement has been shown to decrease quality of life in head and neck cancer patients. Currently, it is estimated that only 10% of people who survive head and neck cancer require PEG for enteral nutrition (EN) [13]. If nutrition is maintained via EN only as necessary but combined with all other treatments (maneuvers, exercises, PO trials, and mucositis treatment) then most patients can expect to avoid permanent feeding tube dependence [14].

With improvements in both imaging and instrumentation, transoral robotic surgery (TORS) and transoral laser microsurgery (TLM) have become increasingly utilized. Compared to traditional approaches, both TORS and TLM are less disruptive of normal and uninvolved anatomic structures, and consequently, the use of these approaches have been associated with a shorter hospital stay, faster recovery, less pain, less need for gastrostomy/tracheostomy tube, and lower cost [15]. However, these advanced surgical procedures do not eliminate the risk of speech impairment or dysphagia, depending on the structures involved in the tumor and surgical resection. As with other surgical approaches and techniques, patients will need to work with a SLP to learn strategies and techniques to improve speech communication as well as training of swallowing exercises and compensatory swallowing techniques for tolerance of oral intake, with the goal to improve PO intake and reduce risk for aspiration pneumonia.

3.4 Speech

Postsurgical outcomes for speech intelligibility depend on the size and location of tumor as well as defect size, configuration, and reconstruction. A lesion on the hard or soft palate, for example, may impact the quality of voice resulting in hypernasality. The use of intraoral prosthetic devices such as obturators, can help optimize voice resonance and speech. If lip closure is affected, it may be difficult to produce bilabial sounds (b, p, m). Speech therapy may then correspondingly target speech exercise to improve lip range of motion (ROM) and strengthening (resistance). The SLP may also give exercises targeting jaw ROM, jaw opening, lateral movement, and rotary movement. When tongue ROM and strength are impacted by treatment, this can lead to difficulty with the coordination required for linguoalveloar sounds (t, d, s, z, n). Communication between surgeon, patient, and ancillary team is imperative for setting up realistic expectations and customizing intraoperative reconstruction and postoperative rehabilitation. The SLP should be involved in discussions at tumor board to ensure strong interdisciplinary decisions are reached and appropriate planning for communication, airway protection, and nourishment are considered.

3.5 Augmentative Alternative Communication (AAC)

For head and neck cancer patients, communication may not be easily achieved using speech modality alone. The medical staff must have the tools and skills to facilitate communication with patients whether or not they can speak [16]. The patient's inability to communicate wants and needs results in an increased risk for unsafe situations and causes marked frustration. Proper education to medical staff can often prevent adverse events. It is the role of the SLP's to educate and train

patients in alternative forms of communication. This will help to maintain the quality of life during hospital admission and bridge the gap of communication to functional speech [17]. The SLP may educate the patient regarding the use of unaided systems (e.g., gestures, signing) and aided systems (e.g., alphabet charts, writing, apps). These can then be personalized to meet the patient's unique communication needs. Benefits of integrating technology-based communication interventions include the expeditious communication of patient needs, as well as healthy emotional outcomes for patients, family, and staff [17].

3.6 Partial or Total Laryngectomy

Depending on the location of the tumor, partial open laryngectomies can be supracricoid partial laryngectomy, supraglottic laryngectomy, or vertical hemilaryngectomy, each of which has different implications on swallowing function, voicing, and airway protection. In most of these procedures, voice production can often be preserved. However, temporary aspiration is common as airway protection postoperatively is affected and requires an intensive rehabilitative effort with exercises, techniques, and swallowing maneuvers to reduce or prevent aspiration of food or liquid. In the case of hemilaryngectomy, chronic dysphonia may persist despite rehabilitative efforts due to the impaired approximation of the contralateral vocal fold and the reconstructed hemilarynx. Conversely, dysphagia symptoms typically recover fairly well with time and swallow training. In cases of large tumors with involvement of both base of tongue and larynx, severe and chronic aspiration may be unpreventable. A laryngectomy may, therefore, be the safest option for the patient if resumption of an oral diet is desired.

The SLP plays a critical role in the postoperative assessment and rehabilitation of laryngectomy patients. A MBSS or esophagram depending on institutional protocol is often performed on postoperative day 7–10 to check for pharyngeal patency and any fistula. Patient can be cleared for PO intake if there are no structural problems in the pharynx. The SLP also provides education on the use of the electrolarynx, esophageal speech technique, tracheoesophageal voice prosthesis, and stomal devices. The SLP also facilitates necessary appliances and care in the perioperative period and beyond. It is important to understand that the presence of dysphagia in the laryngectomy population was historically underreported. As knowledge regarding postlaryngectomy dysphagia and sensitivity to this issue has improved, many patients now receive focused attention to this issue in postoperative rehabilitation including diet modifications, swallow strategies, and exercises [18]. Collaboration with the surgical team and GI collegues is often warranted for management of pharyngeal spasm, stricture, and other post-surgical abnormalities.

3.7 Survivorship

Many head and neck cancer patients live well beyond their cancer diagnosis and treatment and thus enter into a new phase of life: survivorship. This has been defined as the focus "on the health and life of a person with cancer post treatment until the end of life" and includes consideration of the late-effects of treatments, recurrent cancers, and quality of life [19]. The impact of surgical and reconstructive defects on long-term voice, speech, and swallowing abilities as well as the impact of the late effects of radiation on voice, speech, and swallowing are all considered when managing head and neck cancer survivors.

Extensive patient interviews and histories, cranial nerve and oral motor examinations, and instrumental assessments of speech, voice, and swallowing including laryngeal videostroboscopy, MBS, and FEES should be considered when a head and neck cancer survivor presents with complaints of progressive and/or chronic changes to voice, speech, and/or swallow function. It is not uncommon for survivors to present with new onset of cranial nerve paralysis, fibrotic changes, and overall progressive decline of already impaired function of speech, voice, and swallowing.

Despite efforts for functional organ preservation, dysphagia may develop or progress years after radiation-based therapy for HNC [20]. In this situation, the role of the SLP is to help identify the severity and implications of the dysphagia, speech impairment, dysphonia, and/or trismus. Pending results of these assessments as well as the patient's overall medical history, referrals to other medical professionals within the head and neck cancer team may be indicated (i.e., the GI specialist for esophageal dilation of cervicoesophageal web or stricture, the surgeon for consideration and discussion of possible vocal cord medialization, or the dietician for nutritional supplementation and advice within the dietary consistencies recommended). Changes to the function of the head and neck due to the late effects of radiation are uncommon but often refractory to the traditional targeted exercises and strategies taught by the SLP and may require delayed permanent gastrostomy or laryngectomy for severe chronic aspiration and pneumonia [20].

Many comprehensive cancer institutes offer additional long-term support to the head and neck cancer survivors, including opportunities to meet with other survivors to discuss similarities/differences in care, as well as outcomes and impact on quality of life. The SLP may play an integral role in the leadership of such support groups, such as Laryngectomee Support Groups. In addition, many head and neck survivor programs are moving toward including follow-up visits in a similar fashion to that of the physicians (i.e., 6 months followed by yearly visits) to assist patients with long-term toxicities from treatment, with the goal of optimizing quality of life.

3.8 Conclusion

Research and clinical experience demonstrate that quality of life after head and neck cancer treatment is significantly improved when a patient has early access to a SLP in a multidisciplinary setting. The patient similarly benefits when the SLP can follow longitudinally to address late effects of therapy. As treatment advances lead to patients living longer than ever, speech and swallow function have emerged as critical factors in planning and executing treatment. Such priorities on function before, during, and after therapy may redefine what may be considered a successful outcome, beyond just cure.

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Oral and Dental Health in Head and Neck Cancer Patients

4

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_4

Abstract

A diagnosis of head and neck cancer (HNC) is typically followed by therapy that is associated with immediate and long-lasting toxic consequences. HNC patients' oral health needs may be complex and are best addressed in multidisciplinary collaborative teams including surgical, medical, and radiation oncologists, dental providers, nutrition, speech/swallow specialists, and physical therapists. Oral health maintenance also requires patient compliance and caregiver support. The role of dental providers begins prior to cancer diagnosis and continues through survivorship. This includes oral screening and health maintenance, management of common oral complications such as mucositis, pain, infection, salivary dysfunction, altered taste, and dental decay, as well as complex issues that include soft tissue fibrosis, osteoradionecrosis of the jaw, dysphagia, and recurrent/new primary malignancies. As the number of potential therapeutic interventions for HNC increase, so do the spectrum of side effects affecting the oral cavity, oropharynx, and dentition. Specific approaches to oral care must be tailored to the idiosyncrasies of the patient and his/her therapy and condition. Oral and dental care is impacted by the patient's oral and dental status prior to cancer therapy, as well as the specific cancer type, location, stage, and its treatment and potential comorbid conditions. Communication between the dental professional and the oncology team is required for appropriate therapy and is best accomplished by integrated healthcare teams.

Keywords

Cancer treatment protocols · Oral and oropharyngeal complications
Head and neck cancer survivors

4.1 Introduction

Therapy for malignant diseases affects the mouth directly through surgery, and/or radiation therapy, chemotherapy, targeted therapy, and immunotherapy. Common oral complications include pain, mucositis, and stomatitis, salivary gland hypofunction, taste loss/change, oral infections, dysphagia, fibrosis, soft tissue and/or bone necrosis, exacerbation of dental and periodontal diseases, and recurrent or secondary malignancy [1–3]. New therapies are associated with new/altered oral complications.

Head and Neck Cancer (HNC) patients require specialized oral care throughout the continuum of cancer diagnosis, treatment, and survivorship. This chapter will review oral care with a focus on unique oral issues throughout the journey of the HNC patient.

4.2 Head and Neck Cancer Treatment and Its Impact on the Oral Cavity

Treatment modalities employed for HNC that may cause oral complications include surgery, radiation therapy, and chemotherapy (neoadjuvant, adjuvant, and/or concurrent) [4]. Additionally, targeted therapies, including epidermal growth factor receptor (EGFR) inhibitors, tyrosine kinase inhibitors (TKI), mammalian target of rapamycin (mTOR) inhibitors, and emerging immunotherapies can have oral side effects [5–7] Pretreatment oral conditions may increase the risk of complications [2]. Combinations of treatment modalities are expected to cause overlapping and additive toxicities during therapy and survivorship.

Oncologists should recognize the importance of early referral for dental evaluation and appropriate intervention and prophylactic measures to address oral needs. This may include management of preexisting poor dental conditions and prevention and management of emerging oral complications. Therapy for preexisting and developing conditions should ideally be completed before initiation of HNC treatment. Unforeseen or unavoidable oral and dental complications developing during therapy must be managed medically, while oral care in survivorship must be thorough, frequent and personalized.

4.3 Oral Care Prior to Cancer Treatment

Most patients newly diagnosed with cancer tend to be overwhelmed, and preparation of the oral cavity for the upcoming treatment regimen is rarely a part of their concerns. In such circumstances, it becomes imperative for the oncology team to reinforce the need for a so-called “dental clearance”, which consists of diagnosis and treatment of existing infections and physical irritants, as well as the elimination of potential sources of complications during cancer therapy. Community dentists may not have the necessary background or experience in cancer therapies and the burden they place on the patient. Expert dental evaluation and care may be needed to identify and manage oral conditions and diseases in HNC patients. Guidelines for basic oral care have been developed by the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) [7, 8] (Table 4.1). Consensus recommendations for management of selected head and neck toxicities have been recently presented [9, 10]. However, pretreatment dental care must be personalized and tailored to the patient’s oral condition, abilities, and specific expected toxicities from the planned anti-neoplastic regimen. In addition to oral clearance, the dentist must design the oral care package for the duration of therapy, which includes oral hygiene, maintenance of oral homeostasis, and prophylactic measures.

A complete head, neck, oral, dental, and periodontal assessment is recommended as the standard of care and should be conducted as soon as possible after the cancer diagnosis and prior to any treatment [11–13]. In addition to dental evaluation, the

Table 4.1 Oral care prior to and post-cancer treatment in head and neck cancer survivors

Pre-cancer treatment	• Pretreatment assessment >2 weeks prior to cancer therapy • Comprehensive head and neck, oral mucosa, dental and periodontal examination • Radiographs:assess dental/periodontal status • Baseline jaw range of motion (interincisal opening), baseline resting and stimulated saliva • Advanced caries, advanced periodontal disease: definitive treatment may require surgery with goal of 1–2 weeks of healing time • Periodontal debridement/maintenance • Small carious lesions may be treated with fluoride and/or sealants/restoration • Custom fluoride carriers, custom-made oral positioning devices
During cancer treatment	• Individual treatment in context of cancer and cancer treatment • Oral hygiene reinforced • Symptom management: pain: analgesic and topical anesthetic agents; dry mouth: hydration, oral rinses, and coating agents; lip management • Mucositis management: good oral hygiene, hydration/rinses, low-energy laser therapy (LLLT) • Treat dental emergency as indicated • Patient education: – Daily oral hygiene; fluoride application; oral rinsing (1 teaspoon of baking soda and salt in a glass of water) – Oral moisturizing: moisturize mouth rinse and water-based lubricant; lip care using water-based lubricant, wax, or lanolin; avoid glycerin and petroleum jelly products – Diet/nutrition instruction; tobacco cessation
Post-cancer treatment	• Monitoring, prevention, and management of oral complications (mucositis, dry mouth, mucosal pain, taste change, infection, dental demineralization, dental caries, periodontal disease, osteonecrosis, etc.) • Checking for cancer recurrence or secondary primary cancer • Dental caries prevention, periodontal debridement/maintenance • Determine frequency of dental hygiene follow-up based on level of hyposalivation, effectiveness of oral hygiene, demineralization/caries rate • Patient education • As during cancer treatment (above)fluoridated toothpaste; in dry mouth continue use of fluoride in carriers in high-risk patients

assessment should include assessment of salivary gland function and range of jaw opening. Surgical dental treatment within the planned high-dose radiation field should be ideally completed 10–15 days prior to the start of cancer care [14–16]. Compromises in timing and extent of dental treatment may be necessary if initiation of cancer therapy is deemed urgent [17, 18].

Dental extractions in irradiated bone (in particular the mandible), may lead to osteoradionecrosis. Thus, teeth with periodontal involvement (attachment loss or periodontal pockets of >5 mm), retained root tips, or partly erupted teeth should be extracted prior to starting radiation therapy (RT). Rough/irregular dental surfaces

must be eliminated also in order to reduce soft tissue irritation and trauma. Communication between dental and medical providers is essential [19] so that necessary treatment is provided at the correct time in coordination with medical care, and unnecessary care is avoided.

Maintenance of effective oral hygiene and other preventive measures are imperative during cancer therapy. Patients should be advised to brush their teeth after every meal as well as after consumption of sugary foods or drinks. A bland toothpaste is recommended, particularly in the presence of mucosal injury. Interdental cleaning (dental floss, interproximal brush, toothpick) should be included in daily oral hygiene and if discontinued due to mouth pain, resumed as soon as possible. In cases where oral hygiene is anticipated to be difficult to maintain (poor oral habits, physical disability), consideration for risk reduction by extraction of teeth in the high radiation dose volume may be indicated. An alternative may be rinsing with aqueous chlorhexidine (0.12% solution) to reduce gingivitis and caries risk and suppress candida overgrowth [20]. Daily application of fluoride to dentition is recommended and may be more effective using custom-made carrier trays that cover the teeth and gingival margins. For those not able to use trays, brush-on high potency fluoride (5 ppm) gel or paste should be used daily as long as the mouth is dry.

For patients with a large number of metal-containing restorations, custom oral devices (midline blocks or anti-scatter trays) may be prescribed to minimize radiation scatter to oral structures unaffected by cancer by stabilizing and positioning the jaw or soft tissues. This is not necessary for dental implants which are based on titanium.

4.4 Oral Care During Active Cancer Treatment

Nonsurgical therapy for advanced stage HNC typically consists of RT with concomitant use of a radiosensitizer. RT is generally administered in 200 cGy doses 5 days/week to a total of 65–72 Gy. Sensitizing agents usually consist of a platinum agent (cisplatin or carboplatin) or an EGFR inhibitor (cetuximab). The role of immune checkpoint inhibitors is expected to increase as part of multimodality therapy. Each of these agents has oral side effects that can become additive. Additionally, the patient's general condition undergoes significant changes due to the immune-modifying, neurotoxic, emetogenic, and other toxic effects of therapy. For these reasons, and due to oral mucositis, dental treatment is generally contraindicated during and immediately after active cancer therapy, but specific exceptions can be made for resolution of urgent dental pain that requires no surgery. In case a dental or periodontal abscess requires surgical intervention, antibiotics to control the infection may be considered; although it represents only a temporary measure, this strategy may allow completion of cancer therapy without interruption.

Patient education is an integral part of oral supportive care to prevent oral complications and to maintain oral and oropharyngeal function. Education includes dental disease prevention, nutritional guidance, cessation of alcohol, and tobacco

use, and psychosocial support during cancer therapy for successful completion as well as throughout survivorship [21, 22]. Taste change/loss, mucosal sensitivity, and hyposalivation may negatively impact diet affecting energy, nutrient intake, and micronutrients which may affect oral and general health. Oral symptoms and oropharyngeal function require attention from the oncology team to ensure timely diagnosis and appropriate treatment, and support patient compliance with treatment recommendations.

Patients should be instructed in effective, atraumatic tooth brushing (minimum twice daily), interdental cleaning (once daily), and fluoride gel applications, and in high caries risk, oral calcium source and antimicrobial rinse (chlorhexidine) [17, 18]. Supersoft manual toothbrushes should be used, although in some cases ultrasonic or electric brushes may be recommended [23]. Diet and supplements that are high in sugars, as well as sucrose-sweetened medications should be avoided, but when needed should be taken with meals, and following plaque removal by oral hygienist [24].

4.4.1 Pain

The most common oral complication in HNC patients is pain. Oral pain may be due to effects of tumor, following surgery, and due to mucositis during radiation therapy. The severity and duration of mucositis are impacted by radiation therapy plan, complicated by cytotoxic chemotherapy, and targeted therapies. There are specific strategies for prevention and management of mucositis and other mucosal diseases, described in the MASCC/ISOO evidence-based guidelines [2, 8]. For mucositis pain, MASCC/ISOO recommends patient-controlled analgesia (opioid analgesics) for severe symptoms, and topical analgesic/anesthetic agents (e.g., doxepin, morphine, lidocaine, benzocaine, diphenhydramine) for mild–moderate pain. The use of medication for neuropathic pain is increasing with the recognition that pain in mucositis is due to direct tissue damage and neuropathic mechanisms [25]. Study of potential prevention of RT-induced mucositis is ongoing, with a recent suggestion for use of photobiomodulation therapy (PBM, formerly low-energy laser therapy [LLLT]), which may significantly reduce the severity and duration of mucositis [2, 14, 26, 27]. In addition, dietary instruction, frequent use of saline/bicarbonate rinses, and good oral hygiene should be encouraged. Numerous over-the-counter coating agents that may protect ulcerated tissue and thereby reduce pain, are available, but in general have limited data supporting use.

In most cases, RT significantly reduces salivation, which leads to decreased protection of oral soft and hard tissues, as well as microbial shifts that favor increased numbers of cariogenic bacteria [28]. Dental disease prevention during RT should include daily fluoride applications. Fluoride must be continued daily if hyposalivation continues, which is often throughout survivorship. Compliance with needed oral care requires reinforcement at the cancer center, and appraisal of the presence of dry mouth. Furthermore, in patients with dry mouth, a calcium source for maintenance of tooth structure may be critical to prevent structural damage, and

also must be continued if hyposalivation continues. In high-risk patients, management of caries-associated oral flora is needed and daily chlorhexidine rinsing may be added [29, 30].

4.4.2 Mucositis

Mucositis is a dose-limiting toxicity of HNC cytotoxic therapy (Fig. 4.1). Acute mucosal injury develops during therapy, and may continue for weeks to months following completion of treatment. The duration and severity of mucositis are increased in combined chemotherapy and radiation therapy. Targeted drug therapy using epidermal growth factor inhibitors also increases painful mucositis in and outside of the radiation field [31]. It is anticipated that increasing the use of immune checkpoint inhibition will increase oral complications, including mucositis, dry mouth, and taste change [6]. Combination therapy is expected to increase the incidence of oral complications and therefore increase the complexity of management.

Patient education includes the recommendation of the frequent use of non-medicated bland oral rinses, lubricating mucosal coating agents, and topical analgesics/anesthetics as needed. Mouthwashes with alcohol, acidic and spicy foods, and rough/abrasive foods should be avoided [32]. Oral hygiene must be maintained in order to control the growth of oral flora, as well as to reduce inflammatory and infectious complications. Mechanical (brushing, flossing) and/or pharmaceutical (chlorhexidine mouth rinses) methods can be adapted to the patients' oral condition to reduce microbial overgrowth and associated consequences.

Current management of mucositis is focused on palliation of symptoms with coating agents, and topical and systemic analgesics. Photobiomodulation therapy (PBM) has been suggested as the potential for prevention of RT-associated mucositis. Mucositis pain is typically due to inflammation from tissue damage (nociceptive pain), as well as neuropathic sensitization (neuropathic pain). Hence,

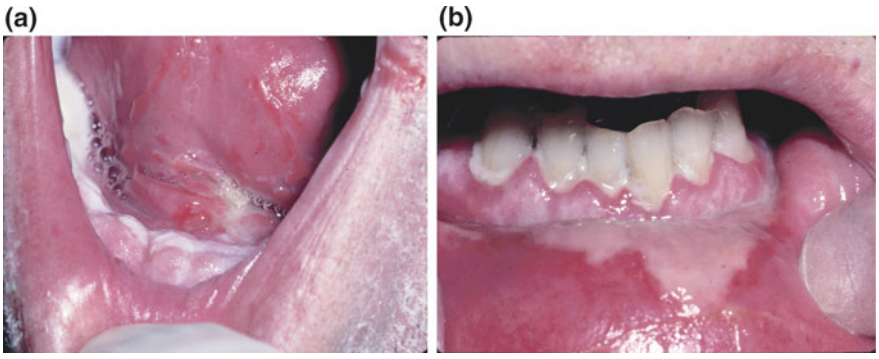

Fig. 4.1 Mucositis. **a** WHO Grade 2 mucositis, compounded by secondary candidiasis (note cracking at the corner of the mouth). **b** WHO Grade 3 ulcerative mucositis

management should include medication like gabapentin and/or doxepin to address the neuropathic causes [33, 34]. Following active therapy, chronic mucosal sensitivity may continue and may be increased in those who had severe acute mucosal damage [35]. This mucosal sensitivity may be due to tissue atrophy, hyposalivation, mucosal infection, and neuropathic mechanisms.

4.4.3 Oral Mucosal Infections—Viral, Bacterial, and Fungal Infections

Oral infections can develop during cancer therapy and diagnosis can be challenging due to potentially overlapping symptoms and signs during mucositis and following treatment due to mucosal changes. Herpes family viral infection may occur; however, reactivation is uncommon in HNC patients. Generally, vesicles and/or ulceration present on oral/oropharyngeal mucosal surfaces should be suspicious for viral reactivation. Diagnosis is confirmed by the presence of multinucleated cells on Tzank smear prepared from scraping of an ulcer base or by culture. Either systemic acyclovir or valcyclovir may be prescribed in herpes treatment [35, 36]. In immunocompromised patients, treatment may need to be administered parenterally. When a severe viral infection is present, pain management, hydration, and nutrition should be addressed.

Local bacterial infection may progress from preexisting chronic dental or periodontal infection. In the setting of mucosal barrier injury including ulceration and possible immune compromise, these infections may become systemic, hence control of bacterial overgrowth is important. Pretreatment dental and periodontal evaluation and control measures are planned to eliminate active/symptomatic foci of infection. In HNC, chronic preexisting dental conditions that may require surgical management in the future should be eliminated prior to cancer therapy. When systemic antibiotics are needed, empiric drug selection should be initiated pending results of culture and sensitivity. Broad coverage may be indicated as initial therapy due to potential shifts in oral flora as HNC treatment progresses, and in patients not responding to therapy as expected [36].

Oral fungal infection is significantly increased in HNC patients during and following cancer treatment. It has a prevalence of 7.5%, 39.1%, and 32.6% prior to, during and following cancer therapy, respectively [37]. The most common organism associated with local infection is *Candida albicans*, but other Candida species (e.g., krusei, dubliniensis, and tropicalis) have been increasing in prevalence in cancer patients (Fig. 4.2). The clinical presentation of oropharyngeal candidiasis may vary from white plaques, to erythema or nodular presentation, and may overlap with mucositis [38]. Other symptoms such as coated sensation, burning sensation, and taste change may be associated with candidiasis and should raise attention. Topical antifungal agents have had inconsistent efficacy and some topical preparations are high in sugar, which increases dental caries risk particularly in the dry mouth dentate patients. Topical antifungals that are not sugar sweetened (e.g., Nystatin vaginal suppositories) are a better choice for topical therapy; oral systemic

agents including fluconazole may also be more effective [39–41]. Of importance is understanding that fungal species with increased resistance to azole antifungal agents are being identified more frequently and effective management may require identification of the fungal species to support the selection of most effective medication, particularly in nonresponding cases [37].

4.4.4 Other Oral Complications

Reduced saliva production (hyposalivation or xerostomia) may continue indefinitely and is associated with many of the long-term oral and oropharyngeal adverse effects of HNC therapy. In some cases, patients may accommodate to the persisting symptoms and not report dry mouth, but if hyposalivation continues, increased risk of oral infection and dental disease continues [37, 42]. Management includes assessment of saliva production, and if residual function remains, stimulation (e.g., hydration, chewing, and taste stimulation), systemic sialagogues such as pilocarpine (Salagen), cevimeline (Evoxac), bethanechol, or PBM. Oral wetting and coating agents are palliative and can be used if salivary gland stimulation is not effective [43]. The increased thickness of oral and pharyngeal secretions as well as dry mouth may represent significant survivorship issues that may lead to trials of mucolytic agents (e.g., guaifenesin, acetyl-cysteine). Good daily oral hygiene and

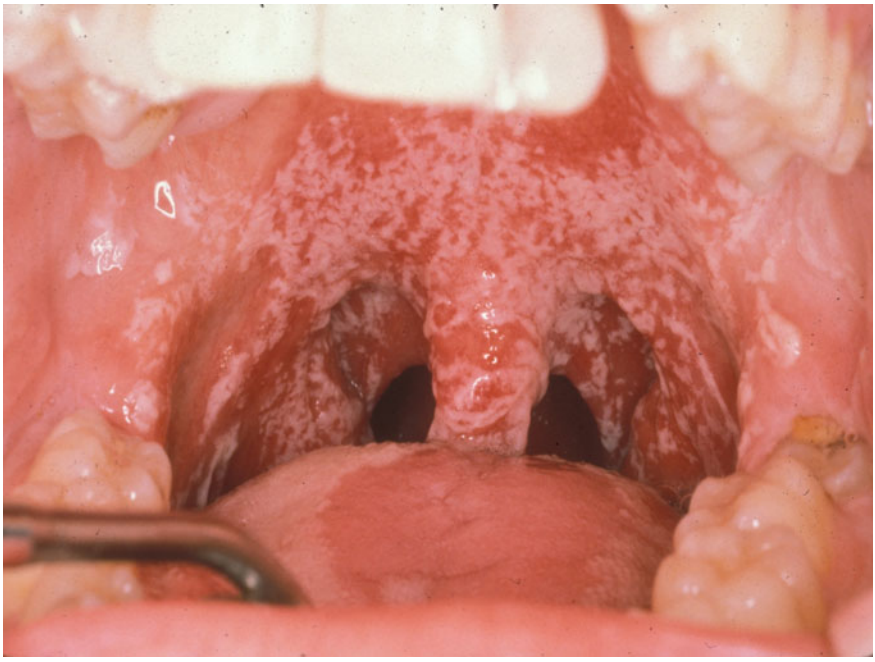

Fig. 4.2 Extensive pseudomembranous candidiasis mixed with erythematous candidiasis

dental fluoride and remineralization supplementation together with frequent dental visits are recommended. For those patients with persisting hyposalivation, wetting and lubrication of oral surfaces and replacement of calcium, phosphate, and use of antimicrobial rinses may be required to replace lost functions of saliva. Lip protection and lubrication should also be recommended. Patients should avoid products with petrolatum, as chronic use may cause atrophy of mucosa and increase the risk of infection, particularly at the corners of the mouth. Wax-based or lanolin-based products are instead recommended.

4.5 Oral Care Post-cancer Treatment for Head and Neck Cancer

Post-therapy HNC patients should be monitored closely to reinforce prevention of oral and dental complications, diagnose and manage late complications, and identify potential cancer recurrence and/or metastasis and/or second primaries [44]. Effective management of oral mucosal and dental infection, residual mucositis, and sensory changes (pain, taste change/loss), screening for dental and periodontal disease, soft tissue/bone necrosis, tissue fibrosis (including temporomandibular joint disorders, dysphagia, tongue mobility) and reduced/altered salivation must be part of post-cancer therapy care [45]. The frequency of follow-up dental visits must be personalized, based on patients' conditions, at a minimum of twice per year basis, although a 3-month schedule may be indicated for cases with ongoing oral/dental complications (Table 4.1).

Dry mouth increases the risk of dental demineralization and tooth cavitation (Fig. 4.3), leading to potential pulp involvement and abscess formation. Hyposalivation also increases the risk for progression of periodontal disease, and may result in increased risk of osteoradionecrosis (ORN). Dental sensitivity to

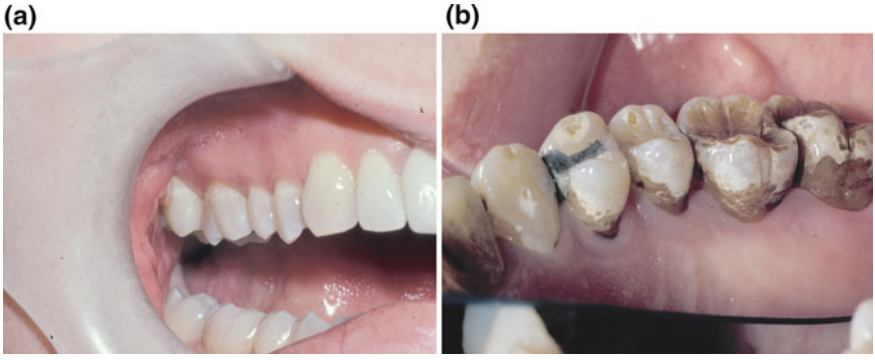

Fig. 4.3 Dental demineralization. **a** Early findings of hyposalivation and dental demineralization along the gum line of teeth. **b** Extensive dental demineralization and cavitation on cusp tips of teeth and along the gum line

temperature is also associated with hyposalivation, dental caries, and lower salivary pH. Temperature sensitivity may be a symptom of progressing dental damage.

Oral burning sensation due to mucosal sensitivity may be aggravated by hyposalivation, secondary candidiasis and/or may result from peripheral neuropathy [2, 46]. Radiation- and chemotherapy-induced neuropathies are associated with inflammation, neurotoxicity, oxidative stress, and ischemia, which may persist long after clinical mucositis resolved [47, 48]. Oral sensitivity may, therefore, be addressed by the management of neuropathic mechanisms when symptoms are affecting the quality of life.

ORN is a known risk following head and neck radiotherapy, particularly when the radiation fields include the body of the mandible. It is associated with dental disease and dental procedures, but can occur without an identified stimulus. This risk may be increased in people on antiresorptive medications such as bisphosphonates or denosumab, on anti-vascular agents, immunosuppressive medications, and/or in people with diabetes, and in tobacco users [49]. Prevention of necrosis is the key concept that mandates expert dental evaluation and necessary extractions in high-dose RT volume prior to HNC treatment, with sufficient healing time from surgery in the planned RT field. In cases where ORN develops, management is based on limited research and clinical experience, and should be provided by an experienced healthcare team due to the complexity of care. The goal of treatment is the prevention of progression, pain control, and management of secondary infection in hard and soft tissues (osteomyelitis, cellulitis). The primary approach for management of ORN has been hyperbaric oxygen therapy, despite high costs and conflicting literature. Medical management based on more recent studies include the use of pentoxifylline and Vitamin E, as well as clodronate [50] with the suggestion in the literature of a potential role for PBM [51]. When medical management fails, referral for surgical intervention with vascularized tissue transfer should be initiated. The patient may require a feeding tube for nutrition support in the meantime.

Up to 75% of HNC patients have dysgeusia or ageusia, which directly impacts nutrition and quality of life. Saliva is required for presenting food molecules to taste receptors. Thus, the first approach to taste complaints may be increasing salivation by use of sialagogues. Dry mouth-associated taste change may also occur with secondary oral bacterial or fungal infection or with use of chlorhexidine rinses. In addition, gastrointestinal upset, mucosal sensitivity, inflammation, and ulceration may limit oral intake, and may lead to nutritional compromise. When local factors have been addressed as best as possible, a dietary instruction to address specific issues of taste may be recommended. Preliminary reports suggest that taste abnormalities may be improved with zinc supplementation, megestrol, and cannabinoids [52].

Trismus may follow internal or external lymphedema in the head and neck. Lymphedema may progress to fibrosis over time [53]. Early intervention with massage and range of motion jaw exercising may prevent severe restriction. Additional approaches to trismus with potential benefit are the use of antifibrotic protocols such as pentoxifylline and vitamin E, and PBM [26].

Recurrent or second primary oral malignancy is a known risk in people with prior upper aerodigestive tract cancer. Post-radiation mucosal changes can make detection of early recurrence difficult due to changes induced by radiation, and the risk of delayed healing of biopsy in the high dose radiation fields make a determination to biopsy more challenging. In such cases, cytology may be helpful, though positive lesions will eventually require tissue biopsy. Continuing expert follow-up is needed in patients with potential recurrence following cancer therapy, and particularly in cases where dysplasia is noted (cytology or biopsy).

4.6 Conclusion

For HNC survivors, physicians and particularly oncologists should recognize the role of specially trained/experienced dental professionals who can provide care as an integral part of the oncology team. These dental professionals can play a role in prevention of oral complications through patient education (improve oral hygiene, maintain nutrition, reduce alcohol and tobacco use), prevention and treatment of dental disease, detection and management of oral complications of cancer therapy (during and following treatment), and early detection of oral malignancy in high-risk patients [54]. The related referral pathways are through dental and medical specialists with oncology experience [55]. The integrated oncology team can contribute to oral complication prevention, detection, and treatment, and considerably improved quality of life.

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Imaging Evaluation of the Head and Neck Oncology Patient

5

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Contents

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_5

Abstract

Imaging plays a multifaceted role in the diagnosis and characterization of head and neck oncological patients and is integral to their care. Given the complexity of treatment, a multimodality approach is often necessary. With the advent of new technologies, imaging can also be used to predict tumor behavior and treatment response. In this chapter, with selected case examples, we describe the various imaging modalities available and offer suggestions on their utilization.

Keywords

Oncologic imaging · PET-MRI · 4D CT · Surveillance imaging
Image-guided biopsies

5.1 Introduction

Head and neck cancers account for roughly 500,000 cases worldwide [1] and comprise 3% of all malignancies in the United States [2]. Head and neck radiology plays a critical role in the initial identification, assessment, and surveillance of these tumors, often requiring a multimodality approach. The head and neck radiologist interpretation during tumor board can restage a tumor, sway decision-making about surgical resectability, or prompt a further workup for suspicious or benign-appearing lesions that are either locoregional or distant. We provide an overview of the various imaging modalities available, offer guidelines for each modality's utility in the cancer workup, and introduce more advanced imaging techniques to characterize tumors on a molecular level.

5.2 Orbits and Sinus

Both CT and MRI play supplementary roles in imaging of tumors in the sinuses and orbits. For the orbits, MRI is the preferred imaging modality as the orbital fat displays an inherent contrast between muscles and nerves. For sinuses/face, CT provides fine bony detail and serves a role for preoperative surgical planning using one of the multiple commercial stereotactic platforms. MRI is helpful for assessment of paranasal sinus soft tissue invasion and perineural spread. PET scan plays a role especially in the postoperative setting given streak artifacts from dental amalgam, surgical clips, and the lack of specificity in an area of the scar.

5.2.1 Sinus/Face/Orbit CT

CT protocols for orbital imaging requires thin-section axial acquisitions with coronal and sagittal reformations performed in both soft tissue and bone algorithms (for assessment of erosive changes). The parameters for a typical orbital CT protocol would include 0.625 mm helical acquisitions, field of view (FOV) of 25 cm, at 0.625 mm spacing with reconstructions at 1.25 or 2.5 mm, tube rotation time of 0.5 s, pitch factor 1.375:1, noise index of 5, kVp 120, and automatic tube current modulation with a minimum of 50 to a maximum of 330 mA. Coverage area for orbital imaging is from above the orbital roof to the mid maxillary sinus. Sinus CT would require coverage from above the frontal sinuses through the maxillary alveolar ridge. Facial CT would require coverage from above the frontal sinuses through the mandible. If volume rendered surface imaging is required for operative planning, the source data should be sent to a three-dimensional workstation for image manipulation. Presurgical planning scans are dictated by the software utilized for intraoperative guidance and may include imaging from the skull vertex to the below the mandible. CT is often preferred in calcified lesions (retinoblastoma), osteolytic lesions, and in the pediatric population due to quick acquisition time not requiring general anesthesia. Both a contrast and non-contrast scan is rarely necessary for facial/orbital imaging and when possible, a contrast-only scan should be performed.

5.2.2 Sinus/Face/Orbit MRI

MRI protocols for orbits differ from their brain counterparts due to the inherent inconspicuousness of contrast enhancement in the setting of orbital fat. Therefore, fat suppression is key for orbital imaging. Coverage area includes from above the orbital roof through the maxillary sinuses and from the pons through the globes. MRI of the sinuses includes the entire paranasal sinuses and nose with MRI face including the mandible. Typical protocols would include axial and coronal T1 TSE at 3 mm intervals, axial and coronal T2 TSE with fat suppression at 3 mm intervals, and axial and coronal T1 TSE fat-suppressed post-contrast imaging. A volumetric post-contrast T1-weighted gradient echo acquisition allows for high isotropic and

spatial resolution with the ability to have additional reformations performed (sagittal, sagittal oblique parallel to the optic nerve). Early acquisition (3 min) post contrast can aid in differentiation from tumors (early enhancement) and inflammatory tissue (delayed enhancement) [3].

5.2.3 Sinus/Face/Orbit PET

PET/CT has proven useful in the setting of identifying distant metastases from a primary metastatic lesion to the face/orbit as well. It is also useful in evaluating recurrent disease in a tumor bed which is often masked by postoperative changes on the anatomic sequences of the conventional CT and MRI imaging [4]. PET scans are limited by the natural FDG avidity of the underlying nasal cavity and sinuses [5]. Given FDG uptake in the extraocular muscles, local disease evaluation is also limited in the orbits. A negative PET study is more predictive of the true absence of tumor than conventional imaging [6].

5.2.4 Select Oncological Imaging Examples

Ocular Metastases—see Fig. 5.1

- most common primary cancer is breast cancer [7]
- melanoma will often be T1 hyperintense on pre-contrast imaging
- PET scan for distant metastases

Sinonasal SCC—see Fig. 5.2

- heterogeneously enhancing irregular mass with bone erosion
- low T2 signal differentiates from obstructive mucosal disease

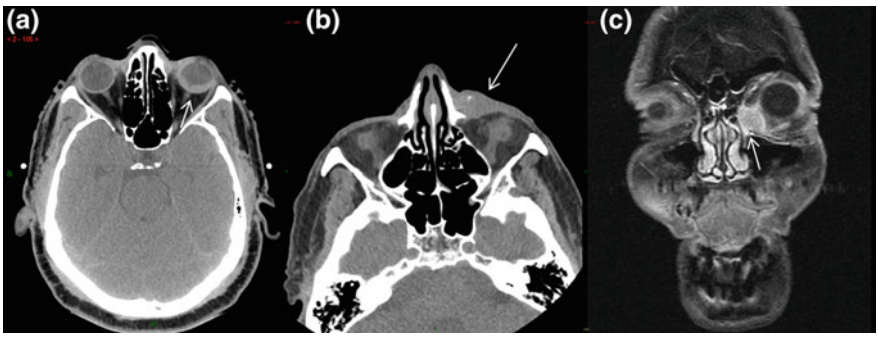

Fig. 5.1 **a** Breast cancer metastases. Axial non-contrast CT for radiation planning with abnormal thickening of the choroid (*arrow*). **b**, **c** SCC of the skin. Axial non-contrast CT showing skin thickening extending to the nasal bone and pre-septal soft tissues (*arrow*). Coronal T1 fat-suppressed post-contrast images demonstrate lesion that abuts the anterior globe and may involve insertion tendon of medial rectus muscle (*arrow*)

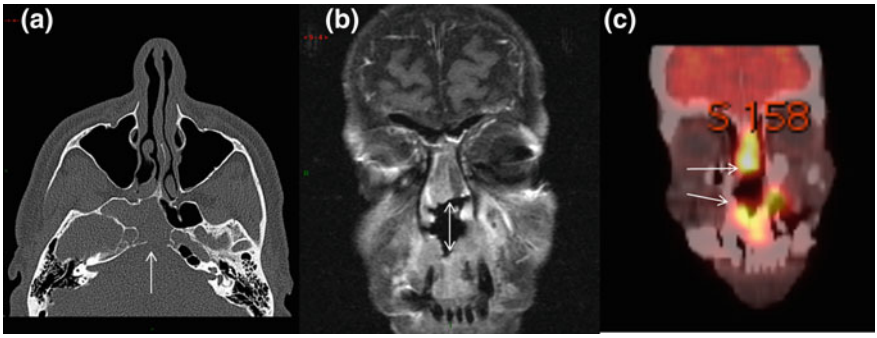

Fig. 5.2 **a** SCC of the sphenoid sinus. Axial non-contrast CT demonstrating expansile sphenoid sinus mass with the erosion of posterior sinus wall (*arrow*). **b**, **c** Recurrent SCC of the sinonasal cavity. Coronal T1 post-contrast MRI shows heterogeneous enhancing tissue in the nasal cavity and maxilla (double arrows) which could be a tumor or less likely scar tissue. Coronal-fused PET-CT confirms residual tumor in both these areas

- MRI useful to evaluate extent of disease into orbit, retroantral fat, and perineural spread
- FDG avid, retropharyngeal/level II adenopathy [8], enhances to lesser degree than adjacent mucosa
- most commonly in maxillary sinuses

Sinonasal Non-Hodgkin's Lymphoma (see Fig. 5.3)

- most commonly occurs in the nasal cavity
- homogenous enhancement, hyperdense on non-contrast studies
- can have regional osseous destruction
- FDG Avid but can be false positive due to inherent FDG avidity of nasal cavity

Sinonasal Undifferentiated Carcinoma (SNUC)

- large fungating lesion, commonly occurs in nasal cavity with sinus extension
- poorly defined with aggressive osseous destruction, heterogeneous enhancement, and rapid growth with distant metastases

5.3 Parotid Space

Although the majority of parotid lesions occur in the superficial lobe and are easily identified on inspection, often by the patient, deeper lesions pose a greater challenge to identify on physical examination alone. This is true of lesions in the deep portion of the parotid gland or exophytic lesions extending into the parapharyngeal space. As a result, many parotid lesions are incidental findings on imaging for other causes (neck trauma, headaches).

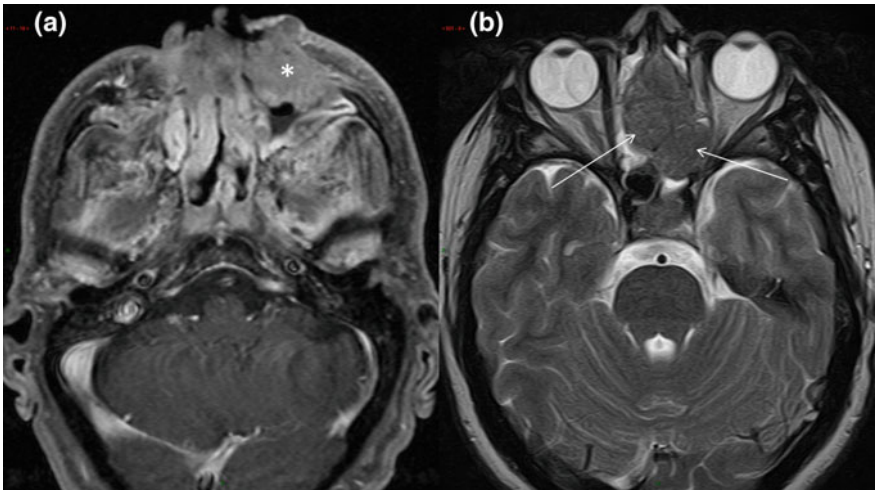

Fig. 5.3 **a** Axial T1 post-contrast images demonstrate enhancing tumor (*asterisk*) in the anterior nasal cavity and invading into the maxillary sinus and overlying soft tissues. **b** Axial T2 demonstrates well-circumscribed mass in the nasal cavity with slightly low T2 signal (*arrows*) invading into the orbit and abutting the medial rectus muscle. This patient had biopsy-confirmed lymphoma of the sinuses

5.3.1 Ultrasonography (US)

Since the bulk of parotid tissue is superficial, ultrasonography is a reasonable first line of imaging. Although underutilized in the United States, ultrasonography is the preferred modality for parotid imaging in Europe and Asia [9], especially in the pediatric population [10]. However, lesions at the stylomandibular notch or in the deep parotid space are not readily accessible with sonography [11].

5.3.2 CT of the Parotid Space

CT has the advantage of higher spatial resolution of the stylomastoid foramen and mastoid bone when perineural spread or bony invasion is suspected. In the normal adult parotid gland, the gland is slightly fatty with Hounsfield units of 15–25 [12] allowing for a clear depiction of most parotid lesions. A denser gland, often seen in a younger population or a post-radiated neck can often mask intraparotid lesions [13]. Additionally, dental amalgam artifact can interfere with tissue evaluation. CT has the advantage of higher spatial resolution of the stylomastoid foramen and mastoid bone when perineural spread or bony invasion is suspected. CT imaging of the parotid gland is often done in conjunction with neck imaging to evaluate for the distal metastatic disease. Additionally, given the variability in parotid size, a larger field of view needs to be employed to account for some glands extending to the mandibular angle. Protocols would include 0.625 mm acquisitions reformatted at 2.5 mm, pitch

0.984:1, 0.5 s rotation time, 120 kVp, smart tube current modulation. Coronal and sagittal reformats in soft tissue algorithm are also provided after nonionic contrast administration. There is rarely any need for both a contrast/non-contrast study.

5.3.3 MRI of the Parotid Space

The normal adult parotid gland has a high T1-weighted signal and low to intermediate T2-weighted signal on conventional MRI due to the inherent fat content. As in CT, the fat content of the parotid gland makes it ideal for MRI. Additionally, the ability to follow abnormal enhancement along the nerves and assessment of the regional vasculature makes parotid space imaging ideal with MRI [14]. Imaging protocols should include axial T1 TSE images in three planes, axial and/or coronal T2 TSE sequences with fat suppression to highlight lesion conspicuity, and axial and coronal T1 TSE post contrast with fat suppression. Coverage is often similar to the neck but can be tailored for just the parotid gland. Additional sequences can include diffusion-weighted imaging and/or post-contrast volumetric acquisition of the parotid glands for isotropic resolution. Performing these tests on a 3T MRI can reduce scanning time while increasing the signal-to-noise ratio. This limits the duration of sedation in pediatric patients and claustrophobic patients [15].

5.3.4 PET/CT of the Parotid Space

PET imaging has had little role in initial workup of parotid tumors. The cost of the test, the time involved, and its low specificity preclude routine use of this test. Furthermore, normal activity in the parotid gland may mask an underlying lesion [16]. Both malignant and benign parotid space tumors have increased glucose metabolism and even some inflammatory processes can demonstrate increased uptake. Specificity can be increased by using multiple tracers. However, these tracers are not readily available. There is a role for PET surveillance for recurrent disease or for assessing distant metastases [22].

5.3.5 Select Oncological Imaging Examples

Pleomorphic adenoma—see Fig. 5.4

- 90% occur lateral to the plane of the facial nerve, 0.5% are multi-centric
- hypoechoic on US, variable enhancement on CT/MRI depending on necrosis
- well marginated, T2 hypointense peripheral rim, higher ADC values than other parotid tumors [17]

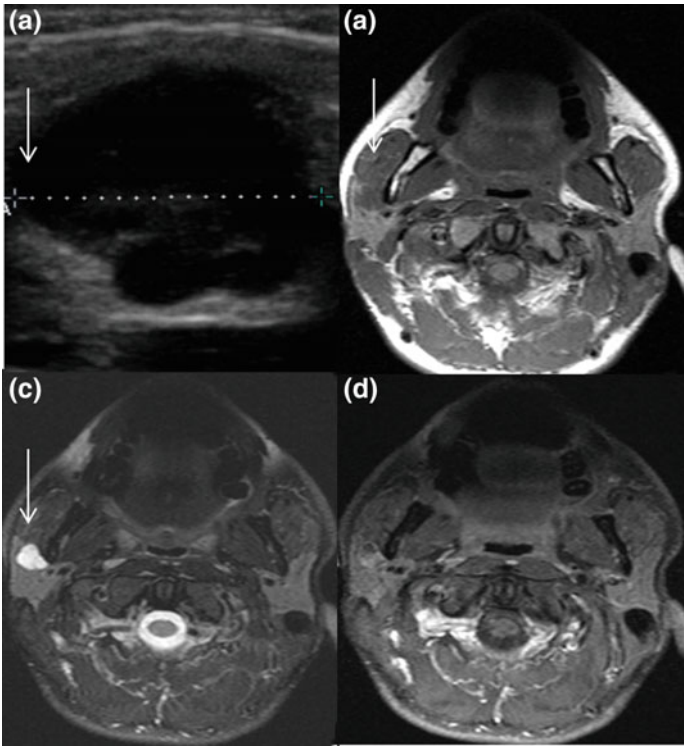

Fig. 5.4 Pleomorphic adenoma. **a** Ultrasound. On US, the lesion is a lobulated hyperechoic solid mass. **b** Axial T1 fat pre-contrast image demonstrating a hypointense mass in the anterior right parotid gland (arrow). **c** Axial T2 image demonstrates well-circumscribed T2 hyperintense lesion in the anterior superficial aspect of the right parotid gland (*arrow*). **d** Axial T1 post-contrast image demonstrates heterogeneous enhancement

Warthin's tumors—see Fig. 5.5

- increased uptake on PET scan
- can be cystic on US
- lower apparent diffusion coefficient (ADC) values than pleomorphic adenomas, variable enhancement

Mucoepidermoid Carcinoma (MEC)—see Fig. 5.6

- well circumscribed when lower grade but more infiltrative if higher grade
- lower T2 values than pleomorphic adenomas with variable enhancement
- higher grades have associated lymphadenopathy
- prone to perineural spread

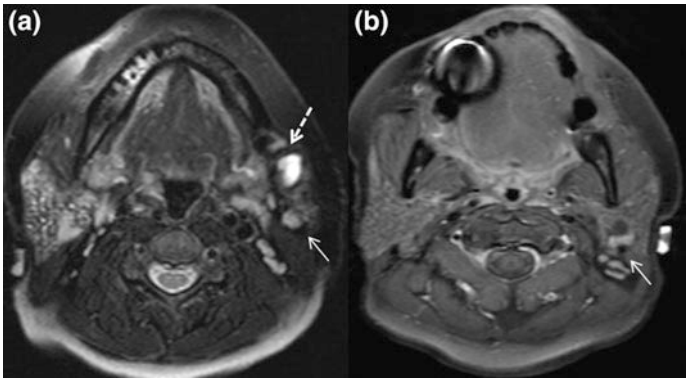

Fig. 5.5 Warthin's tumor. **a** Axial T2 fat suppressed. **b** Axial T1 fat-suppressed post contrast. There is a mixed cystic and solid lesion seen in the posterior left parotid gland (*arrow*) with a second cystic lesion seen in the anterior aspect of the gland (*dashed arrow*). Minimal posterior enhancement is noted

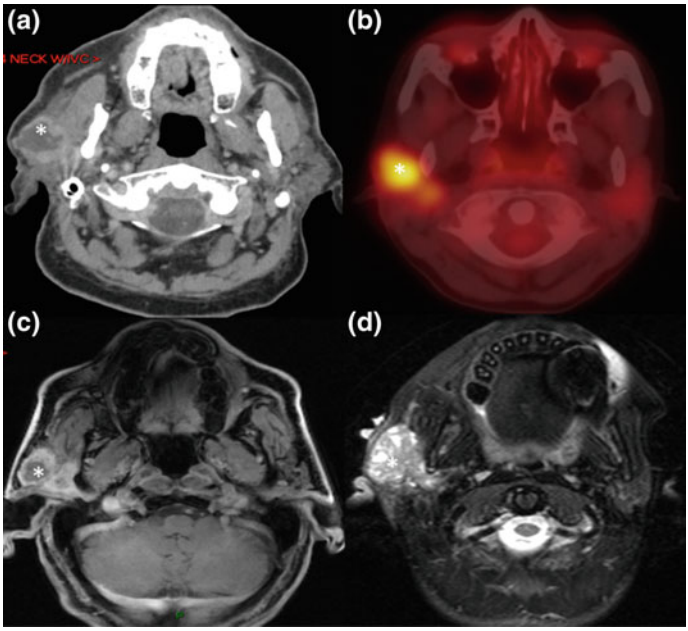

Fig. 5.6 Mucoepidermoid carcinoma. **a** Contrast-enhanced CT. **b** PET-CT. **c** T1 fat suppressed. **d** T2 fat suppressed. There is a heterogeneously enhancing, partially cystic, multilobulated tumor in the superficial right parotid gland (*asterisk*). There is increased FDG avidity in Fig. 5.6c. Figure 5.6d demonstrates classic heterogeneous appearance with low T2 signal as compared to typical pleomorphic adenomas

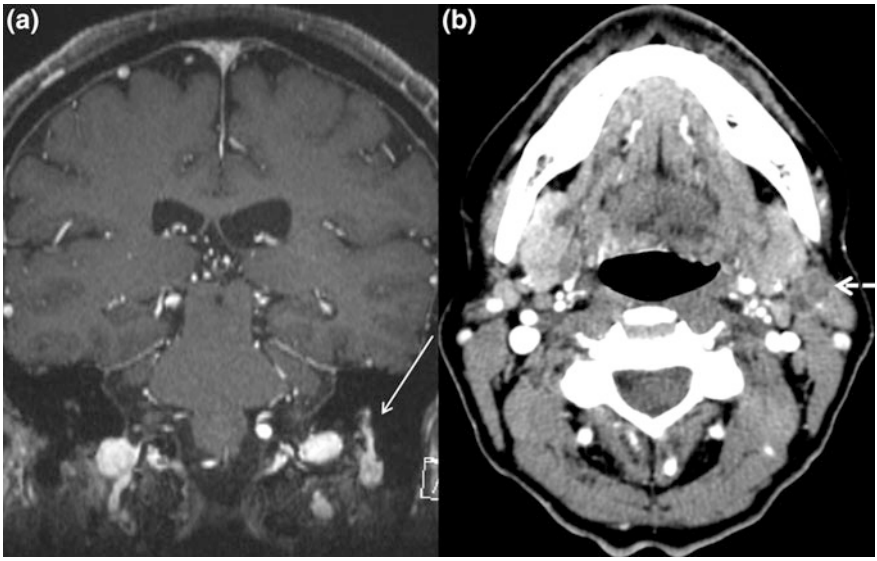

Fig. 5.7 Adenoid cystic carcinoma. **a** Coronal fat-suppressed T1 post contrast. **b** Contrast-enhanced CT. Notice the heterogeneously enhancing lesion in the left parotid gland (dashed arrow in (b)). Perineural spread of tumor along the descending segment of the left facial nerve is seen (solid arrow) on image (a)

Adenoid Cystic Carcinoma (ACC)—see Fig. 5.7

- infiltrative, avidly enhancing, intermediate T2 signal
- high propensity for perineural spread
- lower ADC values than pleomorphic adenomas

Lymphoma—see Fig. 5.8

- systemic parotid lymphoma manifests with multiple nodules in the parotid gland and neck
- primary parotid lymphoma is more infiltrative with possible cystic components [18]

Metastatic Disease—see Fig. 5.9

- 4% of all parotid tumors, often from scalp/skin/external ear tumors
- evaluate for the perineural spread and skull base involvement [19]
- PET/CT scan for systemic surveillance

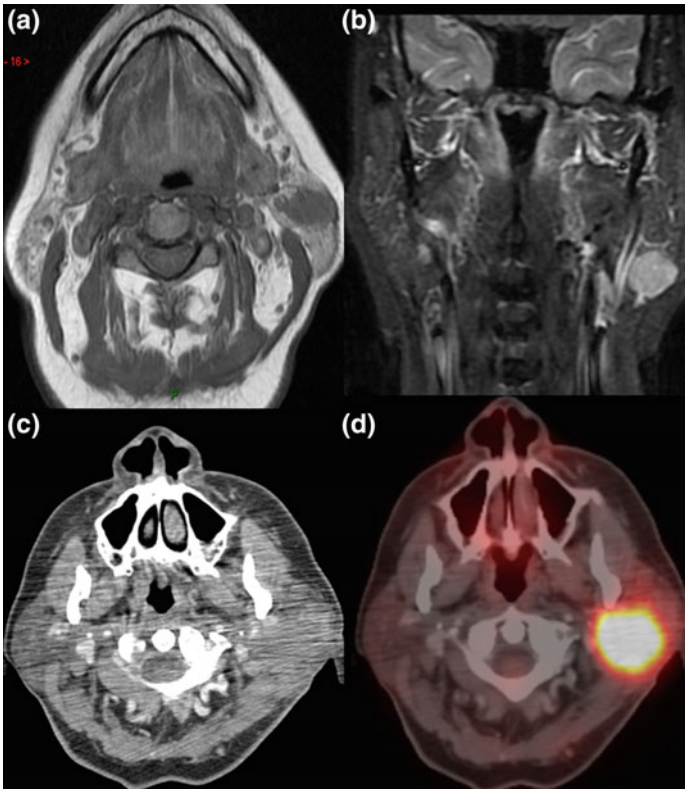

Fig. 5.8 Lymphoma. **a** Axial T1. **b** Coronal T2 fat suppression. **c** Contrast-enhanced CT. **d** PET-CT. Notice how the tumor is readily distinguishable in a and b from the normal left parotid gland. Figure 5.8c, d are images 1 month later demonstrating interval growth of the tumor. The lesion is more infiltrative and less discernible on CT than MRI

5.4 Thyroid and Parthyroid Glands

The thyroid and parathyroid glands are some of the constituents of the visceral space. First line diagnostic imaging is ultrasonography and US-guided fine needle aspiration cytology [20]. Sonography is able to detect small punctate calcifications, a hallmark of papillary carcinoma [21]. CT and MRI have lower sensitivity to thyroid cancer and their role is primarily to define extra-thyroidal tumor extension [22].

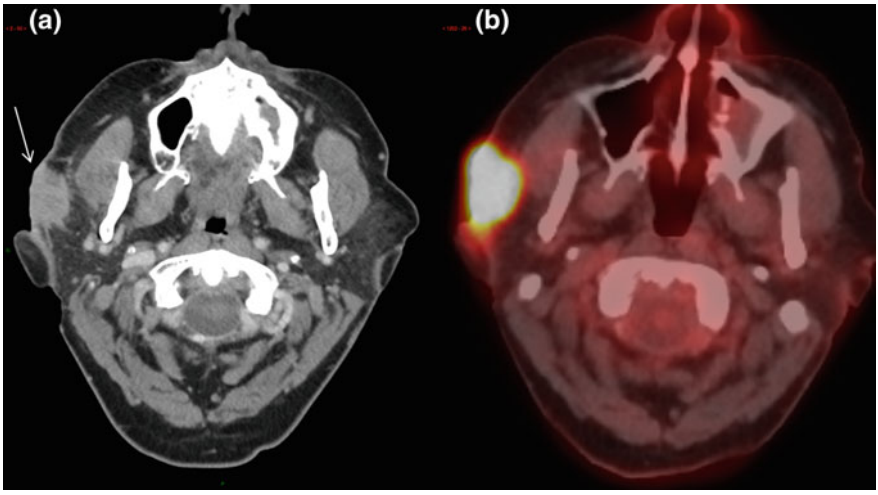

Fig. 5.9 Metastatic SCC to the parotid. **a** Contrast-enhanced CT. **b** PET-CT. Infiltrative dermal cancer invading into the superficial right parotid gland (*arrow*). Avid FDG avidity

5.4.1 CT of the Visceral Space

CT of the visceral space (extending from the hyoid bone to the superior mediastinum) for thyroid evaluation follows the same protocol as a CT of the soft tissues of the neck with coverage from the orbital floor through the thoracic inlet including the aortic arch. This coverage area is more than sufficient for evaluation of distal nodal metastases and covers inferior extents of enlarged thyroid glands that may have a mediastinal extension. Images are acquired at 0.625 mm reconstructed at 2.5 mm, the pitch of 0.984:1, rotation 0.5 s, kVp 120, and smart tube current modulation. Images are reconstructed in coronal and sagittal planes using a soft tissue algorithm. Contrast is helpful in evaluating the postoperative state, tumor recurrence, bulky disease, or in undifferentiated thyroid carcinoma with the understanding that iodine receptors remain blocked for 6–8 weeks when contemplating I-131 therapy [23].

5.4.2 MRI of the Visceral Space

MRI of the visceral space is often in conjunction with ultrasonography. Although the primary tumor is adequately evaluated by US, larger lesions are better assessed with MRI/CT and extension beyond the thyroid capsule is much better evaluated with MRI [24]. Invasion into the thyroid cartilage, involvement of the jugular vein, or invasion into the paraglottic tissues or strap muscles is also better evaluated with MRI than with CT. Additionally, MRI contrast (gadolinium) does not interfere with radioactive iodine uptake. Imaging protocols for MRI of the visceral space are similar to MRI

neck and include multiplanar T1 TSE, axial T2 TSE with fat suppression, axial and coronal T1 TSE post-contrast imaging with fat suppression. Additionally, thin cut 3 mm T2 and T1 post-contrast imaging through the thyroid bed can aid in lesion conspicuity in the postoperative setting.

5.4.3 Nuclear Imaging of the Visceral Space

For differentiated thyroid cancer, whole-body I-131 imaging is still the gold standard in the setting of rising thyroglobulin levels; however, it has a sensitivity of only 50% in picking up metastatic disease [25]. In these cases, PET/CT imaging plays a valuable role in identifying the residual disease. All major subtypes of thyroid cancer are FDG avid to some degree. As thyroglobulin production diminishes, the higher grade/undifferentiated cancers have a greater FDG avidity. Therefore, in differentiated thyroid cancers, the role of iodinated radionuclides supersedes the usefulness of PET scans [26]. PET scans play a vital role in the workup of patients with rising thyroglobulin levels and I-131 negative imaging who are s/p thyroidectomy, as well as in recurrent thyroid carcinoma [27].

5.4.4 Parathyroid Imaging

Historically, under the appropriate clinical scenario, which includes hypercalcemia, bone pain, renal calculi, and lethargy, parathyroid adenomas do not require preoperative imaging. Instead, bilateral neck explorations were often performed. Currently, minimally invasive surgery and unilateral neck dissections often require preoperative imaging to localize the adenoma [28]. Ultrasound and sestamibi scintigraphy are used for localization. In the cases of recurrent disease or possible ectopic disease, the role of dual-phase technetium 99 m (^{99m}Tc) with single photon emission computed tomography (SPECT) has proven very helpful. Although its spatial resolution is inferior to US, its ability to pick up ectopic adenomas, especially mediastinal adenomas, is one of the reasons for its utility [29]. MRI is another tool to evaluate for parathyroid adenomas but its lower spatial resolution, slice thickness limitations, and motion/pulsation artifact in the upper mediastinum can limit its usefulness.

Recently, four-dimensional (4D) CT has served as an alternative tool for adenoma workup. It provides for higher resolution anatomic images with the added benefit of a contrast time curve (the fourth dimension in 4D) that can help distinguish adenomas from thyroid lesions and regional lymph nodes [30]. In surgery-naïve patients, studies have shown a sensitivity of 96.5% in identifying the parathyroid adenoma [31]. The sensitivity does decrease in patients with the recurrent disease with one study reporting 88% sensitivity compared to 54% with ^{99m}Tc-sestamibi scintigraphy and ultrasound. The radiation exposure, depending on the protocol was also less with the 4D CT [32]. The authors suggest the possibility of using 4D CT as a first line diagnostic imaging modality.

There are different protocols that have been adapted for parathyroid imaging. One commonly accepted protocol involves a non-contrast scan, an arterial phase scan, and a delayed venous phase scan. Via a 64-detector row CT (VCT Lightspeed; GE Healthcare, Milwaukee, WI), the angle of the mandible is scanned through the carina in a non-contrast phase, an arterial phase acquired at 25 s after injection of Omnipaque 300 (GE Healthcare, Milwaukee, WI) at 4 cc/sec, and a delayed phase acquired at 80 s after injection. The scanning parameter for all three phases are 0.625 mm thin acquisition, rotation time of 0.4 s, pitch factor of 0.516:1, field of view of 20 cm, kVp 120, noise index of 8, and automatic tube current modulation (100–400 mA for non-contrast and delayed phase and 100–600 mA for the arterial phase.

5.4.5 Selected Oncological Imaging Examples

Thyroid cancer—see Fig. 5.10

- Nodal disease can be Ca++ or hyper-attenuating
- Give contrast if suspect bulky disease
- MRI helpful to evaluate for cartilage invasion

Parathyroid adenoma—see Fig. 5.11

- Tc-99 m sestamibi is the first line of imaging test; consider SPECT-CT to help localize activity
- T2 hyperintense with avid enhancement on MRI
- Early enhancement with washout on 4D CT

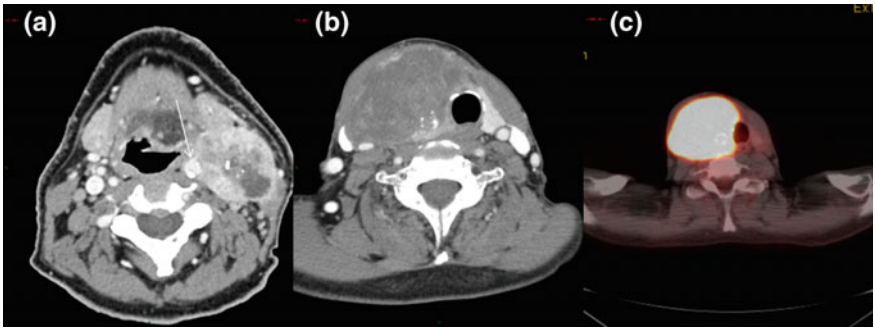

Fig. 5.10 Thyroid cancer. **a** Contrast-enhanced CT. **b** Contrast-enhanced CT. **c** PET-CT. In (**a**) there is a conglomerate nodal mass involving multiple left cervical nodes in a patient with known metastatic papillary thyroid cancer. Notice partial encasement of the left carotid artery (*arrow*) less than 180°. In (**b**) and (**c**) there is large, heterogeneously enhancing mass of the right thyroid lobe with tracheal deviation. This anaplastic thyroid cancer lesion is FDG avid as shown in 5.18c

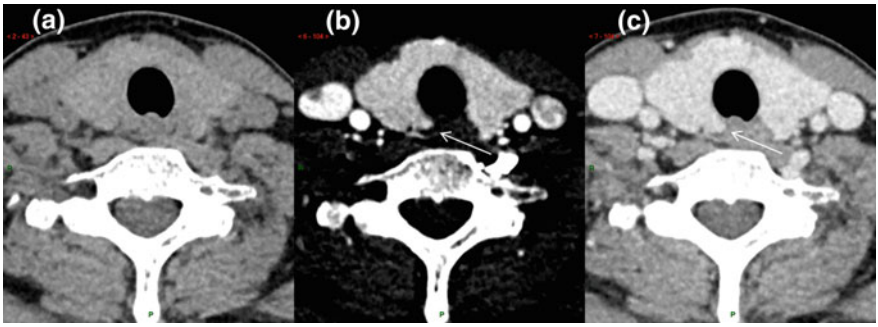

Fig. 5.11 Parathyroid adenoma. **a** non-contrast CT. **b** Arterial phase CT. **c** Delayed phase CT. Notice the parathyroid adenoma (*arrow*) demonstrates early enhancement compared to the thyroid tissue background with early washout on the delayed image

5.5 Suprahyoid Neck (SHN) and Infrahyoid Neck (IHN)

The suprahyoid and infrahyoid spaces cover a bulk of head and neck radiology. The key to understanding pathology and differentials requires understanding the fascial planes and the various sub-compartments created. This section is devoted to providing an overview of the imaging protocols and a few insightful imaging pearls based on case examples. The reader is directed to a number of exhaustive articles and textbooks which cover this area in depth.

5.5.1 CT of the SHN and IHN

The goal of CT imaging of the suspected head and neck malignancy is to define the margins of the tumor, the local spread of the tumor, and regional nodal metastases. As a result, coverage area needs to be larger than the extent of the tumor itself to account for distal metastases. One CT protocol for neck oncologic imaging is as follows: 0.625 mm helical axial thin-section acquisitions on a 64-row detector (Lightspeed VCT, GE Healthcare, Milwaukee, WI), rotation time of 0.5 s, pitch factor 0.984:1, 20 cm FOV, 120 kVp, smart tube current modulation. Axial 2.5 mm reconstructions, sagittal and coronal reconstructions (bone and soft tissue algorithm), in addition to the source axial images are all sent to PACS (source imaging allows for future 3D volume rendered reformation to be generated). These studies are performed after nonionic intravenous contrast with a delay of 80 s. Non-contrast studies are performed if there are known renal insufficiency issues or known allergies to iodinated contrast that cannot be remedied by premedication. Recurrent/residual disease in the resection bed and necrotic lymph nodes are all highlighted by contrast administration. If laryngeal lesions are suspected, the protocol can be further modified with dedicated imaging through the larynx in both

breath holding and straw-blowing technique allowing for improved evaluation of the vocal cord movements and piriform sinus [33]. Laryngeal CTs are performed with a smaller field of view from the vallecula to the subglottis.

5.5.2 MRI of the SHN and IHN

As with CT, the purpose of MRI in the evaluation of SHN and IHN tumors are to evaluate disease location and extent. Like CT, MRIs allow for evaluation of distal nodal burden. The increased soft tissue contrast resolution is helpful for evaluation of perineural spread for skull base tumors and salivary gland tumors, evaluation of cartilage evaluation in thyroid/laryngeal cancer, and differentiation of tumors from scar tissue. Typical MRI protocols will include coverage from the orbits through the aortic arch. This protocol includes sagittal, axial, and coronal T1 TSE pre-contrast images, axial T2 TSE fat-suppressed images, and axial/coronal T1 TSE fat-suppressed post-contrast images. Volumetric T1 TSE post-contrast fat-suppressed images can be obtained for near isotropic resolution. Lesions at the skull base can be further evaluated with dedicated high-resolution T2-weighted images obtained at 1 mm slice thickness for evaluation of skull base foramina and cranial nerves. Lesions at the level of the larynx can also be evaluated with thin-section T2 TSE images at 3 mm intervals with a FOV from the vallecula to the subglottis. Additionally, DWI images have shown promise in tumor evaluation [34].

5.5.3 PET-CT of the SHN and IHN

PET imaging has a role in initial workup of patients, often as an adjunct to conventional anatomic imaging. When tumor histology has a propensity for distal nodal disease (skin cancer, melanoma, metastatic disease) or the primary tumor site is unknown, PET scans can prove invaluable [43]. Its utility is greatest in the postoperative setting when normal anatomy is often distorted by reconstruction or scar tissue masking the area of residual disease. Sensitivity rates for detecting recurrent tumors have been reported to be 96% in one series of 147 patients with recurrent head and neck cancers [35]. The ability to find occult disease aids in directing biopsies [36]. PET-CT can also be useful for quantitative assessment of tumor response by measuring standardized uptake values (SUV) of the primary tumor site.

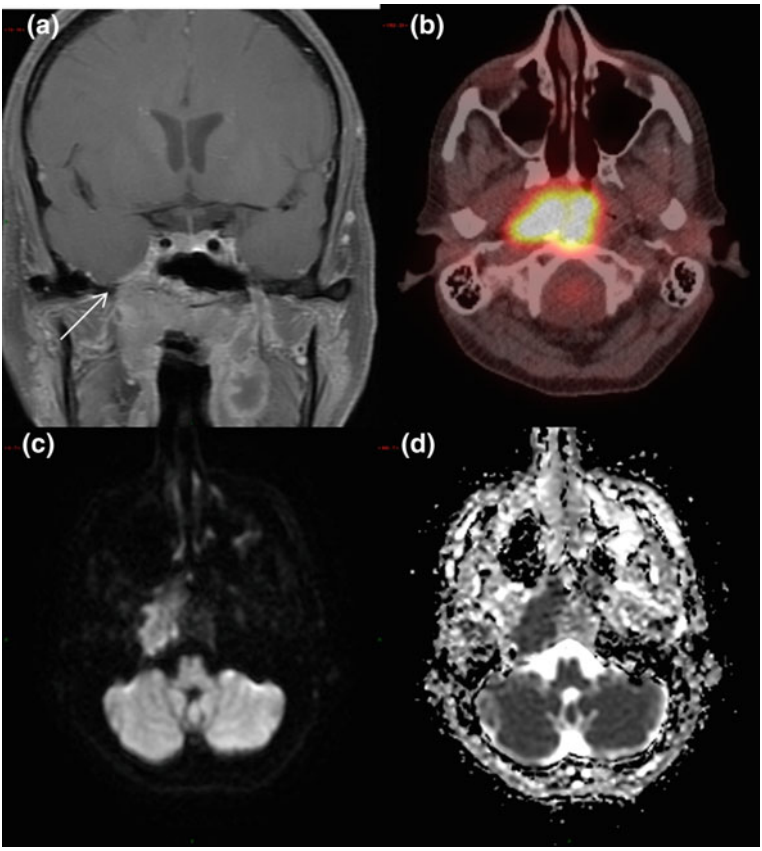

Fig. 5.12 Nasopharyngeal cancer **a** Coronal T1 post contrast. **b** PET-CT. **c** Diffusion-weighted imaging (DWI). **d** Apparent diffusion coefficient (ADC). The lesion is FDG avid with extension across the midline (b). Notice the perineural spread through foramen ovale (*arrow in a*). Portions of the tumor demonstrate diffusion restriction at the skull base (c and d)

5.5.4 Select Oncological Imaging Examples

Nasopharyngeal Cancer—Fig. 5.12

- mildly enhancing tumor with bulky level II, V, and retropharyngeal nodes, high FDG avidity [37]
- can invade clivus with intracranial extension
- high propensity for the perineural spread, MRI is best for evaluation

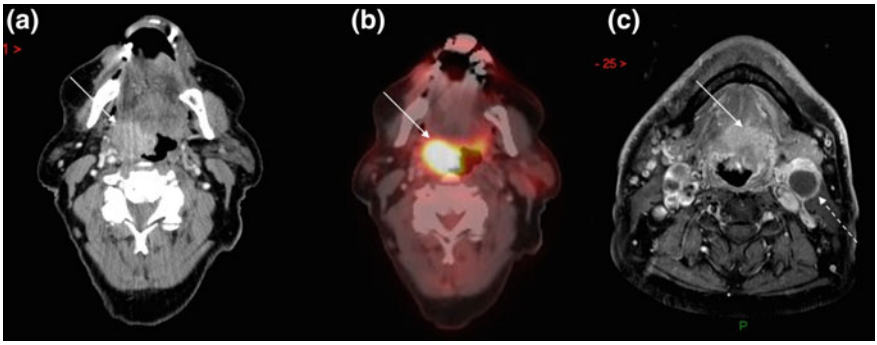

Fig. 5.13 **a** Axial post-contrast CT shows tumor of right oropharyngeal wall (*arrow*). **b** PET-CT shows FDG avidity in the tumor (*arrow*). **c** Axial T1 post contrast shows base of tongue tumor (*arrow*) and necrotic left level IIa node (*dashed arrow*)

Oropharyngeal Cancer—Fig. 5.13

- levels II-III are the most common site of nodal disease
- PET-CT helpful for identifying small occult site
- MRI useful in setting of dental amalgam artifact

Oral Cavity—Fig. 5.14

- Imaging defines depth of invasion for tongue lesions
- Superficial lesions difficult to identify
- MRI useful in setting of dental amalgam artifact
- Evaluate mandibular involvement in floor of mouth tumors

Laryngeal Cancer—Fig. 5.15

- CT preferred due to decreased motion artifact
- MRI has role in cartilage evaluation (inner and outer lamella)
- Tumor upstaged with inner (T3) or outer (T4a) thyroid cartilage involvement

5.6 Posttreatment Imaging

Imaging of the posttreatment and postoperative patient requires knowledge of the extent of surgery, the types of reconstructions performed, and previous treatments used. As normal anatomy is distorted by surgery, and radiation can result in swelling, scarring, and marrow changes, history is key to adequately evaluating these patients. A baseline study is not recommended before 3 months after treatment, as the risk for recurrence in this time is rare and posttreatment effects may confound interpretation [38]. Surveillance imaging interval varies in the literature

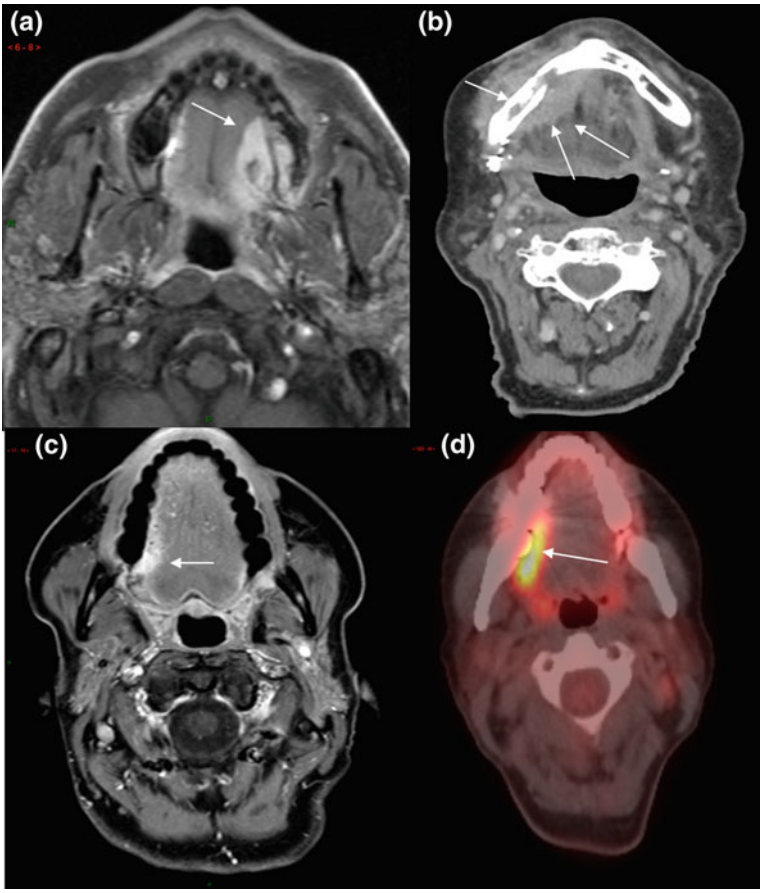

Fig. 5.14 Oral cavity cancers. **a** Axial T1 post contrast shows left hard palate cancer **b** Contrast CT shows right floor of mouth cancer with involvement of adjacent mandible and buccal mucosa (*arrow*) **c** axial T1 post contrast and **d** PET-CT show right lateral tongue mass. This lesion was masked by dental artifact on the conventional CT neck but easily seen on MRI and PET-CT

and on the histology of cancer but should include assessment of any secondary malignancies that may occur because of the treatment [43]. CT and/or PET-CT are usually the imaging modality for surveillance due to its rapid acquisition, higher spatial resolution, and whole-body assessment. MRI is also helpful especially with sinonasal and skull base tumors to evaluate for an intracranial extension, tumors of the larynx to evaluate cartilage invasion, and salivary gland and nasopharyngeal tumors to evaluate for perineural spread [39].

The goal of postoperative surveillance imaging is to identify tumor recurrence early to initiate salvage therapy. Knowledge of the type of surgery aids in identifying tumor recurrence from reconstruction changes. Sharp margins adjacent to normal tissues are typical of myocutaneous flaps and a sign of benignity [40]. Most

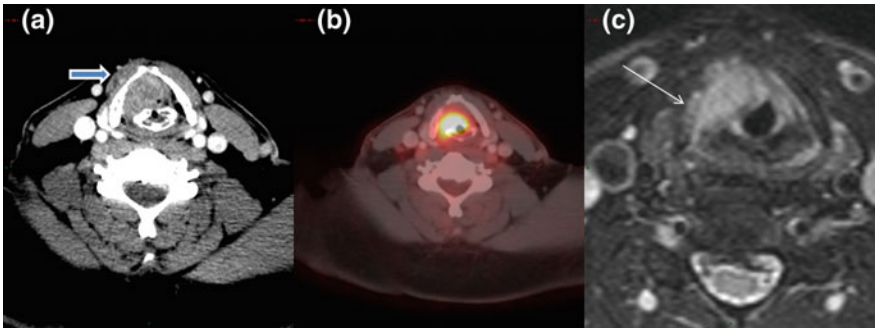

Fig. 5.15 Laryngeal cancer. **a** Contrast CT. **b** PET-CT. **c** Axial T2 weighted. Right laryngeal tumor with extension to the anterior commissure and to the contralateral side. Increased uptake on PET-CT. MRI shows subtle edema in the cartilage (thin *arrow*) and CT shows minimal asymmetric fullness in right strap muscles (*thick arrow*) further contributing to the upstaging of the tumor

local tumor recurrence occurs at the inferior or superior margins of the reconstruction flap and these areas warrant detailed evaluation [41].

After neck dissection, the normal fat planes are obliterated and nodal disease recurrence is more challenging to identify [42]. Many of the normal structures are absent or obscured. A fibrous sheath often forms along the carotid and jugular vessels depending on the extent of the neck dissection which shows diminished enhancement and low T1/T2 signal [43].

Post-radiation therapy changes can be divided into early and late reactions. Early reactions manifest immediately or up to 90 days from the start of radiotherapy. These include mucositis and skin desquamation. These are reversible and usually resolve after radiotherapy cessation. Late complications are usually nonreversible and occur more than 90 days after therapy. The late complications include dysphagia, dental caries, osteoradionecrosis, radiation-induced vascular complications (carotid blow-out, thrombosis), and rarely radiation-induced neoplasms [43]. Some post-radiation changes include thickening of the skin, thickening of the platysma, reticulation of the subcutaneous fat, increased attenuation or intensity of the salivary glands with eventual atrophy. Retropharyngeal or parapharyngeal or paraglottic edema, and increased enhancement of the mucosal space can also occur due to post-radiation changes [38].

Tumor recurrence often will occur within the operative bed and at the margins of the surgical site often within the first 2 years of treatment [44]. On CT, the recurrence will be expansile, slowly growing and hyper-attenuating, and will demonstrate enhancement. On MRI, the recurrence will be infiltrative, intermediate on T1, intermediate to high on T2, and demonstrates enhancement [43, 45] (Fig. 5.16).

Diffusion-weighted imaging (DWI) has recently played a vital role in differentiating vascular scars from recurrent tumors. High DWI signal with low apparent diffusion coefficient (ADC) is suspicious for recurrence with high sensitivity and specificity due to the inherent increased cellularity of tumors as opposed to scar tissue [46, 47] (Figure 5.17). In addition to enlargement, recurrent nodal metastases

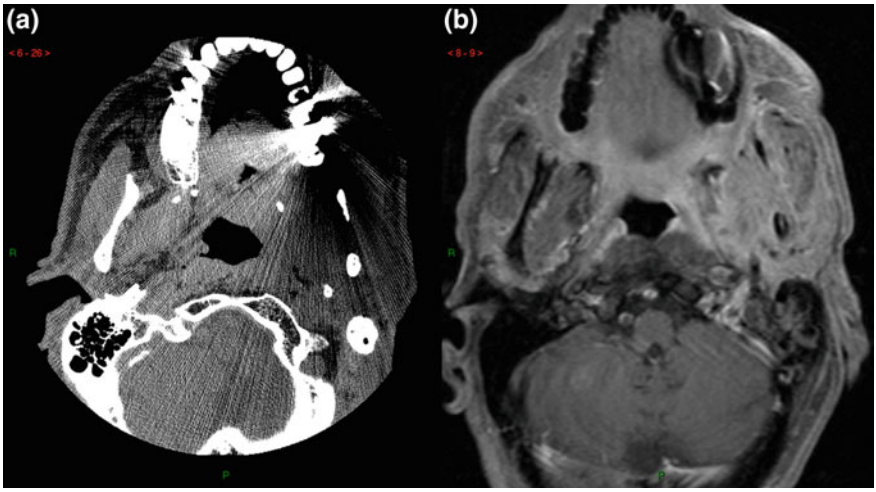

Fig. 5.16 **a** Non-contrast CT. **b** Axial T1 post contrast. Patient with a history of recurrent tumor outside of radiation field. On CT, the lesion is obscured by dental artifact. On MRI, the infiltrative nature of the tumor recurrence is clearly seen within the masticator space

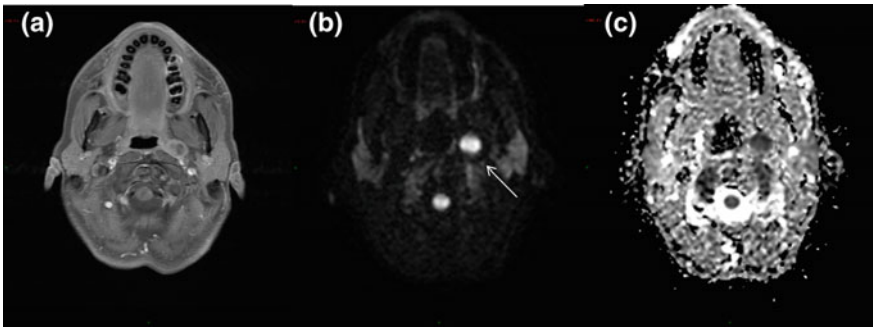

Fig. 5.17 Metastatic lymph node. **a** Axial T1 post contrast. **b** Diffusion-Weighted Imaging. **c** Low Apparent Diffusion Coefficient (ADC). Necrotic appearing left retropharyngeal lymph node demonstrating restricted diffusion (*arrow*)

will also demonstrate slight increased enhancement on CT/MRI imaging and increased diffusion restriction on MRI imaging [51].

Finally, perineural spread is best evaluated on MRI imaging and presents with nerve enlargement, foraminal enlargement, and obliteration of regional fat planes. Denervation injury is a secondary sign of perineural spread of tumor. These findings can be seen with CT but MRI with inherent greater soft tissue contrast increases lesion conspicuity [48].

Treatment-related complications range from intraoperative complications to post-radiation-induced complications. Fluid collections in the postoperative period may simply represent seromas or abscesses. However, persistent collections may indicate chylous fistulas in 1–2% of patients [46]. Persistent fistulas are more common in anemic patients, prior neck dissection, and previous radiation [49]. Flap necrosis occurs often in the first few days after surgery and is related to vascular thrombosis, typically venous in origin [50, 54]. Osteoradionecrosis occurs 1–3 years post radiation therapy and ranges from 0.4 to 22% [51]. On CT, areas of involved bone demonstrate osteolytic changes with cortical destruction and sequestration formation. On MRI, osteoradionecrosis shows increased T2 signal with cortical destruction [52]. A pathological fracture may also be seen with disease progression. Finally, radiation-induced neoplasia is a rare complication with an average latency period of 13.3 years. One study involving treated nasopharyngeal cancer patients showed an incidence of 0.037% of post-radiation osteosarcoma [53].

Imaging Pearls

Postoperative Neck—myocutaneous flaps show sharp margins, benignity, fatty atrophy of the muscles from denervation injury

Post-radiation Neck—induration of fat planes with fascial/mucosal thickening and edema, atrophy of salivary gland in late stages

Tumor Recurrence—lower attenuating mass compared to muscle is unlikely to be recurrence, increased diffusion restriction differentiates from scar tissue, increased enhancement and diffusion restriction in nodes are suspicious imaging findings of recurrence

Complications—osteoradionecrosis and radiation-induced vasculopathy typically occur in the radiation field and can occur removed from the actual tumor site. Radiation necrosis in the brain can be explored with MR perfusion/spectroscopy

5.7 Advanced Imaging

PET/MR hybrid systems allow acquisitions of anatomic, functional, and metabolic activity in one sitting. These systems are fairly new and standardization of techniques and uptake values are still readily being discussed across the literature [54]. The advantages of whole-body PET imaging for evaluation of distant metastases and evaluation of the postoperative bed is benefited by the superior soft tissue contrast of MRI, especially in the oral cavity/floor of mouth, an area often obscured by dental artifact. Third-party software is also readily available for fusion on non-hybrid PET/MRI systems to fuse acquisitions from two different settings [55] (Fig. 5.18).

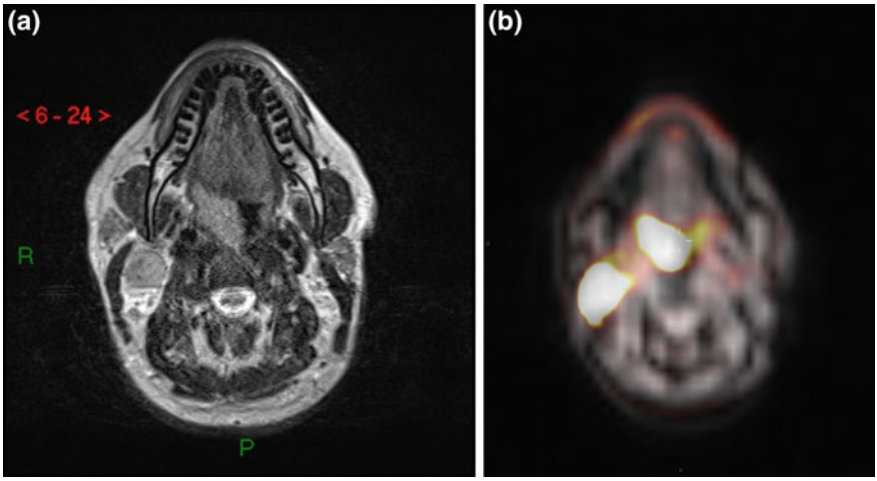

Fig. 5.18 PET/MR. **a** Axial T2 **b** fused PET/MR. Squamous cell cancer of the palatine tonsils (*) and metastatic right-sided nodal disease (arrow). On the fused PET images, there is demonstration of increased uptake in the tonsils and the metastatic lymph nodes

Permeability imaging with dynamic contrast-enhanced MRI (DCE-MRI) is also in its infancy but has proven to be helpful in the workup of head and neck tumors [56]. Lee et al. [57] showed the utility of DCE-MRI to accurately identify undifferentiated tumors from lymphoma and squamous cell cancers in 62 patients. DCE has also been used to predict disease outcome with greater progression-free survival and treatment effectiveness seen in patients with higher pretreatment k^{trans} values [58]. The functional properties measured by permeability imaging have also been used to differentiate diseased versus normal lymph nodes [59]. Metastatic nodal disease from squamous cell cancers was shown to have a longer time to peak contrast enhancement and longer washout of the contrast medium as compared to normal lymph nodes.

5.8 Image-Guided Biopsies

Once a pathologic lesion is identified, tissue sampling can be obtained via palpation, ultrasound guidance, or CT guidance [60]. MRI-guided biopsies are possible but given equipment limitations and acquisition time is not readily available in the clinical setting [61]. US-guided biopsies are commonly performed for tissue sampling in the head and neck. Low cost, lack of radiation, and real-time imaging are some of the advantages afforded by US guidance and has been shown to offer a higher diagnostic yield than with biopsy by palpation [62, 63]. CT guidance with its high spatial resolution is best suited for biopsy of deep head and neck tumors [64]. A contrast CT can be obtained prior to the biopsy to identify vascular structures and

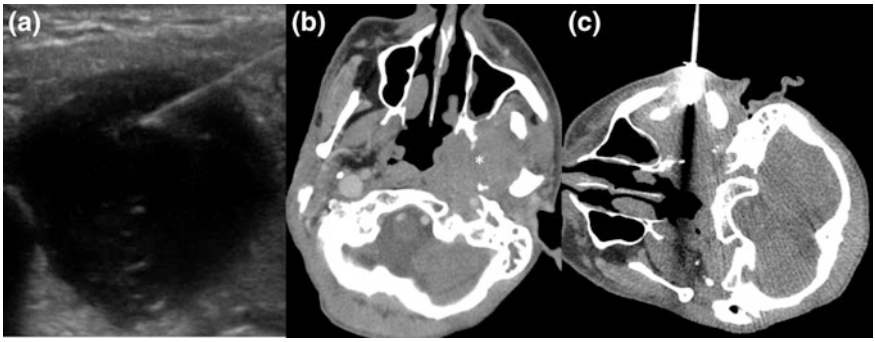

Fig. 5.19 Image-guided biopsies. **a** US-guided fine needle aspiration of a metastatic squamous cell carcinoma lymph node. **b** Pre-procedure contrast CT and **c** CT-guided trans-zygomatic biopsy of the infratemporal fossa in a patient with recurrent squamous cell cancer of the tonsils (*asterisk*)

to plan a trajectory void of critical structures. 20–22 g needles are used for cytological aspiration and 18–20 g cutting needles are used for core biopsy samples. These biopsies are performed routinely with low risk of complications, depending on lesion location [65] (Fig. 5.19).

5.9 Ionizing Radiation Effects

Although diagnostic imaging has significantly improved over the past 40 years with the advent of CT and PET scans, they have come at the expense of radiation exposure to the patients. Radiation poses a defined risk for patients that are exponentially greater for the pediatric population [66]. The newer scanners have wider X-ray beams with multi-detectors to enable larger coverage areas and quicker acquisition with the potential for greater radiation exposure to the patient. Furthermore, the need for continued surveillance further adds to the cumulative effective dose in the patients with both CT and PET imaging. In the setting of malignancies, the benefits often outweigh the risks; however, these risks can often be high for the pediatric population. In a pivotal study by Pearce et al. [67], 178,604 patients were followed over a 24-year period. Pediatric patients who had received scans with dosages of at least 50 mGy had a three times greater risk of developing leukemia and those patients who had received 60 mGy or more also had a three times greater risk of developing brain cancer in their lifetime. This resulted in, on average, one case of leukemia or brain cancer for every 10,000 scans.

Clinicians should be cognizant of the long-term risks of radiation exposure to their patients. Inquiries to the imaging specialists should be made to ensure imaging protocols are periodically reviewed and dose reduction techniques (vendor-supplied or third-party software) are utilized. The imaging protocols should be patient-specific taking into account their size and age. Many of these guidelines have been set forth by

The Alliance for Radiation Safety in Pediatric Imaging as part of the Image Gently campaign (http://www.imagegently.org).

5.10 Conclusion

Imaging fills a critical role in head and neck oncology, aiding in disease diagnosis and surveillance with greater sensitivity than previously possible. In this chapter, we described different modalities used for oncological imaging and imaging pearls for individual disease processes. Coupled with new and emerging technologies, imaging will continue to substantially impact the treatment of various head and neck cancers.

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Challenges in Head and Neck Pathology

6

Anna Laury

Contents

Abstract

The surgical pathologist plays a crucial role in the multidisciplinary team. In nearly all cases, a tissue diagnosis is required to confirm the disease process before treatment begins. Even in settings where the diagnosis appears straightforward, a timely and appropriate report is necessary. The pathologist is also responsible for providing many of the more specific data elements that will guide treatment decisions: examples include evidence of virally driven malignancy, margin status, and the precise depth to which tumor invades. Each of these diagnoses and findings has its own specific set of difficulties and limitations, which require nuanced interpretation by a well-informed pathologist.

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_6

Keywords
p16 · Extranodal extension · Depth of invasion · Frozen section
Margin evaluation

6.1 Introduction

The key to establishing an efficient and valuable relationship with the pathologist is an open line of communication. Communication from the pathologist to the surgeon takes place primarily in the form of surgical pathology reports. These reports can be structured in a variety of formats, and there is no one right reporting style. An appropriate format is one that is consistent and provides the necessary information in a clear manner, which is often most easily accomplished synoptically. Just as important is the surgeon's ability to communicate with the pathologist. Briefly stating the relevant history, clinical impression, or differential diagnosis is often vital to receiving a meaningful interpretation. Withholding relevant information to "test" or avoid "biasing" the pathologist is not advised; at best this will lead to inefficient, delayed reports, excess testing, and inevitable frustration on both sides. At worst, withholding information will lead to misinterpretation and misdiagnosis. Happily, these situations are easily avoided with minimal effort.

6.1.1 AJCC 8th Edition Updates: Depth of Invasion in Oral Cavity Carcinoma, Extranodal Extension

As of the 8th Edition of the American Joint Commission on Cancer (AJCC 8E) staging manual [1], pathologic T staging of oral cavity tumors will depend on the depth of invasion (DOI) in addition to the overall greatest tumor dimension. DOI is also now explicitly distinguished from tumor thickness. Tumor thickness refers to the maximal superficial-to-deep dimension of tumor; DOI refers to the maximal depth of invasion as measured from the nearest intact mucosal basement membrane (Fig. 6.1). This concept, while not novel for the general surgical pathologist (it is already in practice for other sites, including squamous cell carcinoma of the uterine cervix) will be an adjustment and not without challenges. The primary challenge will be assessing DOI in irregularly shaped specimens with convoluted surfaces (Fig. 6.1c). This is best addressed by careful prosection, and cutting the along planes most amenable to this measurement. As the AJCC 8E T-classification system is based on 5 mm increments, the stage in the majority of cases will be unchanged [2], and the overall effect will be to upstage deeply ulcerative tumors (Fig. 6.1b, c) and to downstage minimally invasive exophytic tumors.

Similarly, extranodal extension (ENE), rather than being an optional data point, will now be required information for non-virally related carcinomas. Extranodal extension is defined by tumor extending beyond the capsule of the lymph node and into perinodal tissue; tumor simply within the lymph node sinus or pushing to

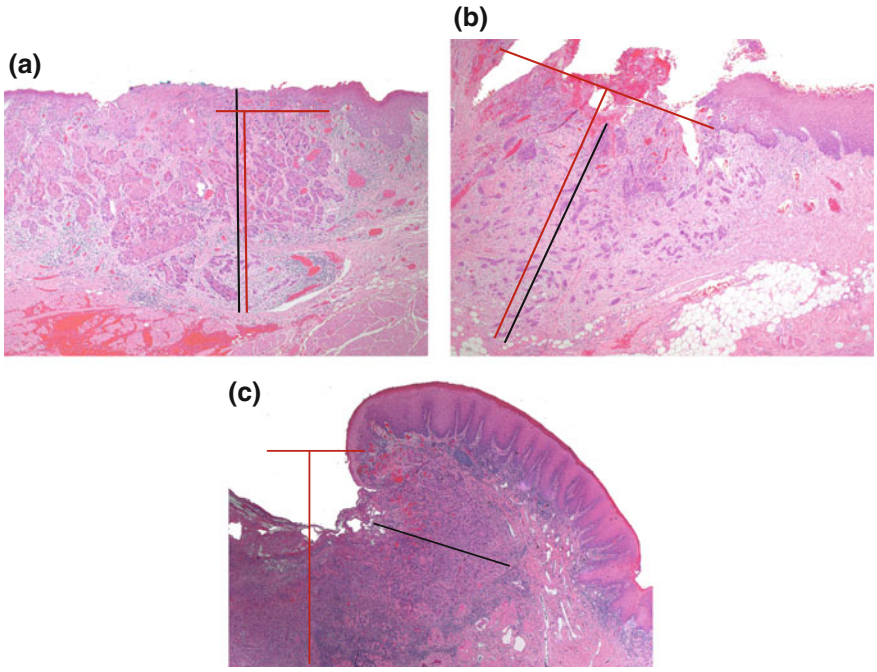


Fig. 6.1 Depth of invasion (DOI). **a** Tumor thickness (black line) is slightly greater than DOI (red line). A line is drawn from the nearest intact basement membrane to create a "horizon" from which the DOI can be measured. **b** For ulcerated tumors, the DOI (red line) will often be greater than tumor thickness (black line). **c** In deeply ulcerative tumors, the DOI (red line) can be significantly greater than tumor thickness (black line). In convoluted tissues, drawing the epithelial "horizon" requires careful consideration; the goal is to best represent where the mucosal surface would have been

expand the capsule does not qualify. All three varieties of ENE will be classified as *ENE: present* and include minor (<2 mm), major (>2 mm), and tumor deposits within adipose tissue (Fig. 6.2).

6.1.2 Margin Assessment

Margin assessment of complex head and neck resection specimens can be challenging. While multiple studies have indicated that en bloc evaluation of perpendicular margins selected by the pathologist is more predictive of outcomes, [3–6] this is not always straightforward. While simple excisions are easily oriented with sutures, complex resections benefit from closer attention. In uncommon specimens, or when the structures are distorted by tumor, some margins and landmarks can be nearly impossible to reconstruct (Fig. 6.3). For these cases, it is ideal to review the specimen with the pathologist or other prosector immediately upon removal. The goals of swift review are orienting the specimen, providing information regarding the most sensitive margins, and identifying surgical defects/tears so that they can be

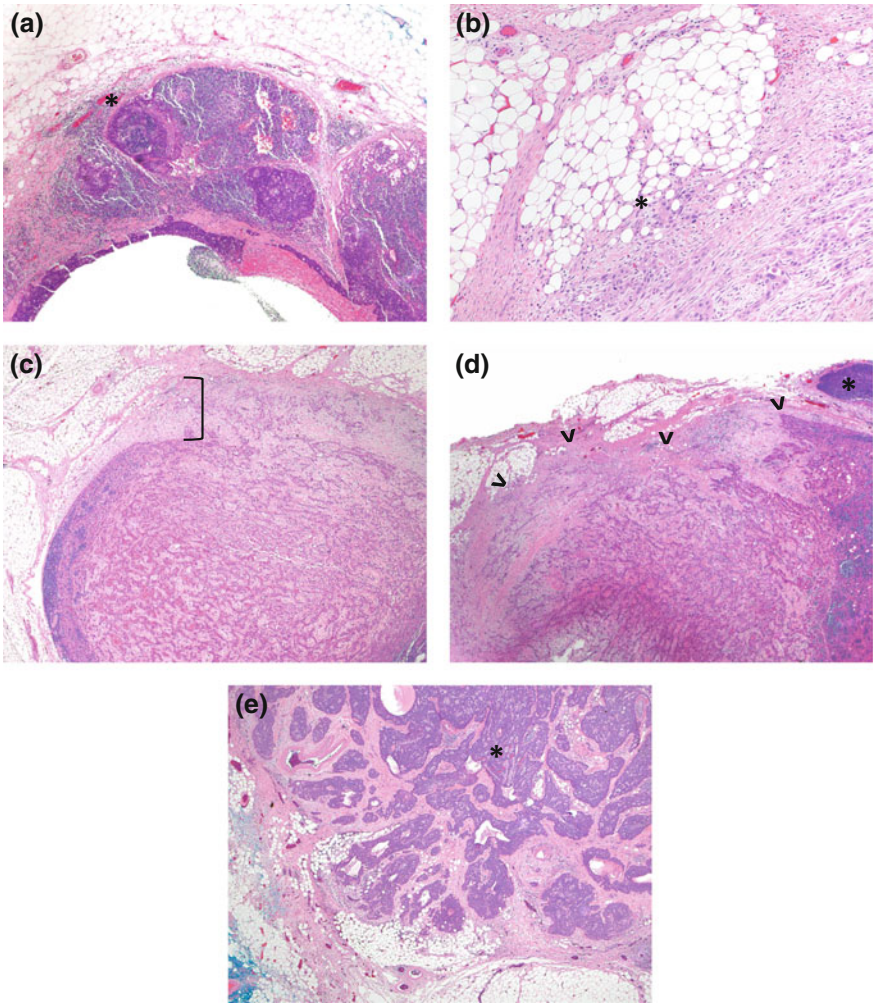


Fig. 6.2 Extranodal extension (ENE). **a** Nodal metastasis without ENE. Tumor is present within the lymph node parenchyma and beneath the capsule (*). **b** ENE. A high magnification image showing tumor cells infiltrating adipose tissue (*). **c** Minimal/minor extranodal extension. Tumor extends into perinodal adipose tissue ( ]) less than 2 mm beyond the lymph node capsule. **d** Major extranodal extension. The tumor front (^) extends broadly into perinodal adipose tissue (>2 mm); no residual capsule is present in this area. Residual node is present in the upper right (*). **e** Tumor nodules (*) in adipose tissue without residual lymph node. These deposits are presumed to represent metastases that have overgrown the node, and are therefore considered extranodal extension

inked a separate color (and not mistaken for margins). Once removed from the patient, tissue quickly undergoes a number of changes and different tissue types shrink and retract to varying degrees, complicating orientation and decreasing

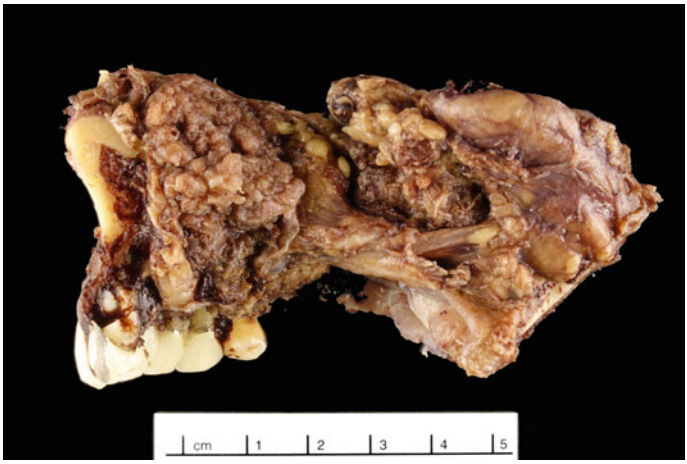


Fig. 6.3 Left mandible, floor of mouth, and tongue. This is an example of a complex specimen that would benefit from the direct review with the surgeon. Some margins (bony, for example) are obvious, but others are less apparent. The distinction between margins and surgical defects is often not appreciated by the prosector

microscopic margin distances. Formalin fixation adds to this, and also renders the tissue less pliable. It should be noted that margins are to be reported as positive only when "cut-through" (ink seen on tumor cells) is present (Fig. 6.4), and the descriptor *close margin* should always be accompanied by a distance.

6.1.3 p16: Interpretation and Usage

Immunohistochemistry (IHC) staining for p16 has been recognized as a useful diagnostic tool and a prognostic indicator for carcinomas of the oropharynx [7, 8]. With the 8th edition of the AJCC Staging Manual, reporting of human papillomavirus (HPV)-related status (usually via p16 positivity) is required for oropharyngeal carcinomas and carcinomas of unknown primary.

p16 is a tumor-suppressor protein, overexpression of which is used as a surrogate marker for HPV infection. It is counterintuitive for overexpression of a tumor suppressor to be an indicator of malignancy, but this is because an HPV oncoprotein (E7) causes degradation of another tumor suppressor (Rb) that also acts as negative feedback for p16; the lack of Rb causes a futile upregulation of p16 in an attempt to halt the cell cycle [8]. With this understanding, it is not surprising that p16 expression is not unique to oropharyngeal SCC, or even to HPV-related tumors. p16 is relatively commonly overexpressed in a variety of malignancies, and therefore, must be interpreted in the appropriate clinical and morphologic context. p16 to date is not considered a useful diagnostic or prognostic marker at head and

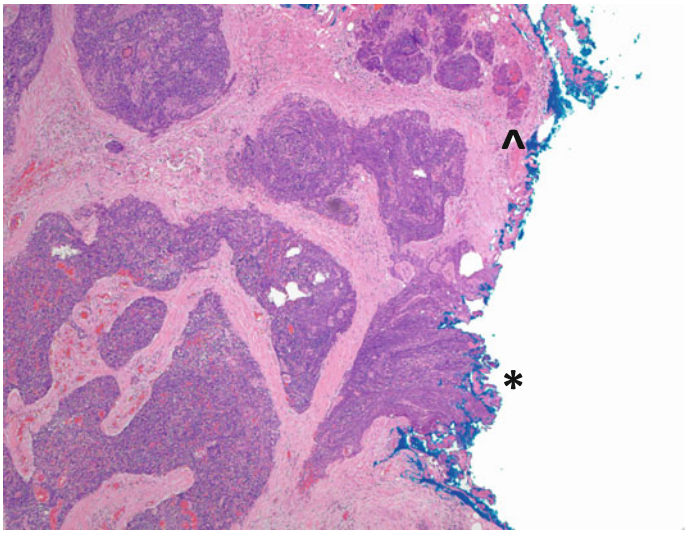
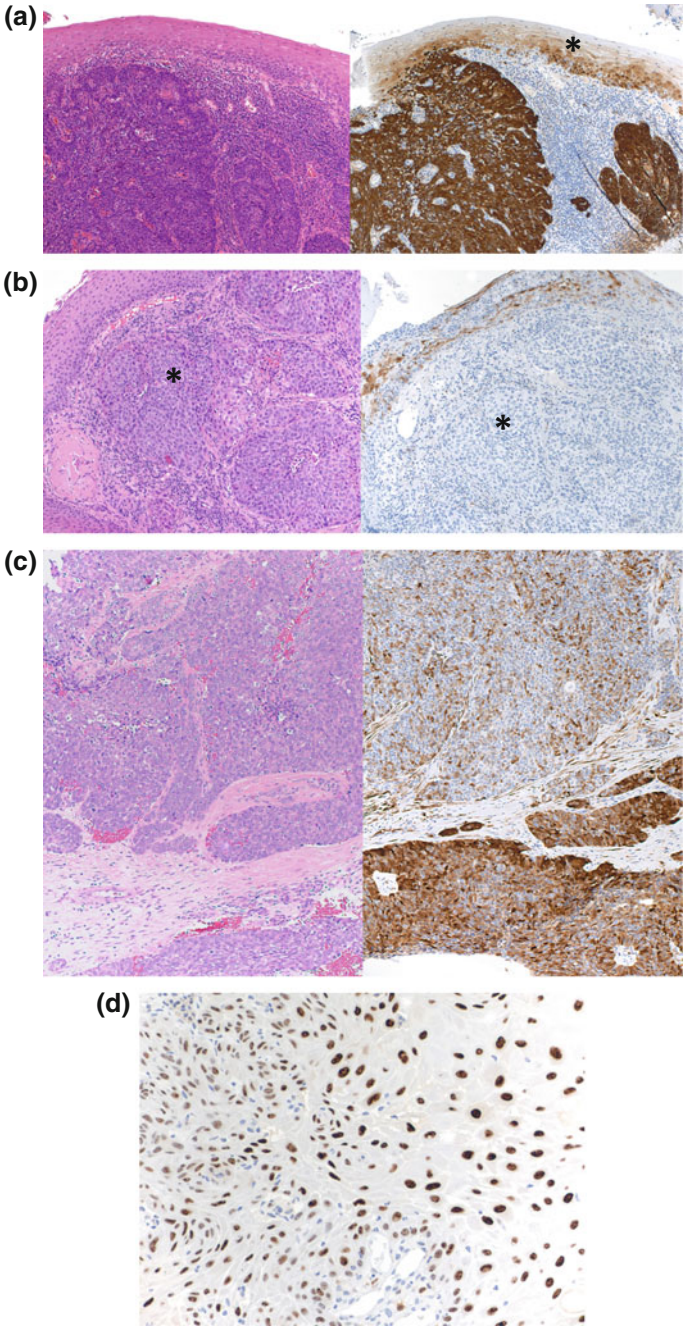


Fig. 6.4 Positive margins. The blue ink on the right has been placed by the prosector to be visible under the microscope. Tumor extends all the way to ink at the center (*)—this defines a positive margin. The focus near the top (^) would require a distance from ink measurement if it were the closest margin

neck sites other than oropharynx [9–12]. As such, p16 staining for oral cavity or laryngeal malignancies is not considered informative.

Interpretation of p16, while generally straightforward, does harbor some potential pitfalls. To be considered positive for the purposes of oropharyngeal squamous cell carcinoma, at least 70–75% of the tumor cells must be at least moderately positive in the nucleus and cytoplasm [1]. In practice, greater than 90% of the tumor cells are usually positive (Fig. 6.5a). Patchy nonspecific staining (Fig. 6.5a, b) should not be considered a positive result. Any unusual staining patterns such as patchy positivity (Fig. 6.5c) or nuclear-only staining (Fig. 6.5d) should be further investigated with direct testing for HPV.

The underlying goal of assessing p16 is to evaluate for the presence of transcriptionally active high-risk HPV (HR-HPV). The advantages of p16 are that it is widely available, validated in many laboratories, and relatively straightforward to interpret: these factors have made its use part of AJCC 8E staging. Though assessment of p16 IHC alone is currently the most accepted practice, this is not universal [13]. Direct testing for the presence of HPV either alone or in combination with p16 is preferred by some groups, though the presence of p16 alone (in the absence of HPV detection) is still prognostic [13]. There are a range of available testing modalities, including identification of HVP DNA, HPV RNA, and viral oncoproteins, with a range of sensitivities, specificities, and technical challenges. The three testing modalities most commonly available to the clinical laboratory are p16, in situ hybridization (ISH) for HR-HPV DNA, and PCR-based HPV detection.


(a)
(b)
(c)
(d)

◀ **Fig. 6.5** Interpretation of p16. **a** p16 positive tumor in the oropharynx. The nests of tumor cells stain strongly and diffusely brown, while the intervening lymphocytes are negative. Note the patchy staining in the overlying tonsillar epithelium (*); this pattern is not considered a positive result in this setting. **b** p16 negative tumor in the oropharynx. The nests of tumor cells (*) are negative, while the overlying tonsillar epithelium again demonstrates a patchy, non-specific staining pattern. **C** Unusual p16 staining pattern. Less than 75% of the tumor cells are staining positively, despite the relatively strong staining at the bottom of the image. This pattern would require additional testing to confirm the presence of HPV. In this case, the tissue was negative for high-risk HVP. **d** Unusual staining pattern. In this case, only nuclear staining is present, though it is strong and present in >75% of the tumor cells. Additional testing to confirm the presence of HPV would be prudent

Overall, staining for p16 is more sensitive, but less specific, while the converse is true for HPV DNA ISH. PCR-based tests, while very sensitive, cannot distinguish a passenger virus from a clinically relevant tumor-driving infection [14]. Interpretation of results from anyone, or a combination of, these studies always requires clinical and histologic context.

6.1.4 Immunohistochemistry Other Than p16

The other virally related group of tumors is Epstein–Barr virus (EBV)-related nasopharyngeal carcinomas. All non-keratinizing nasopharyngeal carcinomas and occult primary SCC should be tested for EBV using in situ hybridization (Epstein–Barr encoding region, or EBER). EBV-LMP is an available immunohistochemistry stain, but is much less sensitive (Fig. 6.6). EBV-related tumors can be of the differentiated and undifferentiated types, and morphology alone cannot predict the presence or absence of EBV. There are reported cases of non-keratinizing nasopharyngeal carcinomas which are HPV-associated; therefore, if EBER is negative it would be prudent to test for HPV, though the significance is not entirely clear [15].

In general, immunohistochemical stains are used as an adjunct to morphologic findings and clinical information. They should not be interpreted in isolation as unexpected reactivity can be found, and any one stain (with rare exception) is expressed in more than one tumor type. For example, thyroid transcription factor-1 (TTF1) is a commonly used stain that is strongly expressed in both thyroid and lung carcinoma. Immunohistochemical stains should always be interpreted as a panel to guide pathologic interpretation and clinical management.

The diagnosis of salivary gland malignancies can usually be made without the help of immunohistochemistry. Specific classification may be improved with the selective use of stains, but it should be again noted that the stains are not exclusive to any one tumor type and must be interpreted as a panel. As an example, androgen receptor (AR) and Her2 are not expressed solely in salivary duct carcinoma: AR expression has been reported in up to 26% of adenocarcinoma (not otherwise specified) and 15% of acinic cell carcinomas [16], and at least one positive case has been reported in nearly all varieties of salivary gland carcinoma (with the exception

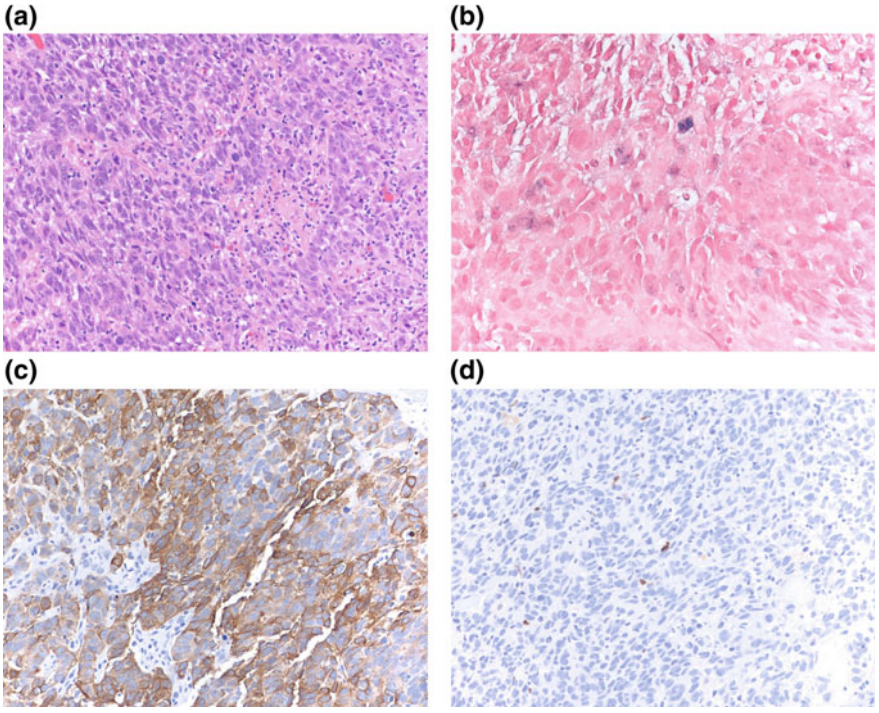


Fig. 6.6 EBV-related nasopharyngeal carcinoma. **a** H&E appearance of the tumor, demonstrating a nonkeratinizing carcinoma. **b** In situ hybridization for EBER (Epstein–Barr encoding region). The blue dots within the nuclei are a positive result, confirming that this is an EBV-related neoplasm. **c** Pankeratin (AE1/AE3). Positive staining confirms the epithelial nature of the malignancy. **d** p16. Negative p16 staining is consistent with the diagnosis of EBV-related nasopharyngeal carcinoma, as the vast majority of nasopharyngeal EBV-related carcinomas are negative for HPV

of myoepithelial carcinoma). Overexpression of Her2, meanwhile, is present in at least 10% of mucoepidermoid carcinomas [17]. In recent years, the identification of specific translocations in salivary tumors has expanded significantly, and in some cases may be more illuminating than a panel of stains when the diagnosis is uncertain. Examples of implicated genes include *MYB-NFIB* in adenoid cystic carcinoma, *PLAG1* in pleomorphic adenoma, *MAML2* in mucoepidermoid carcinoma, and *ETV6-NTRK3* in mammary analog secretory carcinoma [18, 19].

One setting in which immunohistochemistry is invaluable is in the diagnosis of sinonasal small blue cell tumors. In these cases, particularly in small biopsies, the morphology for tumor types with very different implications can be indistinguishable. Olfactory neuroblastoma, melanoma, rhabdomyosarcoma, sinonasal undifferentiated carcinoma, lymphoma, NUT midline carcinoma, and others can usually be reliably distinguished with a panel of stains and molecular studies as

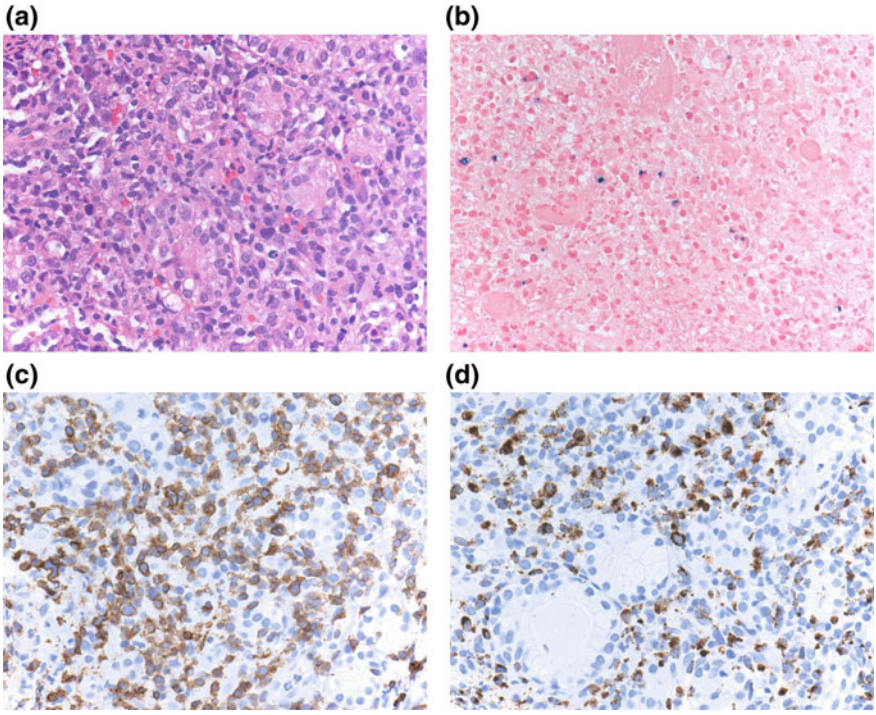


Fig. 6.7 Extranodal NK/T cell lymphoma. **a** H&E appearance of this deceptively bland, polymorphic population of inflammatory cells. **b** EBER. The small blue dot-like staining in the nuclei is a positive result, confirming that this is an EBV-related process. **c** CD3. The tumor cells are highlighted with CD3 staining, confirming the lymphomatous nature of the process. **d** Granzyme. Positivity highlights the cytotoxic phenotype of these tumors, the expression of which is required in some subtypes

long as enough biopsy tissue is obtained. If the sample is very limited, or extensively necrotic, it may not be possible to classify the tumor with certainty.

The other setting in which immunohistochemistry is vital is the diagnosis of extranodal NK/T cell lymphoma, nasal type. Just as this tumor can have a range of clinical presentations, the histology can range from frankly malignant to deceptively bland. Stains for CD56, cytotoxic proteins, CD3, and in situ hybridization (ISH) for EBER are required (Fig. 6.7).

6.1.5 Frozen Section Pitfalls

Despite its limitations, frozen section evaluation is without doubt a reliable and useful tool [20]. In the head and neck, the most common use of frozen section is to evaluate margins for squamous cell carcinoma. For the most part, this is straightforward for any surgical pathologist; invasive carcinoma in this setting is not easily

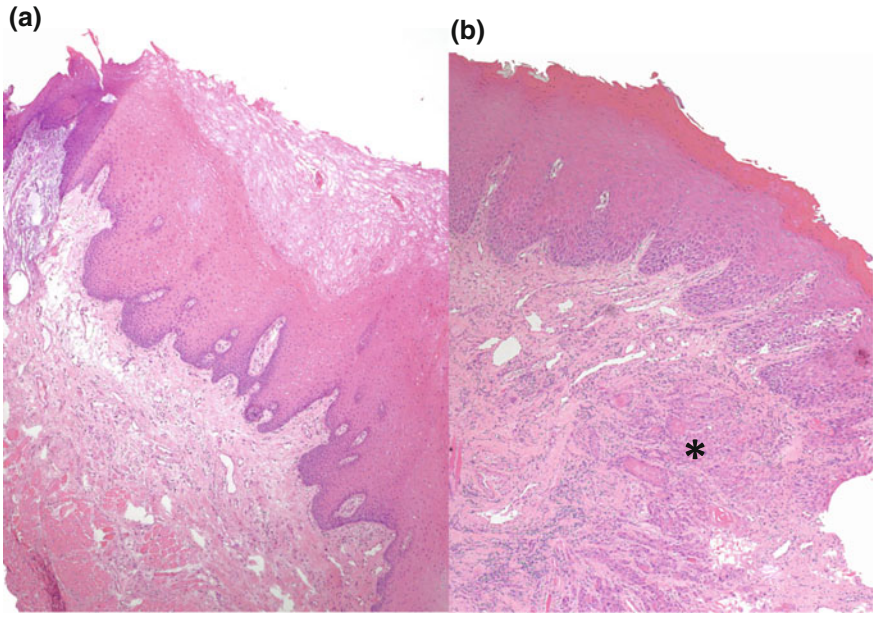


Fig. 6.8 Frozen section discrepancy due to sampling error. **a** Original frozen section slide. Benign squamous epithelium. The stromal component is unremarkable—two levels were prepared and both were free of tumor. **b** Permanent section of the remnant tissue. The overlying epithelium is more strikingly hyperkeratotic, and invasive tumor (*) is clearly present within the stroma

or often misinterpreted. Margins interpreted as "negative" may rarely come back on the permanent section as positive for invasive carcinoma. In these cases, the discrepancy is almost always due to sampling error [21]; the tumor focus was deeper in the block (Fig. 6.8). To avoid this, multiple deeper levels can be examined [22], and the frozen block may even be exhausted.

The greater challenge comes in the interpretation of squamous dysplasia. For dysplasia, the problem is twofold. First, the diagnosis and grading of dysplasia suffer from poor inter- and intraobserver reproducibility [22–24]. One pathologist's low-grade keratinizing dysplasia may be another's moderate. This can become a significant challenge in the oral cavity where moderate to severe dysplasia is potentially considered a positive margin, even on the well-fixed and unfrozen tissue. At the time of frozen section, this challenge is compounded by the fact that freezing tissue introduces significant artifact and it can be difficult to decide if nuclear changes are artefactual or neoplastic; low-grade dysplasia cannot typically be reliably diagnosed on frozen section. Additionally, even in subspecialized pathology departments, the frozen section service is usually covered by pathologists with a wide variety of experience and expertise. Often, the most useful tool is comparing the preoperative biopsy, when available, to the frozen section margins.

Freezing a thyroid nodule with a follicular neoplasm, or follicular lesion of unknown significance (FLUS), fine-needle aspiration (FNA) interpretation

(Bethesda III, IV) should be avoided. This is a very low-yield endeavor, with the vast majority of cases being deferred [25, 26]. To distinguish a follicular adenoma from follicular carcinoma the tumor capsule needs to be extensively sampled, which is often not be feasible in the frozen section setting. The presence of lymphovascular invasion must also be rigorously evaluated, which is not optimal on frozen tissue. For these reasons, this diagnosis is quite frequently deferred to the well-fixed and processed permanent sections. In the case of a suspicious for malignancy/papillary carcinoma (Bethesda V) FNA result, frozen section evaluation is still not particularly revealing. Though the majority of thyroids with this FNA result will have a papillary carcinoma on permanent section, a recent study confirms that more than 30% of the diagnoses will still be deferred at frozen section [25]. The artifact introduced by freezing the tissue can obscure or obfuscate the nuclear features needed to confirm the diagnosis (Fig. 6.9).

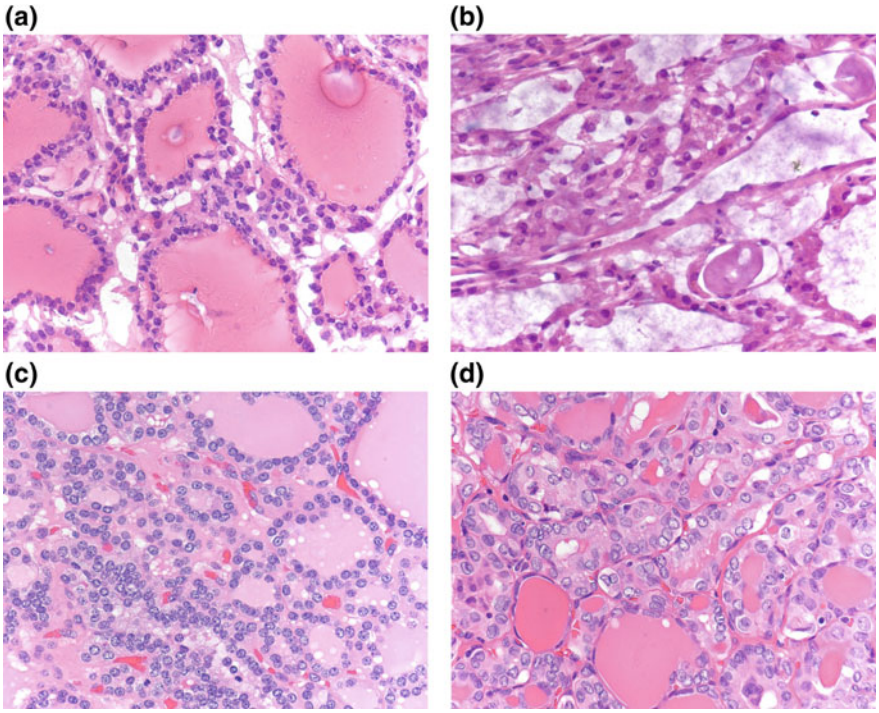


Fig. 6.9 Frozen section of thyroid nodules. **a** Frozen section. Pathologist deferred diagnosis of the nodule. **b** Permanent section. The same nodule as in image **a**, but from a nonfrozen area. With regular processing, the morphology is clearly benign and the final diagnosis was adenomatous nodule. **c** Frozen section from a different patient, also deferred by the pathologist. **d** Permanent section. The same nodule as pictured in **c**, but from nonfrozen area. In this case, the cytologic features of papillary thyroid carcinoma are quite characteristic and striking even from low power. Diagnostic nuclear features including grooves (*), folding (^), clearing ( ]), and crowding (+) are all present in this field. The final diagnosis was papillary thyroid carcinoma

Inappropriate frozen sections, meaning those without any immediate impact on surgical or clinical decision-making, should always be avoided. Utilization of the frozen section service is not a shortcut to a considered diagnosis on well-fixed tissue; the role of frozen section is a form of surgical pathology triage to answer a very specific set of questions. Valid reasons for requesting a frozen section include margin adequacy, the presence of a lesion, adequacy of biopsy, and the potential need for additional tissue for special studies. Potential negative consequences of unnecessary frozen section include wasting of diagnostic biopsy material in the microtome, suboptimal morphology on permanent section due to freezing artifact, and increased opportunity for misdiagnosis and miscommunication [27]. Finally, overuse of the frozen section service for the sake of curiosity tends to dilute the sense of urgency and acuity for all frozen sections. Optimal use of frozen section is a collaborative effort between the surgeon and pathologist to provide quality patient care, rather than a constant source of conflict and consternation.

6.2 Conclusion

The practice of head and neck pathology has become increasingly refined and specific in recent years. The recognition of the importance of HPV-related tumors, histologic parameters such as depth of invasion, and the identification of diagnostically useful molecular alterations in salivary gland tumors are all examples. Each of these changes aims to make the diagnosis of head and neck malignancy more specific and reproducible, in order to provide the most comprehensive and relevant information possible for each patient.

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Surgical Perspectives in Head and Neck Cancer

7

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_7

Abstract

Head and neck cancer treatment is a complex multidisciplinary undertaking. Cancer cure and survival is a primary goal, yet safe-guarding appearance and function to preserve the quality of life are similarly critical. The head and neck surgeon remains central to multidisciplinary cancer care, with deep knowledge of operative technique and an even deeper understanding of cancer biology. The surgeon models practice based on the highest levels of scientific evidence, but also takes into consideration the approaches that may best suit an individual patient. The surgeon's role moreover spans the life history of a head and neck cancer patient, from diagnosis to surveillance. The intimacy of this role makes the surgeon a trusted and frequent frame of reference for the patient. In this chapter, we provide an overview of the surgeon's role in head and neck cancer management. We discuss surgical perspectives within the multidisciplinary care team and selectively highlight some of the more provocative clinical scenarios in the field.

Keywords

Head and neck surgical oncology · Head and neck surgeon
Head and neck cancer · Multidisciplinary care · Quality of life
Role of surgeon

7.1 Introduction

The head and neck surgeon is commonly the initial cancer provider for a newly diagnosed head and neck cancer (HNC) patient. The surgeon must be prepared to balance the disease, the treatment, and the patient to reach optimal outcomes. Detailed knowledge of varied cancer biology is crucial in decision-making: some diagnoses (e.g., angiosarcoma, mucosal melanoma, anaplastic thyroid carcinoma) demonstrate an aggressive pattern of spread with poor prognosis, while others exhibit relatively indolent growth with more favorable prognosis (e.g., early stage glottic cancer, human papillomavirus-positive (HPV+) oropharyngeal cancer, well-differentiated thyroid carcinoma). The treatment regardless of disease category can be devastating on function and quality of life.

The surgeon's role is essential throughout the life history of a patient with a head and neck cancer. This role has evolved to meet the needs of the patient within the context of current multidisciplinary care plans. Most head and neck tumor boards continue to be led by surgeons. Even in an era of organ preservation, the surgeon plays fundamental roles from initial diagnosis through definitive treatment, rehabilitation of form and function, and posttreatment surveillance. In the recurrent setting, the surgeon plays a fundamental role in diagnosis, restaging, and multidisciplinary care. With improved reconstructive techniques and adjunct treatment options, salvage surgery has become more common, and with it increased

challenges in recovery. As such, the head and neck surgeon bridges the many disciplines to reconcile the gains from treatment with its costs.

7.2 Diagnosis and Treatment Selection

Both physical exam and imaging are crucial in the initial surgical assessment of disease burden, resectability, potential morbidity of treatment, and assessment of prognosis. Certain factors on examination such as tumor fixation to overlying skin, gross involvement of mandible, or facial nerve paralysis are ominous indicators that cannot be fully conveyed on imaging. Conversely, imaging modalities may help gauge lesions that are unresectable (Table 7.1) or require more extensive treatment. Whenever possible, the tumor is accurately staged and histopathology is confirmed through appropriate biopsies.

In evaluation and staging, attention is focused on patient factors such as acute symptoms, nutrition and dental status, tobacco and alcohol use, psychosocial resources, body habitus, coexisting medical comorbidities, and performance status. After workup and multidisciplinary consensus, cases may be appropriate candidates for upfront surgery. The surgical benefit to the patient is weighed against the potential morbidities of an operation. Surgical and nonsurgical options for management must be given appropriate consideration, and it is this decision-making that is a key feature of multidisciplinary tumor board discussion [1–3]. Advanced stage disease, in particular, is difficult to treat, in part because it requires careful coordination of care that may be sequenced or combined. Timely completion has a positive impact on outcome: studies have shown that patients who have a longer than 100-day treatment package (time from surgery to end of adjuvant radiation) do markedly worse in terms of overall survival [4, 5].

Overshadowing these considerations is the patient's social support network—the friends and family who drive the patient to treatments, help with home care and nutrition, and provide emotional support to finish the treatment plan. The absence of family present in and of itself signals a poor prognostic feature. Patients who come

Table 7.1 Radiologic factors that may preclude surgery

Radiologic factors that may preclude surgery
Carotid artery encasement
Prevertebral fascia involvement
Mediastinal infiltration
Skull base or dural spread
Cavernous sinus or optic chiasm invasion
Brachial plexus invasion
Distant metastasis

to the clinic alone may, in fact, sway against the decision to operate and toward a palliative approach that may be more realistic given the patient circumstances.

7.3 Surgical Considerations

The overarching goal in surgery is complete resection with negative margins. Positive margins are an indisputably poor prognostic factor in head and neck cancer: they indicate the need for postoperative chemotherapy, substantially increase the likelihood of recurrence, and lead to significantly decreased survival. In optimal situations, negative margins of at least 1 cm on the *en bloc* specimen remain the standard of care (R0 resection). A piecemeal resection with reliance upon negative margins on subsequent frozen sections (beyond the main specimen) is much less ideal and prone to subjective assessment of whether margins are truly clear. Close margins are typically defined as less than 5 mm. Recent data from oral tongue cancer surgery suggest that this cutoff is better defined as less than 2.2 mm [6], whereby locoregional survival was no different for disease with wider margins taken. This is an important consideration given that critical structures may preclude an ideal margin.

Practically, the critical surrounding structures of the head and neck may necessitate leaving microscopic margins (R1 resection). For instance, leaving microscopic disease behind on a partially encased nerve to avoid facial nerve paralysis or hoarseness/aspiration may be worthwhile, if disease histology suggests postoperative radiation will be effective. This decision relies heavily on surgeon judgment and reflects an understanding of the patient's quality of life.

Surgical expertise is also highly germane for neck dissections. It has long been thought that the presence of a single metastatic node may decrease survival by 50% [7]. Recent studies have found that additional positive node confers stepwise risk of mortality, eclipsing conventional staging factors such as node size or contralaterality (Fig. 7.1a) [8, 9]. In addition, the number of nodes harvested, regardless of whether they are cancerous, also seems to predict survival. As a quality metric, some studies suggest that harvesting less than 18 nodes in a neck dissection leads to worsened survival, while others suggest that survival improves with even more thorough neck dissections up to 35 nodes (Fig. 7.1b) [10]. It is unclear if survival is directly related to surgical acumen, or if such thoroughness is an indirect surrogate for institutions that possess other factors such as high-quality radiation or supportive care teams. Regardless, substandard neck dissections or "berry-picking" is ill-advised. Further evidence for the importance of neck dissections was exhibited with a prospective trial randomizing T1-2N0 oral cavity cancer patients to elective neck dissection versus observation, with observed patients undergoing therapeutic neck dissection if they eventually developed nodal metastases [11]. Significantly better survival was seen in elective neck dissection patients, suggesting that meaningful occult nodal disease may exist that is not seen on imaging, and that waiting until subclinical disease declares itself may lead to poorer outcomes.

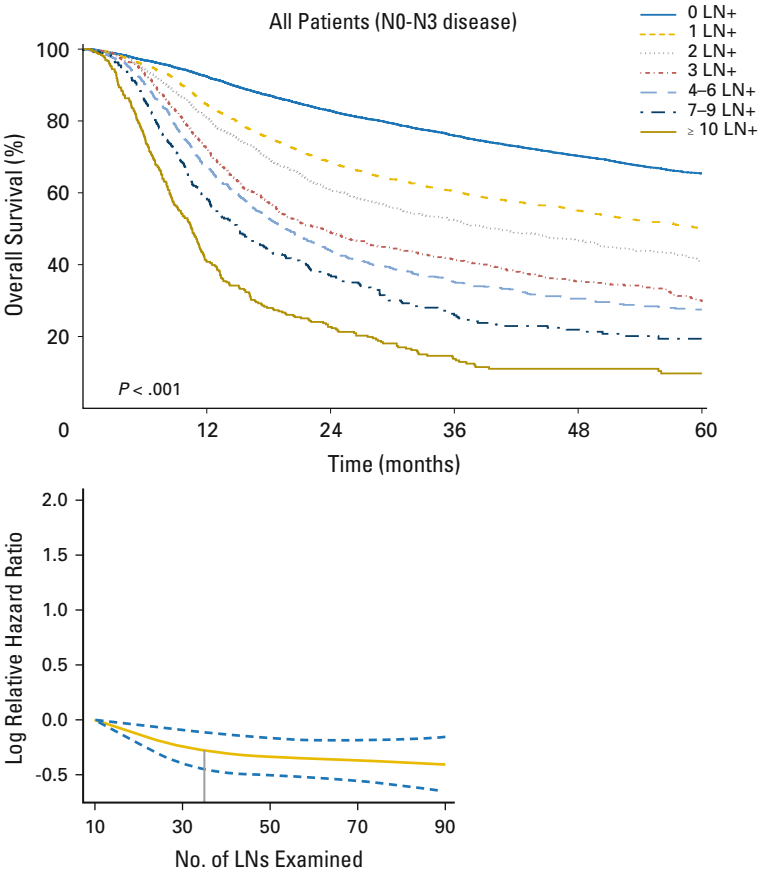

Fig. 7.1 Multivariate spline plot demonstrating **a** increased mortality risk with increasing positive metastatic lymph nodes and **b** decreased mortality risk with increasing lymph nodes examined in a neck dissection, in oral cavity squamous cell carcinoma captured in the National Cancer Database. Plots are adjusted for factors that include T-classification, N-classification, margins, extranodal extension, nodal size, and chemoradiation [8]

Surgery may be definitive, such as for thyroid or salivary cancer, or follow neoadjuvant therapies for certain histologies (e.g., sarcomas) or challenging locations (e.g., sinonasal tumors with orbital or skull base invasion. Regardless of the order of placement, the surgeon plays a critical role in defining areas of direct tumor involvement and areas of high risk for dissemination that need to be accounted for. The surgeon helps facilitate intensity-modulated radiation therapy (IMRT) target delineation in complex cases. This partnership with the treating radiation oncologist is beneficial for optimizing target delineation and reducing marginal misses in both definitive and adjuvant settings [12].

In definitive chemoradiation settings, imaging studies may underestimate macroscopic disease in certain anatomical locations such as anterior commissure, subglottic larynx, and hypopharynx. Imaging may also miss submucosal extension of disease. Direct tumor examination is key in defining gross tumor volumes (GTV) for radiation planning. The head and neck surgeon's knowledge and experience with patterns of disease spread of cancers in different subsites are also critical in defining clinical target volumes (CTV). Clear communication regarding margins of resection and specifics regarding altered surgical anatomy enable adjustment of the radiation field and dose.

7.4 Post-Treatment Surveillance

Close patient follow-up after treatment is critical, as disease relapse can occur in 10–50% of cases depending on the stage of disease and risk factors [13]. Interval physical exams with laryngoscopy over time may best help delineate posttreatment anatomy and changes, and can help overcome artefactual confounders such as inflammation, edema, and fibrosis. Imaging in conjunction with exam remains just as crucial. Though the optimal frequency of follow-up imaging after definitive therapy has not been strictly defined, the National Comprehensive Cancer Network (NCCN) offers general follow-up guidelines (Table 7.2). Notably, most recurrences are detected and reported by patients themselves.

In RTOG 0129 for oropharyngeal cancer, 18.6, 32.5, and 43.2% of enrolled patients experienced disease progression in the low risk, intermediate risk, and high-risk disease categories respectively [14]. The majority of recurrences were locoregional occurring within the first 3 years of surveillance. Nonetheless, when initial posttreatment impression is favorable, a 3-month PET/CT scan confers excellent negative predictive value (NPV) in excess of 90% [15]. Further imaging should, therefore, be prompted by new symptoms or new physical exam findings.

Table 7.2 Surveillance recommendations after treatment completion

Surveillance recommendations (NCCN)	
Clinical exam	Year 1—every 1–3 months
	Year 2—every 2–6 months
	Year 3–5—every 4–8 months
	Year 5+—every 12 months
Imaging	• Consider surveillance imaging of primary within 6 months of completing treatment
	• Chest CT as indicated for patients with smoking history
	• Further reimaging as indicated based on worrisome or equivocal signs/symptoms, smoking history, and areas inaccessible to clinical examination
	• Routine annual imaging may be indicated in areas difficult to visualize on exam

A negligible or short disease-free interval is a poor prognostic indicator. An experienced radiologist can ascertain an equivocal compared to a suspicious FDG-avid lesion on 3-month PET/CT scan, and image-guided needle biopsies can help guide decision-making in suspicious cases earlier than 3 months if needed. Early detection of the persistent disease leads to higher chances of salvage and a better chance of long-term survival.

The role of image-guided surveillance as compared with planned neck dissection in the management of patients with HNSCC and advanced nodal disease (N2 or N3) after chemoradiation therapy has been a matter of debate. In a recent prospective randomized trial, equivalent survival was found for patients who underwent PET-CT-guided surveillance and those who underwent planned neck dissection, but surveillance resulted in considerably fewer operations and was more cost effective [16]. Adams et al. similarly showed that the rate of isolated nodal failure remained low (6%) when following a PET-directed neck management policy after definitive CRT for N3 (>6 cm) HNSCC [17]. Failure was predominately distant metastatic in this setting. Currently, most institutions avoid planned neck dissections and operate only when the PET/CT supports persistent or residual disease.

7.5 Role of the Surgeon in Salvage Therapy

Surgical salvage after chemoradiation can be debilitating, with a decreased chance of survival and considerable potential for complications. The rate of postoperative complications in the salvage setting ranges from 13 to 60% depending on series, with a 5-year overall survival of 22–39% [18]. Surgical salvage when possible is always recommended over re-irradiation or systemic agents when pursuing curative intent [19], though the patient's performance status may make this a difficult decision (Fig. 7.2). The addition of re-irradiation and chemotherapy to salvage

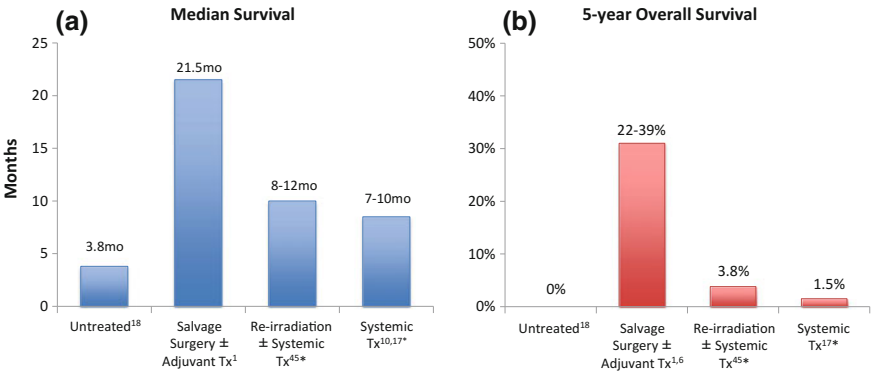

Fig. 7.2 **a** Median survival and **b** 5-year overall survival in recurrent head and neck cancer patients stratified by treatment modality [19]

surgery has been shown to improve local control, but with increased treatment-related toxicity [20]. The experience of the surgical team is paramount in optimizing outcomes and reconstructive techniques are frequently necessary for the salvage setting. In patients in whom recurrence is locoregionally confined, some salvage treatments (such as surgery or stereotactic radiosurgery) provide a possibility of long-term survival but a high chance of treatment-related toxicity.

Recurrent or metastatic HNC generally harbors a poor prognosis with limited median overall survival (OS) (Fig. 7.2), even with salvage therapy. Notably, in patients with suspected recurrence or biopsy-proven recurrence, approximately 25% will demonstrate distant metastases with restaging [18, 21, 22]. Metastastectomy of oligometastases may confer a modest survival advantage. Salvage treatment and its costs to the patient needs to be carefully considered on a case-by-case basis, and every effort should be made to consider a clinical trial or best supportive care.

7.6 Role of a Surgeon in Terminal Disease

Patients with incurable recurrent or metastatic HNC present unique palliative challenges that require sensitive attention. Impending airway obstruction and inability to eat or drink may require surgical remedy with tracheostomy and gastrostomy respectively. Open foul-smelling head and neck ulcerations will require dedicated wound care, and may eventually lead to a terminal bleeding event. The patient and caretakers require delicate education and preparedness regarding this phase of the disease. These discussions are emotionally loaded and difficult even for the most seasoned oncology practitioner. Locoregional resection even in patients with distant metastasis may still be suggested, as fundamental human functions impacted, including breathing, swallowing, speaking, and cranial nerve function may be worth sparing. The primary source of morbidity and mortality in HNSCC is, therefore, often locoregional progression, even for those presenting with distant metastasis. It is best that the surgeon partner with supportive care medicine to steer discussions around patient concerns, needs, and wishes.

7.7 Controversies in Select Disease Types

While guidelines have helped standardize treatment regimens, there remain circumstances that require special management. This may be due to unique histology, difficult locations near critical structures, or sites where the evidence points to different approaches being effective. Several such controversial scenarios are discussed below. Caution is warranted given the lack of definitive evidence for certain approaches.

7.7.1 Angiosarcoma

Angiosarcoma is a rare yet aggressive malignancy, with high rates of local recurrence and early distant metastasis. In the head and neck, it most typically affects the scalp and face where surgical resection frequently fails or is unacceptable to patients [23–25]. Five-year overall survival rates have been reported at approximately 12%, with only half surviving longer than 15 months after presentation [26].

In triaging patients one helpful approach has been to perform mapping biopsies 2 cm or more beyond the visible malignancy in the operating room. If these are positive, then the occult metastatic spread is likely beyond what is surgically feasible, suggesting support for nonsurgical management. Chemoselection is another helpful approach to advanced disease. The degree of tumor response to upfront chemotherapy is used to guide subsequent management. An unfavorable chemotherapy response suggests that curative treatment would have been unnecessary and futile; a favorable chemotherapy response may help identify those patients who may benefit from surgery despite the morbidity. Surgical resection will still aim at the original tumor margins and some patients may have a chance at cure with excellent cosmetic and functional outcomes (Fig. 7.3).

7.7.2 Oropharyngeal Cancers

In the United States, the majority of oropharyngeal cancers are HPV(+). Such disease confers improved cancer cure rates regardless of treatment platform, relative to HPV(−) cancer, and as such quality of life is an important consideration. In general, swallowing outcomes are worsened by compounded toxicities of multimodality treatments. A small but significant fraction of cured patients will develop long-term dysphagia and even gastrostomy tube dependence [27, 28].

There is growing experience with minimally invasive transoral surgical techniques applied to the oropharynx. Transoral laser microsurgery (TLM) and transoral robotic surgery (TORS) are surgical techniques which provide tumor resection through the mouth. These techniques also provide for a more thorough sampling of oropharyngeal lymphoepithelial tissues helpful in localizing small hidden primary tumors, with some reporting identification of the primary upon pathologic examination of TORS-derived tissues in 90% of unknown primary cases [29]. Exact identification of tumor location and extent is helpful in precise tumor targeting and mitigation of unwanted treatment-related side effects. Patient selection is key in successful execution [30–33]. As experience expands, the modality may apply to larger tumors and recurrent salvage settings. Mounting reports from higher volume centers document comparable oncologic and favorable swallow outcomes [34–36]. There is no high-quality evidence comparing outcomes between transoral surgery and chemoradiation.

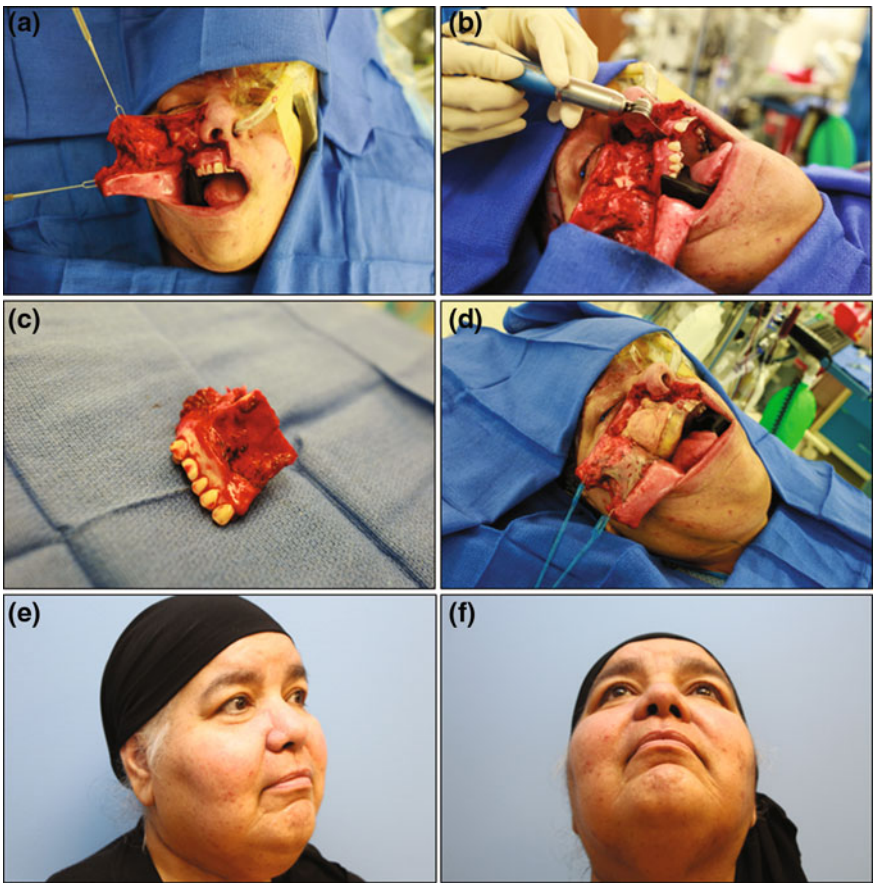

Fig. 7.3 Maxillary sinus angiosarcoma undergoing total maxillectomy with neck dissection. **a** Weber Ferguson incision with upper lip split. **b** Sagittal saw cuts into alveolar ridge after extraction of lateral incisor. **c** Total maxillectomy en bloc resection with margins clear. **d** Obturator placement after obliteration of sinus with xeroform packing. Split-thickness skin graft from thigh placed along mucosa to prevent contracture and facilitate obturator adjustment. **e** Postoperative 3/4 oblique view. **f** Postoperative base view. The patient completed adjuvant chemoradiation and remains free of disease after one year

7.7.3 Anaplastic Thyroid Cancer

Though the clear majority of thyroid malignancies are indolent, anaplastic thyroid carcinomas remain overwhelmingly lethal. Their growth rates are rapid, with both locoregional progression and distant metastases contributing to a 1-year overall survival rate of less than 20% and disease-specific survival approaching 0% [37]. Median survival has been quoted at 8 months if the disease remains locoregional, 3 months if there is distant metastasis, and 1.5 months if there are brain metastases [38]. All anaplastic thyroid cancers are staged IVA at a minimum. Surgical

resection followed by chemoradiation is the ideal curative approach, but like angiosarcoma a palliative approach may sometimes be in the patient's best interests.

The surgeon's role in ATC is multidimensional. A diagnosis must be urgently established through the core or surgical biopsy, as the lesion may masquerade as lymphoma or medullary thyroid carcinoma. The surgeon must furthermore assess the airway for compromise due to impingement, direct invasion, or denervation. Patients with marginal airways and symptomatic distress warrant tracheostomy. Others require a more calculated approach as a premature tracheostomy may become an easy conduit for tumor invasion into the trachea. A tracheostomy may also commit a patient to long-term, complicated nursing care, when the goal should be to keep patients out of the hospital in their potentially final days of life.

Once the patient is stable, goals of care discussion should be had that balances the wishes of the patient with multimodality care. If an R1 resection can be achieved, surgery is preferable as it can ward off imminent problems due to an uncontrollable disease involving the airway. Although the patient may still succumb to disease, it is less morbid to pass away from the distant disease than from suffocation secondary to airway obstruction, which occurs in up to 50% of cases [37, 39]. Note that due to this consideration, the NCCN Guidelines considers surgery reasonable even in the case of distant metastasis (Stage IVC) [38]. Bronchoscopy and esophagoscopy are recommended to ensure no intraluminal involvement, which may discourage curative surgery.

Upfront chemoradiation is a reasonable approach to patients with unresectable or distant metastatic disease. Chemoradiation may increase short-term survival and achieve modest improvements in locoregional control. However, definitive chemoradiation is toxic with a near 100% rate of gastrostomy tube placement. In addition, tumor progression may lead to problematic airway issues. Finally, systemic therapy has not been shown to slow the rate of distant metastasis or improve overall survival [37].

7.7.4 Recurrent Well-Differentiated Thyroid Carcinoma

Though most thyroid cancers are indolent, they paradoxically harbor a high rate of lymph node involvement, with approximately 25% of patients developing new disease after surgery with or without radioactive iodine (RAI) [40]. Nearly 75% of recurrences occur in the lymphatics; this number may, in fact, climb higher as surveillance measures such as thyroglobulin (Tg) assays and ultrasound expertise improves, discovering sub-centimeter disease that previously may have been missed [41]. As such, some recurrent disease is truly persistent disease newly uncovered.

The indolent nature of well-differentiated thyroid cancer contrasts with the potential risks of reoperation. Nearly all patients are asymptomatic, and it is daunting to introduce symptoms to chase a lab value or disease that may never harm the patient. For reoperative central neck dissection, the incidence of temporary and permanent vocal cord paralysis is reported to be up to 22 and 6%, respectively [42].

Similarly, the incidence of temporary and permanent hypoparathyroidism is reported as high as 46 and 10%, respectively [41]. Meanwhile, biochemical recurrence (elevated Tg but no radiologic evidence of cancer) confers a long-term survival nearing 100%. However, structural recurrence (radiologic evidence of cancer) in turn has long-term survival approximating 85%, while distant metastasis leads to long-term survival of less than 50% (higher in younger patients) [43]. These rates for complications and for survival should figure into both the surgeon's and the patient's appetite for intervention.

It has become increasingly clear that small, stable lymph nodes may be observed, in properly selected patients (active surveillance). Moreover, positive but low Tg levels are increasingly being considered acceptable for monitoring, with the Tg trend over time a more important indicator of additional RAI treatment or surgery [44]. In the absence of other patient and tumor factors, the ATA also suggests that lymph nodes ≥ 8 mm (central neck) and ≥ 10 mm (lateral neck) are reasonable thresholds for FNA and potential surgery, even if not causing symptoms [41]. It should be made clear to patients that the surgical removal of metastatic cervical nodes may not eliminate Tg levels in as many as 50% of patients, and may have no impact on overall survival [45–47]. This may sway patients in their decision-making, especially if hypoparathyroidism or bilateral vocal cord paralysis are higher possibilities. Other considerations that impact risk are the degree of fibrosis from earlier surgery and the experience of the surgeon. A compartmental neck dissection mitigates the possibility of nodal persistence and missing the target disease [48]. It is explicitly discouraged to pluck individual nodes or engage in berry picking, as microscopically involved neighboring lymph nodes may easily be missed and the art of surgeon palpation is imprecise.

The ATA Guidelines support that rather than the simple presence of metastatic nodes as predictors of poor outcomes, lymph node metastases larger than 3 cm, the presence of extranodal extension, and more than five positive lymph nodes are more indicative. These factors have been reported to correlate significantly with higher recurrence and decreased survival [49–51]. Nonetheless, the treatment plan is never as straightforward as the guidelines listed above may suggest. The most typical rationale for intervention is to prevent disease progression into vital structures complicating future surgery. In addition, speculation exists that removing locoregional recurrence will prevent seeding to distant metastatic sites.

If the vocal cord is intact preoperatively, preservation of the nerve is usually recommended. Some institutions recommend en bloc resection of the recurrent laryngeal nerve if the vocal cord is known to be paralyzed, as it facilitates an R0 resection and an involved nerve is unlikely to return to function. However, even with known paralysis, nerve continuity may retain some basal tone that helps with phonation and prevents aspiration. Additionally, leaving microscopic cancer on the nerve has not been shown to impair survival or increase rates of recurrence [52, 53]. As such, "shaving" tumor off the nerve may be reasonable in well-differentiated thyroid types due to known excellent prognosis. Similarly, shaving tumor off the trachea rather than performing a tracheal resection or laryngectomy may be preferred.

Nonsurgical options are increasingly available that bridge the conventional modalities of surgery and active surveillance. RAI ablation therapy is possible but less effective for gross disease that does not produce Tg. External beam radiation therapy may also be considered when no further surgery can be performed [54]. Other nonsurgical approaches that are emerging include percutaneous ethanol injection therapy and radiofrequency ablation [55, 56]. Such options may provide meaningful disease control for otherwise inoperable disease or patients not suited for surgery.

7.7.5 Advanced Oral Cavity Cancers

Surgery with or without adjuvant radiation remains the standard of care for oral malignancies. While squamous cell carcinomas of other sites (e.g., oropharynx, hypopharynx, larynx) have done well with a nonsurgical approach, chemoradiation for oral malignancies has not been shown to be as effective, presumably due to greater toxicities of radiation in the oral cavity (e.g., osteoradionecrosis) and ineffectiveness of radiation with bony involvement. This is troubling given that critical functions such as mastication, taste, swallowing, and articulation are irreversibly affected by surgery.

Particularly for advanced stage malignancies, organ preservation is often brought up at multidisciplinary tumor board discussions. Even with excellent reconstruction capabilities, oncologic procedures such as total glossectomy lead to permanent speech and swallow deficits. They may also require a concurrent total laryngectomy to prevent chronic aspiration. Such radical procedures put in stark relief how important a patient's wishes are in determining the quality of life compared to the length of life.

Definitive chemoradiation for T3/T4 oral cavity malignancies has been studied in single institutions, with mixed results. Perhaps the most widely known study advocating chemoradiation involved retrospective analysis of patients undergoing triple-agent chemoradiation at the University of Chicago [57]. More than 90% of patients did not require a feeding tube, with a 5-year overall survival rate of 66.9%. This was comparable to a definitive surgery arm. The authors concluded that advanced tongue malignancies could be spared total glossectomy with this approach.

Despite encouraging results, the chemoradiation regimen used was atypical and has not been reproduced at other institutions. Moreover, other single arm prospective trials have shown poorer outcomes with definitive chemoradiation. Notably, the University of Michigan attempted a chemoselection prospective trial, whereby induction chemotherapy patients with at least a 50% response went on to definitive chemoradiation [58]. Even with chemoselection, chemoradiation patients did worse than patients treated with primary surgery and radiation (5-year overall survival of 32% vs. 65%, $p = 0.03$). A prospective, randomized trial at National Cancer Centre Singapore similarly showed poor results with definitive chemoradiation (5-year disease-specific survival of 12% vs. 68%, $p = 0.04$) [59]. Although

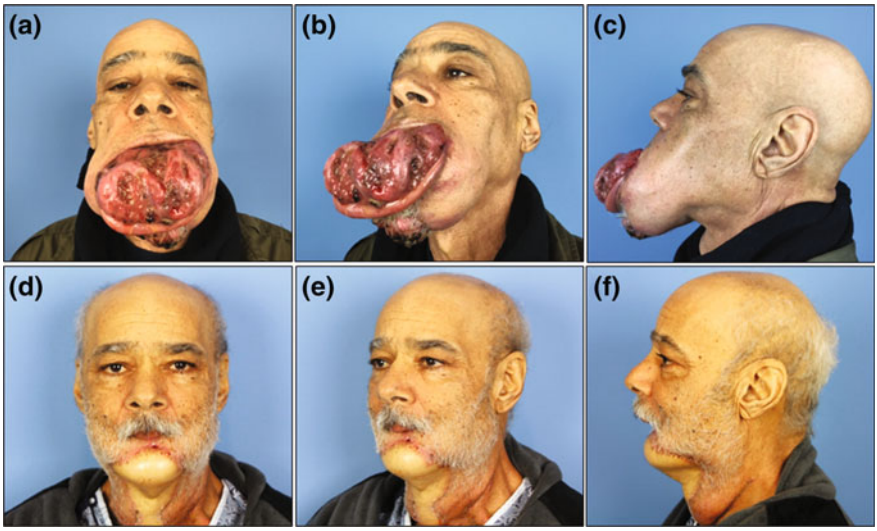

Fig. 7.4 Preoperative **a** frontal, **b**. oblique, and **c** profile views of a 69-year-old male with oral cavity adenocarcinoma. Postoperative **d** frontal, **e** oblique, and **f** profile views after surgical resection. Margins were clear and reconstruction was performed with double fibula and anterolateral thigh flap microvascular reconstruction. The patient retained his baseline speech and swallow function, and remains free of disease after one year [60]

difficult to propose to patients, evidence continues to favor upfront surgery as the standard of care, with functional and cosmetic outcomes potentially excellent (Fig. 7.4).

7.7.6 Advanced Stage Laryngeal Cancer

Advanced laryngeal cancer patients can be a true management conundrum. Conservation approaches such as chemoradiation have made giant strides in organ preservation. High rates of laryngeal preservation were first reported in the Department of Veteran's Affairs (VA) Laryngeal Cancer Group Study, with lower overall rates of salvage laryngectomy for T3 patients (28%) compared to patients with T4 primary tumors (56%) [61]. Moreover, RTOG 91-11 established concurrent chemoradiation as the definitive treatment for patients with advanced laryngeal squamous cell carcinomas, but excluded large-volume T4 disease [62, 63].

It is these T4 lesions that are the most challenging for patients and physicians. Cartilage invasion or extralaryngeal spread is often considered contraindications to organ preservation approaches. Yet although total laryngectomy offers the greatest chance of cure, the costs of a laryngectomy stoma and voice impairment are daunting. Chemoradiation holds some opportunity for cure, but also confers the

possibility of a nonfunctional larynx, chronic aspiration, and recurrence that would require salvage surgery.

Interestingly, there have been no significant studies investigating cancer patient perceptions and preferences. There is a clear discrepancy between what physicians and patients prefer. The initial treating physician also plays a strong role in swaying what the patient ultimately decides for treatment, and it is important to understand the dangers of making assumptions about patient attitudes and their goals. Data suggest that, at least pretreatment, survival is of primary importance: one study of 131 head and neck cancer patients showed that being cured was the top priority in 75% of patients [64]. There was, however, individual variability observed that highlights how personal a decision this is. For laryngeal cancer, there are largely surveys of healthy volunteers to consider. Perhaps the most widely cited is the "firefighter study", where healthy patients collectively were willing to trade 15–30% of life expectancy in order to preserve their larynx [65]. A more recent French study of 269 healthy patients found that 29% would not trade any drop in cure rate for voice. After being educated about the surgery including the risk of permanent gastrostomy tube placement, the rate of patients preferring cure above all rose to 56% [66].

Patient preferences remain highly variable, and some patients will want to avoid surgery at all costs. Indeed, some institutions report laryngeal cancers are highly radio-responsive, and may be cured despite large volumes or cartilage involvement. The University of Michigan has studied a chemoselection approach for T4 laryngeal cancers, reserving laryngectomy only for a patient with poor response to chemotherapy [67]. Of 97 eligible patients, 75% achieved >50% response rate and went on to chemoradiation. Of those with chemoradiation, 14% eventually needed total laryngectomy. The overall rate of total laryngectomy, including early surgery after a single induction cycle, was 30%. This study suggests that the inherent biology of a tumor (i.e., responsiveness to chemoradiation) may be more important than the presence of either bulky disease or cartilage invasion on imaging studies. Given relatively good rates of laryngeal preservation, NCCN suggests consideration of this approach for patients who decline surgery, but with surgery as the preferred option.

7.7.7 Early Stage Laryngeal Squamous Cell Carcinoma

The ideal treatment of laryngeal malignancies considers both the survival and functional consequences of the approach chosen. The high cure rates (>90%) of early stage disease have indicated that patients do well with either surgery or radiation, if appropriately selected. The high likelihood of cure has enabled greater flexibility in approach and place a higher priority on preserving speech and swallow functions.

Effective larynx-preservation treatment typically requires expertise and a dedicated support team. More specialized surgical techniques, including endoscopic KTP laser ablation, transoral laser microsurgery, robotic laryngeal surgery, or open partial laryngectomies, are emerging but are not widespread outside of several

institutions, and only for select patients with favorable features. Their advantages include excellent voice outcomes in experienced hands, faster treatment, and the avoidance of radiation sequelae. Voice quality has been difficult to assess in controlled, prospective fashion: outcomes are hard to measure across different surveys, different surgeons, and different subsites across the larynx. A rough consensus, however, is that voice outcomes after surgery are equal or inferior to that after radiation [68].

If the tumor is in a favorable location, then endoscopic resection is recommended. This includes tumors that are superficial, positioned on the free edge, and within the middle third of the cord. Endoscopic resection still requires close surveillance and a certain percentage of patients will need repeat OR evaluation to ensure disease has been cleared. Nonetheless, it preserves radiation for recurrent or persistent disease [68].

Conversely, indistinct lesions, especially those arising in carpet-like fashion with infiltrative margins are more suitable for radiation. Anterior commissure involvement similarly appears to be an indication for radiation, given that postsurgical scarring can lead to webbing and impaired voice. The drawback to radiation is the lengthiness of treatment, risk of secondary malignancies, and the likelihood of needing a total laryngectomy in the case of recurrence, perhaps one of the most feared and stigmatized operations in all of the surgery by patients. The choice of treatment relies heavily on patient counseling on the risks and benefits of approaches, patient wishes, and institutional expertise.

One controversial issue has been how to treat the neck. In laryngeal malignancies limited to the glottis, regional metastasis is quite rare and the neck does not warrant treatment. However, T1 supraglottic lesions or T2 glottic lesions that have spread to the supraglottis or subglottis are a different matter, as lymphatic drainage patterns are much less impeded and bilateral lymphadenopathy is not uncommon. Historical rates of occult neck metastasis in supraglottic cancers have been greater than 20–30%, even in early stages [69]. Furthermore, monitoring the neck and treating it only in the case of relapse is not suggested. Such undertreatment has been shown in multiple institutions to impair survival [70, 71]. Therefore, if endoscopic resection of such lesions is performed, the surgeon must be prepared to perform unilateral or bilateral neck dissections. A mix and match approach of resecting the primary and radiating the necks is highly discouraged: in those instances, the patient would have been better served undergoing single-modality radiation.

7.8 The Future of Head and Neck Surgery

The modern head and neck surgeon remains central to multidisciplinary head and neck cancer care. Translational studies with surgeon input and tissue procurement have helped unveil mechanisms of carcinogenesis and factors predictive of treatment resistance. Clinical trials have also unveiled new targets and novel approaches to management. Minimally invasive surgeries, image- and molecular-guided techniques,

tissue engineering, and 3D printing are just several promising developments that will change the surgical landscape. These assure that the modern head and neck surgeon will remain intimately involved in refinement and delivery of HNC care, championing both survival and functional outcomes for the benefit of patients above all.

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Head and Neck Reconstructive Surgery

8

Edward Ray

Contents

Abstract

Head and neck reconstruction following surgical extirpative management of head and neck cancer requires critical assessment and meticulous correction of both aesthetic and functional deficits to optimize the physical and psychological well-being of the patient. Unique to head and neck cancers is the potential alteration of one's senses, breathing, speech, and swallowing functions, as well as overall head and neck aesthetics. When possible, tissue defects are replaced

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_8

with similar tissues, though donor sites may be anatomically local, regional, or distant. The "reconstructive ladder" provides a heuristic approach to restoring the functional and aesthetic integrity of the head and neck cancer patient. Local tissue-rearrangement, grafts, flaps, and prosthetics are all options in the armamentarium of the reconstructive surgeon. The aim of this chapter is to familiarize the reader with the aims of reconstructive surgery, techniques employed to restore form and function as well as challenges and outcomes.

Keywords
Head and neck reconstruction · Cancer reconstruction · Flaps
Tissue transfer · Microvascular surgery

8.1 Background

The first task of the reconstructive surgeon is to define both the defect to be reconstructed as well as the goals and priorities of reconstruction. Removing a tumor of the mandible may require reconstruction of the bone and oral lining. Extirpation of a maxillary tumor may leave a defect of the orbital floor and/or oral roof. A neoplasm that invades the skull base may leave exposed dura. Compromises are sometimes required to achieve wound closure, while optimizing functional rehabilitation and minimizing aesthetic concerns.

Once the defect has been created, the surgeon then establishes priorities, which typically include (1) repairing and covering any exposed dura, especially when in proximity to the nasal cavity, (2) providing rigid support to the orbital contents, (3) providing bone to the maxilla and mandible to allow dental rehabilitation and mastication, (4) replacing soft tissue (bulk), mucosa, and skin (lining) for restoration of both function and aesthetic appearance, (5) covering vital structures in the face and neck, (6) restoring the integrity of the aerodigestive tract to allow normal respiratory function, oral continence, and deglutition, (7) restoring animation after sacrifice of mimetic motor nerves and/or muscles, and (8) providing tissue support for any anticipated prostheses (e.g., ocular, nasal, palatal, auricular).

Once the goals and priorities of reconstruction are established, potential donor sites are evaluated. Patient factors, such as limited cardiopulmonary reserve or peripheral vascular disease may influence the choice of operations offered. As with any surgical endeavor, the risks and benefits of each option need to be considered and discussed with the patient. Imaging studies are often employed to help in decision-making, particularly when patient comorbidity increases the risk of certain procedures. For example, a CT angiogram of the lower extremities may be obtained when considering a free fibula flap to reconstruct the mandible in a patient with abnormal vascular exam findings [1]. The presence of three-vessel runoff below the popliteal artery would reassure the surgeon that removing the peroneal artery in a fibula free flap harvest is unlikely to cause distal limb ischemia.

While tissues are ideally replaced with *like* autologous tissues, occasional deviations may be in the patient's best interest. The reconstructive armamentarium includes alloplastic or metallic meshes, plates, and/or customized prosthetics. Choice of reconstruction and rehabilitation technique depends on both the defect and patient factors, and must be individualized on a case-by-case basis. Reconstruction must not add the undue risk of morbidity or mortality. Two different patients having a partial mandibulectomy are not necessarily reconstructed in exactly the same way; a healthy patient might be offered a vascularized bone flap to optimize healing and dental rehabilitation while the frail patient with end-stage renal disease might be better served with a local muscle flap and a reconstruction bar to shorten surgical time and minimize the risks of prolonged recovery and rehabilitation.

The "reconstructive ladder" is a heuristic approach to reconstruction, and illustrates the idea that the simplest and safest approach to a problem (i.e., the lowest "rung") is frequently the preferred solution [2]. When that solution fails to achieve the goals of reconstruction, the next higher "rung" on the ladder is considered. For example, a simple skin defect should be closed primarily when possible and if it does not lead to unacceptable functional or aesthetic issues. (One could argue that an even lower "rung" on the ladder is *allowing a wound to heal by second intention*, which, as in the example of a medial canthal skin defect, might actually lead to a better aesthetic result). Proceeding up the ladder, when simple closure of a wound is not possible, a local skin flap or skin graft should be considered. Should that not suffice, a local/regional flap would be entertained. When that option is deemed inadequate, free tissue transfer with microvascular anastomoses could be employed. Whatever technique is ultimately chosen, the surgeon should have one or more "back-up" plans for reconstruction should intra-operative circumstances change.

As the technology evolves, an even higher "rung" could involve allograft tissue transplants or engineered tissues. While tissue transplantation in head and neck reconstruction has been proven feasible, there remain ethical, technical, and economic limitations to its widespread use [3]. Due to the potential ramifications of immunosuppression in cancer patients, a history of malignancy is considered a contraindication to allotransplantation.

The terms "graft" and "flap" are not interchangeable. A *graft* is a quantity of tissue transferred from one part of the body to another without its own blood supply. A graft requires ingrowth of a new blood supply from surrounding tissue in order to "survive" the grafting process. Grafts may be from the same individual (*autograft*), a same-species donor (*allograft*) or tissue from another species (*xenograft*). Autografts are by far the most commonly utilized, though allografts are sometimes used (e.g., acellular dermis and demineralized bone are commercially available allografts).

A *flap*, contrastingly, is tissue transferred with its own supporting vessels. Flaps that are moved without disrupting their blood supply are called *pedicled* flaps. Examples include the pectoralis major muscle flap which can be raised and mobilized on its own vascular pedicle for inset into the oral cavity. On the other

hand, *free* flaps are flaps that are transferred by transection and release of their vessels at the donor site. These flaps require attachment to vessels at the recipient site to reestablish flow using microvascular techniques. There are many types of flaps and each can be classified by the tissue being transferred. Common types of flaps include skin (*cutaneous* flaps), skin + fascia (*fasciocutaneous* flaps), skin + muscle (*myocutaneous* flaps), bone + skin (*osteocutaneous* flaps), and bone + muscle + skin (*osteomyocutaneous* flaps). Flaps that involve multiple tissue types (e.g., bone, muscle, and skin) are often referred to as *composite* flaps. Examples include the radial forearm flap which is commonly used to repair floor-of-mouth and tongue defects. *Perforator* flaps are a subtype of free flaps whose blood supply comes from separately identified branches of a named nutrient vessel [4]. Free tissue transfer has revolutionized reconstructive surgery, giving the surgeon the ability to replace sizeable amounts of tissue or to close difficult wounds when locoregional tissues are inadequate. Experience in head and neck reconstruction and microsurgical technique is critical to ensure good outcomes when this option is employed.

8.2 Evaluating Reconstructive Options

When discussing reconstruction, it is helpful to classify techniques by anatomic area and tissue type. Each area of the head and neck has its unique functional and aesthetic concerns and typical approaches used to address them.

8.2.1 Skin, Mucosa, and Soft Tissue

Skin defects require thoughtful planning to achieve restoration and scar camouflage with minimal to no disruption of adjacent facial aesthetic units (Fig. 8.1). The major facial units are the forehead, eye/brow, nose, lips, cheek, and chin. Millard and others emphasized that when the majority of an aesthetic unit is to be reconstructed, a better aesthetic result often accompanies reconstruction of the entire unit rather than just the damaged portion [5].

Repairing a defect of the skin or mucosa may be as simple as primarily closing the wound. Larger defects, or those bordering structures that may be distorted by primary closure, require a more thoughtful approach. As an example, a wound following removal of a skin cancer close to the lid–cheek junction may be reconstructed with the wide mobilization of adjacent tissue to achieve tension-free closure in a manner that does not cause an ectropion of the lower eyelid. The well-vascularized facial skin is ideal for raising large flaps to repair wounds, as in the Mustardé cheek advancement flap (Fig. 8.2).

The reconstructive surgeon should be familiar with local skin flaps that borrow skin from areas of less tension, or redistribute skin tension, in order to minimize distortion of adjacent structures (Fig. 8.3). Although the details of all described types

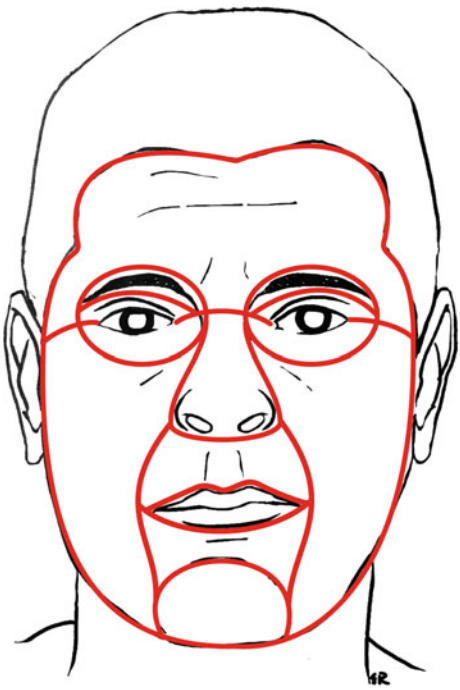


Fig. 8.1 The major aesthetic units of the face

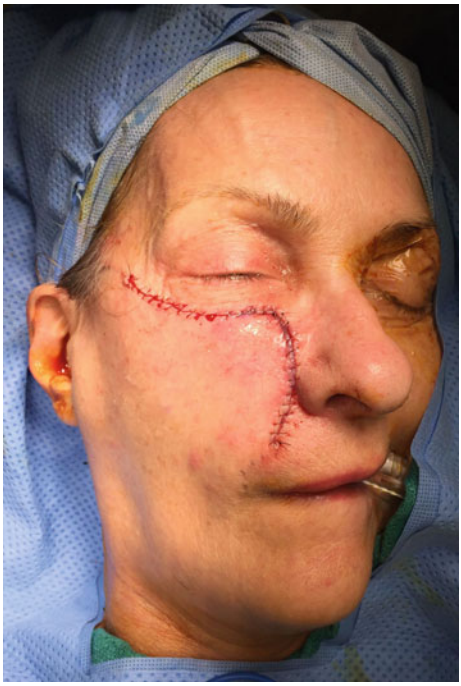


Fig. 8.2 Cheek advancement flap used to reconstruct a cheek skin defect after Mohs surgery for skin cancer

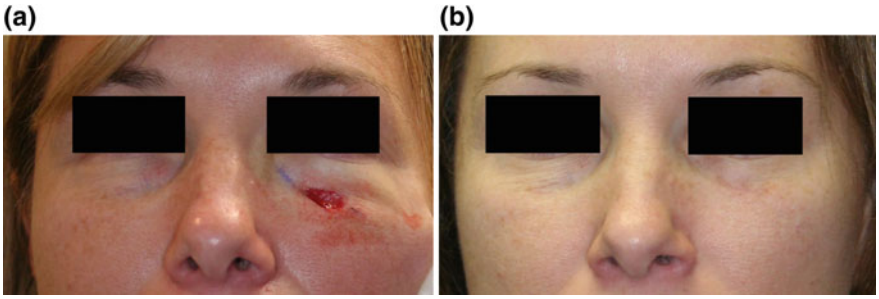


Fig. 8.3 **a** A lid–cheek junction skin defect—before primary repair along skin tension lines to minimize visibility of scars and distortion of the lower eyelid, **b** the same patient after healing is complete

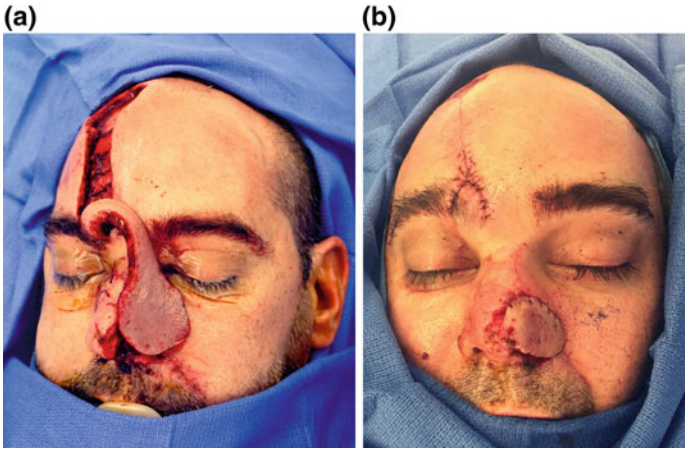


Fig. 8.4 **a** A paramedian forehead flap raised to repair a defect of the left ala and nasal sidewall, **b** the same patient at the time of flap pedicle division, with the blood supply to the flap now provided by the recipient site, and **c** late follow-up after scar revision and cartilage graft for alar support

of skin flaps are beyond the scope of this chapter, the most commonly employed tissue-rearrangement schemes are classified as *advancement*, *bipedicle*, *transposition*, *rotational* and *rotation-advancement* flaps. Local tissue-rearrangement may also involve techniques such as the Z-plasty, the A-T plasty, the M-plasty, the H-plasty, among other "plasties". While most skin flaps utilize a *random* blood supply, *axial* flaps are skin flaps with a known blood supply (or *pedicle*) that facilitates transfer of the skin to more distant areas by mobilizing the attached vessels [6]. The forehead flap, similar to the design used in ancient India, is a classic example of an axial flap used in head and neck reconstruction, and finds its greatest utility in nasal reconstruction (Fig. 8.4). The donor site can sometimes be primarily

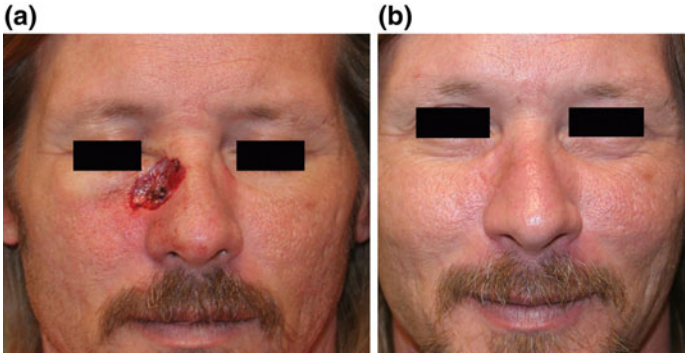


Fig. 8.5 **a** A skin defect following Mohs surgery for skin cancer, **b** the same patient 2 months after full-thickness skin grafting (neck donor site)

closed, or allowed to heal by second intention with remarkably acceptable aesthetic results.

When local skin is inadequate to achieve wound closure, the surgeon must choose a different approach. Although tissue expansion is used in head and neck reconstruction, it requires multiple stages and prolongs recovery. It is often best suited to allow revision of skin-grafted areas, in patients who are not candidates for free tissue transfer procedures, or in facilitating restoration of hair-bearing skin to areas of the scalp after another reconstructive procedure.

Skin grafts, either full or partial thickness, are sometimes used in head and neck reconstruction (Fig. 8.5). Donor skin should match the color and quality of the missing skin when possible. Suitable full-thickness skin graft donor sites for small defects of the face include the base of neck, upper chest, subclavicular skin, upper eyelid, and pre- or post-auricular skin, all of which can potentially be primarily closed after graft harvest. Skin from more distant sites may not provide as acceptable a color or texture match.

Large and deep defects of the head and neck soft tissue may require pedicled flaps or free tissue transfer. For thin but large defects, a free radial forearm flap (usually harvested from the non-dominant upper extremity) can be very useful. Deeper defects, especially when large spaces such as the maxillary sinus need to be filled, are better reconstructed with bulkier flaps such as the rectus abdominis myocutaneous flap or an anterolateral thigh fasciocutaneous (ALT) flap. It should be noted that flaps that transfer muscle without accompanying motor innervation will predictably lose bulk over time as the muscle atrophies [7]. This is in contrast with flaps consisting solely of skin, fascia, and fat, which tend to maintain their bulk (for better or worse). Secondary procedures to "thin" bulky flaps are sometimes needed to correct this issue.

A pedicled pectoralis major muscle or myocutaneous flap based on the pectoral branch of the thoracoacromial artery may provide sufficient bulk as well as coverage of bone and critical structures of the neck and the lower margin of the oral

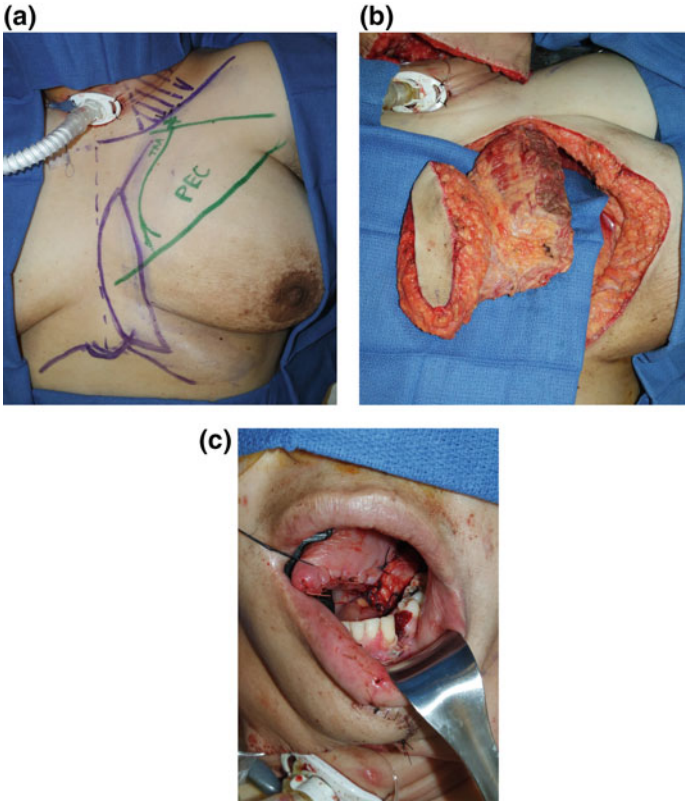


Fig. 8.6 **a** A pectoralis major myocutaneous flap planned for reconstruction of a floor-of-mouth defect after removal of a squamous cell cancer, **b** after flap elevated, and **c** following flap inset

cavity (Fig. 8.6). However, this flap has a bulky pedicle that leaves a lump over the clavicle with some distortion of neck contour to be expected.

8.2.2 Scalp

An ideal scalp repair avoids visible alopecia and may be achieved with local scalp advancement and/or rotation of primary closure. This approach is ideal for smaller soft tissue deficits but requires elevating the full thickness of the surrounding soft tissue: skin, fat, and galea. Because of the cranium's rigid convexity, small defects often require the wide mobilization of scalp flaps to achieve closure, particularly near the vertex. The reach of scalp flaps can be augmented slightly by scoring the galea. When this is not enough, skin can be grafted directly onto galea or periosteum, or (when periosteum is absent) onto bone that has been burred down to a deeper layer of outer cortex. Scalp tissue expansion is sometimes performed in an

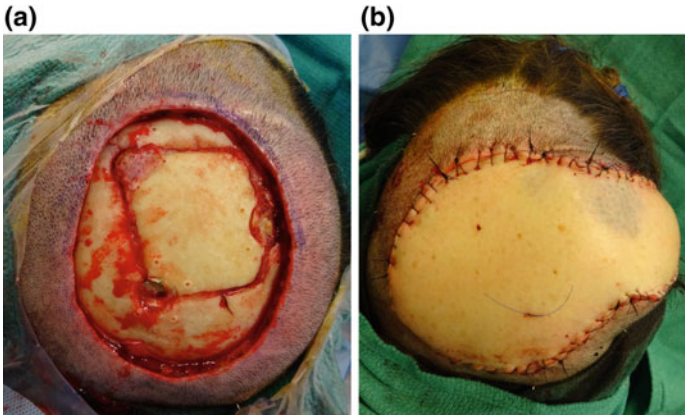


Fig. 8.7 **a** Full thickness scalp defect, **b** the scalp after reconstruction with a free anterolateral thigh (ALT) flap

immediate or delayed fashion to allow the advancement of hair-bearing scalp into wounds or previously grafted areas to restore a more natural appearance [8]. The introduction of engineered *dermal regeneration templates* has provided a way to enhance the durability of grafted scalps. One example is the use of Integra®, a bilayer collagen substrate, which is grafted directly onto a cranial defect. After the material has become vascularized a few weeks later, its occlusive outer silicone layer is removed and a skin graft can be applied [9].

When the defect is large or involves bone resection, the solution is often more complex. Bony defects can be covered with titanium mesh, with or without replacement of the cranial bone segment. Prosthetic materials and/or exposed bone require robust vascularized soft tissue coverage to minimize the risk of infection and hardware extrusion (especially if radiation therapy is planned). Free tissue transfer has become the mainstay of large scalp defect reconstruction [10]. The anterolateral thigh (ALT) flap has become a popular choice for large scalp defects [11], as shown in Fig. 8.7. Pure muscle or omental flaps require skin grafts to complete the reconstructive effort. Intermediate-sized defects may be reconstructable with either radial forearm fasciocutaneous or rectus abdominis myocutaneous flaps. The superficial temporal and occipital vessels provide the most accessible recipient vessel choices.

8.2.3 Skull Base, Paranasal Sinuses, and Orbit

Major tumor resections that involve the orbit, sinuses, or skull base require special consideration. Exposed dura, for example, should be separated from the nasal cavity and sinuses using pericranial flaps or with a free flap. When orbital contents are preserved but the orbital floor is resected, some form of support is required.

Typically this is accomplished with either a free osteocutaneous flap or a bone graft covered with a free soft tissue flap [12]. As with bone grafts, prosthetic materials such as titanium mesh require healthy vascularized tissue coverage to minimize the risk of implant exposure. In cases of orbital exenteration, pre-operative consultation with an ocular prosthetist may be helpful. A thin fasciocutaneous flap or skin graft in the orbit is superior to a bulky flap for the support of a prosthesis.

8.2.4 Hypopharynx and Cervical Esophagus

The primary goal of pharyngeal, hypopharyngeal, and esophageal reconstruction is to restore oral alimentation, ideally within 2 weeks of tumor extirpation. Small, superficial defects involving only mucosa can often be closed primarily or allowed to heal secondarily without any further intervention. Full thickness defects of the pharyngeal wall, if not amenable to primary closure, may require a regional myocutaneous flap, such as the pectoralis major pedicled flap, or a free flap [13]. Because these procedures necessitate disruption of the upper aerodigestive tract, the possible need for a temporary tracheostomy and nasogastric or gastrostomy tube should be anticipated and performed concurrently.

Laryngectomy sometimes involves removal of a portion of the hypopharynx. Partial defects may be patched or reinforced with a pedicled pectoralis major myocutaneous flap or a small free fasciocutaneous flap, such as the radial forearm flap. Wider resections, involving the full circumference of the hypopharynx, necessitate an evaluation of the length of segmental loss. Short segments are reconstructable with either a tubed fasciocutaneous flap (radial forearm or anterolateral thigh in thinner patients) or a length of free jejunum. When an esophagectomy results in a longer segmental defect, a gastric transposition or "gastric pull-up" may be necessary to restore continuity with the upper alimentary tract.

Less reliable but occasionally used local flaps include the supraclavicular artery flap, which is a pedicled fasciocutaneous flap based on a branch of the transverse cervical artery that originates close to the base of the lateral neck [14]. Because the vascularity of the supraclavicular flap is random toward the tip, this option is more commonly used in salvage procedures, for example, to help repair leaks following prior pharyngeal repairs or to cover skin defects of the neck and lower face.

8.2.5 Oral Cavity and Mandible

The goals of oral reconstruction are multiple: restoration of speech, oral continence, tongue mobility, dental occlusion, mastication, deglutition, airway protection, as well as avoidance of nasal regurgitation. Support of the labial skin in addition to maintenance of the lower facial height and chin prominence are key aesthetic objectives in reconstruction.

Small mucosal defects, as in the case of cutaneous wounds, may be allowed to heal secondarily or repaired primarily. For deeper defects, adjacent tissue transfer

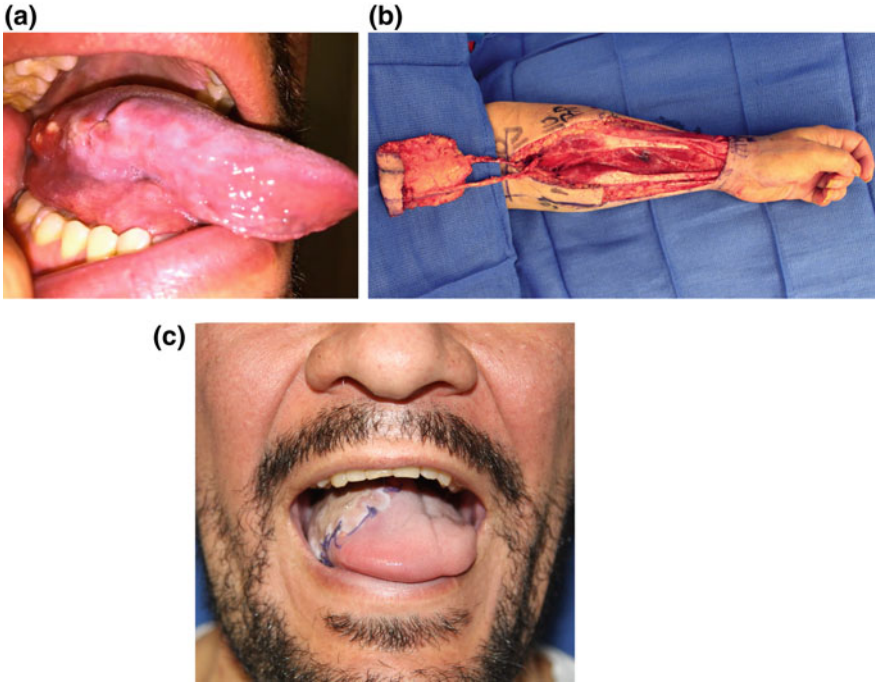


Fig. 8.8 **a** Squamous cell cancer of the tongue, **b** radial forearm free flap elevated, and **c** same patient 1 month after flap reconstruction

may be needed, e.g., using the *facial artery musculomucosal* (FAMM) axial flap. Moderate-sized superficial mucosal defects that only require lining over vascularized tissue (such as the tongue or floor-of-mouth) will sometimes be covered with split-thickness skin grafts. More complex or larger defects, especially those that connect with other cavities (e.g., sinuses, nasal cavity, skull base) typically require free tissue transfer. The radial forearm free flap is commonly used to provide oral lining for shallow defects, such as those following glossectomy, or resections of the palate, pharynx or floor-of-mouth (Fig. 8.8).

As described previously, the pectoralis major muscle is a workhorse flap for neck and oral reconstruction. When a skin paddle is included, the flap provides epithelial lining for oral floor defects or mandible coverage. This bulky muscle can be useful in obliterating neck and submental dead space and in providing a reliably well-vascularized wound bed where healthy tissues are otherwise scarce. Typical applications are a primary reconstruction of floor-of-mouth defects and secondary reconstructive or salvage procedures (e.g., following resection of an orocutaneous fistula after radiation). It is also helpful for protecting an exposed carotid artery, shielding vessels from potential salivary fistula, and separating laryngectomy stomas from large vessels.

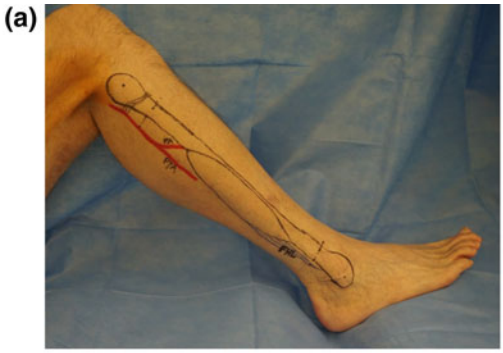
Marginal mandibulectomy (i.e., resection of the lower alveolus) typically only requires soft tissue coverage. Segmental mandibulectomies, in contrast, usually require some sort of bone reconstruction. For short segments (bone defects less than 6 cm), a bone graft secured with plates and screws may be sufficient to restore mandibular integrity. Non-vascularized bone grafts heal more slowly and are more susceptible to infection, nonunion and fracture compared with vascularized bone. Longer segments typically require a composite free flap, such as a fibula osteocutaneous flap (Fig. 8.9), arguably the best choice for total or subtotal mandibular reconstruction [15]. Many reconstructive surgeons now utilize 3D computer modeling to plan the bony reconstruction. Thin slice CT images are used to create cutting guides that help determine exactly where to perform osteotomies (in both the fibula and the mandible), so that the fibula segments fit together precisely and bridge the mandibular defect in a predictable manner. Some knowledge of the predicted extent of bone resection is needed for 3D modeling to work as intended. 2D templates generated from 1:1 reproductions of axial and sagittal views of the mandible are helpful in making accurate angled cuts in the fibula once the defect has been created. Figure 8.9b illustrates these 2D and 3D templates used in mandible reconstruction.

Other options for mandible reconstruction include the radial forearm osteocutaneous flap (best suited to short segments due to limited bone stock), the scapular osteomyocutaneous flap, or the iliac crest osteomyocutaneous flap [16] (which has a natural curve but can be quite bulky) as shown in Fig. 8.10. Replacing bone is most critical for anterior mandibular defects; in some circumstances, body defects are reconstructed with hardware and soft tissues alone. There is some debate about what type of plating is best for mandibular reconstruction, and whether to utilize mandibular-maxillary fixation during the acute healing phase [17, 18]. Dental implants require solid vascularized cortical bone, which may be one consideration when choosing a reconstructive option following partial mandibulectomy [19].

Maxillary alveolus resections seldom require bony reconstruction as dentures will often serve as a satisfactory substitute for dental rehabilitation. Free tissue transfer is mainly beneficial for the purpose of obliterating communication between the oral and nasal cavities, sometimes in conjunction with a palatal obturator. Bulkier flaps suited to this purpose include the ALT and rectus abdominis muscle or myocutaneous flaps.

8.2.6 External Ear

The auricle is one of the more common locations for skin cancers and thus is frequently subjected to resections of all sizes and thicknesses. The shape of the external ear provides both unique challenges and advantages in reconstruction. Lesions inside the helical rim may be excised as wedges, sometimes with Burow's triangles to facilitate closure. Outer helical rim excisions may be repaired with primary closure, wedge excisions (Fig. 8.11), rim advancement procedures, or the more extensive Antia-Buch advancement [20]. It should be noted that the overall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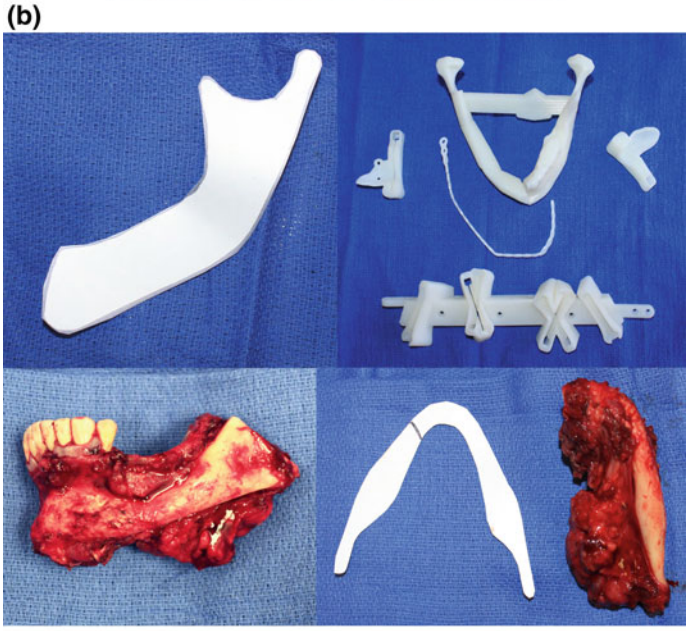
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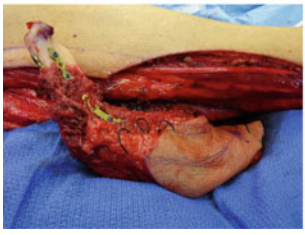
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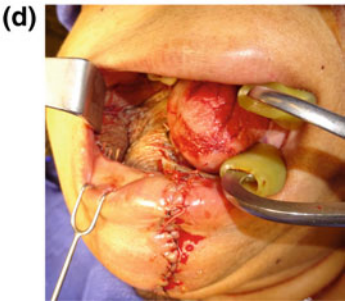
(d)

◀ **Fig. 8.9** **a** Planning reconstruction of a hemi-mandibulectomy using a free fibula composite (skin, muscle and bone) flap, **b** multiple types of templates can be generated from pre-op radiographic studies and used to assist in harvesting and shaping the fibula. The flat templates are generated using 1:1 lateral and coronal views of the mandible. The 3D printed model and cutting guides (upper right) are made from CT images of the face and fibula, **c** the fibula is cut, shaped and plated while still connected to its blood supply, and **d** after flap inset

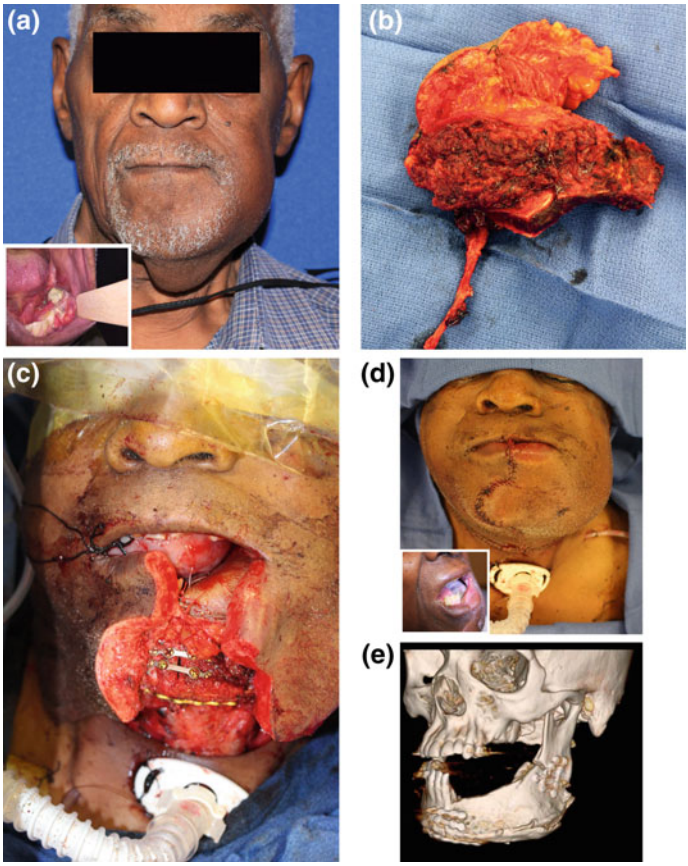

Fig. 8.10 **a** A patient with an oral cancer involving the mandible and floor-of-mouth, **b** an iliac crest composite (skin, muscle, and bone) flap harvested, **c** following inset of the bone with mini reconstruction plates, **d** after skin closure (inset shows skin paddle in the mouth several weeks later), **e** 3D computed tomography scan showing the iliac crest bone flap in situ

height of the ear can be reduced to a significant degree without noticeable aesthetic deformity. When skin is removed and underlying perichondrium left intact, skin grafts may provide a simple and aesthetically acceptable solution. Small degrees of skin undermining and closure under moderate tension are well tolerated, but excessive tension may result in buckling of the auricular cartilage and a "cup ear"

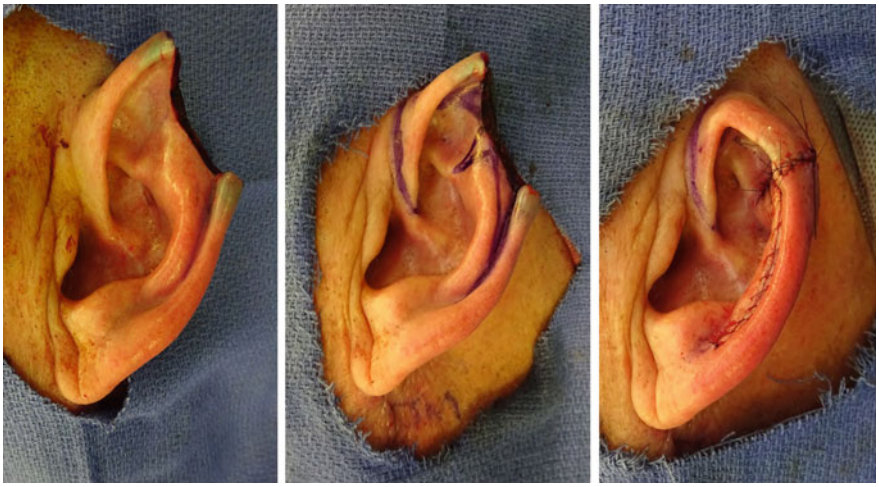

Fig. 8.11 A patient with squamous cell skin cancer removed from the upper third of the helical rim, repaired with wedge excisions and helical advancement

deformity. Because the underlying cartilage defines the shape of the ear, attention should be paid to ensuring that cut and mobilized cartilage is properly repaired. When needed, cartilage grafts may be obtained from the contralateral ear or from distant sites such as the ribs [21].

More central defects of the ear or those resulting from the excision of larger surface areas can frequently be reconstructed with local mastoid skin flaps. Because they are relatively hidden behind the auricle, the donor site of these flaps can be skin-grafted without aesthetic concerns. When the majority of the ear is excised, reconstruction becomes more problematic. A total ear reconstruction can be accomplished with a skin-grafted temporoparietal fascia flap wrapped around a carefully planned framework of cartilage or porous polyethylene [22]. However, an auricular prosthesis attached to the cranium by an osseo-integrated anchor will often provide a superior aesthetic result over autologous reconstruction.

8.2.7 Nose

Sometimes described as the focal point of the face, much attention has been paid to reconstructing the nose. There are more textbooks and treatises on nasal reconstruction than any other facial aesthetic unit. As with other facial reconstructive challenges, the two goals are the preservation of function (i.e., breathing) and restoration of appearance. The nose requires an inner lining, strong structural support, and durable external coverage. Partial reconstruction should follow the rules of aesthetic subunits discussed previously. Local skin and soft tissue flaps that

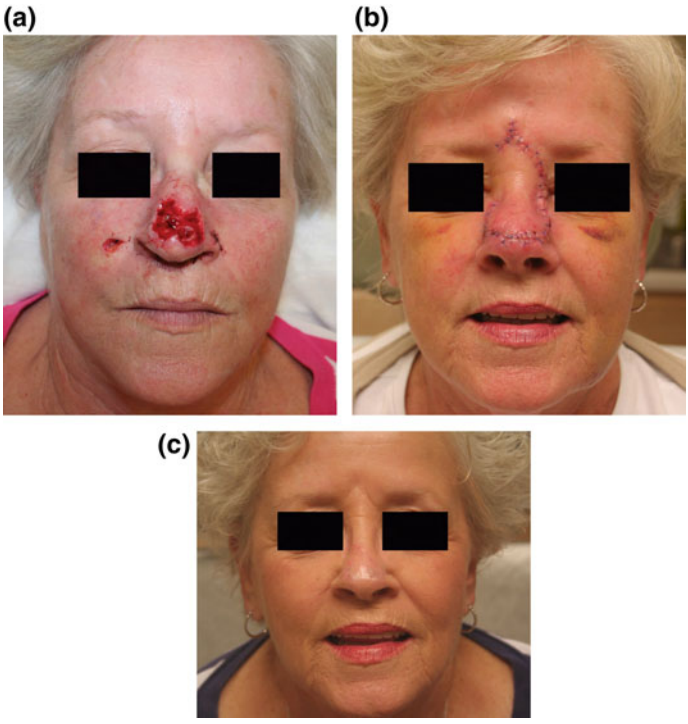

Fig. 8.12 **a** A large defect of the nasal tip and dorsum following skin cancer removal, **b** one week after an axial frontonasal flap used in reconstruction, and **c** same patient 3 months later

may be helpful include nasolabial flaps, septal mucosal flaps, and the forehead flap. Superficial defects of the nose can be repaired as described in the previous section on the skin and soft tissue reconstruction (Fig. 8.12).

For total or subtotal nasal reconstruction, support of the external nasal envelope will require rigid tissue such as bone or cartilage. A cantilever rib graft secured to the nasal radix with or without a columellar strut of similar tissue serves this purpose. Inner nasal lining may come from septal mucoperichondrial flaps, skin grafts or from flap skin that is turned inside upon itself. A thin fasciocutaneous free flap, sometimes combined with a forehead flap, may be needed to bring sufficient epithelium for both lining and external coverage [23]. The radial forearm flap is suited to this purpose because of its thin pliable quality and a long vascular pedicle. The facial or superficial temporal artery and vein are used most often as recipient vessels for these free flaps.

When autologous tissues are insufficient, the anatomy is unfavorable, or patient factors make extensive reconstruction untenable, nasal prosthetic devices should be considered. Single or multiple aesthetic units (e.g., nose, cheek, and periorbital area) can be covered with an external silicone prosthesis designed using 3D modeling and anchored to the maxilla with osseointegrated anchors. Disadvantages

of prosthetics include limited durability of these devices, lack of animation, and potential for complications related to the bone anchors.

8.3 Caveats and Controversies

Reconstruction of the head and neck cancer patient requires careful patient assessment and reconstructive planning for success. Pre-operatively, the need for ancillary supportive measures such as tracheostomy and feeding tubes should be anticipated. Difficult airway access and/or suboptimal airway patency should prompt a temporary tracheostomy. The patient's overall health with careful attention to cardiopulmonary reserves and any peripheral vascular disease will impact the choice of reconstruction. A history of trauma, previous surgery, radiation therapy, and any comorbid conditions such as poorly controlled diabetes or collagen vascular disorders should also trigger a closer study of both donor and recipient sites.

A careful assessment of a patient's psychological health, ongoing substance abuse issues, social support system, and likelihood of postoperative compliance should also be employed in the patient selection process for more complex and potentially morbid procedures. The need for adjunctive postoperative radiation therapy is common in head and neck malignancies; the effects of radiation should be considered when performing tissue reconstruction and potential secondary or tertiary procedures. Furthermore, radiation is most effective at locoregional control when employed in a timely fashion, so patients at risk for delayed healing may benefit from more conservative reconstructive options to minimize any delay in initiation of radiation therapy [24].

During the acute postoperative phase, close monitoring of free flaps by nurses trained in care of head and neck patients is mandatory, as timely recognition of compromised free flaps will increase the chance for successful flap salvage. Flap checks usually occur every 15–60 min for the first 24 h, becoming less frequent over the next few days. After about 5 days, the risk of flap loss becomes much lower [25]. Flap monitoring should include an assessment of the flap's color, turgor, capillary refill and blood flow. Arterial and venous blood flow can be evaluated using an external handheld Doppler or, when that is not possible or reliable, with an implanted Doppler, such as the Cook–Swartz Doppler Probe (Cook Medical, Bloomington, IN). Flaps with compromised venous outflow will often appear swollen, dark pink or purple, have a rapid capillary filling (less than 1.5 s) and bleed dark blood when pricked. Arterial insufficiency produces a pale flap with slow or absent capillary refill and bleed slowly or not at all when pricked. Nursing staff should be educated on signs of early flap distress and be instructed to contact the surgeon when concerns arise. Because every flap is different and staff experience in caring for these patients varies, the surgical team should engage postoperative nursing staff on what to look for, as a matter of standard practice.

Some surgeons prefer to use low-dose anticoagulants and antiplatelet agents during postoperative recovery to lower the risk of flap loss due to intravascular thrombosis. As an example, 30 mg Lovenox SQ BID plus Aspirin 325 mg once daily or Toradol 30 mg IV q6 × 5 days is a typical regimen. That said, there is little evidence to show that routine use of anticoagulation reduces flap loss after uncomplicated free tissue transfer. Similarly, the benefit of *prolonged* antibiotic prophylaxis following head and neck reconstruction has not been proven and remains controversial [26].

One issue not often discussed but frequently encountered when using a flap with a dermal component (and sometimes in the case of a full thickness skin graft) to replace missing mucosa is the presence of hair follicles. Hair growth continues in the transferred skin. Under some conditions, hair follicles can be removed with the help of lasers or electrolysis. Otherwise, tweezing or shaving may be necessary.

8.4 Complications

Problems after head and neck reconstruction can be minimized by anticipating potential complications and taking steps to avoid them. For example, with the abundance of oral flora bathing tissues exposed during oral reconstruction, wounds should be thoroughly irrigated to reduce the level of contamination and thus reduce the risk of postoperative infection. The choice of postoperative antibiotic prophylaxis is controversial, but both anecdotal experience and recent data suggest a short course of broad-spectrum antibiotic regimen may reduce infection rates [27]. Avoiding excessive tension and careful attention to tissue handling and suturing technique can reduce the risk of wound dehiscence and orocutaneous or pharyngeal fistula formation. Early recognition of such problems followed by appropriate imaging, antibiotic optimization, and surgical management are paramount to preventing a bad situation from becoming much worse.

Ischemic tissues lead to wound breakdown and excessive scar formation. This, in turn, can contribute to stricture formation (in cases of pharyngeal reconstruction) or a poor aesthetic result when involving skin flaps. In the worst case, loss of entire tissue flaps may result from poor planning or use of flaps with unreliable blood supply. Flap monitoring as described previously can help identify a troubled flap while it is still salvageable. If early signs of impending flap failure are recognized and reported to the reconstructive team, the patient can quickly be returned to the operating room and the cause investigated. The most common cause of flap failure, especially in the early postoperative period is venous thrombosis, followed by arterial occlusion [28]. Venous thromboses have higher salvage rates than arterial causes, in part due to earlier detection (venous congestion in a flap is more obvious than ischemic changes). Whatever the cause, early exploration is key for flap survival. Warm ischemia survival time varies among types of flap tissues, but animal studies have found that after 4 h, fat and muscle begin to develop irreversible cell death [29]. Jejunum is even less tolerant of ischemia, with irreversible tissue loss starting around 2 h.

Possible reasons for early vessel thrombosis (within 48 h of surgery) include a hematoma compressing the vessels, poor quality recipient vessels (insufficient inflow or outflow), kinking of the pedicle due to twisting or anatomic position, as well as occult intimal injury. Late causes of flap failure include infection, tumor progression or patient-systemic factors such as hypercoagulability. At the time of re-exploration, the anastomoses are typically excised and revised after thrombectomy. Any technical cause for failure, such as vessel orientation or inadequate recipient vessel choice is addressed. Thrombolytics such as tissue plasminogen activator (tPA) are often used intra-operatively (especially in the presence of venous thrombosis) to help reestablish flow through the flap. Salvage rates vary from 28 to 90% in series of head and neck cancer reconstruction procedures [28].

When flap salvage is unsuccessful, a second-choice flap may need to be pursued. This choice depends mostly on the probability of success, and may include a free flap or a pedicled flap. Whatever approach is used, reconstruction should be completed in a timely fashion to avoid wound-related complications.

Excessively bulky flaps may cause obstruction of the aerodigestive tract or contribute to poor aesthetic results. In many cases, experience in selecting appropriate choices for given situations is the most predictive factor toward an ideal outcome. Having a back-up or salvage plan is critical to averting catastrophic results when the initial reconstructive effort fails.

8.5 Conclusions

From simple wound closure to microvascular tissue transfer, the reconstructive surgeon has a wide array of choices to consider when addressing oncologic defects. A combination of careful planning, patient selection, and experience in handling technical challenges are needed to achieve success, as in any complex and resource-intensive endeavor. With allotransplantation, tissue engineering, and other emerging technologies, science continues to push the boundaries of what is medically possible. With this change comes the need for the surgeon's expertise to expand, evolve, and accommodate.

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9 Radiation Therapy for the Head and Neck Patient: Advances, Challenges, and Perspectives

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_9

Abstract

Radiation therapy for head and neck malignancies has made remarkable advances in treatment technology, resulting in improved clinical and functional outcomes. It is necessary for the radiation oncologist to have a complex understanding of the patient's tumor and its relationship to the surrounding normal anatomy, in order to safely limit dose to normal tissues. Complications following radiation can be managed with timely intervention, usually on an outpatient basis. This chapter will discuss the technological advances in the field, the impact of human papillomavirus (HPV)-mediated disease on radiation treatment, efforts to limit dose to critical salivary and swallowing structures, and management of certain radiation-related toxicities.

Keywords

Radiation · IMRT · Side effects · HPV · Protons

9.1 Introduction

Radiation therapy for head and neck cancers is arguably the most challenging and sophisticated radiation treatment delivered to any anatomic subsite. Multiple studies have demonstrated that radiation quality and physician experience directly impact both locoregional control and overall survival in head and neck cancer (HNC) [1–4]. There have been substantial advances in radiation technology over the past two decades, including the development of intensity-modulated radiation and image guidance, leading to an improved acute and late toxicity profile of this treatment. This chapter provides an introduction to the basics of radiation techniques used in modern practice for head and neck cancers, and details some of the potential toxicities from treatment.

9.2 Intensity-Modulated Radiation Therapy

Intensity-modulated radiation therapy, or IMRT, is now considered the standard radiation treatment technique for HNC. IMRT allows highly conformal radiation dose distributions that minimize radiation doses to adjacent normal structures. Since

its introduction approximately 20 years ago, it rapidly gained widespread acceptance in the clinic, especially with HNC treatment planning. Prior to this, a technique known as three-dimensional conformal radiation therapy (3D-CRT) resulted in a significantly larger area of normal tissue adjacent to the tumor receiving the tumoricidal prescription dose. Examples of such normal tissue include the parotid glands and constrictor muscles. With IMRT, the tumoricidal dose is highly conformal to the tumor itself. This results in significant sparing of normal tissues. Lambrecht et al. [5] has shown significantly improved rates of xerostomia with IMRT compared to 3DRT. Dose coverage of the tumor itself is also superior with IMRT compared to 3DCRT, due to multiple beam angles being used, which has resulted in improved local-regional control (LRC) rates. In nasopharynx cancer (NPC), for example, single institution series report LRC at 4–5 years of approximately 90–97% [6, 7]. In patients with T4 disease, 5-year LRC has been shown to be 80% [8].

A randomized control trial of 60 patients comparing 3DCRT and IMRT demonstrated a substantial reduction in both acute (59% vs. 89%) and late patient-reported xerostomia rates with IMRT [9]. Subcutaneous fibrosis was also substantially reduced with IMRT. No significant differences were seen in the 3-year LRC or survival between the arms. Quality of life (QOL) data from this same trial showed improved scores in the IMRT versus the 3DRT patients [10].

In a large retrospective pooled analysis of patients treated on RTOG 0129 and 0522, Yao et al. compared the toxicity of those treated with 3DCRT versus IMRT [11]. IMRT was associated with a significant reduction of xerostomia at 1-year (grade 2–3 20% vs. 33%) and 2 years (grade 2–3 15% vs. 28%). IMRT patients were also less likely to have a feeding tube at 1 year (16% vs. 21%).

On the basis of the above data and multiple other reports, IMRT is the accepted technique for the treatment of head/neck cancer.

9.3 Radiation Treatment Design

The design of radiation treatments for HNC is complex, requiring a thorough understanding of the regional anatomy, patterns of spread, and radiation physics. In addition, the toxicity from radiation this area is relatively high, especially when delivered with concomitant chemotherapy. Because of this, National Comprehensive Cancer Network recommends all HNC patients be treated at centers with access to a full range of support services and “specialists with expertise in the management of HNC” [12].

The first step in radiation treatment design is a simulation. The purpose of a simulation is to develop a three-dimensional map of the patient’s anatomy in the exact position that they will be treated in each day. In order to accomplish this, the patient is immobilized in a custom-designed thermoplastic mask that limits motion of the head, jaw, and shoulders. In some cases, a device to immobile the tongue and physically separate it from the palate, known as a bite block, is utilized. Once the

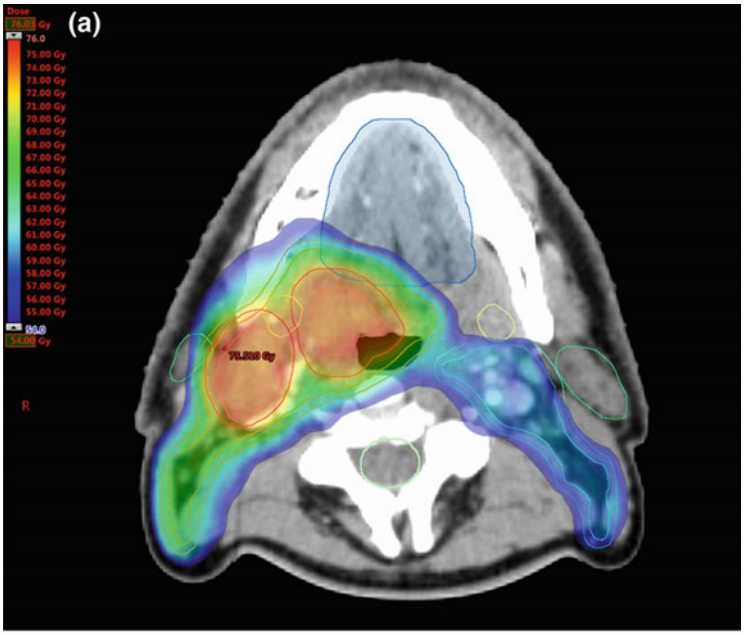
patient is properly positioned, a thin-slice CT scan, often with IV contrast, is performed. This scan is used for subsequent radiation planning.

After the simulation, the radiation oncologist needs to define the targets that will be treated, and critical normal structures that should be avoided. This process is known as contouring or target delineation. In definitive cases, the first step is defining the gross tumor volume (GTV) at both the primary site and any regional lymph nodes. The GTV is defined based on the CT simulation images, other pre-radiation imaging studies, clinical exam including flexible fiberoptic nasopharyngoscopy, and operative reports. In addition, separate imaging studies, such as PET-CT and MRI scans, can be rigidly or deformably fused to the CT simulation to aid in defining the GTV.

Next, several clinical target volumes (CTVs) are defined to account for potential sites of radiographically occult microscopic disease. Typically, the various CTVs encompass a margin around the GTV, areas surrounding the primary site that are known to be at risk for microscopic extension, and the draining lymph node basins, although each CTV can be treated to a different dose depending on if it considered high-, intermediate-, or low-risk of harboring disease. Finally, a planning target volume (PTV) is created, typically defined as an isotropic margin around the CTVs to account for small changes in patient positioning each day. The PTV is often 3–5 mm beyond the CTV. Radiation dose is ultimately prescribed only to the PTV.

As an example (Fig. 9.1), for a T2N2b tonsil cancer extending more than 1 cm onto the base of tongue and two level II lymph nodes, the radiation oncologist would draw GTV for the primary tumor and gross lymph nodes. These would then be expanded to create a high-dose CTV (usually 70 Gy). Then, two intermediate dose CTVs for the primary and nodal volumes are defined (usually treated to 54–63 Gy). The intermediate dose primary CTV includes a margin around the high-dose CTV and other structures at risk of microscopic spread, including the entire tonsillar fossa, the ipsilateral or entire base of tongue, the ipsilateral glossotonsillar sulcus, the ipsilateral soft palate, and the ipsilateral pharyngeal wall and parapharyngeal space to the skull base. In some bulkier cases, the intermediate dose primary volume can be extended out to include the retromolar trigone and pterygomandibular raphe, or down to the vallecula depending on the extent of base of tongue involvement. The intermediate dose nodal CTV includes ipsilateral cervical lymph node stations IB-V and the ipsilateral retropharyngeal lymph nodes, although some experts advocate sparing ipsilateral IB and V if radiographically negative based on modern surgical series showing infrequent involvement of these areas for oropharyngeal cancers (Sanguinetti IJROBP 2009). The low-dose CTV

Fig. 9.1 Comparison of **a** IMRT to **b** conventional radiation techniques. The GTVs are contoured ► in pink. The red lines represent PTV70, inner and outer orange lines represent CTV60 and PTV60, respectively, and the inner and outer cyan lines represent the CTV54 and PTV54, respectively. The color wash represents that actual calculated dose delivered. The IMRT plan is highly conformal, and minimizes dose to adjacent normal structures. Of note, the conventional radiation plan shown uses only photons. However, in clinical practice, midway through the treatment, posterior electrons fields would match to the photon fields in order to decrease dose to the spinal cord


(a)
Dose
76.03 Gy
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74.00 Gy
73.00 Gy
72.00 Gy
71.00 Gy
70.00 Gy
69.00 Gy
68.00 Gy
67.00 Gy
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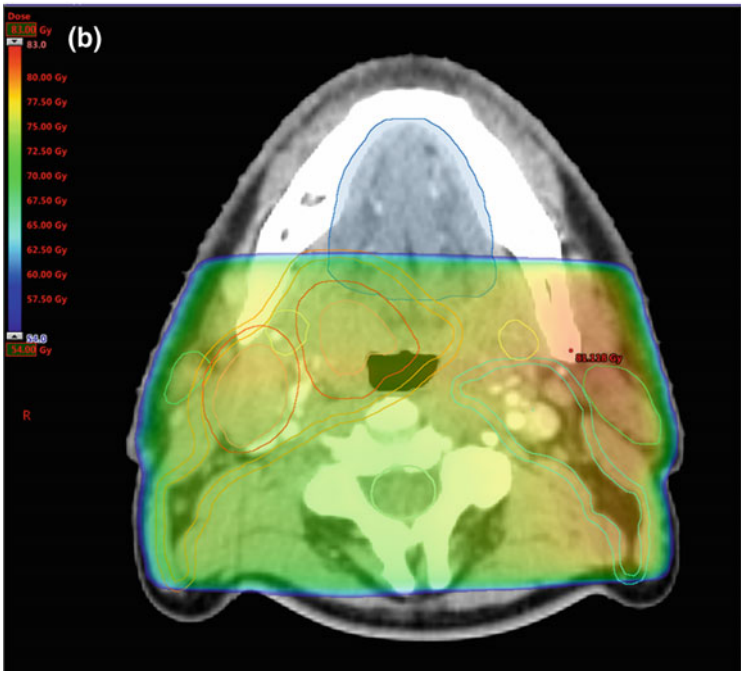

(b)
Dose
83.00 Gy
83.0
80.00 Gy
77.50 Gy
75.00 Gy
72.50 Gy
70.00 Gy
67.50 Gy
65.00 Gy
62.50 Gy
60.00 Gy
57.50 Gy
54.00 Gy
R

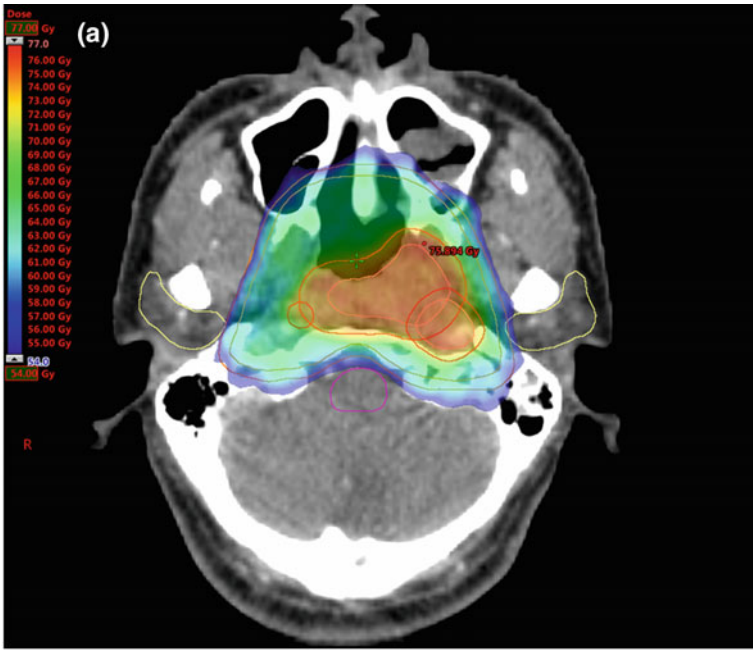
(usually treated to 50–54 Gy) includes the contralateral levels II–IV and the contralateral retropharyngeal lymph nodes. All CTVs would then be uniformly expanded to account to patient set up error to create final PTVs. Target delineation is unique for each anatomic site, and for each cancer (Fig. 9.2).

Following completion of target delineation, the radiation oncologist gives the dosimetrist or physicist specifications for both target coverage and normal tissue constraints. Typically, a maximum and minimum dose for each PTV is specified, and goals for minimizing dose to critical structures are stipulated. The dosimetrist or physicist then uses sophisticated inverse planning algorithms to determine the optimal orientation, shape, and intensity profile of each beam in order to most closely match the ideal plan specified by the physician. The process can take several weeks, and usually involves numerous iterations, including communication between the clinicians and planners in order to ensure that the proper trade-offs between the myriad of factors involved are being incorporated into the final plan.

9.4 Postoperative Radiation Design Considerations

Radiation treatment design is similar in many ways in postoperative and definitive cases. However, there are several differences in the postoperative setting that warrant discussion. There is typically no GTV following surgery, so the radiation oncologist can define the preoperative GTV and the operative bed as part of the CTV. As a general rule, anything manipulated surgically needs to be included in the postoperative CTV. Thus, although the tumor has been removed, the volume required for treatment is often larger in the postoperative setting than in definitive cases. The standard postoperative dose for all surgically manipulated tissue, including dissected cervical lymph node chains, is 60 Gy in 30 fractions. Generally, fraction sizes less than 2 Gy are avoided for surgically violated areas given the theoretical concern that these tissues are more hypoxic following surgery, and may be less sensitive to radiation. However, the undissected node-negative neck can be treated to 54 Gy in 1.8 Gy fractions if not dissected. In cases of very close/positive margins, or with extranodal extension, areas at high risk of harboring residual

Fig. 9.2 An IMRT plan for a patient with a cT3N3b nasopharyngeal cancer undergoing ▶ chemoradiation. The GTV's are contoured in pink. The red lines represent PTV70, inner and outer orange lines represent CTV59.4 and PTV59.4, respectively, and the inner and outer cyan lines represent the CTV54 and PTV54, respectively. This plan is delivered over 33 fractions using "dose-painting" (simultaneous-integrated boost) to deliver 2.12, 1.8, and 1.64 Gy per fraction. In this case, the entire nasopharynx, entire clivus, bilateral parapharyngeal space, bilateral pterygopalatine fossa, posterior maxillary sinuses, posterior nasal cavity, entire sphenoid sinus, bilateral foramen rotundum, bilateral foramen ovale, and bilateral cavernous sinuses are covered in the CTV59.4. In addition, the bilateral cervical and retropharyngeal lymph nodes are also covered. The dose color wash represents the calculated physical dose delivered to the patient each day. Daily cone-beam CT's are used daily for image guidance to ensure accurate setup, given the proximity of the tumor to the adjacent brainstem and optic structures


Dose
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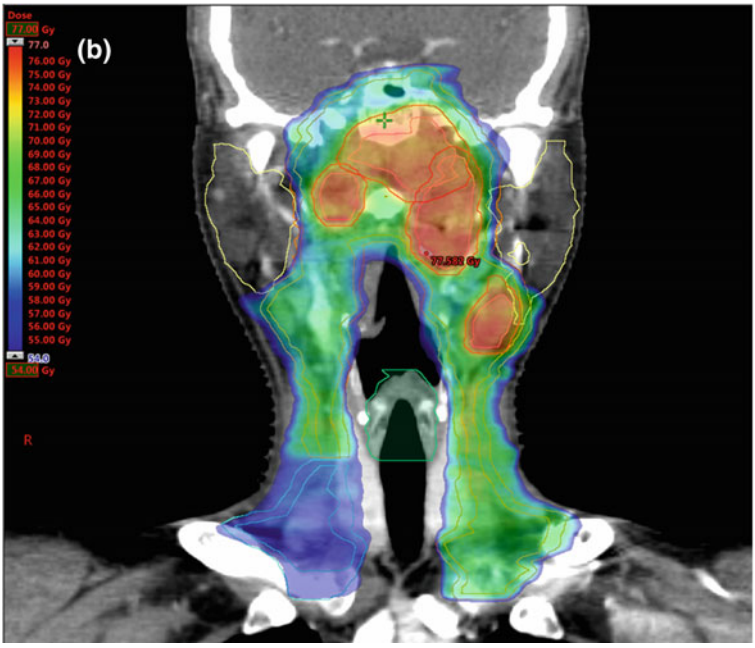
(a)


Dose
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(b)

microscopic disease are often boosted to 66 Gy in 33 fractions. The extranodal extension also can impact the treatment target. For example, if pathologic extranodal extension is noted, the skin around the scar can be treated to full dose using tissue equivalent bolus, and the entire underlying sternocleidomastoid muscle is included in the CTV.

In addition, the optimal time to start radiation following surgery is typically 4–6 weeks. Multiple studies have shown poorer local control and overall survival when the treatment package time, consisting of the time from surgery to the end of radiation, is prolonged [13]. This is presumably due to the phenomenon of accelerated repopulation, whereby cancer cell under duress will proliferate, leading to a higher tumor burden the longer treatment is extended.

9.5 Fractionation Patterns

Radiation treatment is typically administered daily for approximately 7 weeks. However, a variety of alternative schedules can be employed, including 6 treatments per week [14], twice a day treatment [15], or daily treatment for the first 18 days followed by twice daily treatment for the remaining 12 days [15], to name a few. These altered fractionation regimens are most commonly used when patients are not receiving concomitant chemotherapy [16, 17]. Altered fractionated regimens can have different purposes. Hyperfractionated treatment, typically referring to twice daily treatment, aim to minimize the individual fraction size in order to either dose-escalate or minimize late effects, which are known to depend on fraction size for late-responding tissues. Accelerated fractionation refers to given the same dose and fractionation over a short period of time (e.g., 6 fractions per week) in order to minimize the effect of accelerated repopulation. Hypofractionated regimens were given in a small number of large radiation fractions, and are typically used in the palliative setting.

9.6 Dose Delivery

Several techniques can be used to deliver different dose levels to the high-, intermediate-, and low-dose PTVs over the course of treatment. Patients can be treated using a sequential boost, or cone-down, technique, where fraction size of each day is constant, but the volume treated becomes progressively smaller as therapy progresses. An alternative technique uses simultaneous-integrated boost, or "dose-painting". In this technique, a single plan with multiple fraction sizes is delivered daily. Although this can simplify planning, a pure simultaneous-integrated boost plan will limit the range of maximum to minimum doses delivered to the target volumes. This is because radiation oncologists tend to favor fraction sizes between

approximately 1.6–2.0 Gy for head and neck cancer, which are thought to optimize tumor-killing efficacy while minimizing the risk of late toxicity from daily radiation. Therefore, in a 35 fraction simultaneous integrated boost plan, is possible to treat targets only from 56–70 Gy if a 1.6–2.0 Gy fraction size range is utilized. If a physician wanted to treat targets with doses ranging from 45 Gy to 70 Gy, for example, using a pure simultaneous boost technique, fraction sizes either larger than 2.0 Gy or smaller than 1.6 Gy would be necessary (e.g., 1.29–2.0 Gy in 35 fractions, or 1.6–2.5 Gy in 28 fractions). It is also possible to combine sequential and simultaneous-integrated boost techniques in a single plan in order to take advantage of the relative benefits of each technique.

9.7 Image-Guided Radiation Therapy

Image-guided radiation therapy, or IGRT, is a technique that involves obtaining detailed imaging of the patient's internal anatomy while on the treatment table. This information is obtained immediately prior to delivery of that day's treatment. It is known that there are day-to-day differences in positioning of the patient when compared to the original CT simulation position. In head/neck cancer, a custom rigid thermoplastic mask is used to immobilize the face, chin, neck, and shoulders of the patient. It is accepted that a mask setup can limit the motion of the patient to less than 5 mm. However, during the course of therapy, changes in body weight and tumor size can affect the daily reproducibility of the patient's setup, potentially impacting the accuracy of delivery. Reliance on bony anatomy alone with planar X-rays, is not sufficient to detect such changes. Cone-beam-computed tomography (CBCT) technology has been built into modern linear accelerators to allow for soft tissue imaging to be reviewed in the treatment position. Treatment table adjustments can then be made to modify the position of the patient to match the original simulation position in three-dimensional space, which allows for the use of decreased PTV margins given there is less uncertainty in patient setup.

How has IGRT made an impact in the clinic? Chen et al. [18] examined their outcomes in head/neck cancer patients who received IGRT and were treated with a 5 PTV margin around the clinical target volume (CTV), and compared these to patients treated with a 3 mm margin. No differences in overall survival or local-regional control were observed, and this was confirmed with more mature follow-up [19]. In addition, the 3 mm margin cohort had a significantly reduced risk for gastrostomy tube dependence at 1 year (3% vs. 10%) and esophageal stricture (7% vs. 14%) compared to the 5 mm group. In another retrospective analysis, Hsieh et al. reported a significantly improved 5-year survival rate in oral cavity cancer patients who received postoperative IMRT with IGRT compared to those received IMRT alone (87% vs. 48%) [20]. More patients in the IGRT cohort were able to complete the treatment in the prescribed time, and the rate of local failure in the IGRT group was also improved. These data give support to combining both IMRT

and IGRT in the treatment of HNC. The recommended form of IGRT is either kilovoltage (kv) or megavoltage (mV) CBCT to be performed on a daily basis prior to treatment.

9.8 Radiation Side Effects and Management

During radiation treatment, HNC patients experience significant side effects. Side effects are more severe when radiation is combined with chemotherapy. In a study of RTOG 95-01 adjuvant chemoradiation, the frequency of acute grade 3 (or more severe) toxicities was 77% in patients receiving chemoradiation versus 34% in patients receiving radiation therapy alone ($P < 0.0001$) [21]. The most frequent acute adverse side effects observed for chemoradiation are mucositis, dermatitis, hematological toxicities, and secondary infection. Late toxicities include xerostomia, soft tissue necrosis, and osteoradionecrosis. These side effects and late toxicities are managed by a multidisciplinary team.

9.8.1 Skin Reactions

After radiation, the skin may remain normal and pliable, or patients may experience a variety of acute skin reactions. Erythema can be treated with non-alcohol-containing creams, including Aquaphor, Miaderm, or pure aloe vera gel. Dry desquamation may be treated similarly. If a patient develops moist desquamation, use of a cream or ointment containing sulfonamide-based drugs, such as Silvadene, or application of foam dressings such as Mepilex products, may be helpful.

Submental edema (turkey gobbler) and/or lymphedema usually appear 4–6 weeks post treatment. The patient may also develop chronic fibrosis. These conditions usually respond to massage treatment, and referral to physical therapy is helpful.

9.8.2 Mucositis

To reduce the extent of mucositis, it is essential to carefully plan radiation treatment. Special attention must be paid to reduce radiation exposure to normal structures.

To minimize the impact of mucositis, good oral hygiene is encouraged. This includes gargling with a pinch of salt and baking soda 3–4 times a day; use of a soft toothbrush; use of a humidifier at night; and avoidance of spicy food, alcohol, or smoking. Once mucositis has developed, systemic opioids may be needed to effectively treat mucositis-associated pain, and close monitoring of nutrition and hydration must be offered.

Antifungal medication and antibiotics may also be required. If there is evidence of fungal infection, use antifungal medication, such as Mycelex Troche (clotrimazole; dissolve lozenge in mouth 5 times a day), Nystatin oral suspension (5 cc; swish well for 2 min and swallow 4 times a day), or Diflucan (fluconazole; 200 mg by mouth for first day, then 100 mg by mouth once a day for 7 days). Use of glutamine supplements may help reduce mucositis [22]. For oral mucositis, one can use Radiation Mixture ([79 mL 2% Lidocaine, 47 mL Benadryl, 345 mL Mylanta]; 1 tablespoon, swish and swallow before each meal and before bed time) or Miracle Mouthwash ([60 cc tetracycline oral suspension (125 mg/5 cc), 30 cc Mycostatin oral suspension (100,000 units/cc), 30 cc hydrocortisone (10 mg/5 cc), 240 cc Benadryl (12.5 mg/5 cc)]; 2 teaspoons, swish and swallow/spit four times a day).

9.8.3 Xerostomia

The incidence of xerostomia is directly related to the radiation dose to the salivary glands (mainly parotid and submandibular glands) and to the oral cavity. Intensity-modulated radiation therapy (IMRT) as a strategy for sparing the parotid glands may decrease both the occurrence and severity of xerostomia. Delivered doses lower than 24–26 Gy to the parotid glands seem to be crucial to preserve salivary flow rates after radiation therapy [23]. Every attempt should be made to limit exposure of the submandibular glands and uninvolved oral cavity mucosa to less than 30 Gy.

Patients should be followed by a dietitian to ensure they receive sufficient protein and calories. It is common to consider gastrostomy feeding tube placement if a patient loses more than 10% of initial body weight.

Prior to the start of radiation treatment, patients should be evaluated by a dentist. A pretreatment discussion between the radiation oncologist and dentist may be extremely helpful to address management of teeth that will receive high radiation doses. Any teeth that require an extraction should be removed before the start of treatment to prevent complications such as osteoradionecrosis or non-healing ulcer. Post treatment patients should also be followed by a dentist for regular checkups and for prophylactic prescription fluoride treatment.

9.8.4 Soft Tissue and Joint Stiffness

It is important that patients are seen by the rehabilitation department prior to, during, and post treatment, particularly to manage and prevent trismus and neck stiffness from radiation fibrosis.

9.8.5 Soft Tissue Necrosis

With improved surgical and radiation techniques, patients with HNC are achieving better organ and functional outcomes. As clinicians, it is important to continue to reduce treatment-related morbidity. Several studies have shown the feasibility, safety, and promising oncologic results of using transoral robotic surgery (TORS) [24]. In selected high-risk groups of patients, adjuvant radiotherapy or concurrent chemoradiotherapy (CCRT) after TORS is recommended to improve local control and overall survival.

However, soft tissue necrosis (STN) has been reported at the site of TORS surgery when followed by postoperative radiation treatment (PORT). Radiation-induced mucositis is typically resolved through the body's regeneration process, which requires proliferative stem cells and vascular and connective supplies. However, TORS or wide excision (WE) without reconstructive surgery may cause disruptions to the lymphovascular supply and injuries to connective tissue, along with the reduced repopulation of stem cells in surgical beds. This can result in unexpected complications, such as STN, after PORT [25].

Lee et al. [26] reviewed their experience with 67 HNC patients evaluated for STN, which was defined as ulceration and necrosis of the surgical bed with pain, after PORT with or without chemotherapy. STN developed in 13 HNC patients (19.4%). STN incidence in oropharyngeal cancer patients was even higher (23.4%). STN risk factors were depth of invasion >1.4 cm and maximum dose per fraction >2.3 Gy. Lukens et al. [27] also described an incidence of STN of 28% in TORS patients who received PORT with or without chemotherapy. Risk factors included tonsillar location, depth of resection, radiation dose to the surgical bed, and severe mucositis. STN risk was significantly decreased by carefully avoiding a radiation dosage of >2 Gy maximum dose per fraction to the surgical bed.

Comorbidities such as diabetes and hypertension [28] are also risk factors for the development of soft tissue necrosis.

Treatments for STN include: adequate pain management; cessation of tobacco use (if not already achieved prior to irradiation); high protein nutritional intake; and trial of vitamin E, pentoxifylline, and chlorhexidine rinse. If this regimen does not relieve STN, and if the patient does not have residual cancer, hyperbaric oxygen treatment can be considered. However, identifying the presence of residual cancer can be challenging, and requires biopsy under anesthesia. Furthermore, the use of hyperbaric oxygen treatment is controversial, as some clinicians believe it can promote cancer regrowth.

9.8.6 Osteoradionecrosis

Osteoradionecrosis (ORN) is defined as exposure of the mandibular bone in the absence of improvement following conservative treatment. Risk factors for ORN are radiotherapy in the head and neck region, total mandible dose, lack of dental prophylaxis before treatment, and a dental extraction that fails to heal.

ORN has a multifactorial origin. Prevention is the best alternative. This includes pretreatment dental prophylaxis to avoid the subsequent need for tooth extractions as well as close monitoring and surveillance post treatment to identify early symptoms, caries, and periodontal disease.

IMRT spares radiation dose to the salivary gland, limiting xerostomia, but may increase the dose to portions of the mandible, increasing the possibility of ORN. In particular, Rosenthal et al. [29] demonstrated that IMRT allowed for substantial dose reduction to the parotids, optic nerve, and central nervous system, but IMRT also resulted in a higher toxicity profile for the mandible than three-dimensional conformal (3D) radiation therapy and two lateral beam approach. With two lateral port radiation fields, ORN arose most frequently in the body of the mandible. In contrast, with IMRT, ORN was most commonly located in the anterior segments of the mandible [30]. IMRT treatment typically requires at least nine radiation beams to achieve a satisfactory plan. Thus, due to the variety of beams, it is crucial to contour the entire bone during planning [31]. It is generally accepted that the risk of ORN is high at doses >60 Gy, moderate between 40 and 60 Gy, and null at <40 Gy. At present, the recommended dose constraint is a maximum dose of 70 Gy. Mandible tolerance is reduced by concomitant chemotherapy. It is recommended to decrease the total dose to the mandible bones as much as possible and to avoid "hot spots" within it.

The RTOG 00-22 multi-institutional trial failed to demonstrate a potential for clinical implementation of IMRT in terms of ORN risk reduction [32]. Dosimetry of the ORN sites was available and was related to hot spots in the mandible with a biologically equivalent dose well above 70 Gy.

Chen et al. [33] presented a large cohort of 1692 HNC patients treated by IMRT. ORN was recorded in 6.2% of cases. They found a higher ORN incidence in patients with primary tumors in the floor of the mouth, buccal mucosa, retromolar trigone, and gum regions. Data on maximum and mean doses were not available from this study.

To yield an acceptable ORN risk, the recommended maximal dose constraint is (D_{max} < 70 Gy) and small volume dose constraints are (V50, or 50% of the radiated volume = 62 Gy and V60, or 60% of the radiated volume = 20 Gy) for the mandible [31].

Treatment of ORN is difficult. It is typically conservative and relies on analgesics, antibiotics, or hyperbaric oxygen [34]. If symptoms do not resolve following treatment, surgery may be required. In some cases, removal of necrotic bone sequestrations may promote healing.

However, a simple step toward preventing ORN includes scrupulous oral care. Prophylactic extraction of teeth in poor condition within the proposed irradiated area should be recommended. Dental extraction should be carried out as atraumatically as possible, and a generous healing period should be allowed before initiation of irradiation. Excellent nutritional intake and cessation of tobacco are extremely important to promote healing.

9.9 Future Directions

9.9.1 Treatment De-intensification and Human Papillomavirus-Mediated Oropharynx Cancer

Human papillomavirus (HPV) has been shown to a significantly favorable prognostic factor in patients with oropharyngeal SCC [35]. Due to the significantly higher rate of local control and survival in these patients, emphasis has been placed on reducing treatment toxicity while still preserving clinical outcome. Reducing the dose radiation dose has been investigated as a means to reduce late toxicities including dysphagia and feeding tube dependence. The results from three trials incorporating this strategy are reported below.

The Eastern Cooperative Oncology Group (ECOG) 1308 study was a phase II trial, which included patients with stage III–IV SCC of oropharynx [36]. Patients received induction chemotherapy for 3 cycles consisting of cisplatin, paclitaxel, and cetuximab. This was followed by an assessment of the primary site and involved neck with endoscopic and radiographic evaluation. Patients with complete clinical response (cCR) received 54 Gy in 27 fractions (reduced dose) to originally involved areas of gross disease, while partial responders received 69.3 Gy in 33 fractions (full dose), both with concurrent cetuximab. Of the total of 80 evaluable patients, 70 and 58% achieved cCR at the primary and nodal sites, respectively. The 2-year progression-free survival was 78%, with overall survival of 91%. Smoking status was a significant variable for PFS, 57% versus 92%, in patients with >10 pack-years versus ≤ 10 pack-years, respectively. Those receiving ≤ 54 Gy dose had significantly lower rates of dysphagia to solids at 12 months compared to the full-dose arm (40% vs. 89%).

Chera et al. [37] conducted a phase 2 de-escalation trial with a different design in which HPV-positive oropharynx cancer patients were treated uniformly to a lower dose of 60 Gy with concurrently weekly cisplatin. Eligibility criteria were also more restricted compared to ECOG 1308, enrolling patients with T0-3N0 p16-positive oropharynx cancer with ≤ 10 pack-year smoking history or ≤ 30 pack-year smoking history and abstinent for the past 5 years. The primary endpoint was the rate of pathological complete response (pCR), which was determined by post-treatment biopsy of the primary site and nodal excision of original grossly involved disease. In 43 patients, the pCR rate of 86%. Thirty-nine percent of patients required a feeding tube.

Finally, Chen et al. reported results using a study design similar to ECOG 1308 [38]. Induction chemotherapy consisted of carboplatin and paclitaxel for 2 cycles, followed by concurrent chemoradiation with paclitaxel. Responders to induction chemotherapy received 54 Gy, while nonresponders received 60 Gy, both of which would be considered reduced dosages. With a median follow-up of 22 months, 2-year PFS was 91%. No patients had a gastrostomy tube in place 3 months following completion of therapy.

The results above provide early encouraging data to support further investigation of using reduced-dose radiation in treating HPV-positive patients. Although there are multiple competing strategies, exploring these innovative paradigms are necessary in order to reach the ultimate goal of providing tailored-treatment recommendations for a specific patient. The NRG cooperative group HN-002 randomized trial is also comparing two dose-reduced cohorts, comparing 60 Gy with weekly chemotherapy over 6 weeks versus 60 Gy alone over 5 weeks. Other competing strategies for treatment de-intensification are also being studied in clinical trials, including TORS with reduced-dose radiation and avoidance of chemotherapy (ECOG 3311).

9.9.2 Proton Therapy

The number of proton beam therapy centers has exponentially increased over the past decade, both in the United States and worldwide [39]. However, how to best integrate proton therapy into the management of HNC remains to be determined. There are some physical characteristics of a proton beam that offers dosimetric advantages of standard photon therapy in certain situations. Most notably, protons deposit the majority of their dose within a small defined volume, known as the Bragg peak (Fig. 9.3). Additionally, proton beams have virtually no exit dose. These properties are theoretically advantageous in many head and neck cancers, given that tumors are often located in close proximity to normal structures, including the salivary glands, larynx, oral cavity, brain stem, and optic structures. There is some evidence that the physical characteristics of proton beams may lead to improved toxicity profiles, particularly in patients with tumors that are well lateralized, near the skull base, or in previously irradiated fields [40–43]. Moreover, one retrospective study suggested improved cancer outcomes for patients with

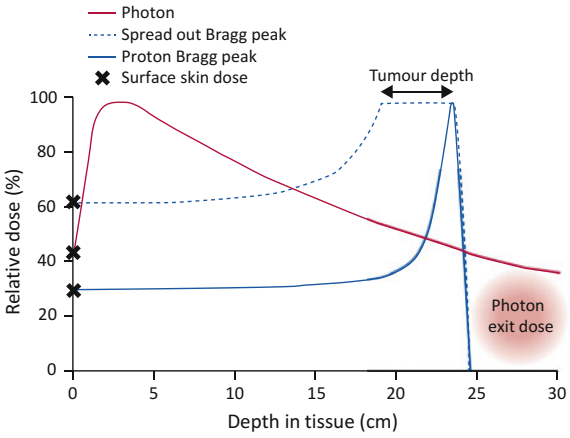

Fig. 9.3 Comparison of dosages with increasing depth in tissue. Photons have a higher exit dose, while protons exhibit a Bragg peak with the sharp elimination of exit dose. Conversely, photons have a lower surface skin dose compared to the modulated, spread-out proton modality [45]

paranasal sinus tumors receiving proton therapy [44]. However, protons have some potential disadvantages as well, including uncertainties in dosimetry and range near the Bragg peak, increased skin dose, and possible increases in neurologic toxicity and temporal lobe necrosis [41, 44]. Ongoing prospective clinical trials will help better define the role of proton therapy for head and neck cancers in modern radiation oncology practice in the future.

9.10 Conclusions

Radiation therapy is a cornerstone of the treatment of head and neck cancers. Radiation techniques for head and neck cancers continue to evolve, and are among the most complicated in all of radiation oncology. Improved outcomes are associated with provider and facility experience, and therefore patients should be referred to providers with subspecialty expertise whenever possible. Although there have been dramatic improvements in radiation delivery over the past several decades, toxicity remains a significant challenge for patients undergoing this treatment. Nevertheless, ongoing clinical trials should help optimize the therapeutic ratio of this treatment.

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Perspectives in Head and Neck Medical Oncology

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_10

Abstract

The modern treatment of locoregionally advanced disease often requires a multimodality combination approach. A number of chemotherapeutic agents can be combined with radiation, but the platinum agent cisplatin, a potent radiation sensitizer, is best studied in head and neck cancer. Newer agents such as cetuximab can be used in combination with radiation therapy for those patients who cannot tolerate cisplatin. For chemotherapy-naïve patients with metastatic head and neck cancer who demonstrate a good performance status, platinum doublet regimens are commonly used. Doublet regimens generally improve response rates compared to single-agent chemotherapies, although they have not demonstrated a survival benefit over single agents and they have added toxicity. Immunotherapies, alternative cytotoxic chemotherapies, and targeted therapies are second-line options for patients with disease that has progressed on platinum-based therapy. Immunotherapy, in particular, has gained focus by enhancing the ability of the immune system to recognize and destroy malignant cells. When multimodal approaches are used, as in combined chemotherapy and radiation therapy, toxicities are increased. It is imperative that patients are followed closely in order to maximize treatment benefit while minimizing complications.

Keywords

Head and neck · Cisplatin · Nivolumab · Pembrolizumab
Carboplatin · Docetaxel · Paclitaxel · Nab-paclitaxel
Fluorouracil · Methotrexate · Cetuximab · Squamous cell carcinoma
HPV

10.1 Introduction

Head and neck cancers are a highly diverse group of tumors that account for over 500,000 cases diagnosed annually worldwide [1]. Most head and neck neoplasms arise from surface epithelium and are squamous cell carcinomas. There is a strong association between head and neck squamous cell carcinoma and alcohol and tobacco use. Any form of tobacco use, smoked or smokeless, increases the risk of malignancy in the head and neck. Alcohol consumption is an independent risk factor and has a synergistic effect with smoking.

Viral infections also play a role in carcinogenesis. Epstein-Barr virus (EBV) infection is associated with the malignant transformation of cells in nasopharyngeal cancers. Human papillomavirus (HPV) has been identified as a causative agent in the oropharynx. Over the last two decades, there has been a shift in the etiology of oropharyngeal squamous cell carcinomas (OPC), with the majority (about 60%) in the United States thought to be associated with HPV infection [2]. Patients with HPV-associated OPC have exhibited comparatively improved survival rates [3]. Other associated risk factors include betel nut chewing and occupational exposures to perchloroethylene, asbestos, pesticides, and polycyclic aromatic hydrocarbons [4, 5–6]. Genetic factors such as defects of the CDKN2A locus causing loss of function of the cyclin-dependent kinase inhibitor p16INK4A5 and the hMDM2 regulator p14ARF have also been associated with familial head and neck cancers, which are usually seen in patients less than 40 years of age [7].

10.2 Curative Multimodality Approach for Advanced Locoregional Disease

A large proportion of HNSCC patients present at an advanced stage of disease. Historically, chemotherapy has been used in different ways in the treatment of locally advanced disease: as neo-adjuvant or induction therapy, as definitive therapy when combined sequentially or concurrently with radiation, and as postoperative adjuvant therapy with radiation therapy.

A number of chemotherapeutic agents can be combined with radiation, but the platinum agent cisplatin, a potent radiation sensitizer, remains the best studied [8]. Radiation-induced free radicals may enhance the formation of toxic platinum intermediates and enhance cellular platinum uptake [9]. Adding chemotherapy to other modalities has been shown to improve outcomes when used as adjuvant therapy with radiation after surgery in patients with high-risk features, including positive surgical margins or extracapsular extension in the regional lymph nodes [10].

10.2.1 Definitive Chemoradiation

The rationale for using combined chemoradiation as the primary treatment for locally advanced HNSCC is well-supported. Pignon et al. performed a meta-analysis of 63 randomized studies of nonmetastatic HNSCC to evaluate the impact of adding chemotherapy to locoregional therapy. The initial analysis, published in 2000, looked at 10,741 patients receiving neo-adjuvant, concomitant, or adjuvant chemotherapy in addition to locoregional therapy versus locoregional treatment alone. The results showed a significant improvement in survival in the patients who received any form of chemotherapy (4% absolute survival benefit at

5 years). A subset analysis of patients who received concurrent chemoradiation showed a greater absolute survival benefit of 8% at 5 years [11].

In 2009, the MACH-NC Collaborative Group updated their original meta-analysis to increase the statistical power of the analysis by adding patients from studies performed between 1994 and 2000. The update included 93 trials and 17,346 patients, and focused on trials using concurrent chemoradiation and induction chemotherapy. It confirmed the previously seen absolute survival benefit of 6.5% at 5 years for patients who received concurrent chemoradiation. The hazard ratio for death was significantly lower when a platinum-based chemotherapy regimen was used (0.75 vs. 0.86, $p < 0.01$). The timing of chemotherapy (concurrent versus neo-adjuvant versus adjuvant) proved to be prognostic, with a significant survival benefit seen only in the patients receiving concurrent chemoradiation (HR 0.81 vs. 0.96 for induction chemotherapy and 1.06 for adjuvant chemotherapy) [12]. Overall, the updated MACH-NC meta-analysis validated the survival benefit of chemotherapy in HNSCC, with the greatest benefit seen with concurrent chemoradiation utilizing a platinum agent (cisplatin or carboplatin).

10.2.2 Adjuvant Chemotherapy

Two additional major trials (RTOG 9501, EORTC 22931) explored specifically the use of chemoradiation versus radiation therapy alone in the adjuvant setting after surgery for operable tumors. Patients had completely resected disease with high-risk characteristics, defined as two or more involved lymph nodes, extracapsular extension, perineural involvement, vascular tumor emboli, or positive margins. Both trials showed significantly better local control and disease-free survival in the chemoradiation therapy group when compared to radiation alone. Overall survival was improved in the EORTC trial but not in the RTOG trial, likely due to differing definitions of high-risk features. However, the incidence of grade 3 and 4 adverse events, primarily mucosal events, was significantly increased in both trials [13, 14]. In addition, the frequency of distant metastases in both trials was not significantly improved with the addition of chemotherapy to radiation, suggesting that the cisplatin mainly added benefit by potentiating the effects of radiotherapy. A retrospective pooled analysis of both trials showed that patients with extracapsular extension and/or positive surgical margins were the only group that significantly benefited from combined chemoradiation therapy [10]. Therefore, adjuvant chemoradiation can improve outcomes when these high-risk features are present.

Cisplatin remains the most commonly used chemotherapy agent in combination with radiation. The dosing schedule of 100 mg/m^2 given every 3 weeks was initially used in induction chemotherapy regimens and then adapted for use in combined chemoradiation regimens. This high-dose schedule has not been prospectively compared directly to a weekly low-dose regimen (40 mg/m^2). This regimen exhibits decreased toxicity and theoretically distributes the radiosensitizer effect more evenly throughout the radiation course, and is now the standard regimen used in clinical trials. Notably, a recent prospective Phase III trial demonstrated inferior locoregional control

with a lose-dose regimen (58.5% for low-dose vs 73.1% for high-dose, p = 0.014) [15]. However, overall survival was the same, and their particular low-dose schedule (30 mg/m^2 weekly) differed from the 40mg/m^2 regimens more commonly seen.

10.2.3 Cetuximab

Newer agents have been evaluated in combination with radiation therapy for those patients who cannot tolerate cisplatin. Cetuximab is a monoclonal antibody against epidermal growth factor receptor (EGFR), which is pathologically overexpressed in 90% of HNSCC [16]. The Bonner trial compared radiation therapy alone to radiation given concurrently with weekly cetuximab in patients with stage III-IV HNSCC. The addition of cetuximab significantly improved locoregional control (HR 0.68, $p = 0.005$ and the duration of locoregional control improved to 24.4 months from 14.9 months). Overall survival was favorable in the cetuximab arm (49.0 months vs. 29.3 months, $p = 0.03$) [17]. These findings prompted studies evaluating the addition of cetuximab to platinum-based chemotherapy with concurrent radiation. RTOG 0522 compared cisplatin versus with cisplatin and cetuximab, in Stage III-IV HNSCC patients receiving chemoradiation. No significant differences were seen in disease-free or overall survival, and higher rates of mucositis and treatment interruptions were seen in the cetuximab-containing arm [18]. More recent studies utilizing cetuximab monotherapy with radiation reported a higher incidence of toxicities, and suggested a more modest benefit than initially reported [19–22]. An improvement in overall survival has been noted among cetuximab-treated patients who experienced an acneiform rash of at least grade 2 severity compared with patients with no rash or grade 1 rash (HR 0.49, 0.34–0.72; $p = 0.002$) [23]: this suggests that the rash potentially serves as a proxy for efficacy. In current practice, cetuximab is generally used as monotherapy with radiation for patients who cannot tolerate platinum-based chemotherapy.

10.2.4 Induction Chemotherapy

Induction chemotherapy has been studied with the goal of decreasing risk of distant metastases, improving survival for locally advanced HNSCC, as well as to allow for organ preservation. Many earlier trials evaluated the role of induction chemotherapy, followed by definitive radiation, to improve outcomes in locally advanced disease. The most used chemotherapy regimen at that time was a combination of cisplatin with 5-fluorouracil (5FU). Of particular interest was induction chemotherapy in laryngeal cancer for organ preservation [24, 25]. Lefebvre et al. showed similar treatment failure at local, regional, and second primary sites in both induction and immediate surgery arms, (17% vs. 12%, 23% vs. 19%, and 13% vs. 16%, respectively). Induction chemotherapy led to a significant improvement in distant failure rate (25% vs. 36%, $p = 0.041$) and a trend toward survival benefit (44 months vs. 25 months) when compared to immediate surgery. The MACH-NC meta-analysis showed no survival benefit for induction chemotherapy treatment protocols; however, the patient

characteristics were heterogeneous in terms of tumor site and stage and approximately 50% of the trials did not use a "standard" combination of platinum and 5-FU. The updated MACH-NC analysis confirmed the lack of survival benefit for induction regimens. There was a decreased risk of distant metastases seen, but this did not seem to impact survival [12].

Subsequently, the addition of a taxane to induction cisplatin and 5FU was tested in an effort to improve survival outcomes. Vermorken et al. compared docetaxel, cisplatin and fluorouracil to cisplatin, and fluorouracil alone in locoregionally advanced, unresectable squamous cell carcinoma. A statistically significant improvement in progression-free survival (11.0 months vs. 8.2 months, $p = 0.007$) and overall survival (18.8 months vs. 14.5 months, $p = 0.02$) was found with the addition of a taxane [26]. A phase III trial compared the three-drug combination of taxane, cisplatin and fluorouracil to cisplatin, and fluorouracil alone as induction chemotherapy in unresectable patients. Again, the triplet combination showed better efficacy than the doublet in regards to overall survival (71 months vs. 30 months, $p = 0.006$) [27]. A meta-analysis of five large randomized trials evaluating 1,772 patients compared three-drug combinations including a taxane to doublet regimens. Results showed that the three-drug combination significantly improved progression-free survival, overall survival, distant failure, and locoregional failure. Most notably, the main criticism of the meta-analysis was that it did not compare the triplet combination with the standard of care, i.e., definitive chemoradiation.

When utilized, induction chemotherapy is generally followed by radiation therapy alone, or in combination with weekly cetuximab or carboplatin. High dose cisplatin is generally not recommended after induction chemotherapy due to the increased potential for toxicity [28]. Induction chemotherapy prior to chemoradiotherapy has yet to show improved overall survival when compared to chemoradiotherapy alone (PARADIGM, DECIDE trials) [29, 30] with the possible exception of nasopharyngeal carcinoma [31]. The benefit seen with induction strategies may be mitigated by the delay to definitive treatment, the inability to give high dose cisplatin during concurrent chemoradiation, and the potential for neutropenic infection or other complications prior to definitive therapy. Therefore, in the current era, induction chemotherapy is generally reserved for situations in which organ preservation is desired, or when radiation cannot be started in an appropriate timeframe (Table 10.1).

10.3 Treatment of Recurrent and Metastatic Disease

Recurrent/Metastatic HNSCC confers a poor prognosis, with a median overall survival of 6–9 months. Survival beyond 2 years is infrequent. Performance status, comorbidities, prior treatment regimens, bulk of disease at the time of presentation, HPV status, and tobacco use are important prognostic factors [32]. In patients with locoregional recurrent disease, surgery, radiation therapy, or combined chemoradiation can provide long-term control [33, 34]. However, if the local recurrence is not amenable to surgery or radiation, then treatment goals and outcomes are palliative. With the advent

Table 10.1 Induction chemotherapy considerations

Pros	Cons
1. Decreases risk of distant metastases	1. No improvement in overall survival for HNSCC*
2. Enables immediate treatment initiation when radiation cannot begin in appropriate timeframe	2. Significantly higher toxicities, including 1–3% fatality rate
3. May minimize high-dose radiation fields, reducing dose to nearby critical structures (optic chiasm, brainstem)	3. Delays time to definitive treatment modality (radiation)
4. May shrink radiation fields in air-filled spaces (sinus, airway)	4. Longer overall treatment duration (13 weeks vs 7 weeks)
5. May reduce tracheostomy risk in patients with potential airway obstruction, limiting consequences of radiation-induced laryngeal edema	5. May prevent ability to give high-dose cisplatin during concurrent chemoradiation phase
6. Facilitates chemoselection, with tailored definitive treatment (intensification for responders, deintensification for non-responders)	

*Induction chemotherapy recently shown to improve overall survival in nasopharyngeal carcinoma [31]

of checkpoint inhibitor immunotherapies and molecular targeted therapies, newer options are available for the treatment of metastatic disease. Treatment plans should take into account previous lines of therapy, burden of metastatic disease, and availability of more definitive treatment with surgery or radiation therapy.

10.3.1 Recurrent/Metastatic HNSCC

10.3.1.1 First Line Therapy

For chemotherapy-naïve patients with metastatic HNSCC who demonstrate good performance status, platinum doublet regimens are commonly used. Doublet regimens generally improve response rates compared to single-agent chemotherapies, although they have not demonstrated a survival benefit over single agents and they have added toxicity. A Southwest Oncology Group study evaluated the use of a platinum doublet compared to single-agent methotrexate in patients with metastatic HNSCC. 277 patients were randomized to receive either cisplatin and fluorouracil, carboplatin and fluorouracil, or weekly methotrexate alone. The study did not demonstrate any significant difference in overall survival among the groups. Better response rates were observed in the cisplatin-containing arm (32%), as compared to the carboplatin containing arm (21%) or methotrexate (10%). However,

hematologic and non-hematologic toxicities were significantly increased in the cisplatin-containing arm compared to methotrexate [35].

The combination of cisplatin and a taxane has also been compared to the combination of cisplatin and fluorouracil. The Eastern Cooperative Oncology Group conducted a phase III randomized study to compare cisplatin (100 mg/m^2 day 1) and fluorouracil (1000 mg/m^2 per day continuous infusion for four days) with cisplatin (75 mg/m^2 day 1) and paclitaxel (175 mg/m^2 over 3 h on day 1). Results of the study showed no differences in overall survival (median survival 8.5 vs. 8.1 months) or response rates (27% vs. 26%) between the two groups. It is worth noting that the paclitaxel regimen was generally better tolerated.

More recently, biologic agents that target the EGFR pathway have been studied in combination with cytotoxic chemotherapy. Cetuximab was approved in 2011 for first-line use in patients with recurrent or metastatic HNSCC in combination with a platinum agent and fluorouracil. Its approval was based on results of the phase III EXTREME trial which evaluated 442 patients randomized to receive either a platinum derivative in combination with fluorouracil and cetuximab versus a platinum derivative and fluorouracil. The study showed an improvement in overall survival from 7.4 months to 10.1 months in the cetuximab-containing arm. The anti-EGFR monoclonal antibody panitumumab has also been studied but has failed to show a survival benefit in this setting (CONCERT-1, CONCERT-2, [36]). Therefore, cetuximab is the anti-EGFR agent of choice in metastatic HNSCC.

For patients with poor performance status or multiple comorbidities who cannot tolerate a platinum doublet therapy, a number of single-agent chemotherapies can be used. Response rates are generally lower with single agents than with doublet therapies. Active agents that are options in this setting include cisplatin, carboplatin, taxanes (docetaxel, paclitaxel, nab-paclitaxel), fluorouracil, methotrexate, and cetuximab.

10.3.1.2 Second Line Therapy

Immunotherapies, cytotoxic chemotherapies, and targeted therapies are second-line options for patients who have progressed on a platinum-based therapy. The programmed cell death protein 1 (PD-1) inhibitors pembrolizumab (Keytruda) and nivolumab (Opdivo) have received regulatory approval as second-line treatments for metastatic HNSCC. Nivolumab was approved in 2016 on the basis of the results of the phase III Checkmate-141 trial. In this trial, 361 patients with platinum-refractory disease were randomized to receive nivolumab or methotrexate, docetaxel, or cetuximab. Patients receiving nivolumab had higher response rates compared to standard chemotherapy (13.3% vs. 5.8%, respectively). Overall survival was significantly longer with nivolumab (HR 0.71; $p = 0.0048$). Eighteen-month overall survival was significantly improved in the nivolumab arm (21.5% vs. 8.3%). Greater survival benefit was observed in patients who had programmed death ligand 1 (PDL-1) expression $\geq 1\%$ as well as patients with HPV-positive tumors. Toxicities were significantly lower with nivolumab than with chemotherapy. Common side effects of the PD-1 inhibitors include fatigue, hyperglycemia, transaminitis, and dyspnea (Fig. 10.1).

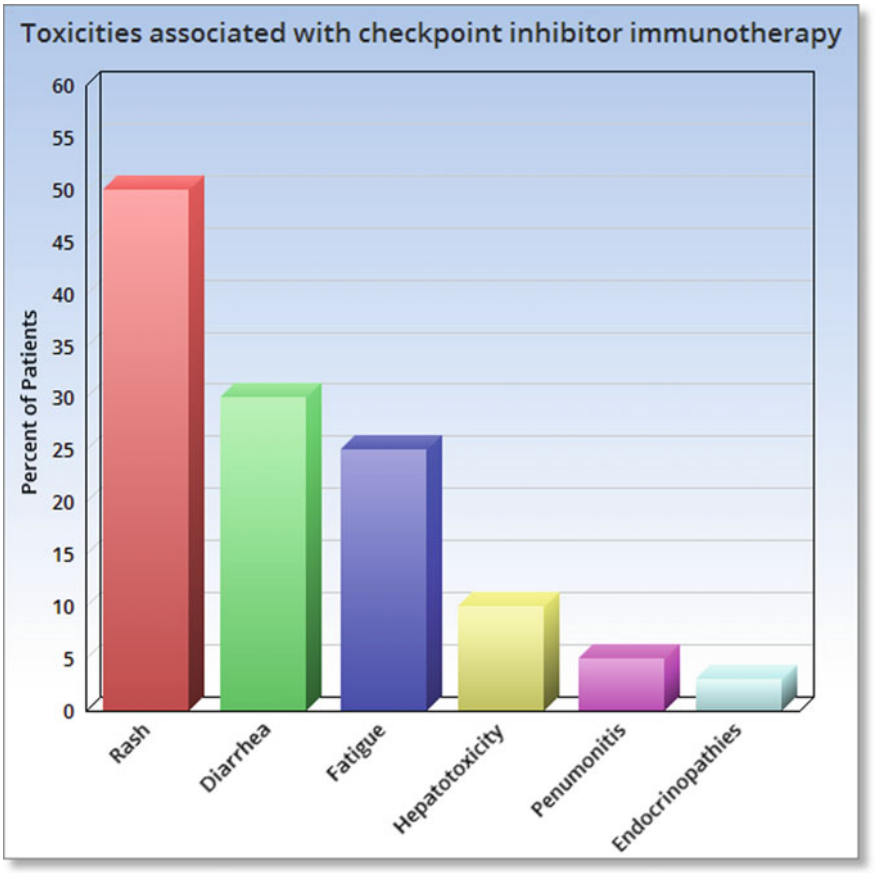

Fig. 10.1 Toxicities associated with checkpoint inhibitor immunotherapy

Similarly, pembrolizumab was granted accelerated FDA approval for R/M HNSCC based on KEYNOTE-012 results. In the trial, 17.7% responses were seen with 7 CRs and 27 PRs in patients who were treated with pembrolizumab after they had progression on platinum-based chemotherapy. Durable responses lasting 6 months or longer were seen in 85% of the responding patients. Benefit was observed regardless of tumor PDL-1 expression, but patients with PDL-1 expression over 1% showed a trend toward greater benefit [37]. The phase III KEYNOTE-040 showed overall survival was marginally higher in pembrolizumab compared to standard of care (8.4 vs. 7.1 months, HR 0.81, $p = 0.02$). However, patients with PDL-1 expression over 1% showed much greater benefit. Among patients with >50% PDL-1 expression, overall survival was 11.6 months compared to 7.9 months (HR 0.54, $p = 0.0017$) [38].

Cytotoxic agents have limited efficacy after progression on chemotherapy. As such, single-agent chemotherapies are preferred to minimize toxicities, given low

overall benefit. Any active agent as described previously may be used, and the choice of agent depends on its toxicity profile, the patient's performance status, and previous therapies received. Historically, methotrexate has been used at the dose of 40 mg/m^2 intravenously weekly. Response rates are higher at the dose of 60 mg/m^2 weekly but there is increased risk of mucositis without improvement in overall survival [39, 40]. Gemcitabine has also been studied in the metastatic setting in early phase trials with limited number of patients. A phase II trial performed in France enrolled 61 patients and showed a response rate of 13% with a relatively favorable side effect profile. This drug may be an option for some patients with metastatic disease who cannot tolerate other agents.

Other tyrosine kinase inhibitors such as gefitinib, afatinib, erlotinib, and lapatinib have been evaluated and have not shown efficacy in the metastatic setting. Patients with poor performance status may benefit most from best supportive care.

10.4 Current Clinical Trials for Future Therapy

Recently there has been an increased focus on treatment of HNSCC with combinations of immune therapies which enhance the ability of the immune system to recognize and destroy malignant cells. Immunotherapy can be classified broadly into four categories including vaccine therapies (DNA vaccines, peptide vaccines, and biological vaccines), monoclonal antibodies (receptor tyrosine kinase inhibitors and check point inhibitors), oncolytic viruses and other active immunotherapeutics, and immunomodulators (immune receptor agonists and exogenous cytokines). Many of them have shown promising results in animal models and are currently being tested in humans in phase II/III clinical trials [41–44]. There are numerous ongoing trials in patients with HNSCC, many of them combining PD1 checkpoint inhibitors with other immune modulators, and the results of these trials are eagerly awaited. HPV-specific therapeutic vaccines alone or in combination with immunotherapy are also being currently studied in animals.

10.5 Toxicities with Therapy

When multimodal approaches are used, as in combined chemotherapy and radiation therapy, toxicities are increased (Table 10.2). It is imperative that patients receiving multimodal treatments are followed closely to maximize treatment benefit while minimizing complications. Breaks in radiation therapy result in lower locoregional control and survival rates [45]. Suboptimal symptom control may lead to patient poor compliance and even treatment discontinuation. Therefore, patient education

Table 10.2 FDA-approved chemotherapeutic and biologic agents in the treatment of head and neck cancer

Drug name	Mechanism of action	Potential treatment-related toxicities
Cytotoxic agents		
5-Fluorouracil (5-FU)	Fluoropyrimidine	Mucositis, diarrhea, cardiac vasospasm, sun hypersensitivity, hand-foot syndrome
Capecitabine	Oral fluoropyrimidine	Mucositis, diarrhea, cardiac vasospasm, sun hypersensitivity, hand-foot syndrome[a]
Cisplatin	First-generation platinum analogue	Cumulative peripheral neuropathy, nephrotoxicity, myelosuppression, ototoxicity
Carboplatin	Second-generation platinum analogue	Electrolyte abnormalities, myelosuppression, hepatotoxicity and delayed hypersensitivity reaction
Docetaxel	Taxane derivative	Alopecia, nail discoloration, stomatitis, myelosuppression, pulmonary toxicity, neuropathy
Gemcitabine	Pyrimidine analogue	Peripheral edema, skin rash, myelosuppression
Methotrexate	Antimetabolite	Arterial and venous thrombosis, alopecia, PJP infection, HSV infection,
Paclitaxel	Taxane derivative	Alopecia, myelosuppression, hepatic toxicity, peripheral neuropathy, arthralgia, hypersensitivity reaction
Vinorelbine	Vinca alkaloid	Peripheral neuropathy, alopecia, myelosuppression, hepatoxicity
Epidermal growth factor inhibitors		
Cetuximab	Chimeric monoclonal antibody against the EGFR	Acneiform rash, fissuring of distal fingertips, paronychial, infection, hypomagnesium and hypocalcium, diarrhea, and, allergic hypersensitivity reaction
Afatinib	Irreversible covalent inhibitor against tyrosine kinase EGFR	Acneiform rash, fissuring of distal fingertips, paronychial, infection, hypokalemia, stomatitis, diarrhea
Immunotherapy—targeting agents		
Pembrolizumab	Humanized monoclonal antibody against the programmed cell death 1 receptor (PD-1)	Pruritis, rash, hypo/hyperthyroidism, hepatitis, pneumonitis
Nivolumab	Humanized monoclonal antibody against the programmed cell death 1 receptor (PD-1)	Pruritis, rash, hypo/hyperthyroidism, hepatitis, pneumonitis

and early, aggressive symptom management is paramount. Supportive care services and specialists including social work, nutrition, speech and swallow, dentistry, rehabilitation, audiology, and palliative care services should be systematically utilized as integrated parts of multidisciplinary management.

10.5.1 Platinum Agents

Platinum chemotherapeutic drugs cause a broad spectrum of toxicities. Cisplatin is the most common agent used in combined chemoradiation for HNSCC. Cisplatin at the traditional doses of 75–100 mg/m^2 intravenously every 3 weeks can be associated with gastrointestinal, hematological, renal, neurological, and otologic toxicity.

Cisplatin is one of the most emetogenic chemotherapeutic agents, with a dose-dependent effect. Aggressive prophylactic premedication with combinations of 5HT antagonists, steroids, and NK1 antagonists should be systematically used from treatment initiation (primary prophylaxis) to prevent acute and delayed nausea and vomiting. Benzodiazepines can prevent anticipatory nausea. Recently, the use of olanzapine has also been associated with a decreased incidence of severe nausea/vomiting [46]. Patients should be counseled to appropriately use antiemetics and to maintain adequate oral hydration. Intravenous hydration should be given with each cycle of cisplatin and whenever necessary.

Cisplatin nephrotoxicity can present in various ways, including acute kidney injury, hypomagnesemia, renal salt wasting, chronic renal failure, among others [47]. However, the most serious and most common presentation is acute kidney injury. In the kidney, cisplatin causes proximal tubule injury, leading to a decrease in the glomerular filtration rate, as well as magnesium and salt wasting. The risk of nephrotoxicity increases with dose level and with subsequent doses as well as with baseline dehydration, age, hypoalbuminemia and preexisting renal disease [47, 48]. Cisplatin-related acute renal toxicity is typically, albeit not always, reversible. Aggressive measures to prevent nephrotoxicity should be used in patients receiving cisplatin. These include IV fluids pre and post cisplatin to establish a urine output of 100 mL/hr, and consideration of mannitol to force diuresis. Dehydration due to radiation-induced mucositis or nausea can increase the risk of nephrotoxicity and should be managed promptly. Hypomagnesemia should be corrected with oral or IV supplementation. If acute kidney injury is noted while on cisplatin, aggressive supportive measures should be instituted and alternative chemotherapeutic regimens considered. These include administration of lower weekly doses of cisplatin, or substitution with carboplatin or cetuximab. Amifostine is approved in the US for reducing the cumulative nephrotoxicity of repeated cisplatin dosing in patients with advanced ovarian cancer, but very limited data exist regarding its use in other tumor types [49].

Cisplatin additionally may cause neurotoxicity, which commonly manifests as a peripheral neuropathy and/or ototoxicity. The toxicity is dose dependent and cumulative, and may develop after a total dose of approximately 300 mg/m^2.

Symptoms are related to the damage of large myelinated sensory fibers and include numbness, paresthesias, and pain, which develop in the digits and spread proximally to involve the extremities. Late symptoms include loss of deep tendon reflexes. In patients with mild neuropathy, cisplatin can be continued cautiously, but discontinuation is recommended prior to reaching grade 3 toxicity, due to the potential for permanent and irreversible nerve damage [50]. Gabapentin or pregabalin can be used in case of chemotherapy-related neuropathy.

Ototoxicity can occur with cisplatin or carboplatin, although it is more commonly seen with cisplatin. In a study performed in almost 500 germ cell tumor survivors who had received cisplatin, 80% of them had some degree of hearing loss at 4 years post-therapy [51]. It manifests as a bilateral high-frequency sensorineural hearing loss and can be accompanied by tinnitus. Its incidence is dose-dependent and it is generally irreversible. Early detection with audiometry may prevent further hearing loss, and alternative agents used if confirmed.

Carboplatin causes less ototoxicity and should be substituted for cisplatin in cases of high-frequency hearing loss. Carboplatin is considered less toxic than cisplatin, but is more myelosuppressive and may be less active than cisplatin. For patients at high risk of infection, colony stimulating growth factors may be used to shorten the duration of neutropenia with carboplatin.

10.5.2 Antimetabolites (Methotrexate and Fluorouracil)

Methotrexate (MTX) and fluorouracil (5FU) are antimetabolites that are active in HNSCC. Methotrexate has been known to cause nephrotoxicity from intratubular precipitation of the drug and its metabolites in acidic urine. However, the incidence of renal toxicity has been reduced by the use of hydration and urine alkalinization. Higher doses of MTX can also cause acute transaminitis and hyperbilirubinemia which resolve after discontinuation of the drug [52]. Less common but occasionally severe side effects include generalized skin rash, interstitial alveolitis, pulmonary fibrosis, central nervous system toxicities ranging from headaches and drowsiness to confusion and encephalopathy, vasculitis, and allergic reactions.

The main side effects of fluorouracil include diarrhea, mucositis, palmar and/or plantar erythrodysesthesia, and myelosuppression. Of particular relevance for HNSCC patients is oral mucositis/stomatitis which is a major overlapping toxicity with radiation therapy and has limited the use of 5-FU in HNSCC. Good oral hygiene and mouthwashes should be implemented early to reduce the frequency and duration of high-grade oral mucositis. Early use of anti-diarrheal medications such as loperamide together with adequate dietary recommendations can prevent severe diarrhea. Rare side effects of cerebellar ataxia, upper motor neuropathy and coronary vasospasm have also been reported [52]. Dihydropyrimidine dehydrogenase (DPD), an enzyme encoded by the DPYD gene, is the rate-limiting step in pyrimidine catabolism. Patients with DPD deficiency develop severe and potentially life-threatening side effects when treated with 5FU or capecitabine. However, because true DPD deficiency is rare, screening for mutations prior to initiating

therapy are not warranted [53]. Therefore, 5-FU related toxicities should be carefully monitored and appropriate measures, including administration of uridine triacetate in patients with early onset, should be implemented [54].

10.5.3 Taxanes

Paclitaxel and docetaxel can be used as single agents or in combination with other agents in the treatment of HNSCC. Neuropathy is a common side-effect encountered in patients receiving taxanes. It manifests in a stocking-glove distribution and can be persistent or irreversible in some cases. Dose reductions or treatment discontinuation may be required for significant neuropathy. Cardiac toxicity in the form of sinus bradycardia can also be observed in 30% of patients [55]. Patients who are considered to be at high cardiac risk should have routine cardiac monitoring. Cytopenias may also occur and are more likely when used in combination with other myelosuppressive agents. Other common side effects associated with taxanes are reversible dose-related alopecia, nail disorders, and transaminitis. Fluid retention can be seen and is more common with docetaxel [56]. This side effect can be prevented with steroid premedication and can be managed with diuretics if it occurs. Hypersensitivity reactions can be seen with paclitaxel and docetaxel and may present with flushing, chest tightness, chills, shortness of breath, or rash. Patients who experience hypersensitivity should be managed by stopping the infusion and administering steroids, antihistamines, fluids, and epinephrine as needed. Premedication with steroids and antihistamines is advised to reduce the risk of hypersensitivity reactions.

10.5.4 Targeted Agents (Cetuximab)

As a biologic agent targeting EGFR, cetuximab has a unique side effect profile. The most common adverse event is skin toxicity, which occurs due to the presence of EGFR in the skin and hair follicles [21]. This may manifest as acneiform rash, dry skin, and nail changes. Acneiform rash occurs in 60–80% of patients and is generally mild to moderate in nature, although grade 3–4 rashes have been reported in 5–20% of patients [57]. Paradoxically, the rash correlates with treatment efficacy. In a phase 3 clinical trial evaluating cetuximab added to standard chemotherapy in metastatic head and neck patients, 9% of patients in the cetuximab arm experienced grade 3 skin reactions [58]. The rash is reversible and usually completely resolves within 1 month after discontinuing treatment. Patients should be counseled on general preventive measures such as using sunscreen, keeping skin hydrated with alcohol-free products, and avoiding excessive beard growth. Grade 2 toxicity can be managed with topical antibiotic treatments and/or oral tetracyclines. For Grade 3 toxicities, treatment should be interrupted until symptoms improve. Oral or IV corticosteroids, oral retinoids, antihistamines, and antibiotics can be used in cases of

severe or nonresponsive skin toxicities. Grade 4 reactions are an indication for permanent discontinuation of cetuximab [59].

Hypersensitivity infusion reactions with cetuximab have been reported in 3–22% of patients, with incidences [21]. Symptoms generally occur soon after the first or second dose and may include fever or chills, laryngeal edema, urticaria, bronchospasm, and hypotension. Patients should be monitored closely with the first administration of cetuximab. Premedication with an H1 antagonist is recommended, and corticosteroids or H2 antagonists can also be used, although data on prevention with these is lacking. When reactions do occur, the infusion should be stopped immediately and corticosteroids, antihistamines, and epinephrine should be administered as needed.

10.5.5 Immunotherapy

Nivolumab and pembrolizumab are PD-1/PDL-1 inhibitors with side effect profiles (Table 10.3) that are distinct from chemotherapy. In the phase III Checkmate 141 trial, the most common adverse events with nivolumab were fatigue, nausea, rash, decreased appetite, diarrhea, and asthenia. 13% of patients experienced a grade 3 or 4 toxicity, which included fatigue, anemia, asthenia, and stomatitis. No patients were seen to have alopecia or neutropenia. Similar side effects were observed with pembrolizumab in trials. Of particular interest for this class of drugs are the autoimmune side effects which can affect a broad spectrum of organs. The most common are various forms of skin toxicity which are generally manageable and rarely lead to treatment discontinuation, followed by autoimmune endocrine disorders and more rarely autoimmune hepatitis, colitis, and pneumonitis. In the Checkmate study, 7.6% of patients experienced endocrine abnormalities, including primary hypothyroidism, adrenal insufficiency, hypophysitis, and panhypopituitarism [60]. Rarely the autoimmune toxicities such as colitis, pneumonitis, and hepatitis can be severe and even life-threatening if unrecognized and/or inadequately treated. Patients receiving immunotherapies should be monitored closely. In some cases, the PD-1 targeted therapy can be restarted once the symptom is controlled and steroids can be slowly tapered off. Rapid steroid tapering can result in toxicity rebound. Interestingly, steroid therapy administered for management of side effects does not seem to impact treatment efficacy [61].

10.5.6 Radiation Therapy

Mucositis is the main dose-limiting toxicity when radiation is utilized. Radiation in standard dose fractionation is associated with grade 3 and 4 mucositis in approximately 25% of patients in the major RTOG trials [62, 63]. When accelerated regimens using boosts or hyperfractionation are used, the incidence of grade 3–4 mucositis approaches 50% [63]. The addition of radiosensitizing chemotherapy agents increases the rates of grade 3 mucositis by up to 80% [64–68]. Severe

Table 10.3 Toxicities associated with immune checkpoint blockade

Toxicity	Examination	Management	Comments
Skin: Grade 1–2		Continue Anti-PD-1 Topical Steroids	For persistent rash or pruritis use urea containing ointments or oral antipruritics
Skin: Grade 3–4	Biopsy	Delay or Stop Anti-PD-1 Oral Steroids 1–2 mg/kg/d[a]	In case of improvement resume Anti-PD-1
Colitis: Grade 1	Stool test for pathogen	Ant diarrheal drugs, hydration and electrolyte replacement	
Colitis: Grade 2	Consider colonoscopy	Delay Anti-PD-1 Oral Steroids 0.5–1 mg/kg/d[a]	In case of no change stop Anti-PD-1
Colitis: Grade 3–4	Colonoscopy	Stop Anti-PD-1 Oral Steroids 1–2 mg/kg/d[a]	In case of no change or worsening consider Infliximab if suspected infection or perforation
Pneumonitis: Grade 1	Lung function test and ABG Frequent controls q2-3 days	Continue Anti-PD-1	
Pneumonitis: Grade 2	Lung function test and ABG Daily symptom control Consider bronchoscopy	Delay Anti-PD-1 Oral Steroids 1–2 mg/kg/d[a]	In case of improvement resume Anti-PD-1
Pneumonitis: Grade 3-4	Lung function test and ABG Bronchoscopy with biopsy	Oral Steroids 2–4 mg/kg/d[a]	In case of no change or worsening consider micophenolate mofetil
Endocrinopathies: Grade 1	Check TSH, fT4 and fT3 Consider imaging	Continue Anti-PD-1	
Endocrinopathies: Grade 2	Check TSH, fT4 and fT3 MRI	Delay Anti-PD-1 Oral Steroids 1–2 mg/kg/d[a] Consider HRT	In case of improvement resume Anti-PD-1 In case of no change or worsening consider HRT
Endocrinopathies: Grade 3	Check TSH, fT4 and fT3 MRI	Consider HRT IV steroids	In case of improvement resume Anti-PD-1
Renal injury: Grade 1	Control for signs of renal dysfunction	Continue Anti-PD-1	

(continued)

Table 10.3 (continued)

Toxicity	Examination	Management	Comments
	Check Cr q week		
Renal injury: Grade 2	Consider renal biopsy Check Cr q2-3 days	Delay Anti-PD-1 Oral Steroids 0.5–1 mg/kg/d[a]	In case of improvement resume Anti-PD-1
Renal injury: Grade 3–4	Renal biopsy	Stop Anti-PD-1 Oral Steroids 1–2 mg/kg/d[a]	
Hepatic Injury: Grade 1	Control for signs of hepatitis	Continue Anti-PD-1	
Hepatic Injury: Grade 2	Frequent controls Transaminases	Delay Anti-PD-1 Oral Steroids 0.5–1 mg/kg/d[a]	In case of improvement resume Anti-PD-1
Hepatic Injury: Grade 3–4	Very frequent control q1–2 day Consider biopsy	Stop Anti-PD-1 Oral Steroids 1–2 mg/kg/d[a]	In case of no change or worsening consider micophenolate mofetil
Infusion Reaction Grade 3–4	Vigilant controls/imaging	Stop Anti-PD-1 Oral Steroids 2–4 mg/kg/d[a] or IV Steroids	

[a]following improvement steroid taper of at least 1 month should be given

mucositis may further complicate the therapeutic course of patients receiving combined modality therapy by increasing the risk of dehydration, renal failure, malnutrition, and fatigue, escalating the risk of other chemotherapy-induced toxicities.

The initial treatment of mucositis involves topical coating agents, anti-inflammatory drugs, antimicrobials, as well as local and systemic analgesics. Xerostomia can develop when the salivary glands are radiated and may exacerbate mucositis via decreased salivary production. Pilocarpine is a cholinergic agonist that is FDA-approved to treat xerostomia in HNSCC. The approval was based on placebo-controlled trials that showed improved symptoms of oral dryness and discomfort and increased ability to speak [69]. If mucositis or xerostomia interfere significantly with the ability to maintain adequate nutrition or hydration, nutrition specialists should be consulted. Nutritional supplements can be used to increase caloric intake. If nutrition or hydration goals still cannot be attained or significant weight loss occurs, enteral feeding tubes should be placed. Published rates of feeding tube use in trials are 15–40% when radiation is used alone, and 35–50% when chemotherapy is added [13, 23, 68, 70, 71]. Patient factors associated with an increased risk of dysphagia necessitating feed tube placement include significant pre-treatment weight loss, older age, poor performance status, and heavy alcohol or tobacco use. Tumor-related factors include larger size of the primary tumor and

Table 10.4 Landmark Head and Neck Cancer Trials

Setting	PMID	Significance
Organ preservation		
VA Larynx Trial	2034244 [77]	Organ preservation can be achieved in a high number of laryngeal SCC patients, with equivalent survival rates compared to surgery
EORTC 24891	8656441 [24] 22492697 [78]	Organ preservation can be achieved in a high number of hypopharyngeal SCC patients, with equivalent survival rates compared to surgery
GORTEC 2000–01	19318632 [79] 26681800 [80]	TPF induction chemotherapy is superior to PF induction chemotherapy for overall survival and laryngeal preservation
Induction setting		
DECIDE PARADIGM	25049329 [30] 23414589 [29]	Induction chemotherapy not superior to concurrent chemoradiation in advanced HNSCC
EORTC 24971/TAX323 TAX 324	17960012 [26] 17960013 [27]	Triplet induction (TPF) superior to doublet induction (PF) chemotherapy for overall survival
Definitive setting		
RTOG 91-11	14645636 [81] 23182993 [82]	Concurrent chemoRT superior to induction chemotherapy
Bonner trial	16467544 [83]	Cetuximab with RT superior to RT alone
GORTEC 9401	10601378 [71]	ChemoRT superior to RT alone in oropharynx SCC
Intergroup 0099	9552031 [65]	ChemoRT superior to RT alone in NPC
MACH-NC	19446902 [12]	Meta-analysis showing 6.5% absolute survival benefit from chemoRT compared to RT alone; concomitant chemoRT superior to induction chemo
Adjuvant setting		
RTOG 9501 EORTC 22931	15128893 [84] 15128894 [85] 16161069 [10]	Patients with ENE/ECS or positive margins benefit from adding chemotherapy to adjuvant radiation
Recurrent/metastatic setting		
Janot Re-irradiation Trial	18936479 [86]	Full-dose reirradiation combined with chemotherapy after salvage surgery significantly improved DFS, but not OS.
EXTREME SPECTRUM	18784101 [58] 23746666 [87]	As compared with platinum-based chemotherapy plus fluorouracil alone, cetuximab plus platinum-fluorouracil chemotherapy improved overall survival when given as first-line treatment in patients with R/M HNSCC
Checkmate-141 KEYNOTE-012	27718784 [88] 27247226 [89]	Among patients with platinum-refractory, recurrent squamous cell carcinoma of the head and neck, immunotherapy (nivolumab, pembrolizumab) resulted in longer overall survival than treatment with standard, single-agent therapy
Miscellaneous		
RTOG 0129	20530316 [90]	Accelerated RT not superior to standard RT; HPV status is prognostic

hypopharyngeal or laryngeal primaries [72–76]. Patients with multiple risk factors should be counseled on the placement of a prophylactic feeding tube prior to the start of treatment. Prophylactic placement may reduce the rate of weight loss and hospitalizations for dehydration, allowing patients to maintain treatment schedules and minimize treatment breaks. Conversely, routine prophylactic placement may lead to long-term dysphagia or even permanent PEG dependence.

10.6 Conclusion

HNSCC management continues to evolve, with landmark trials (Table 10.4) continuing to advance progress made in systemic agents and when to employ them. Whether as an induction agent, a radiosensitizer, an adjuvant modality, or for R/M disease, systemic therapy increasingly plays a greater role in HNSCC treatment. Well-tolerated agents with a minimal side effect profile and durable treatment effect remain elusive but increasingly possible in effectively managing this challenging disease.

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Nutrition Management for the Head and Neck Cancer Patient

11

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_11

Abstract

Head and neck cancer (HNC) patients often face multiple nutritional challenges before, during, and after treatment due to the close proximity of the cancer to organs that are vital for normal eating function. Common treatment-related side effects, such as dysphagia, odynophagia, dysgeusia, xerostomia, thick saliva, mucositis, nausea, and vomiting, all further impair the patient's ability to maintain adequate oral intake. Malnutrition and unintentional weight loss in HNC patients during and after treatment are associated with poorer treatment outcomes, increased morbidity and mortality, and poor quality of life, even in overweight and obese patients whose Body Mass Index (BMI) is not suggestive of malnutrition. The main nutrition goal for HNC patients is thus to maximize nutrition intake either orally or through nutrition support therapy in order to prevent or limit weight loss, preserve lean body mass, minimize treatment delays and unplanned hospitalizations, and improve treatment outcomes. This chapter will discuss nutrition interventions to manage common symptoms before, during, and after treatment for HNC. Guidelines will be provided for patients that require enteral nutrition or less commonly, parenteral nutrition.

Keywords

Head and neck cancer · Malnutrition · Dysphagia · Mucositis · Xerostomia Nasogastric tube · Percutaneous endoscopic gastrostomy · Enteral nutrition Parenteral nutrition

11.1 Introduction

Head and neck cancer (HNC) may greatly impact the alimentary tract, and patients can experience difficulty with chewing and/or swallowing due to impairment or tumor-related pain. HNC patients are often malnourished at time of diagnosis with 25–50% of patients having involuntary weight loss prior to starting treatment [1].

The high incidence of malnutrition in this population is further exacerbated by potential pre-existing chronic malnutrition associated with alcohol and tobacco use, which are two important risk factors for HNC [2]. Studies have shown higher rates of complications and reduced survival rates after surgery in HNC patients with weight loss of 10% or more during the 6 months before diagnosis [3].

Cancer treatments may further compromise a HNC patient's nutrition status. Surgery may necessitate a temporary or permanent feeding tube to adequately meet nutritional needs. Common toxicities from chemotherapy and radiation treatment such as mucositis, taste changes, xerostomia, nausea and vomiting, and loss of appetite will all compromise an individual's ability to eat. Malnutrition and unintentional weight loss in HNC patients during and after treatment are associated with poorer treatment outcomes, increased morbidity and mortality, and poor quality of life, even in overweight and obese patients whose Body Mass Index (BMI) is not suggestive of malnutrition.

This chapter will discuss nutrition interventions to manage common symptoms before, during, and after treatment for HNC. Guidelines will be provided for patients that require the use of enteral nutrition or less commonly, the use of parenteral nutrition.

11.2 Nutrition Assessment

Early detection of HNC patients who are at risk for malnutrition is vital to prevent or minimize weight loss during and after treatment. Weight maintenance is an important nutrition goal for HNC patients since weight loss has been shown to reduce survival rates and increase rates of complications after treatment. Urgent nutritional management is necessary for patients that lose $\geq 10\%$ body weight within 6 months of treatment or $\geq 5\%$ within one month of treatment. Weight loss in excess of 20% significantly increases infection, hospitalization, and early death rates. An outpatient Registered Dietitian (RD) consult for nutrition assessment should be considered before treatment to establish a patient's baseline nutrition status. HNC patients should then be reassessed on a weekly basis during treatment with a focus on symptom management and weight maintenance [4]. The goal of nutrition intervention is to continue a safe oral diet, manage symptoms, and supplement as necessary during treatment. Enteral Nutrition (EN) may be necessary in patients with new surgery wounds, or in patients with dysphagia and aspiration risk. See Table 11.1 for components of nutrition assessment.

11.3 Treatment Methods and Associated Common Side Effects

Treatment options for HNC may include surgery, radiation therapy, chemotherapy, and targeted therapies alone or in combination. Surgery may cause temporary or permanent impairment in oral food intake based on tumor location, extent of

Table 11.1 Components of nutrition assessments

Medical history	Location of head and neck tumor, planned treatment regimen and anticipated side effects, comorbidities (e.g. diabetes, hypertension, cardiovascular disease), and dental history (full, partial, or absent dentition)
Social history	Focus on personal resources and social support to aide in food preparation, food access, and nutrition supplementation
Physical exam	Look for signs of muscle wasting, ascites/edema, pressure ulcer/wound, mucositis, stomatitis, glossitis
Anthropometric assessment	Height, usual weight, current weight, weight change over time, BMI, fluid status
Relevant laboratory data	Albumin, pre-albumin, glucose, electrolytes, CBC (complete blood count) panel, lipid panel, liver function, renal function
Nutrition intake history	Detailed usual oral intake versus current oral intake, use of food records if appropriate, personal or prescribed diet restrictions (e.g. diabetic diet), food allergies and intolerances, nutrition impact symptoms (e.g. swallowing/chewing difficulty), use of dietary supplements (e.g. vitamins, herbs, probiotics), use of high calorie high protein oral supplements (e.g. Ensure, Boost), use of appetite stimulants (medicinal marijuana), use of enteral nutrition or parenteral nutrition prior to treatment

resection, and need to abstain from oral intake to facilitate wound healing. HNC patients often require ongoing intervention by a speech and language pathologist (SLP) to maintain speech and swallowing function after surgery. The goal of the RD is to facilitate adequate nutrition intake with appropriate food choices and/or oral supplements, and if medically appropriate, nutrition support therapy (enteral nutrition or parenteral nutrition). Good nutritional management is essential to patient's ability to complete the prescribed treatment course, minimize nutrition related side effects, and foster healing [5].

Radiation therapy can cause mucositis, xerostomia, thick saliva, and dysgeusia. Chemotherapy can exacerbate nausea, vomiting, mucositis, dysgeusia, and anorexia. Multimodality sequential or concurrent treatment is frequently necessary for patients with advanced stages of HNC. The more modalities employed in treatment, the more toxicity is to be expected and the more susceptible to malnutrition the HNC patient will be.

11.4 Dysphagia and Odynophagia

Dysphagia is a common symptom of HNC patients. Impaired mastication is also common and can contribute to dysphagia. Masticatory difficulty follows anorexia as the most significant predictor of reduced food intake. Removal of teeth during surgical treatment of HNC as well as poor baseline oral health may result in masticatory difficulty [6]. Odynophagia often results from mucositis during and

immediately following radiation and/or chemotherapy treatment [7]. Odynophagia may necessitate pain medication prior to oral intake. Patients should follow dietary guidelines for mucositis to minimize pain from food choices.

Patients experiencing dysphagia may exhibit observational symptoms such as drooling, choking, or coughing during or following food and beverage intake. Other signs include the inability to suck from a straw or hold food in the buccal recesses, gurgled voice quality, and an absent gag reflex. A common complaint is food "sticking in their throat". In addition to reduced oral intake, dysphagia can lead to aspiration. This can result in pneumonia from the bacteria in the oral cavity or the food or beverage entering the lungs and is referred to as aspiration pneumonia [8].

Swallowing assessment should be a part of the routine care for the HNC patient. SLPs assess patient's ability to masticate and swallow different liquids and food textures to determine the consistency needed to prevent aspiration. The SLP works closely with the RD to ensure patients are eating safely and adequately. RDs play an important role in the care of patients with dysphagia by providing modified consistency diet education and dietary recommendations to promote optimal oral intake.

Recommended food and fluid consistencies should be consistent with The National Dysphagia Diet (Tables 11.2 and 11.3). These dietary guidelines were developed by the American Academy for Nutrition and Dietetics (AND) in 2002 to standardize food consistency recommendations for dysphagia. For many patients with dysphagia, liquids need to be thickened. Patients may have difficulty controlling the fast flow of thin liquids (thickened liquids move slower and allow the patient to coordinate a bolus for safe swallowing). Modified liquid consistencies range from thin to thick and in order of increasing viscosity include thin, nectar, honey, and pudding thick liquids. Commercial thickeners or modified starches such as tapioca or cornstarch are used to thicken liquids to the desired consistency (Table 11.2). Thickeners may be added to beverages such as water, tea, coffee, juice, broth, milk, and liquid consistency foods such as soups.

Foods are modified to the following consistencies for dietary management of dysphagia and masticatory difficulty: pureed, mechanically altered, and advanced. The pureed diet is the most restrictive and recommended for patients with minimal or no dentition. Mechanically altered, advanced, and regular diets require mastication. The advanced diet is often used as a transition to a regular diet for patients with mild dysphagia (Table 11.3) [9].

11.5 Dysgeusia

Distortion of taste (dysgeusia), absence of taste sensation (ageusia), and reduction in taste sensitivity (hypogeusia) are common side effects associated with radiation fields that reach the tongue and chemotherapy treatment. Taste changes can also occur with biologic therapies and medication. Other factors that may contribute to taste changes include poor oral hygiene, infection such as Candidiasis, postnasal

Table 11.2 Modified consistency liquids

Category	Consistency	Examples	
Thin liquids	Pours like water	Coffee, tea, milk, thin cream soup, broth, liquid supplements, ice cream, sherbet, Italian ice, milkshakes	
Nectar-thick liquids	Similar to the consistency of tomato juice when stirred	Apricot, peach, or pear nectar; tomato juice	
Honey-thick liquids	Pours slowly, similar to the consistency of honey when stirred	Commercially thickened honey-thick liquids	
Pudding-thick liquids	Very thick	Pudding, Greek yogurt, custard	

Adapted from the American Academy of Nutrition and Dietetics (AND)

drip, gastrointestinal reflux, and oral mucositis [10]. Taste dysfunction is associated with anorexia, and decreased enjoyment of food [11]. Patients may describe their taste as impaired, unpleasant, distorted, or absent.

A review conducted primarily on HNC patients reported that 50%-75% of patients treated with radiation and or chemotherapy experienced dysgeusia [10]. Both chemotherapy and radiotherapy damage cells with a high turnover rate which includes taste bud cells. Cisplatin and Fluorouracil can cause a metallic taste sensation as they permeate the taste and odor receptive cells from the blood stream [10, 12]. Taste changes during radiotherapy usually worsen during treatment as the

Table 11.3 Modified consistency diets

	Dysphagia level 1	Dysphagia level 2	Dysphagia level 3
	Pureed foods	Mechanically altered	Advanced
Consistency	Pudding	Blended, chopped, ground, or mashed	Soft and non-sticky; bite sized
Foods to choose	Smooth pudding, custard, yogurt; pureed vegetables and fruits; pureed meat, pureed soups; farina and wheat cereals; pureed meats, poultry, eggs, and tofu	Well cooked pasta, oatmeal, corn flakes, wheat flakes, and puffed rice cereals; moist well-cooked vegetables; canned and cooked fruit, fruit pie; cottage cheese; moistened ground meat, moist casseroles, tuna, egg, or meat salad; baked beans	Well-moistened breads and cereals ex: pancakes with syrup and butter; canned and cooked fruits, soft peeled fruits (peaches, mangos, melon without seeds); ground meats and poultry, well moistened fish, eggs, rice, potatoes
Foods to avoid	Dry cereals, bread, rice; fruits and vegetables that have not been pureed, yogurt with fruit or nuts, cottage cheese, whole or ground meats, fish, or poultry, beans, cheese, scrambled eggs	Fruit with seeds, coconut, nuts, pizza, sandwiches, rice or bread pudding, sausage, bacon, whole grain cereals	Apples, grapes, pineapple, coconut, seeds, nuts, pizza, crusty bread, course cereals (shredded wheat, all bran), raw vegetables, chowders should be strained; nut butters unless used as part of a sauce or preparation that makes it easy to swallow ex: smoothies
Preparation tips	Prepare foods with blender or food processer to pudding consistency. Use a small amount of liquid to moisten foods to desired consistency. Examples: milk, water, broth, sauce, juice, cream. Use potato flakes or commercial thickeners to thicken foods	Use blender, food processor or masher to alter food consistency. Serve foods with sauces or gravies to moisten and add flavor. Vegetables should be cooked tender enough to mash with a fork	Moisten dry foods to soften and cut food in small pieces. Avoid sticky, crunchy, and hard textures

Adapted from the American Academy of Nutrition and Dietetics (AND)

cumulative dose increases; taste changes normally resolve after treatment, but may be permanently impacted depending on the radiation fields [10].

Medical nutrition therapy for HNC patients with dysgeusia includes oral hygiene and manipulation of food flavors. Patients should be instructed to brush their teeth twice daily with a soft toothbrush and use a non-alcohol mouth rinse as needed; alcohol dries the oral mucosa and causes pain in the presence of mucositis. Dentures and dental plates should be cleaned within 30 min after eating and before bedtime. Rinsing the mouth with a solution of warm water, salt, and baking soda

prior to eating may help remove lingering foul tastes and will also provide oral hygiene [13].

An individualized approach to managing taste changes is best due to the transient nature of dysgeusia during treatment. Patients are encouraged to experiment with different foods to determine what is acceptable to them. Cool or cold foods may be less offensive to a patient with dysgeusia as most cold foods are less pungent than hot foods [8]. However, for HNC patients treated with radiotherapy to their tongue, dysgeusia is often a persistent discomfort throughout treatment despite intervention.

The manipulation of flavors may improve taste. For example, adding salty and bitter flavors may increase the intensity of sour taste, sweet flavors may improve bitter tastes, and acidic flavors may increase sweet taste perception. Patients should be cautioned against foods that may increase oral or throat pain from mucositis. For example, acidic foods such as citrus fruits, tomatoes, pickles, and vinegar should be avoided. In the absence of mucositis, acidic foods may improve taste sensitivity [13].

Zinc deficiency may contribute to a decreased sense of taste and assessment of taste changes should include consideration for zinc deficiency prior to the start of treatment [8]. The relationship between zinc deficiency and taste perception is not well understood. One explanation is zinc is a cofactor of alkaline phosphatase, which is found in the taste bud membrane. Zinc may also play a role in regulation of the pores of taste bud microvilli [10]. However, current research does not support the use of supplemental zinc to prevent or treat dysgeusia resulting from treatment for HNC [10, 14].

11.6 Mucositis

Mucositis is a common side effect associated with chemotherapy and radiation therapy for HNC. It is manifested by inflammatory ulcerated lesions in the mouth and throat [15, 16]. Mucositis is often a serious complication which can limit treatment course, cause infections, dysphagia, weight loss, and pain. The pain and infection caused by mucositis often lead to nutritional deficiencies [17]. Certain foods can cause irritation to an inflamed mouth and throat while other foods are easier to consume which will allow for good nutrition. See Tables 11.4 and 11.5 for Nutritional Management and Supportive Care strategies to manage mucositis.

L-glutamine (glutamine) is an amino acid derived from foods rich in protein such as fish, red meat, beans, and dairy products. During times of serious illness and stress, decreased protein consumption and diminished ability to extract glutamine from consumed foods, places the body in a significant glutamine deficit and supplementation is recommended [18, 19]. Multiple studies have shown that glutamine supplementation can mitigate the incidence and severity of oral mucositis [20–23]. In a double blind, randomized, placebo-controlled trial by Tsujimoto et al. the incidence of oral mucositis (grade 2) was 22% lower with glutamine supplementation as compared to placebo ($p = 0.026$) as well as the duration ($p = 0.048$) [19].

Table 11.4 Nutritional management of mucositis

Recommended items to avoid	
Acidic foods	Oranges, grapefruits, limes, lemons, pineapple, tomatoes, plums, green apples, tomato sauce, vinegar and vinegar-based dressings, and pickled foods
Spicy foods/spices	Hot sauces, curry dishes, salsa, chili peppers, black pepper, mustard, garlic, cloves, cinnamon, ginger, peppermint spearmint in gums, candy, teas, lozenges, mint flavored liquid anti-acids, flavoring extracts
Salty foods	Salt, pickles, olives, potato chips, bouillon, and salt substitutes that contain potassium. Be cautious with hot dogs, bologna, salami and pastrami
Crunchy foods	Granola, bran, potato chips, corn tortilla chips, crackers, deep fried hard foods, toasted breads, pretzels, sunflower seeds, other large seeds, nuts, and popcorn
Carbonated beverages and caffeine	Carbonated beverages such as soda and sparkling water. If suffering from esophageal reflux consider avoiding caffeine containing beverages such as coffee, tea, and cola
Alcohol	Beer, wine, hard liquor, mouthwashes, cough syrup (use children's if needed), medications in liquid form that have alcohol (check the label or ask a pharmacist)
Tobacco	Cigarettes, cigars, pipes, and chewing tobacco
Recommended items to choose	
Complex carbohydrates	Soft breads, muffins, pasta, rice, oatmeal and other cooked cereals, dry cereals that are softened in milk, puffed rice, green peas, split peas, beans and hummus. High moisture casseroles and low acid soups such as cream of chicken
High protein foods	Beef, chicken, turkey (ground if needed) with gravy, canned tuna, salmon, eggs, custard, pudding, Ricotta cheese and other cheeses, cottage cheese, yogurt, milk, milk shakes, peanut butter, lentils, and tofu
Fruits and vegetables	Applesauce, canned non-acidic fruits, peaches, pears, apricots, melons, blueberries, cherries, grapes, bananas[a], avocado[a] and nectars of low acid fruits
Seasonings, sauces and condiments	Basil, dill, rosemary thyme, sage, and parsley; non-acidic, non-spicy sauces, gravies, hollandaise sauce, béarnaise sauce, cheese sauce, butter, and margarine

[a]Some high potassium foods can cause burning
Information adapted from eating hints: before, during, and after cancer treatment (2011). In N.C. Institute (ed.): U.S. Department of Health and Human Services National Institutes of Health

In recommending supplemental glutamine to HNC patients, it is important that the glutamine be of pharmaceutical grade and dosed at 30 g per day, up to 0.57 g/kg body weight. The majority of clinical trials have analyzed the effects of using 10 g of glutamine mixed into a liquid suspension and administered orally 3 times per day [19, 23]. Supplemental glutamine is available as a powder. In clinical practice, patients are recommended to mix 10 g (normally 2 teaspoons) into 4 oz of room temperature water and swish the solution in their mouth and swallow 3 times

Table 11.5 Supportive care strategies to manage mucositis

• Cook foods until they are soft and tender. Use a crock-pot or a pressure cooker to soften tough meats
• Cut food into small pieces to aid with ease of chewing or blend foods in a food processor • Topical application of pasteurized honey to coat sores may provide brief pain relief • Use a straw to drink liquids to minimize food contact with sores in mouth • Use oral anesthetics prescribed by physician to help control pain or numb oral mucosa prior to meal consumption • Consume room temperature foods. Extreme temperatures may be irritating and exacerbate pain • Use a very soft tooth brush and mild tooth paste. Ask your dentist for suggestions • Rinse your mouth out 4–6 times a day, before and after meals with ¼–½ teaspoon of baking soda and/or salt mix in 1 cup of water. Use only alcohol free labeled mouthwashes • Supplement with a total 30 grams of glutamine/day divided over 2 or 3 times a day

per day during radiation treatment for HNC. Patients are cautioned against mixing glutamine into acidic or hot liquids as these can denature the glutamine.

11.7 Xerostomia and Thick Saliva

Xerostomia or dry mouth is the most common late and permanent side effect of radiation treatment to the head and neck and significantly impacts patients' quality of life [24]. The parotid glands are often in the radiation field. Parotid dysfunction starts at 10–15 Gy and at levels of 40–50 Gy can translate to a 75% reduction in salivation [25]. Often, patients experience thick, ropy saliva. This problem can be further compounded by underlying predisposing medical conditions or medications.

Dry mouth can impact eating by affecting chewing, forming a bolus, swallowing, taste sensitivity, and speech. Increased dental caries and infections are also sequelae of dry mouth [24]. Dietary management guidelines of food preparation techniques, including moist foods, increasing fluid consumption, frequent rinsing of the mouth during the day and good dental hygiene are all necessary to aid patients with xerostomia [8].

There are a variety of over the counter sprays and tablets to help with a dry mouth along with pharmacological interventions. Xerodent™ tablets containing malic acid with and without fluoride have been investigated for their impact on dry mouth. Investigators found a 15-fold increase in saliva flow rate compared to unstimulated levels. This tablet was well accepted by most patients. These sugar-free tablets also increased the saliva bicarbonate secretion along with pH [26]. Diet modification strategies for xerostomia help the patient eat more comfortably while staying well-nourished to foster healing (Tables 11.6 and 11.7 and 11.8).

Table 11.6 Nutritional management of dry mouth

Recommended foods to avoid	
Tough to chew foods	Tough meats, dried meats like jerky, and dried fruits
Dry, crumbly foods	Cakes, crackers, dry chips
Sticky foods	Nut butters such as peanut butter and almond butter
Recommended foods to choose	
Complex carbohydrates	Cream of wheat, oatmeal, mashed potatoes, baked potatoes with butter or gravy lentils, split peas, and beans
High protein foods	Casseroles, meat loaf, chicken and dumplings, ground meat and chicken, tuna, egg salad, eggs (soft boiled and scrambled), cottage cheese, macaroni and cheese, stews, soups, hummus, milk shakes, fruit smoothies, pudding, yogurt
Fruits and vegetables	Canned fruits, applesauce, and most fresh fruits: apples, melons, banana, peaches, nectarines, pears, berries, avocados, and citrus fruits (if not experiencing mucositis); most vegetables
Other foods	Non-spicy sauces, gravies, sour cream, butter, margarine, custard, and ice cream

Information adapted from eating hints: before, during, and after cancer treatment (2011). In N.C. Institute (ed.): U.S. Department of Health and Human Services National Institutes of Health

Table 11.7 Supportive care strategies to manage dry mouth

- Soak foods into liquids: tea, coffee, milk, hot cocoa, and juices
- Chew on sugar-free gum (5 min of exposure is effective in increasing saliva production) or suck on sugar-free hard candy
- Eat popsicles, frozen tart green grapes or melon balls to help stimulate saliva production
- Use a cool mist humidifier, especially at night
- Drink plenty of fluids: juices, milk, and high calorie high protein beverages. Carry a water bottle or thermos. Keep water at bedside
- Rinse your mouth out frequently throughout the day with alcohol free mouthwashes, or ¼–1/2 tsp salt and/or baking soda in 8 oz of water solution
- Moisten lips with salves or lip balm
- Avoid all alcoholic beverages
- Try over the counter products that coat and moisten your mouth/throat such as oral lubricants, sprays, gels, lozenges, and rinses

11.8 Constipation

HNC patients may experience constipation as a result of chemotherapy treatments or medications such as opioid pain medications or anti-emetics with anticholinergic side effects, treatment-induced electrolyte abnormalities, lack of physical activity,

Table 11.8 Supportive care strategies to manage thick saliva/thick mucus

• Rinse mouth before eating with baking soda, salt and water solution (¼–1/2 tsp salt and baking soda to 8 oz water)
• Rinse mouth with sparkling water • Drink fluids throughout the day to maintain adequate hydration • Use a humidifier in your home, especially while sleeping and on dry windy days or when using the heater in the home • Experiment with fresh papaya fruit or juice of the fruit. Papain, the active enzyme in the fruit, can help dissolve thick saliva. Freeze the fresh juice in ice trays and use throughout the day for relief • Experiment with rinsing the mouth with unseasoned meat tenderizer that contains papain—dissolve 1 tsp in 8 oz of water, then swish, gargle and spit. DO NOT swallow meat tenderizer

and dehydration. In general, increasing intake of foods high in fiber such as whole-grains, fruits, and vegetables help alleviate constipation, but many of these food choices are contraindicated for a HNC patient experiencing dysphagia, mucositis, and xerostomia. Consider encouraging intake of warm juices and senna tea to help stimulate a bowel movement. An appropriate bowel regimen which includes laxatives and stool softeners should be prescribed, in addition to oral hydration and fiber as tolerated.

11.9 Nausea and Vomiting

Nausea and vomiting are potential side effects of highly emetogenic chemotherapy agents. Nausea and vomiting can also result from swallowed oral secretions during radiation treatment [27]. Excessive oral secretions cause coughing, gagging, and queasiness. Persistent nausea and vomiting contributes to malnutrition, which can be as high as 88% in HNC patients [27, 28]. Management of nausea and vomiting should include pharmacotherapy, medical nutrition therapy, and lifestyle interventions.

Medical nutrition therapy for nausea and vomiting include consuming low-fat, bland, starchy foods such as potatoes, crackers, bananas, and cereals when symptoms are present. Patients benefit from eating small, frequent meals and eating slowly. Foods that may contribute to stomach upset include fatty, spicy, or very sweet foods. Patients should be encouraged to drink fluids such as diluted fruit juices, low-sugar sports drinks, or rehydration formulas for adequate hydration. Often, nauseated patients tolerate rehydration formulas or sports drinks better than water.

Lifestyle recommendations include eating in a peaceful environment with fresh air and avoiding strong odors such as perfumes, cleaning chemical products, and cooking odors [13, 27]. Eating prior to receiving chemotherapy, especially a high protein meal, may be helpful in reducing chemotherapy induced nausea and vomiting [27].

11.10 Anorexia and Cachexia

Anorexia is the loss of appetite or desire to eat. It can be a side effect of the cancer treatment, psychosocial stressors, depression, or medications, as well as a result of the compounding effect of the multitude of symptoms affecting the ability to eat described in this section. Cachexia is a syndrome characterized by anorexia, weight loss, inflammation, muscle wasting, immunosuppression, abnormalities in fluid status, weakness, and increased morbidity and mortality. It is important to recognize that weight loss related to treatment-related side effects that are anticipated to resolve once treatment is completed, should not be characterized as cachexia [29]. Medical nutrition therapy goals include behavior and lifestyle changes such as eating small, frequent, easy-to-prepare meals, choosing nutritionally dense foods to maximize intake of energy and protein, use of oral nutrition supplements as a meal replacement if solid food is unfavorable, and increasing physical activity as medically able to help stimulate appetite. Other interventions include creating a pleasant dining atmosphere such as using fancy dishes and silverware, opting for non-traditional meal choices such as breakfast foods for dinner, eating with others, and scheduling meals. For HNC patients experiencing anorexia, it is important for the clinical team to encourage patients to view eating as a necessary part of the treatment and goals should be set to encourage oral intake despite the lack of desire to eat.

11.11 Oral Nutrition Supplements

Many patients undergoing treatment for HNC will need to supplement their diet with nutrient-dense liquids and potentially follow a full liquid diet during their treatment if they are unable to eat enough solid foods to meet their needs. For most patients receiving radiation therapy to the oral area, the cumulative side effects will impair the patients ability to masticate and swallow solid foods. For these patients, oral nutrition supplements can be vital to ensure adequate intake of nutrition and aid in minimizing weight loss during treatment. Patients may wish to prepare smoothies and milkshakes; however, given the degree of fatigue normally seen in patents undergoing treatment, food preparation can be difficult. Blenderized fruits and vegetables may be too thick for patients to tolerate and it can be difficult to achieve the thin consistency found in commerical shakes. Given these barriers, commerially

produced shakes with concentrated calories and protein can be used as meal replacements. Shakes that provide the most nutrition for the smallest volume are encouraged. High calorie, 1.5 kcal/ml, and high protein formulations include brands such as Ensure Plus and Boost Plus, by Abbott Laboratories and Nestle Nutriton Healthcare Inc. respectively. Boost Very High Calorie (VHC) is a 2.25 kcal/ml shake also made by Nestle Nutrition Healthcare Inc and is thicker than the 1.5 kcal/ml formula. There are many other commerically available brands and other shakes such as Kate Farm shakes, Kate Farms Inc. which is USDA Organic. All of the aforementioned examples are nutritionally complete and can be used as enteral formula as well as an oral supplement.

11.12 Nutrition Support Therapy for Head and Neck Cancer

The American Society of Parenteral and Enteral Nutrition (ASPEN) clinical guidelines recommend initiating nutrition support therapy in patients receiving anticancer therapy who are malnourished and anticipated to be unable to ingest and/or absorb adequate nutrients for a "prolonged period", which is defined as seven to fourteen days [30].

Nutrition support therapy (the provision of nutrients by routes into the body bypassing oral intake) can be delivered in the form of enteral nutrition (EN) through the gastrointestinal tract via a tube (preferred), or parenteral nutrition (PN) intravenously. For HNC patients with severely limited oral intake, EN is preferred and PN is rarely used. Early initiation of EN is essential in order to minimize the decline of nutritional status, offering better tolerance to treatment, and improving quality of life and survival [31]. Studies have shown that 84% of patients that refuse recommended tube feeding ended up being hospitalized for severe dehydration and malnutrition [32].

EN is preferred for individuals with an intact gastrointestinal tract to promote maintenance of gut integrity. Some patients may be encouraged to continue to consume foods and fluids orally although EN is providing most their nutritional needs, if it is safe to do so, to exercise swallowing muscles and decrease risk of long term EN dependence or for mere oral gratification. Although PN is not routinely used in HNC patients, it can be used in patients who are not able to tolerate EN or in patients with a chyle leak after extensive neck surgery [33, 34].

11.13 Route of EN Administration

The route of administration of EN is largely determined by the anticipated duration of need for nutrition support. Generally, nasogastric tubes are used for short-term therapy (<4 weeks). For long-term therapy (>4–6 weeks), percutaneous endoscopic gastrostomy (PEG) tubes are preferred [35].

It should be noted that the ASPEN clinical guidelines advise against routine use of nutrition support therapy in patients undergoing head and neck irradiation [30]. A comprehensive review of the literature conducted by Locher et al. concluded that there is insufficient evidence to support prophylactic PEG tube placement in HNC patients [36]. There is currently no consensus on whether prophylactic versus reactive placement of PEG tubes is preferable in this population. In one study, 33% of HNC patients treated with IMRT and concurrent chemotherapy required prophylactic PEG placement because of >10% weight loss in the setting of severely reduced oral intake. Furthermore, age remained the single most significant factor in predicting need for EN ($p = 0.003$). For adults aged 60 or greater compared to younger adults, the odds ratio was 4.188 (95% CI, 1.587–11.16; $p = 0.0019$) [37]. The NCCN Guidelines has published useful recommendations for prophylactic feeding tube placement (Table 11.9).

11.14 Method of Administration

There are three methods of EN administration: continuous, intermittent drip, or bolus [35]. Enteral feedings may be provided on any combination of feeding method and schedule that works for the patient or caregiver and meets the feeding goals of the patient. Since the PEG tube feeds directly into the stomach, the optimal method of administration is bolus or intermittent drip feeding since these closely mimic normal eating patterns. Bolus feedings are defined as formula delivered by gravity via a 60 ml catheter tip syringe over approximately 15 min and intermittent

Table 11.9 Indications for prophylactic feeding tube placement

- Severe weight loss prior to treatment, 5% weight loss over prior 1 month, or 10% weight loss over 6 months
- Ongoing dehydration or dysphagia, anorexia, or pain interfering with the ability to eat/drink adequately
- Significant comorbidities that may be aggravated by poor tolerance of dehydration, lack of caloric intake, or difficulty swallowing necessary medications
- Severe aspiration; or mild aspiration in elderly patients or in patients who have compromised cardiopulmonary function
- Long term swallowing disorders are likely

Adapted from NCCN guidelines for head and neck cancer version 2.2017

feedings are delivered via a feeding bag over 30–45 min with or without an enteral feeding pump. Feedings are administered 3–8 times per day, with increases of 60–120 mL every 8–12 h as tolerated up to the goal volume [30]. Pump-assisted continuous feeding is recommended for feeding into the small bowel or for patients who prefer to have feeding administered overnight or cannot tolerate bolus or intermittent feeding into the stomach.

11.15 Formula Selection

Enteral formulas may be classified as standard or polymeric, elemental, or specialized [35]. The selection of the appropriate formula is often directed by the RD (Fig. 11.1). Standard or polymeric formulas are suitable for HNC patients with intact gastrointestinal tracts [38]. A higher caloric density formula (1.5–2.0 kcal/ml) is ideal for patients unable to tolerate large volumes at one time, but it is important to remember that formulas of lower caloric density (1.0 kcal/ml) may be easier to digest. Elemental formulas containing hydrolyzed proteins (peptides) are reserved for patients with malabsorption or pancreatic dysfunction and are rarely used in the HNC population. Specialized formulas designed for a particular condition such as renal disease, hepatic disease, diabetes, or pulmonary disease require documentation of medical necessity for insurance coverage and are typically more expensive [35].

11.16 Optimization

The success of EN relies on the collaborative effort of the multidisciplinary team to monitor patients medically, but also help patients address issues that may arise related to delivery of formula and supplies, insurance/cost issues, and appropriate feeding administration [38]. It is imperative that the patient and caregiver receive education regarding the purpose of EN, the appropriate method of EN administration, PEG tube and site care, signs of feeding intolerance, and when to contact the multidisciplinary team. One of the most important parts of monitoring a patient receiving EN is to assess achievement of estimated nutritional needs [35]. Stable patients tolerate a rapid progression of EN, generally reaching the established goal within 24–48 h of initiation [30]. After initiation, patients should be instructed to report signs of intolerance such as nausea, vomiting, abdominal distension, abdominal cramping, and diarrhea. If bolus feeding is not tolerated, then feedings

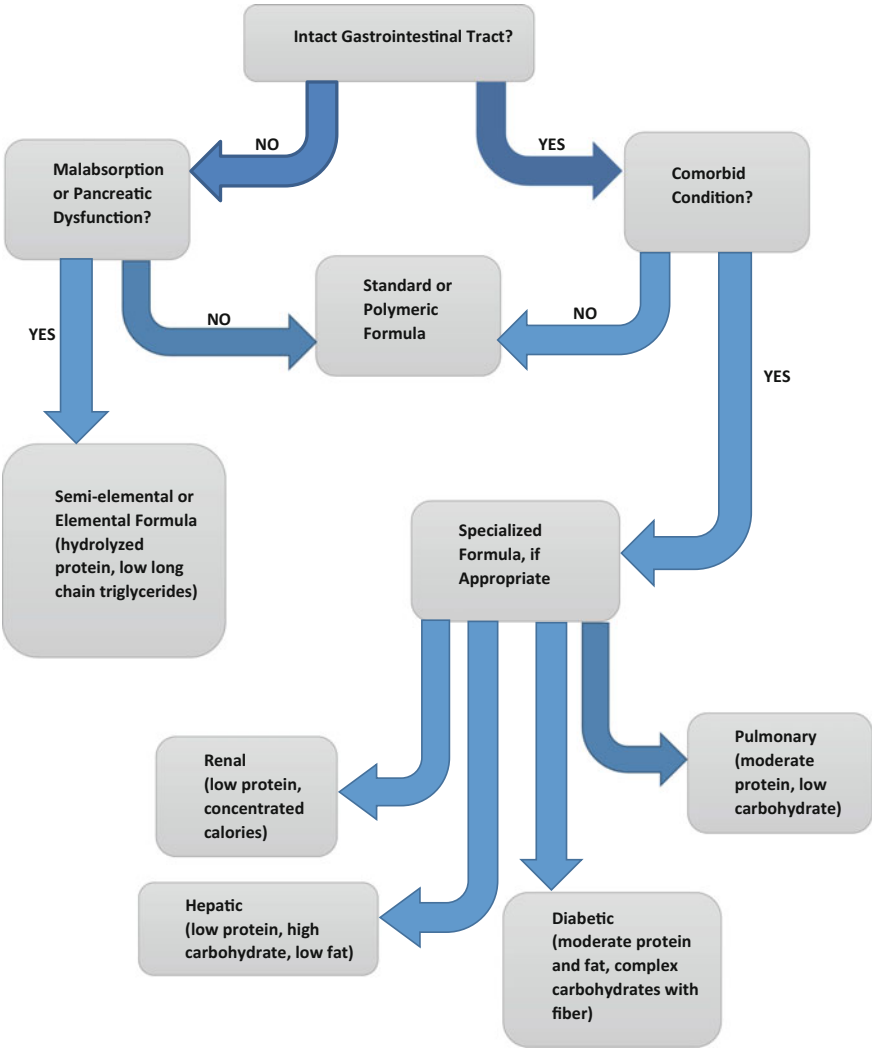

Fig. 11.1 Algorithm of formula selection for nutrition support

should be administered by intermittent or gravity feeding, allowing more gradual delivery of formula over longer duration. Timely nutrition assessments and follow up during the duration of treatment will ensure adequate delivery of nutrition via EN or combination of EN and oral intake. Nutritional guidelines, including EN, are more likely to be followed if a RD is a part of the multidisciplinary team [29].

11.17 Complications

Complications associated with long-term home EN include diarrhea, constipation, leakage from the tube site, tube site infection, tube dislodgement, and tube clogging [38]. These complications do not usually require hospitalization and can be managed in an outpatient setting. To prevent tube clogging, ASPEN recommends to flush feeding tubes with 30 mL of water every 4 h during continuous pump-assisted feeding or before and after intermittent feedings in an adult patient. It is also suggested to elevate the patient's backrest to a minimum of 30°, and preferably to 45° unless a medical contraindication exists, to prevent aspiration and pneumonia, as well as reduce symptoms of gastroesophageal reflux and nausea.

Long-term EN dependence and prolonged dysphagia are the main complications that deter clinicians and patients from appropriate placement of PEG. While the tube placement itself typically carries low procedural risk, data suggest that EN can induce long-term tube dependence and disuse of the swallowing mechanism which has been linked to complications such as prolonged dysphagia and esophageal constriction [31]. Collaboration between the RD and SLP on the multidisciplinary team is important to ensure treatment goals are aligned to promote swallowing rehabilitation, encourage safe oral intake when appropriate, and prevent long-term EN dependence.

11.18 Transition from EN to Oral Nutrition

Oral nutrition should be attempted when safe swallowing is established by the SLP. Patients may be more motivated to attempt oral intake as nutrition impact symptoms begin to resolve. Some patients may experience long-term swallowing problems and difficulty with eating or dry mouth and may require a modified-texture diet for a year or more following treatment [29]. The RD will assess oral intake and recommend gradual decrease of EN to ensure nutrition needs are met by combination of EN and oral intake and weight has stabilized. Patients can continue to supplement oral intake with oral nutrition supplements once EN is discontinued until oral intake is adequate to meet nutrition needs with whole foods.

11.19 Parenteral Nutrition (PN)

PN should be managed by an interdisciplinary nutrition support team that includes physicians, RDs, pharmacists, and nurses to reduce complications and improve efficacy and safety. PN is rarely used in HNC patients. Contraindications for PN include a functional GI tract, inability to obtain intravenous access, and if therapy is needed for fewer than 5 days for patients without severe malnutrition [34].

A patient who has been malnourished for greater than 2 weeks should be monitored carefully for refeeding syndrome, which is characterized by the development of potentially life-threatening metabolic changes (hypokalemia, hypophosphatemia, and hypomagnesia) along with the development of edema, cardiac, and respiratory distress [39]. The risk of refeeding syndrome can be decreased by correcting metabolic abnormalities prior to initiation of PN.

PN is initiated slowly by starting at 15–20 calories per kg body weight per day or no more than 1000 calories a day, and then titrate to goal over several days as tolerated while monitoring for undesirable drops in potassium, phosphorus, and magnesium levels [40]. Lab data, weight changes, physical exam and fluid balance are closely monitored to assess patient's tolerance to PN. Transitioning to EN or oral nutrition should be attempted as soon as the patient has adequate GI function to prevent GI mucosal atrophy and biliary sludge. PN should be gradually decreased once oral or EN intake reaches 500 calories per day, and PN should be discontinued once patient is meeting greater than 60% of energy and protein needs either orally or through EN [34].

Chyle leaks typically occur after extensive left neck surgery, due to the proximity of the thoracic duct [41]. Chyle leak is generally characterized with an increase in milky drain output with enteral feeding [42]. Management includes use of a middle chain triglyceride diet (MCT) or very-low fat diet, with the chyle leak commonly closing with time. Occasionally, PN may be used for a prolonged chyle leak. Output of >400–600 cc of chyle per day usually requires intervention beyond dietary adjustments: they include neck exploration with ligation, thoracic duct clipping from the chest performed by thoracic surgery, or embolization by interventional radiology.

11.20 Conclusion

Head and neck cancer patients often face multiple nutritional challenges before, during, and after treatment due to the close proximity of the cancer to organs that are vital for normal eating function. Common treatment-related side effects, such as dysphagia, odynophagia, dysgeusia, xerostomia, thick saliva, mucositis, nausea, and vomiting, all further impair the patient's ability to maintain adequate oral intake. As discussed earlier, weight loss has been validated as the strongest independent predictor of survival in patients with HNC. Multiple studies have shown that undernutrition is associated with poor treatment outcomes. The goal of the RD is to maximize patient's nutrition intake either orally or through nutrition support therapy with enteral or parenteral nutrition to prevent or limit weight loss and to preserve lean body mass, which will improve treatment outcomes by minimizing treatment delays and unplanned hospitalizations. Nutrition assessment before

treatment is often recommended for HNC patients to establish a baseline nutrition status. Continuous monitoring during and after treatment with a focus on symptom management and weight maintenance are all vital to optimize the treatment outcome of the HNC patient.

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Physical Therapy Challenges in Head and Neck Cancer

12

Dwight Baldoman and Ron Vandenbrink

Contents

Abstract

Treatment sequelae such as trismus, shoulder dysfunction syndrome resulting from spinal accessory nerve palsy, and radiotherapy-induced neck fibrosis are often overlooked when in the management of head and neck cancer patients. This chapter examines these underappreciated issues and their corresponding physical therapy intervention based on current evidence. Head and neck cancer survivors must contend with these disabilities for years after treatment has been concluded. A few quit their jobs which puts a tremendous burden on them and their families with a diminished quality of life. The physical rehabilitative needs

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_12

of head and neck cancer patients and useful interventions to help meet them are addressed.

Keywords
Radiotherapy-induced trismus · CNXI/Spinal accessory nerve palsy
Radiotherapy-induced fibrosis · Physical therapy · Prehabilitation
Survivorship · Shoulder dysfunction syndrome · Jaw-mobilizing device
Neck stiffness · Rehabilitation

12.1 Introduction

Physical therapists are professionals who examine, diagnose, and manage conditions that limit the body's ability to move [1]. They are uniquely qualified to assess and assist with the physical debilitating side effects of cancer treatment. This chapter will shed some light on what physical therapists do as part of the interdisciplinary head and neck cancer team. As cancer treatments have improved, so have long-term survival rates. Since cancer survivors live longer, they desire for better quality of life over longer periods. This has made physical therapy an indispensable part of the cancer management team.

Each patient's goal in physical therapy is unique. A professional driver, who lost his neck mobility due to radiation-induced fibrosis of his neck muscles, may want to regain his ability to turn his head for safe driving. A carpenter may wish to restore his ability to hold his arm up for a sustained period without neck pain after spinal accessory nerve palsy. Any patient could benefit from jaw-opening exercises to help mitigate trismus. Severe trismus could limit one's ability to eat by mouth or even get routine dental care. Several other treatment-related impairments that physical therapists address affect head and neck cancer patients. They include balance difficulty from chemotherapy-induced peripheral neuropathy, pain, physical deconditioning and cancer-related fatigue, frozen shoulder, cervical dystonia, postural dysfunction, disfiguring facial and neck lymphedema, post-surgical myofascial restriction, and neck weakness. All can significantly impact careers, self-image, families, and quality of life.

A recent systematic review on neck dissection reported that the most commonly reported outcomes were shoulder pain, shoulder droop, and loss of active shoulder range of motion. Prevalence rates for shoulder pain were slightly higher after radical neck dissection (RND) (incidence 10–100%) compared with modified radical neck dissection (MRND) (0–100%) and markedly higher compared to selective neck dissection (SND) (9–25%). Similarly, RND (44–100%), MRND (0–30%), and SND II–V (56%) displayed greater rates of shoulder droop than SND I–III (13%). In addition, reduction in shoulder abduction was found in unilateral RND (92–94%), and bilateral RND (100%), and MRND (23%) [2]. Outside of neck dissection, incidence of radiation-induced trismus has been reported as high as 42% of head and neck patients [3]. This chapter describes the more common complications of head and neck cancer treatment and their corresponding physical therapy solutions.

12.2 Prehabilitation

To date, it remains controversial as to whether a head and neck cancer patient should be seen by physical therapy before their cancer treatment has begun. The ideal pre-evaluation in this patient population should include but is not limited to a baseline functional assessment of the neck and shoulder, overall strength, mouth opening including any deviation and or TMJ involvement.

The issues arising with prehabilitation include whether it would unnecessarily increase the already considerable high anxiety level of the patient. In addition, the patient is often overwhelmed with visits to other providers. However, other patients may benefit from an informed visit that adjusts their expectations, should physical therapy be needed after treatments. To date, there is no data to support this approach for physical therapy in the head and neck cancer population. A selective approach by the MD may be more effective and could affect the outcome and the post-functional quality of life of the patient.

12.3 Rehabilitation

12.3.1 Trismus

12.3.1.1 Overview

Trismus, in head and neck oncology, is defined as a decrease in the maximum interincisor distance (MID) to <35 mm [4]. There are many different causes of trismus. Trismus can result from tumor invasion in the temporomandibular joint (TMJ) and neighboring muscles, fibrosis of masticatory muscles from radiation therapy and buccal tissues from surgery and/or radiation therapy. It is important to delineate radiotherapy-induced trismus (RIT) (Fig. 12.1) from other types, as its management is significantly more intensive. The impact on the patients' quality of life can also be very severe [5]. Pain and inability to open one's mouth preclude proper nutrition, oral hygiene, breathing, tumor surveillance, communication, and social interactions [6, 7].

To treat RIT effectively and efficiently, it is paramount for the clinician to understand its pathogenesis. RIT results from a localized inflammatory response which triggers a cascade of events leading to excessive collagen deposition, impaired local circulation, and scar formation [8]. It is associated with the upregulation of transforming growth factor (TGF) beta one [9–12]. RIT is multifactorial but MRI findings in severe trismus seem to suggest that most patients have fibrotic changes of masticatory muscles [13]. It usually occurs 4–12 months after radiation therapy, progresses rapidly in the first 9 months and persists for years [8, 14].

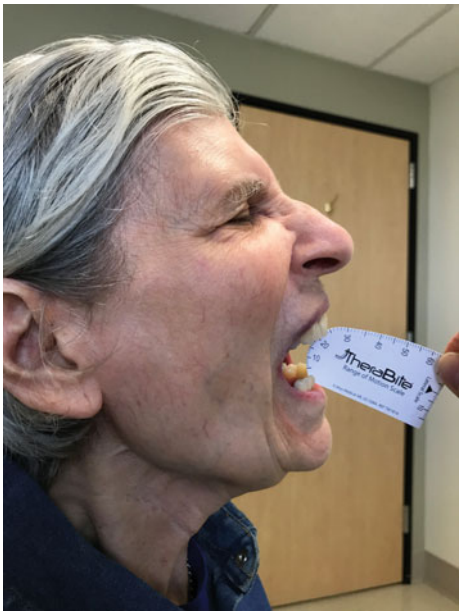

Fig. 12.1 Radiotherapy-induced trismus

12.3.1.2 Risk Factors

The incidence of RIT in head and neck cancer ranges from 5 to 46% [3, 4, 15]. Poor baseline physical function, radiation dosage above a certain threshold, concurrent chemotherapy, and radiation therapy exposure of ipsilateral masseter, pterygoid muscles and TMJ have shown to increase the risk for trismus [3, 16–19]. Non-modifiable risk factors include pre-radiation therapy MID of ≤ 40 mm and large tumors that necessitate big resections and free flap reconstruction plus adjuvant radiotherapy [20, 21].

12.3.1.3 Prevention

As with any disease, prevention is key. Advances in radiation oncology, such as intensity-modulated radiation therapy (IMRT), have reduced the incidence of RIT but have not completely eliminated it [22, 23]. In susceptible patients, self-care rehabilitative exercises have been tried without much success [24–26]. Part of the reason for this could be lack of compliance. Aside from movement pain, head and neck patients' poor physical function may preclude proper adherence to these exercises.

12.3.1.4 Treatment

Physical therapists have been in the forefront in helping patients with RIT, but due to the paucity of research, there have been no specific protocols on how to approach this condition. This has led to variations in practices that make it challenging to

empirically demonstrate the efficacy of physical therapy. Nevertheless, lack of physical therapy in many head and neck patients would be deleterious to the return of functional abilities and quality of life for patients as well as their families [27].

Exercise therapy is the centerpiece of RIT management. For it to be effective it must begin early after radiation is complete [18, 28–31]. It is important to recognize the etiology for reduced MID. Mouth-opening limitation could be intra-articular and/or extra-articular in origin; therefore, a detailed examination is warranted. The physical therapist commonly performs an assessment of posture, neck mobility, and the TMJ including intra-oral joint testing and palpation of muscles of mastication. In most cases of RIT, muscles of mastication become stiff and rigid, limiting muscle extensibility.

Exercises, when combined with jaw-mobilizing devices, have proven to be the most effective strategy in increasing MID [32]. Physical therapist supervision of jaw-mobilizing device use is critical as there are factors that warrant patient understanding for the treatment to succeed, especially in first 4–6 weeks [33]. For example, when patients experience pain in the process without a professional guiding them and helping control pain, early termination of treatment could result. The first 4 weeks is also when patients can regain the largest increase in mouth opening with jaw-mobilizing device [34]. Manual therapies such as masticatory muscle stretching and massage, temporomandibular/cervical joint mobilization, and myofascial release to neck musculature also augment the effectiveness of treatment [35].

Two of the most commonly utilized and studied jaw-mobilizing devices are TheraBite (Atos Medical, Horby, Sweden) and Dynasplint (Dynasplint Systems, Inc., Maryland, USA) (Fig. 12.2).

With TheraBite, patients manually squeeze the handle to apply torque, while with Dynasplint, patients incrementally increase torque and jaw opening by turning a handle. Such differences become important when chemotherapy-induced neuropathy impairs grip strength for TheraBite usage [36]. In addition, painful rebound muscle spasms, which cause setbacks, can potentially occur if the torque is exceeded. Once maximum MID has been reached, patients are advised to maintain daily stretching, as MID may regress quickly without continued usage.

A low torque-sustained stretch was superior to a high-torque short duration stretch in lengthening muscle contracture in an animal study [37]. In a prospective intervention study using TheraBite in a structured 10-week exercise program (30 s hold of passive stretch five times daily), the mean increase in MID was 7.2 mm after 3 months, with concurrent improvement in quality of life [38]. In a preliminary report using Dynasplint, an 11 mm improvement in MID was demonstrated after using the device 30 min three times daily for 3 months in combination with physical therapy, pain medications, and botulinum toxin injections [39]. Despite their benefits, jaw mobilization devices are expensive and not often covered by insurance: TheraBite is available for purchase for $500 while Dynasplint is usually for rent at $300 monthly. Of note, when initial mouth opening is less than 7 mm, exercises often starts with stacked tongue depressors (Fig. 12.3) since most jaw-opening devices would require a minimum MID to be utilized [40].

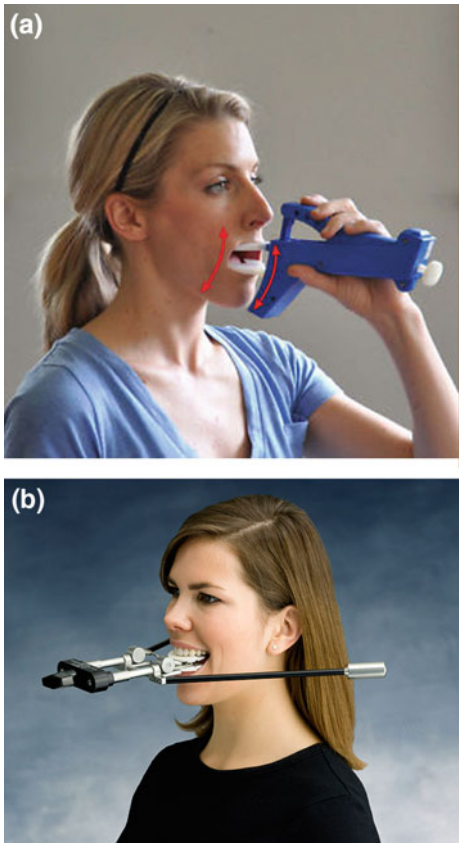

Fig. 12.2 Jaw mobilization systems. **a** TheraBite® Jaw Motion Rehabilitation. **b** Jaw Dynasplint® System

Since pain is a major issue in RIT management, it is essential to be in close communication with a pain specialist who can prescribe appropriate medication and administer Botox when necessary [41].

12.3.1.5 Goal Setting

It is important to note that physical therapy is subject to the same insurance reimbursement issues that affect other providers. When patients have reached their maximum potential for MID improvement, they are discharged and must take responsibility for maintenance of their gains in physical therapy through a home exercise program. The length of the physical therapy course will be influenced by several factors which include the patient's goals and determined mode of nutritional intake. A return to $\geq$36 mm MID is not always an appropriate objective. For instance, a patient who has a very poor prognosis of regaining the ability to eat by mouth may only aspire to recover the ability to brush his teeth which requires much lesser MID. On the other hand, a patient, who has intact swallowing ability but can only get back to MID of 24 mm, will have to adapt by cutting his food up first in

Fig. 12.3 Stacked tongue depressors to treat severe trismus <7 mm MID (maximum interincisor distance)

small pieces. Patients who have chronic trismus may not expect to regain pre-radiation therapy MID. Therefore, it is necessary to have the patient, physical therapist, and referring physician mutually agree on realistic goals in the plan of care.

12.3.1.6 Precautions

To avoid pathologic fracture, jaw-opening devices should not be used in patients with mandibular osteoradionecrosis [42, 43]. Osteoradionecrosis usually occurs in the first 3 years after irradiation but the risk remains throughout life [44]. A rare but fatal complication of radiation therapy is carotid blowout syndrome which has an incidence rate of 2.6% among patients who received salvage head and neck re-irradiation [45]. In addition, osteoradionecrosis of the first and second cervical vertebrae was noted in 1% of nasopharyngeal cancer patients who received radiation therapy [46]. In these situations, manual therapy should be used with caution.

12.3.1.7 Surgical Options

In recalcitrant trismus, resection of bilateral mandibular coronoid processes has demonstrated respectable outcomes. In a prospective case series of 18 patients who failed to improve after a minimum of 3 months of physical therapy, a mean improvement in MID of 21.8 mm was maintained 1 year postcoronoidectomy [47]. The subjects, 83% of whom received bilateral coronoidectomy at an average of 10 months after radiation therapy was completed, had a baseline MID of 20 mm or less.

12.3.1.8 Adjunctive/Alternative Therapies

There are adjunctive therapies that have shown some benefits. They are not yet widely accepted due to lack of robust empirical data to support their use. In a pilot study specifically addressing RIT, pentoxifylline, given at a dose of 400 mg two to three times daily for 8 weeks, resulted in a mean increase of 4 mm in MID [48]. At another study using case-control, neuromuscular electrical stimulation using surface electrodes twice weekly for an hour after each radiation therapy in the clinic with traditional swallow therapy done 2 weeks before and ended 2 weeks after the course of radiation therapy helped prophylactically reduce fibrosis in muscles [11]. Lastly, low-level laser therapy or photobiomodulation has shown promise in reducing fibrotic changes in injured muscles, but has not yet been proven to be beneficial in RIT [49].

12.3.2 Shoulder Dysfunction Syndrome

The quality of life following a radical neck dissection with the sacrifice of the spinal accessory nerve (cranial nerve XI or CNXI) remains of great concern. It is generally accepted that the return of shoulder function to a normal quality of life (QOL) depends largely on the healing of the spinal accessory nerve and in the prevention of injury to the cervical plexus. Patients who were subjected to a selective or a modified neck dissection (with sparing of CNXI) show normal to near-normal functional levels of the shoulder in the long term compared to those who underwent a radical neck dissection [50–52]. In accessory nerve-sparing surgeries, Sobol et al. [53] have shown that healing of the CNXI starts at 4 months post-surgery and could take up to 1 year for it to recuperate, and in some cases 2 years. Unfortunately, in the radical neck dissection with the sacrifice of CNXI, a shoulder drop is almost immediately apparent (Fig. 12.4).

To understand the drooped shoulder or shoulder dysfunction syndrome, it is instructive to review the force couples acting on the shoulder girdle. A force couple is defined as equal forces producing a rotation by pulling in opposite directions. The three couples include the *glenohumeral force couple*, which is the deltoid-supraspinatus versus the infraspinatus-teres minor-subscapularis; and *the serratus anterior and the trapezius force couple*.

In a radical neck dissection with the sacrifice of the CNXI, the shoulder girdle will be without the trapezius muscle group, causing a shoulder drop. In the drooped shoulder, the passive supporting role of the upper trapezius for scapular elevation is lost. Only the levator scapulae and the rhomboids remain as elevators, and are unable to fully compensate. The scapula drops since the lateral end of the clavicle drops down. As a result, the "serratus anterior and trapezius force couple" becomes ineffective. Loss of this force couple leads to an impairment of proper scapular rotation when the arm is elevated, and consequently, the humeral head loses its centrally located position at the glenoid fossa. Gradually the supraspinatus tendon is lengthened, leading to a loss in supraspinatus strength, which then unleashes the shearing force of the deltoid as it forces the humeral head upward. This impairs the

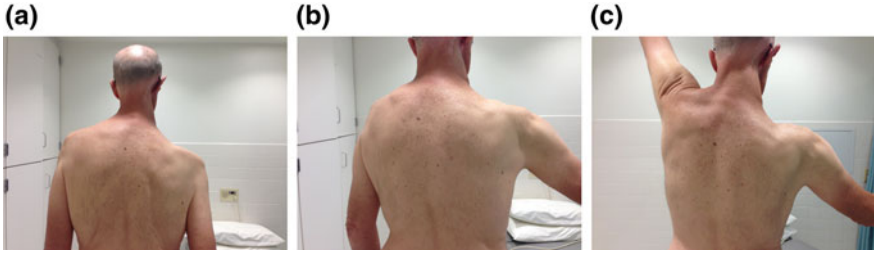

Fig. 12.4 Shoulder dysfunction after neck dissection. **a** Drooped right shoulder at rest with the winged scapula. **b** Right shoulder weakness on upward rotation, with the inability to raise an arm to 90-degree horizontal plane. **c** Normal left shoulder upward rotation

glenohumeral force couple. Without scapular rotation, the deltoid would shorten excessively at 90 degrees of abduction, and active abduction is severely restricted past this point. An excellent reference for further sturdy is Kelley and Clark's text [54], where the biomechanics of abduction and flexion are well explained.

12.3.2.1 Treatment

As mentioned, shoulder weakness after SND and MRND does better in the long term compared to after RND, where the CNXI is sacrificed [51, 55]. Kuntz and Weymuller [56] observed that the MRND group reported greater shoulder disability at 6 months compared to the SND group, but by 12 months there was no difference. In these two neck dissections, normal shoulder rehabilitation with a progressive resistance program is recommended depending on the patient's level of pain [57, 58]. Strengthening the scapular muscles is important since trapezius weakness has altered scapular biomechanics [59].

Patients with an RND with CNXI sacrifice are advised to wear a shoulder sling during the entire radiation treatment period. The foremost reason for the sling is to prevent any injury to the cervical plexus (traction injury) [60]. Slings also shorten the coracohumeral ligament, enabling it to support the humeral head and preventing excess descent.

A physical therapy evaluation is initiated after the surgery and before the first radiation treatment. This is not only to obtain a good baseline and to provide education, but also to instruct the patient to maintain neck mobility as much as possible during the radiation period until pain starts to exceed the patient's level of pain tolerance. Caution is advised to not place undue strain to the soft tissue within the field of radiation.

It is important to start the active supervised physical therapy immediately after the entire radiation period has been completed. Patients typically at this time may discontinue use of their sling. No matter what type of surgery, range of motion and stabilization exercises and short arc dynamic activities are initiated. For the next 4 months, low weight training with sub-maximal contractions are performed since the nerve begins to recuperate at four months post cancer treatment [53], unless CNXI is sacrificed.

For the selective and the modified neck dissection where CNXI is preserved, it is advisable to start with passive and active ROM exercises to prevent the development of adhesive capsulitis. Some studies suggest that the pain in the radical neck dissection may itself result from adhesive capsulitis. Another possibility is that the mass gravity effect of shoulder droop may lead to a cervical plexus traction injury and subsequent pain.

For patients with a radical neck surgery, it is advisable not to exceed the 90 degrees of elevation or abduction due to the excessive shearing and compression forces of the deltoid in the glenoid fossa. Strengthening the shoulder up to 90 degrees of abduction and elevation is more important, in order to protect the cervical plexus from sudden harmful stresses such as a traction injury.

Another important point is that only two elevators remain after RND: the levator and the rhomboids. While the levator is a tonic muscle, the rhomboids are phasic muscles that over time may become atrophic if left in a sedentary position. When that occurs, only the levator remains as an active elevator muscle for the shoulder. But if the levator (C3-4-5) is also injured, the patient will have no shoulder elevator at the involved side, and the entire shoulder girdle will drop completely, which causes injury to the cervical plexus. Therefore, strengthening the rhomboids through neuromuscular electrical stimulation and progressive strengthening exercises is critical. In the RND with the sacrifice of CNXI, a shoulder brace should be issued to the patient to protect the cervical plexus. The purpose of the shoulder brace is to provide proper support to the dysfunctional shoulder during lifting. For RND patients, it is advisable to wear a brace at all times during the day, especially when the patient is physically active or working at the computer for long periods.

12.3.3 The Stiff Or the Fibrotic Neck

The fibrotic neck after head and neck radiation remains poorly understood. In the presence of neck swelling, it is often wrongly diagnosed as lymphedema. Studies have shown that any irradiated area could become 5–6 times thicker in collagen formation due to the hyperactivity of the fibroblast cell in the connective tissue, especially of collagen type I and III [61]. The number of cells containing type I + III collagen mRNA increases in the upper dermis of irradiated skin, leading to fibrosis and thickening of the dermis. The rate of collagen synthesis is proportional to the level of mechanical tension, and as the skin increases in tension, the rate of collagen formation will also escalate [62]. Due to increased mechanical tension, the fibroblast cell is stimulated to produce distorted collagen, making the irradiated area more dense, avascular, and fibrotic. Hypoxia generates reactive oxygen species, which promotes inflammation, vascular damage, and profibrotic cytokines, further promoting collagen formation [63]. This clinically leads to contractures of the skin, muscles, and joints such as the temporomandibular joint, inducing trismus (Fig. 12.5).

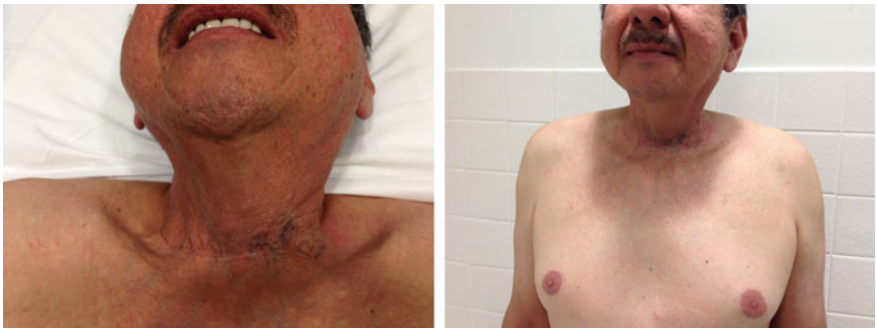

Fig. 12.5 Fibrotic neck changes after radiation

It is of utmost importance to address the stiff and fibrotic neck immediately. The key is early prevention through education and proper treatment. Most of the complaints are of a pressure-like tightness as of being choked, or a feeling that the airway is being trapped. One of the functions of the skin is the regulation of body temperature. Loss of normal skin pores result in heat that is trapped at the core of the neck and as a consequence the production of reactive oxygen species whose free radical activity could affect the deeper tissues such as vocal cords, with swelling as an end result [64–67]. This type of edema is not lymphedema, but edema due to the formation of molecular oxygen. The end product of molecular oxygen is swelling and inflammation, further triggering a cascade of further swelling. This distinction is critical since the management for lymphedema versus fibrosis is very different.

12.3.3.1 Treatment

Quantitative assessment of neck stiffness vs fibrosis is very difficult. According to Moloney et al. [68], there are many methods but not one that is preferred. Many mainly rely on hand palpation. The stiff neck is usually amongst the first complaints during radiation, and when untreated the stiff neck could result in fibrosis.

The stiff neck is different from the fibrotic neck. For the *stiff neck*, the goal is to prevent fibrosis from occurring. This is not only done by active or passive stretches but also through connective tissue mobilization. The rate of collagen synthesis is proportional to the level of mechanical tension. The goal is to decrease the mechanical tension on the fibroblast cell and to keep the skin pores open for proper core heat transference from the inside to the outer environment to prevent molecular oxygen to develop. When the mechanical tension on the fibroblast cell decreases, then the need to make more tissue stops, halting the development of fibrosis. Gradual strengthening of the neck flexors is introduced.

The goal for the *fibrotic neck* is to prevent the development of torticollis. Stretching the anterior neck and chest prevents the development of a flexion contracture. Anterior neck and chest stretching exercises such as done for thoracic outlet syndrome are also helpful. Cervical traction in a horizontal plane seems to be an effective treatment option for both the stiff and the fibrotic neck. Strengthening

of the interscapular muscles and neck extensors are meaningful, since the interscapular muscles are phasic muscles and will weaken over time when sedentary. One effective neck brace to prevent neck extensor weakness, but also to prevent a torticollis from occurring is the Headmaster Cervical Collar [69].

In this type of cancer population, good patient education is vital. To prevent heat build-up, the spontaneous flow of thermal energy is always from a higher temperature to a lower temperature difference. Therefore, the patient is advised to use the air conditioner on hot summer days, never to take hot showers, never to walk in the hot midday sun, and to use cold wet towel compresses instead of cold packs since plastic is not a heat conductor. Additionally, the patient must adhere to daily home regimens to prevent serious long-term side effects. The ultimate goal is to prevent irreversible, radiation-induced fibrosis.

12.4 Conclusion

In the head and neck cancer population, an individualized physical therapy program is needed rather than a "one size fits all" approach. To improve survivorship amongst head and neck patients, an interdisciplinary approach is advisable. Early education and prompt treatment to address physical therapy needs can substantially improve quality of life. Rischin et al. reported that amongst head and neck cancer patients "currently more than 60% of survivors have unmet needs." [70]. Other studies have found that decreased neck mobility remains one of the most unreported side effects of treatment, with an incidence of 60% [71]. Shone and Yardley [72] reported that 46% of those employed prior to RND surgery gave up their current line of work due to pain related to their shoulder, and 30% complained of moderately severe to severe shoulder pain. Despite these disparities, few reports have described the long-term effects of physical therapy [58, 73]. Ultimately, more research is needed to understand the lasting impact of intervention, with the goal of improving the livelihood of patients and their families.

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Occupational Therapy for the Head and Neck Cancer Patient

13

Priscilla Park and Mahjabeen Hashmi

Contents

Abstract

Occupational therapy is a health profession concerned with promoting health and well-being through occupation. A diagnosis of head and neck cancer (HNC) often invokes fear and anxiety because of the potential negative impact of the diagnosis and/or treatment on lifestyle and well-being. Occupational therapists perform a unique and important role in addressing quality of life concerns for HNC patients through applied expertise in lifestyle management,

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https://doi.org/10.1007/978-3-319-65421-8_13

facilitating the use of positive coping strategies and daily routine management. Occupational therapy concurrently assists HNC patients to effectively manage the debilitating stress and anxiety associated with HNC diagnosis, treatment, and recovery while facilitating a return to prior or adapted daily routines.

Keywords
Occupational therapy · Lymphedema · Prehabilitation
Complete decongestive therapy · Survivorship

13.1 Introduction

Occupation consists of work, play, leisure activities that are part of everyday life [1]. The primary goal of occupational therapy is to enable people to participate in the activities of everyday life and effectively engage in the occupations they want to, need to, or are expected to do. The Occupational Therapy Practice Framework serves as a conceptual framework that describes four subscales: Areas of Occupation, Body Function, Performance Skills, and Psychosocial Well-Being [2]. It is within these critical areas that occupational therapy can bring about improvement.

Individuals with HNC tend to rate highest on scales for psychosocial distress, depression, and suicide compared to patients with other cancer types [3]. Quality of life, as defined by the World Health Organization, is an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns. Quality of life is closely connected to, and affected by, numerous factors including one's degree of physical autonomy, social relationships, and environment. Many factors affecting quality of life are suddenly altered with an HNC diagnosis and the severe ramifications may easily go unaddressed.

Occupational therapists perform a unique and important role in addressing quality of life concerns for HNC patients through applied expertise in lifestyle management, facilitating the use of positive coping strategies and daily routine management. Occupational therapy concurrently assists HNC patients to effectively manage the debilitating stress and anxiety associated with HNC diagnosis, treatment, and recovery while facilitating a return to prior or adapted daily routines.

13.2 Prehabilitation

Prehabilitation is defined as engagement with rehabilitation services prior to the commencement of treatment of the disease for baseline functional evaluation, needs assessments, and to provide the patient an introduction to helpful strategies upon diagnosis. New models propose including rehabilitation services such as occupational therapy from diagnosis through treatment [4]. Rehabilitation has physical, psychological, and social aspects [5]. Occupational therapists partner with patients and caregivers to provide education regarding the potential side effects of treatment as well as coping strategies to mitigate their impact on important daily functions. As part of the multidisciplinary team, the occupational therapist works with the patient to prioritize goals that are meaningful to his or her quality of life from the outset of diagnosis.

Spending time with patients prior to the initiation of treatment gives the therapist an opportunity to obtain an occupational history and to understand the patient's roles and values. The patient may have concerns about roles and responsibilities they are not able to fulfill during their treatment. If necessary, referrals can be made to clinical social work or psychology to address these concerns more comprehensively. A variety of validated tools exist that can be used for prehabilitation assessment (Table 13.1) [6–13].

Depending on the patient's functional status and physical health before treatment, a conversation should be held about exercise and nutrition to optimize health. Patients may need guidance to help set realistic expectations regarding the change in performance capacity during and following treatment. Education on sleep hygiene and energy conservation should be provided for the patient to utilize before, during and after the commencement of treatment. Other useful strategies include monitoring fatigue levels throughout treatment and structuring daily and weekly routines to maximize participation in important activities while being careful to avoid overexertion.

13.3 Rehabilitation

Rehabilitation is the second phase of occupational therapy. It begins during the acute stage of cancer treatment and continues through the post-acute stage. Rehabilitation entails assessments of appearance, scars, lymphedema, facial weakness, oral coordination, pain, neurologic deficits, mobility, and range of motion limitation. Strategies are implemented to facilitate mobility, communication, energy conservation, and psychosocial well-being. HNC patients face a range of problems in the acute and post-acute stages (Table 13.1).

Table 13.1 Assessment tools and common interventions performed by occupational therapy throughout the continuum of treatment

Stages	Assessment tools	Physical	Functional	Psychosocial
Prehabilitation	– NCCN distress thermometer – FACIT—fatigue – FACT; head and neck – University Washington—QOL – Pittsburgh enjoyable activities scale (PEAT)	– Baseline measurements of cervical range of motion (CROM) – Assessment of and education on shoulder mobility and posture – Instruct on exercise routine	– Assessment of activities of daily living – Instrumental activities of daily living – Sleep hygiene – Energy conservation – Work simplification	– Coping strategies for anxiety and depression – Strategies for improved self-esteem, appearance
Acute care/Inpatient rehabilitation	– NCCN distress thermometer – FACIT fatigue – MOCA-cognitive screening – Hospital anxiety and depression scale (HADS)	– Pain management – CROM – Wrist and hand mobility and positioning – Facial impairment interventions – Delirium management – Sensory stimulation – Managing incisions and drain tubes – Managing tracheostomy – Lymphedema treatments – Management of xerostomia	– Bed mobility and positioning – Independence in self-care – Improve sleep patterns – Fatigue management – Work simplification – Oral and G—tube feeding	– Coping strategies for anxiety or depression – Appearance and self-esteem – Stress management
Outpatient/Long-term rehabilitation	– NCCN distress thermometer – FACIT fatigue – FACT; head and neck – MOCA-cognitive screening – University Washington—QOL	– CROM, shoulder, wrist, and hand mobility – Skincare and scar mobility – Management of radiation-induced fibrosis – Lymphedema – Pain management – Management of xerostomia	– Correct posture in functional activities – Improve sleep hygiene – Functional use of bilateral upper extremities – Oral and pharyngeal coordination exercises	– Coping strategies – Stress management – Improve self-esteem – Socialization

(continued)

Table 13.1 (continued)

Stages	Assessment tools	Physical	Functional	Psychosocial
	– Pittsburgh Enjoyable Activities scale (PEAT) – Canadian Occupational Performance Measure (COPM) – Occupational Performance History Interview (OPHI-II)	– Sensory stimulation – Fatigue management – Trismus interventions	– Eating, choices of food, planning for meal times alone and in social gatherings. – Independence in driving – Strategies to improve sleep – Oral/G—tube feeding – Energy conservation – Work simplification – Sexuality	

13.3.1 Physical Function

Significant impairments resulting from HNC treatments include facial weakness, oral incoordination, and shoulder impairment. Pending clearance from their doctors, patients may need to be taught facial exercises to improve coordination. Shoulder and upper quadrant movements will be facilitated with soft tissue and joint mobilization, therapeutic exercise and activities. Patients are often unaware of movements they can safely perform in the weeks following treatment and may need specific guidance on appropriate exercises. Education on how their treatment can affect anatomy, muscle strength, and range of motion is beneficial for patients and caregivers. Extended periods of immobility should be avoided, as this can lead to more difficult recovery. The occupational therapist can provide exercise programs as well as suggestions for sleep positioning to assist with comfort and facilitate timely healing. Certain patients will benefit from splints or braces for daytime and nighttime wear. These may be modified or omitted depending on a patient's tolerance and functional status as treatment progresses.

13.3.2 Fatigue

Cancer-related fatigue is defined as a "distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" [14]. Fatigue may be related directly to the cancer or its treatment and may continue for years after treatment is completed [15]. Fatigue can be magnified by ongoing stress, anxiety, or depression. The occupational therapist should discuss modifications to activities and routines to better cope with fatigue, and also explain the significant role exercise and physical activity play in overcoming fatigue. Patients, therefore, benefit from instruction on what they can expect in terms of fatigue and on how they can continue to participate in valued activities in order to maintain or increase the quality of life. In addition, education on ways to cope with stress and anxiety can mitigate fatigue.

13.3.3 Lymphedema

Lymphedema is swelling of soft tissues due to an accumulation of protein-rich fluid, debris, and fat within a congested lymphatic system with inefficient drainage [16]. Head and neck lymphedema (HNL) is a common side effect of head and neck cancer (HNC) and its treatments.

Tumor involvement of the head and neck lymphatic network, treatment-related interruption in normal head and neck lymphatic vessel drainage, as well as surgery and/or radiation therapy disruption of the lymphatic vessels can all contribute to HNL. It has been estimated that more than 50% of treated HNC patients will develop some degree of HNL [17]. Lymphedema can be external—involving the

Table 13.2 MDACC head and neck external lymphedema rating scale [18]

Levels	Description
0	No visible edema but patient reports heaviness
1a	Soft visible edema; no pitting, reversible
1b	Soft pitting edema; reversible
2	Firm pitting edema; irreversible, no tissue changes
3	Irreversible; tissue changes occur (normal tissue is replaced by scar-like structures, and increase in fibrosis)

external soft tissues of the head and neck or be internal—involving the aerodigestive tract. External lymphedema of head and neck is visible and is graded by the MDACC head and neck scale [18] (Table 13.2), modified from Foldi's classification of lymphedema. Internal lymphedema is difficult to measure, but it is visualized during endoscopy or stroboscopy.

The key to successful treatment of HNL is early diagnosis, referral, and start of treatment. The treatment can be started as early as 1–2 weeks after surgery. For patients receiving chemoradiation, manual lymphatic drainage can be performed in areas that are not in the direct field of radiation, depending on the patient's tolerance. More aggressive treatment should be held until chemoradiation is complete and the skin has an opportunity to recover from treatment. Complete decongestive therapy (CDT) is widely regarded as the most effective treatment for lymphedema (Table 13.3).

Manual lymphatic drainage is effective for decongestion of the face and neck, but is contraindicated in patients with hyperthyroidism, hypersensitive carotid sinus, and carotid arrhythmia. The frequency of CDT can be from one to three times per week depending on both the patient's needs and the severity of lymphedema. Patients should be instructed on how to perform self-manual lymphatic drainage as well as daily head and neck exercises that will facilitate fluid drainage. Techniques can be performed in front of a mirror, and a video can be made in the clinic to follow at home. The patient's caregiver can be instructed in manual lymph drainage and massage techniques to help with consistency of routine at home. A home exercise program for oral exercises can help with draining excess fluid from internal structures of the head and neck, and are often successful in relieving congestion. Different sleep positions can be beneficial, as some patients benefit from sleeping with their heads elevated. The occupational therapist may work with the patient to

Table 13.3 Complete decongestive therapy interventions

Complete decongestive therapy (CDT)
Pain management
Manual lymphatic drainage (MLD)
Skin and scar mobility
Compression bandages/garments
Head and neck exercises
Risk reduction education

determine which garments or bandages are feasible for the patient to wear, and the optimal timing for them to be worn. These treatments will be modified depending on the patient's progress.

13.3.4 Psychological Distress and Social Isolation

HNC can have devastating effects on patients including disfigurement, functional impairment, body image changes, anxiety, depression, speech and swallowing difficulty, and social isolation. The occupational therapist helps patients identify sources of distress and work through practical ways to reduce them. This can include identifying social support networks such as friends, family, religious groups, or support groups. The occupational therapist finds modified activities during the course of treatment so they can continue to feel productive. Patients often benefit from a discussion on the balance of work, play, rest, and leisure in their daily and weekly routine. A conversation about the patient's individual values can help them prioritize their objectives and give perspective on their current situation. The occupational therapist ensures the patient is receiving sufficient support from other care providers that can assist with their psychological health.

13.3.5 Sleep Hygiene

Sleep hygiene refers to good sleep habits. HNC patients often must deal with multiple issues that may interfere with sound sleep such as altered anatomy, inability to handle secretions, xerostomia, lymphedema and fibrosis, and supportive devices such as a tracheostomy or feeding tubes.

The occupational therapist educates HNC patients on options according to their specific problems. Some helpful tips include avoiding stimulants such as caffeine or nicotine, avoiding screen time before bedtime, avoiding large meals before bedtime, creating a healthy sleep environment (including reducing light, sound, and temperature) with a set bedtime routine, and daily regular exercise. The occupational therapist can review progressive muscle relaxation and meditation techniques, which can be beneficial. Patients often benefit from the use of meditation tapes and the practice of journaling before they sleep, which can also help to reduce anxiety associated with tasks that need to be completed the next day. If appropriate, patients should discuss sleep medication options with their doctor.

13.3.6 Intimacy and Sexual Health

Sex is a normal and necessary human behavior. Sexual activities are a vehicle for expression of love, procreation, intimacy, and pleasure. HNC patients may be limited by oral coordination, pain, xerostomia, thick saliva, disfigurement, body

image, impaired posture, lymphedema, fatigue, psychosocial problems, and fear of deficient performance, undesirability, or rejection.

As the occupational therapist meets with the patient regularly, they often build the rapport necessary for the patient to be comfortable discussing their sexual health. Barriers to intimacy and practical ways to eliminate them can be discussed. Strategies to address fatigue can be reviewed. The patient and their partner may be lacking clear communication, and covering ways to vocalize needs and emotions is often helpful. Depression and anxiety may lead to lack of interest in sexual activities and can be addressed using practical techniques. Referrals can be made to other healthcare providers if extensive counseling or medication is necessary. Once informed, the patient's doctor can decide if further testing for metabolic or hormonal imbalances may be beneficial.

13.4 Survivorship

The conclusion of cancer treatment is a welcome relief, but is also a time of adjustment. Moving forward with one's life entails coping with the fear of disease recurrence and both physical and emotional recovery. Studies show that cancer survivors experience psychosocial symptoms such as depression, anxiety, and social avoidance after their treatment. The occupational therapist partners with the HNC survivor to identify functional goals that will help them engage in meaningful roles and occupations. Occupational therapists address an individual's support structure, coping strategies, and participation in leisure, employment, and education [19].

Quality of life is a primary focus in the survivorship phase. This can be complicated due to the reality that quality of life is subjective and multidimensional, encompassing many aspects of life [5]. Occupational therapy provides tools to address symptoms that linger after treatment, such as fatigue, cognitive changes, neuropathy, pain, and lymphedema. Self-image is a common concern that may affect an individual's ability or willingness to reengage at work, home, and the community. A negative self-image can impede interpersonal relationships and sexual function.

Depending on how a patient's functional status has changed by the conclusion of their treatment, they may find it difficult to move forward with their lives in the same manner they did prior to diagnosis. The occupational therapist plays the role of a coach to define client-centered goals with the patient and works on a functional approach to meet them. If chronic fatigue is a concern, the therapist educates the patient on fatigue management. Activities can be prioritized according to importance and urgency and distributed at a manageable pace throughout the week. Incorporating exercise for increased endurance is crucial, and the therapist can help strategize with the patient to include an exercise routine as part of the patient's lifestyle. If lymphedema persists in the head and neck area, the therapist works with the patient to find proper garments and a compression routine to address swelling.

If the patient is struggling with cognitive deficits, the therapist can review compensatory strategies such as minimizing distractions, avoiding multitasking, and making lists. They additionally review factors that affect cognitive function, such as exercise, stress, nutrition, and sleep.

Patients often have difficulty settling themselves in a productive daily schedule after following a structured treatment schedule. They may be affected by shifts in the roles they had as father, wife, employee, athlete, etc. They could benefit from brainstorming steps to achieve their goals, whether it be returning to work/school, finding new employment, returning to previous family responsibilities, or finding meaningful activities in the community. It is important for the therapist to continually screen for clinical depression, anxiety, and other concerns that may need to be addressed by other healthcare professionals on the multidisciplinary care team. Because the patient sets goals pertaining to health self-management, activities of daily living, and participation in the community with the occupational therapist, most insurance providers will cover these treatments as part of the patient's plan of care. If a patient is limited in the number of visits they are allocated, the therapist will ensures they are used most effectively. The occupational therapist remains in communication with the patient's doctors for additional prescriptions or paperwork if indicated.

13.5 Conclusion

In summary, occupational therapists play a crucial role in the care of HNC patients throughout the continuum of care. Occupational therapists are key members of a multidisciplinary team, working with the patient to identify the aspects of their lives that contribute to their identity and well-being. Through skilled interventions the therapist assists the patient in navigating the hardships of diagnosis and treatment to facilitate active engagement in life, and ultimately, to enhance the quality of life throughout each stage of their care, and beyond.

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Psychosocial Needs of Head and Neck Cancer Patients and the Role of the Clinical Social Worker

14

Natalie Thome, Nellie Garcia and Karen Clark

Contents

Abstract

In this chapter, we examine the demographics and risk factors in the population diagnosed with head and neck cancer (HNC), what challenges these patients face post-treatment and what the role of psychosocial support through clinical social work is in managing these stressors. While many forms of head and neck cancer found in the early stages have a high cure rate, the side effects of treatment for these cancers have major life-altering effects. Previously, the majority of those

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https://doi.org/10.1007/978-3-319-65421-8_14

diagnosed with head and neck cancers were those who used excessive alcohol and tobacco, but the numbers are changing to include the human papillomavirus (HPV) as a major risk factor. Due to the behavioral risk factors that are often causes of head and neck cancers and the effects of treatment that often lend to psychosocial distress, the role of psychosocial intervention at time of diagnosis throughout the disease trajectory is essential for compliance with treatment and healthy coping post-treatment. Clinical social workers play an essential role within the multidisciplinary team of assessment and interventions for managing patient's psychosocial distress.

Keywords
Head and neck cancer · Clinical social work · Psychosocial distress
Depression · Anxiety · *SupportScreen* · Cognitive behavioral therapy

14.1 Demographics and Risk Factors of Head and Neck Cancer

Head and neck cancers (HNC) include cancer of the lips, mouth, pharynx which include the nasopharynx, oropharynx, and hypopharynx, larynx, salivary glands, paranasal sinuses and skin, soft tissues, and bones of the head and neck [1]. "Oral and oropharyngeal cancer is the sixth most common cancer worldwide, with the annual incidence of oral cancer estimated to be 275,000. This disease is associated with significant mortality, especially in the developing nations, with global 5 year survival rates estimated to be 50% [2]." While substance abuse and HPV are the major risk factors in the United States, worldwide there are several other risk factors that have been found to cause head and neck cancer. These include paan or betel quid in Southeast Asia [3, 4], maté in South America, [4, 5] preserved or salted food in childhood [6, 7], poor oral hygiene, occupational exposure such as asbestos, synthetic fibers, wood, nickel dust, or formaldehyde [6–8]. But 75% of head and neck cancers are caused by alcohol and tobacco use, and therefore, this disease has historically impacted men more than women [9].

The demographics are changing though as human papillomavirus (HPV) becomes a greater cause of HNC, especially in developed countries. This has caused an increase in diagnosis of HNC in women and younger people [10]. The incidence of HPV-related HNC is rising with numbers in the USA set to surpass the numbers of cervical cases by 2020 if the current trend continues [11]. Patients with HPV-positive HNC are typically younger than those with HPV-negative disease and tend to be white, male, married, educated, and employed [12]. Risk factors are thought to be a greater lifetime number of sexual and oral sex partners due to greater exposure to HPV [12–15].

Lifestyle risk factors are believed to be the greatest cause of head and neck cancer. These can pose challenges as patients face diagnosis, treatment, and treatment side effects as people often resort to their coping mechanisms in times of distress. As will be discussed in further depth in a later section, continuing to use alcohol and tobacco can cause more intense side effects, make the treatment less effective, and lead to greater likelihood of recurrence of cancer. For those with disease caused by HPV, less intensive treatment may be needed, and it has been found that these head and neck cancers have greater potential for cure. There are similar challenges of stigma attached to the diagnosis of HNC for those caused by HPV as those caused by alcohol and tobacco though which may lead to similar psychosocial distress.

14.2 Treatment and Its Physical Effects

Treatments offered to patients with head and neck cancer can include any combination of chemotherapy, radiation, and surgery. The treatment choices are dependent on the stage and location of the patient's cancer. When a patient has a tumor removed and/or radiation to the head and neck area, their ability to continue with life's daily activities and functioning is dramatically affected. Treatment for oral cancer is frequently disruptive to core functions of daily life including an individual's ability to eat, speak, and interact with others, and as such, the treatment of oral cancer is associated with a significant physical and psychological burden [16, 17]. Typically, the greatest side effects occur in the final weeks of radiation treatment and continue on for several months post-treatment, which can disrupt a person's daily functioning. The length of symptoms and side effects can vary depending on each person's situation, complications, and healing process. The recovery time for surgery is also dependent on each situation, but similarly, it can take weeks to months to recover function if full recovery to all functional capabilities is possible.

Some of the physical challenges that patients with head and neck cancer face post-surgery or due to radiation can include significant changes to their appearance and disfigurement. Surgery can cause a change in facial shape, visible scars, and change in ability to make facial expressions. Radiation can also cause disfigurement in changes to skin color, skin tissue, and its elasticity. Also, patients often need to have teeth extracted prior to having radiation [17]. Beyond the physical changes that others can see, the functional impairments can pose challenges to daily life. These can include difficulty speaking, swallowing, breathing, and pain. Further symptoms of oral dysfunction include dry mouth, limited to no taste buds, excessive saliva, or inability to control one's saliva. People at times experience limited mobility in their neck, shoulder(s), or arm(s). And often at final stages of radiation and for several months afterward, many experience significant weight loss due to

inability or difficulty with swallowing. Due to these side effects affecting daily functioning in some of the seemingly simplest bodily functions often for months post-treatment and for some permanently, HNC has been described as more emotionally traumatic than any other form of cancer.

14.3 Psychological Results Due to Diagnosis and Treatment

HNC is often associated with decreased quality of life and increased psychological distress [18, 19]. Psychological distress can be described as a combination of symptoms including anxiety, depression, cognitive, and behavioral impairments. Psychological distress ranges from transient, normal feelings of vulnerability, sadness, and fear to severe and crippling depression and anxiety [20]. Percentages of HNC patients with significant levels of distress range from 11 to 52% [21–25]. Howren found that depression was significantly correlated with disfigurement. This study looked at 82 patients 2 years out of treatment who continued to experience depression [10].

HNC patients report a worse quality of life and higher support needs with instrumental activities of daily living [17]. Due to the physical changes that impair these patients' ability to return to daily life as it was previously and their decreased functional status, depression and anxiety are common psychological effects that HNC patients experience. Approximately, 15–50% of HNC patients experience depression across the disease trajectory [22, 26] which may affect immunocompetence, treatment adherence, self-care behaviors, and resocialization [27–29]. A study done in Australia followed 37 HNC patients up to 18 months post radiotherapy to follow the psychological trajectory. This study identified fluctuating anxiety levels but younger patients and those with more severe physical symptoms were at higher risk. In addition, one-third of HNC patients reported symptoms above the cut-off threshold for depression following radiotherapy [30].

Another way that the high level of psychological distress that HNC patients often experience is manifest in a high suicide rate. One study has also found that the suicide rate for HNC patients is more than four times the rate in the general US population [31]. According to Moore, patients with oral cancer have a much higher suicide rate than not only the general cancer population but also the general population as a whole [17]. Therefore, ongoing monitoring for signs of distress is important following completion of acute therapy.

14.4 Disfigurement and Body Image as Predictors of Psychosocial Distress

Disfigurement is a common side effect of head and neck cancer treatment. HNC patients with facial disfigurement are vulnerable to distress, intimacy issues, and social isolation [32–35]. Whether side effects are caused by surgery or radiotherapy, post-treatment symptoms such as dry mouth, inability to speak clearly or eat safely can affect patient's self-image and interaction with others. HNC survivors indicate feelings of discomfort going out for meals or other social activities because they are unable to eat or swallow as they did before. One patient, depressed by her appearance after jaw cancer surgery, reported that she and her husband no longer socialized with friends over dinner as she could not mentally cope with their reaction to her condition. This patient is not alone in the psychosocial distress experienced from disfigurement that results in isolation; her husband is also impacted. Psychosocial distress impacts head and neck cancer patient caretakers and family members in a significant manner. This is discussed in further detail in the chapter on Supportive Care Medicine.

For many patients, returning to work helps to return to a sense of normalcy and purpose as well as financial stability. Treatment side effects, loss of functional abilities, social isolation, continued tobacco and alcohol abuse, anxiety, and depression can interfere with job performance and ultimately gainful employment [36]. Not only does continued alcohol and tobacco use challenge the ability of patients to return to work, but it can also reduce the efficacy of the received treatment, worsen symptoms, contribute to a lower functional status and ultimately is linked to a higher chance of recurrence or a second primary cancer diagnosis [28]. A study done in Germany and a separate study done in the Netherlands found results that the unemployment rate among patients with head and neck cancer was higher than in the general population. Other than patients who have survived central nervous, blood, and lymph cancers, head and neck cancer patients have the highest rate of disability or quitting gainful employment with lack of success in resuming significant work and ability to provide financially [37, 38]. Many of our patients report distress related to the side effects they experience and how this affects their ability to return to work. For example, one of these patients struggled in coping with how he would return to work where he spent his time speaking to clients on the phone in a customer service role post-laryngectomy.

Poor body image and loss of function ultimately lead to intimidation and social isolation making it difficult to maintain intimacy with their significant other or attempt a new intimate relationship. This sensitive issue is further addressed in the supportive medicine chapter.

14.5 Psychosocial Distress Screening at City of Hope Medical Center

The NCCN Clinical Practice Guidelines in Oncology and ASCO's Quality Oncology Practice Initiative (QOPI) recommends regular screening of cancer outpatients as a standard of clinical care. One tool includes *SupportScreen*, which assesses new patients during their first outpatient visit [37]. Patients answer questions by a handheld computerized device regarding 30 problem-related distress items (e.g., nutrition, psychosocial, spiritual concerns, and physical symptoms). A summary report of biopsychosocial concerns is printed and emailed in real time to appropriate providers. Patients themselves have a choice in the level of distress they identify and types of assistance they request.

Table 14.1 Demographics of head and neck cancer outpatients using the *SupportScreen* tool ($N = 322$)

Age groups		Education		Ethnicity		Gender	
Age groups	Valid percent	Education level	Valid percent	Ethnicity	Valid percent	Gender	Valid percent
18–39	7.8	Less than high school	3.3	Non-Hispanic	87.3	Female	26.4
40–64	54	Some high school	7.7	Hispanic	12.7	Male	73.6
65+	38.2	Completed high school	16.9				
		Some college	28.3				
		Completed college	18.8				
		Beyond college	19.5				

Household income		Marital status		Preferred language		Race	
	Valid percent		Valid percent		Valid percent		Valid percent
0–$40 k	42.7	Single	20.5	Armenian	2.2	Asian	16.8
$40–100 k	31	Life partner	0.4	Cantonese	2.9	Black	2.3
$100 k+	26.3	Married	58.5	English	86.5	White	80.9
		Separated	0.8	Farsi	0.7		
		Divorced	8.1	Korean	0.4		
		Widowed	6.6	Mandarin	2.2		
				Russian	0.7		
				Spanish	2.9		
				Vietnamese	1.5		

Table 14.1 shows the breakdown of demographics of the 322 screened HNC patients. The highest percentage of patients are males between the ages of 40 and 64, who have completed at least some college education, make less than $40,000 annually, are married, English speaking, and Caucasian.

Table 14.2 includes the highest reported biopsychosocial concerns triaged to social work. The greatest concerns include physical side effects including eating, swallowing and chewing, pain, and other not specified side effects. Other concerns include finances, anxiety, fatigue, ability to sleep, and family. As this screening is typically done at the first or second appointment with each physician, most patients have experienced minimal interventions or treatments at the time of screening. They likely are experiencing side effects of their cancer but not yet experiencing side effects of treatment. As

Table 14.2 Percentage of high distress (moderate to very severe) for head and neck cancer outpatients using the *SupportScreen* tool (N = 322)

Biopsychosocial problem triaged to social work	(%)
Eating, chewing, or swallowing	45.4
Side effects of treatments	40.5
Pain	37.2
Finances	35.3
Sleeping	33.9
Feeling anxious or fearful	31
Fatigue	30.4
How my family will cope	28.4
Fear of medical procedures	26.9
Questions and fear about end of life	25.2
Swelling	23.6
Feeling irritable or angry	21.6
Solve problems	21.6
Physical appearance	21.3
Needing help coordinating my medical care	21
Managing my emotions	20.7
Recent weight change	19.6
Managing work, school, or home	19.4
Understanding my treatment options	18.1
Transportation	17.4
Finding community resources near where I live	15.5
Walking, climbing stairs	15
Bowel movement/constipation	14.7
Becoming too ill to communicate	14.5
Needing practical help at home	10.4
Sexual function	9.1
Talking with the doctor	9.1
Tobacco use	7.4
Substance use	5.9
Ability to have children	3.1

previously mentioned, side effects and functional status are the greatest factors that lead to depression, anxiety, and a lower quality of life overall for this population.

14.6 The Role of the Clinical Social Worker and Psychosocial Interventions

Clinical social workers are a key part of the multidisciplinary team in the oncology setting and play an essential role in response to patient's biopsychosocial distress. Distress items are triaged to a team of clinical social workers for further screening of patients. Written information regarding clinical social work support availability is provided to patients who express a low to moderate level of distress so that patients are able to reach out for support if they are interested. For patients who respond with a severe level of distress, a volunteer makes a phone call while a clinical social worker is available to speak to them at the time of the call for initial psychosocial intervention.

An oncology social worker is fundamental to personalized cancer care and ultimate treatment outcomes, and has specialized expertise in identifying psychosocial distress. The clinical social worker can delicately communicate points of distress offering resources and coping strategies for both patients and their caretakers enabling completion of treatment. "Social workers serve as a component of the healthcare system by supporting, advocating, informing, educating, sensitizing, counseling, and synergizing all available resources and inherent strengths to the benefit of the patient, family and healthcare team" [38].

There are few studies demonstrating the effectiveness of psychological interventions for HNC patients. Cochrane ENT group evaluated several studies to determine effectiveness. They were unable to draw conclusions due to shortcomings in the studies designs or how they were reported [39]. Yet psychosocial intervention is a necessity in the treatment of these patients and their families. Without management, psychological distress in the form of anxiety and depression can result in noncompliance with treatment, more complications, delayed or stunted recovery, and inability to return to the highest level of function [21, 40, 41]. Recognition of anxiety and depressive disorders in cancer patients is therefore important because effective psychotherapeutic and pharmacologic treatments exist which can reduce morbidity and improve quality of life (QOL) [42–44].

Numerous randomized controlled trials (RCTs) have successfully tested and shown psychological interventions to be efficacious for cancer patients in reducing cancer stress, enhancing positive coping and QOL [45–47], improving health behaviors (diet, exercise, and adherence) enhancing biological responses such as immunity, and in some circumstances, reducing risk for disease progression and death [48–51]. However, open discussions about psychosocial difficulties and referral to appropriate services are uncommon [52]. Cognitive behavioral therapy

has been found to be an effective treatment for cancer patients with advanced disease who also have anxiety and depression.

The few psychological intervention trials that have been done in HNC confirm the efficacy of psychoeducational strategies, cognitive behavioral therapy (CBT), and problem-focused interventions [10]. One RCT was conducted with newly diagnosed HNC patients in which patients either received CBT or supportive counseling. Patients from both groups reported a significant reduction of anxiety, depression, and post-traumatic stress disorder symptoms, although more patients who received CBT experienced a remission of these symptoms [52]. While there are limited specific tools studied to determine the effectiveness of psychosocial intervention, CBT has been found as an effective mode of intervention for cancer in general and specifically for HNC patients.

14.7 Conclusion

HNC treatment is debilitating and has been found to have a significant impact on patient's practical, psychological, social, and spiritual well-being. Many HNC survivors experience psychosocial distress and struggle with returning to life as it was. Many suffer from depression and anxiety as a result and may experience other tangible consequences including a reduction in income related to their inability to return to work. The role of the oncology social worker is essential throughout the disease trajectory of an HNC patient from initial encounter for diagnosis and treatment through recovery and return to function. Utilization of psychosocial interventions by a clinical social worker will help patients adhere to the necessary treatment for their disease, reduce patient's psychosocial distress, and improve their overall outlook and quality of life.

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Supportive Care for the Head and Neck Cancer Patient

15

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_15

Abstract

Patients with head and neck cancers (HNC) face multiple psychosocial and physical challenges that require multidisciplinary attention and care throughout their disease process. The psychoemotional symptoms may be triggered by cosmetic disfigurement and/or functional deficits related to the cancer itself or cancer-directed treatments. These physical and emotional symptoms can be demoralizing and require acute and long-term professional assistance throughout a patient's lifespan. HNC remains one of the most challenging cancers to treat due to disfigurement, emotional suffering, social isolation, and loss of self-esteem. The emotional and physical symptoms a supportive care team can address are discussed in this chapter.

Keywords

Supportive care · Palliative care · Hospice · End-of-life care

Abbreviation List

HNC	Head and Neck Cancer
NCCN	National Comprehensive Cancer Network
MDD	Major Depressive Disorder
EOL	End of Life
ENT	Ear, Nose, Throat
5-HT3 receptor	5-hydroxytryptamine receptor antagonists
QOL	Quality of Life
CNS	Central Nervous System

15.1 Introduction

The involvement of a specially trained healthcare team that addresses holistic symptom management for HNC patients is of great importance. This specialty team is known as the palliative care team, and more recently, the supportive care team. Either term is intended to identify a group of healthcare providers such as physicians, nurse practitioners, social workers, psychiatrists, psychologists, child-life specialists and chaplains who focus on holistically addressing a patient's specific needs to achieve quality of life, as the patient defines it. Palliative or supportive care care can also be described as the promotion of physical and psychosocial health, regardless of the diagnosis or prognosis. An individual therefore does not have to be dying to benefit from supportive care involvement. The supportive care team is often consulted to assist with the care for the terminally ill and dying, so the association with hospice has resulted and continues to prevent early consultation that could be beneficial. HNC comprises only 5% of all cancers in the Western world, but it remains one of the most challenging cancers to treat and maintain quality of life because of its association with disfigurement, emotional suffering, social isolation, and loss of self-esteem [1–3].

15.2 Psychological Distress

Psychological distress encompasses a wide spectrum of symptoms ranging from transient feelings of fear or sadness to the more disabling symptoms of anxiety or depression. Patients with head and neck cancer face the gamut of stressors and challenges inherent to cancer in general (e.g., uncertainty, intrusive treatments, dependency, disability, threat of recurrence and mortality). In addition, their distress can be magnified by unique issues stemming from specific functional difficulties (e.g., speaking, eating, and breathing) and the stigma of disfigurement [4].

Studies have shown that patients with HNC have experienced increased distress at the time of diagnosis, as well as during and following treatment. Undetected and untreated psychological needs are associated with reduction in patient quality of life (QOL), extended hospital stays, malnutrition, complications with treatment, and treatment non-compliance [5].

The Distress Management Panel of the National Comprehensive Cancer Network (NCCN) has established guidelines for the recognition, monitoring, documentation, and treatment of distress [6]. According to these guidelines, all patients should be screened for distress during their initial visit and at appropriate intervals thereafter, particularly during changes in disease status and treatment.

A number of cancer centers have implemented distress screening tools in order to identify and flag distress in head and neck cancer patients at risk for illness-related biopsychosocial complications [7]. Such tools survey for nutrition, psychosocial, spiritual concerns, and physical symptoms. In addition to rating their level of distress, patients have the choice regarding the type(s) of assistance

requested. These surveys allow early discovery of patient stressors and allow triage to appropriate providers for timely intervention. In addition, statistical analysis allows for the identification of major areas of distress that warrant institutional resource allocation. Data collected indicates that functional impairment is a top source of distress in this patient population [7, 8]. Other significant stressors are pain, side effects of treatment, and impact on finances.

15.3 Body Image Disturbance

Body image is the subjective picture of one's own physical appearance established both by self-observation and by noting the reactions of others [9]. According to Rhoten et al. [10] conceptual model, the two primary causes of body image disturbance are disfigurement and dysfunction. Patients with HNC often not only experience changes to their physical appearance but also to function. Swelling and scarring, sensory changes such as pain or numbness, and functional impairment such as dysarthria or dysphagia may be temporary or long term, and have a significant impact on one's psychological well-being, social functioning, and overall QOL. Numerous studies have shown that body image concerns in patients with HNC have been associated with higher levels of anxiety and depression, poorer quality of life, and difficulties with sexual functioning [11–18]. The impact of such disfigurement and dysfunction on personal identity, ability to communicate or relate to others, and ability to feel successful interpersonally are all important considerations for the treatment team [19]. There appears to be a significant correlation between distress related to physical appearance and feeling anxious or fearful ($p < 0.001$) and between physical appearance and feeling irritable or angry ($p < 0.001$).

Fingeret et al. [16] noted that research in the area of body image in HNC is in its infancy. It is clear that further attention is needed to address body image concerns as part of comprehensive treatment for head and neck cancer. Clinical experience and data demonstrate the importance of understanding, and when possible, addressing body image concerns in patients with HNC, yet it is an understudied and undervalued problem many patients face [17]. Given the association with increased anxiety and depression, it is important to assess patients for emotional distress including symptoms of depression and anxiety related to body image. Identifying and treating distress in one area substantially impacts others.

15.4 Depression and Anxiety

Recurrent disease, radiation, low household income, and lack of perceived social support are significantly associated with higher levels of emotional distress [20, 21]. When patients are first confronted with the diagnosis of HNC, anticipatory anxiety is commonly seen, along with symptoms of distractibility and poor sleep. However,

once the patients are more adapted to the disease and treatment, the rate of anxiety significantly declines [20]. On the other hand, fear of recurrence and the unknowns related to mortality are common concerns for patients with cancer. Changes in appearance often create a visible reminder that one has, or has had, cancer and so does the ability to swallow or salivate. These reminders can contribute to anxiety, whether conscious or unconscious. Simply looking in the mirror can often trigger an anxiety response.

Depression is seen in HNC patients with a frequency ranging from 11 to 52% [20]. The potential triggering factors for depression include difficulties with eating and communicating, body disfigurement, changes in sexuality, presence of comorbidities, a history of substance abuse, impaired ability to work, dissatisfaction with care, and poor delivery of information by the medical team [22, 23]. Smith et al. [22] found the incidence of depression to approximate 15% in the period of acute survival stage (defined as time from diagnosis to treatment) followed by a rise in incidence in the period of extended survival stage (defined as time from the treatment completion through recurrence or surveillance) that was succeeded by a drop in incidence in the permanent survival stage (defined as >5 years after completing treatment). However, Chen et al. concluded that the incidence of depression remains high even in the extended and permanent survival stages with 17, 15, and 13% of the patients reporting feeling depressed at 1, 3, and 5 years after completing treatment. The same authors acknowledged that mental health services were underutilized despite such a relatively high rate of depression [24].

Due to high levels of distress, patients with HNC are at higher risk for suicide. Misono et al. [25] found that patients with oral cavity, hypopharyngeal, and laryngeal cancers comprised three of the top five cancer populations with the highest risk for suicide, the other two being patients with lung and stomach cancers. A study by Kam et al. [26] found that HNC patients were three times more likely to commit suicide than the general US population, with the prototypical profile being an older white male with advanced stage Iaryngeal and/or hypopharyngeal cancers. This appears linked to impairment of speech and swallowing functions that along with tracheostomy or gastros tomy tubes may further deteriorate body image and QOL. Other important predictive factors for suicide are preexisting substance abuse, psychiatric comorbidities, and poor family support [21].

15.5 Pain

Pain was defined by the International Association for the Study of Pain as “an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage” [27]. Pain in the HNC patient may be acute (lasting for less than 6 weeks) or chronic (lasting for longer than 3 months). It may be a direct consequence of the tumor or secondary to treatment. Pain can occur with the initial cancer presentation, during treatment, after

completing treatment, or with cancer recurrence [27]. van den Beuken et al. [28] concluded that HNC patients exhibited the highest prevalence (70%) of cancer-associated pain. Other literature reviews found that 80–100% of patients with advanced disease experience pain [27].

HNC-specific pain is often a combination of somatic and neuropathic pain. Somatic pain can result from direct invasion of the bones and soft tissue, infections, ulcerations, and radiation-related mucositis. Invasion and destruction of local nerves and plexuses can occur from cancer treatment and result in the development of neuropathic pain with the optic, vagal, and hypoglossal nerves being the most affected [29, 30]. The intensity of this pain can be amplified by normal daily activities such as chewing, swallowing, and speech.

Scharpf et al. analyzed 339 HNC patients and concluded that the presence of pain was associated with younger age, comparatively poor physical and mental health, depression, worse survival rates, and recurrence within the first year after treatment. Moreover, the intensity of pain correlated with survival. They found that HNC patients with low post-treatment pain exhibited an 81.8% of 5-year survival rate, compared to those with high levels of pain with a rate of 65.1% ($p = 0.04$) [31].

The incidence and intensity of pain are dependent upon the complexity of the cancer treatment itself. Early-stage HNC is usually managed with single modality treatment. More advanced cancers often require multimodality therapy regimens that have a greater impact on musculoskeletal and nervous tissue function, and in turn may lead to lifelong disabilities. Two studies noted that patients with advanced stage cancers who had both surgery and radiotherapy were significantly more likely to experience pain than those who received radiotherapy alone [29, 32]. Bianchini et al. [33], in a study on 164 patients, found no association between age, gender, and postoperative pain, whereas stage, surgery complexity, and tumor site were directly associated with increased risk for postoperative pain. Pain is often the only indication of disease recurrence. According to Smith et al., 70% of patients with recurrent HNC disease reported a change in pain sensation as the first reason they sought medical attention. Studies continue to emphasize the need for prompt and aggressive work-up for HNC patients with new or worsening pain [22].

Despite research showing that effective screening for pain and aggressive pain management are of paramount importance to ensure quality of life for HNC patients, pain continues to be under-addressed and under-managed. Several possible reasons include the following:

(1) Negative attitudes of healthcare providers who fear opioids side effects particularly addiction, cross-addiction, or chemical coping with this group of patients already known to be at higher risk for abusing alcohol and tobacco.
(2) Negative beliefs and fears of patients taking opioids regarding addiction, accidental death, side effects, dislike of taking medications, and difficulties in communicating symptoms.
(3) Negative impact of the opioid epidemic resulting in increased restrictions from the government and the healthcare system.

The effective management of HNC pain requires a multidisciplinary, non-pharmacological, pharmacological, and procedural approach.

The non-pharmacological approach includes

(a) Cutaneous stimulation, involving application of superficial heat (thermotherapy) or cold (cryotherapy).
(b) Massage therapy, especially when dealing with tissue scarring.
(c) Transcutaneous electrical nerve stimulation, which produces a low-voltage electrical charge to large, myelinated pain fibers.
(d) Acupuncture (manual acupuncture, ear acupuncture, electroacupuncture, or acupressure), which may relieve not just pain, but also dysphagia, xerostomia, and anorexia [34].
(e) Relaxation therapy measures, including focused-breathing exercises, pleasant imagery, meditation, and art/music-assisted relaxation.
(f) Hypnosis, which may decrease pain, nausea, fatigue, discomfort, and emotional distress [35].
(g) Psychotherapy, which may be helpful for patients with a history of psychiatric disorders or who develop depression.

HNC pain should be addressed pharmacologically in accordance with the World Health Organization pain ladder model (Fig. 15.1):

1. Non-opioids such as nonsteroidal anti-inflammatories (NSAIDs) or acetaminophen [36].
2. Anticonvulsants such as gabapentin and pregabalin. They should be gradually increased every 3–7 days up to the maximum daily dose of 1800–3600 mg for gabapentin and 450–600 mg for pregabalin, respectively. They should be weaned slowly due to the risk of seizures.
3. Other anticonvulsants such as carbamazepine, valproic acid, or lamotrigine and some antiarrhythmics like lidocaine or mexiletine [37]. Lidocaine is used in an oral solution for radiotherapy-related mucositis and intravenously for opioid-refractory cancer pain with a neuropathic component. Many institutions use lidocaine oral solution ("magic mouthwashes") in combination with antacids, diphenhydramine, steroids, antifungals, and antibiotics. However, there is insufficient data regarding its efficacy for treatment of mucositis. Clarkson et al. found that the oral solution with lidocaine, diphenhydramine, and aluminum hydroxide was not effective in treating oral mucositis. However, Miller et al. concluded that oral lidocaine was effective in reducing oral mucositis pain [38, 39].
4. Antidepressants particularly tricyclic antidepressants (TCAs) or serotonin-norepinephrine reuptake inhibitors (SNRIs), which can be used to address both the depressed mood and the neuropathic pain [36].
5. Skeletal muscle relaxants such as baclofen, tizanidine, and cyclobenzaprine [36].

6. Corticosteroids especially when pain is due to significant local inflammation. They may be used orally, parenterally, or topically, such as to address radiodermatitis after radiation. Side effects including suppression of the hypothalamic–pituitary–adrenal function, Cushing's syndrome, osteoporosis, secondary diabetes, and poor wound healing must be considered. Bur et al. found that long-term corticosteroid use was associated with a higher incidence of unplanned readmission after HNC surgery along with age, the presence of diabetes, preoperative dyspnea at rest, disseminated cancer, and contaminated wounds [40]. For cases requiring chronic corticosteroids, the goal should be using the smallest effective dose for the least amount of time.
7. Opioids are the standard pharmacological management choice for pain. Their action occurs on the mu, kappa, and/or delta receptors in the central and peripheral nervous systems [36, 37]. All opioids act as agonists on the mu receptors, whereas others additionally act on the delta or kappa receptors like morphine (kappa receptor agonist), hydrocodone and hydromorphone (delta agonist), oxycodone (delta and kappa agonist), and tramadol and tapentadol (mu agonists and norepinephrine reuptake inhibitors). Fentanyl, especially the transdermal (patch) form, is indicated for patients with impaired renal function or inability to swallow, or in patients who have experienced unwanted side

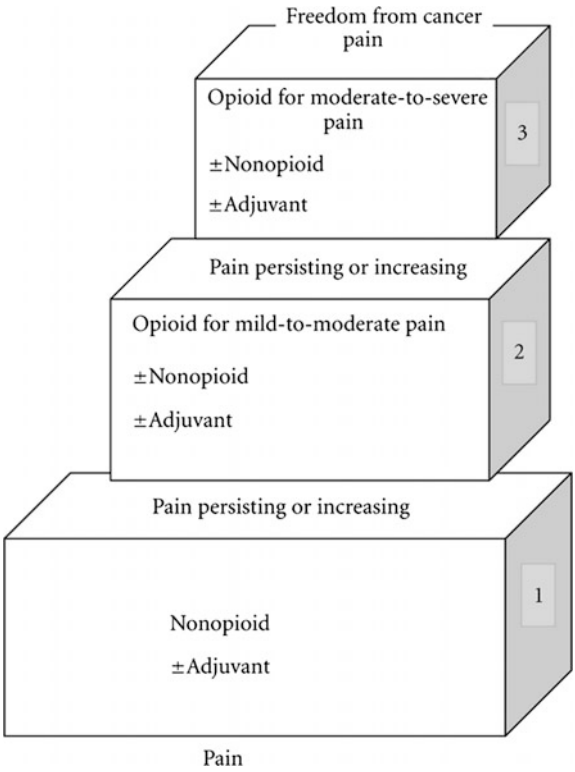

Fig. 15.1 World Health Organization pain ladder model. Reproduced from Namukwaya E, Leng M, Downing J, Katabira E—Cancer pain management in resource-limited settings: a practice review. Pain Research and Treatment—2011; 2011:393404

effects from other opioids. It should be avoided in cases that require a rapid opioid titration. The transmucosal fentanyl is a reasonable option for patients who are opioid-tolerant, with breakthrough pain and with difficulty swallowing. Codeine, morphine, oxymorphone, hydrocodone, and hydromorphone should be avoided in patients with an acute or chronic kidney disease, because such patients may develop opioid-induced neurotoxicity, secondary to accumulation of the renally cleared metabolites. Tramadol and Tapentadol should be avoided in combination with other serotonergic drugs such as SSRIs, SNRIs, and TCAs, due to the risk of serotonin syndrome.

Particular attention needs to be paid when initiating patients on long-acting opioids that are indicated solely for opioid-dependent patients, defined as taking at least 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid for 1 week or longer. Though the oral route is preferred, the parenteral administration of boluses or patient-controlled analgesia (PCA) is indicated for urgent relief or rapid titration.

8. Inhibitors of the N-methyl-D-aspartate (NMDA) receptors such as Ketamine or Methadone. Methadone is also a mu receptor agonist and is widely used to address both nociceptive and neuropathic pains. It also has the advantages of having a long half-life and low cost. However, the variations in individual pharmacokinetics make it unpredictable, and therefore it is recommended to first consult with a palliative care or pain management physician. Notably, there may be potential significant drug–drug interactions and QT interval prolongation associated with methadone.

Aggressive pain management is imperative for HNC patients or for any patient approaching end of life (EOL). Concerns regarding opioid dosing and side effects, particularly sedation, do not apply for the actively dying. At EOL, the desired outcome for pain management is to relieve suffering. This approach should not be misinterpreted as euthanasia or physician-assisted suicide. The goal to relieve suffering is protected by the "rule of double effect [42]," as the benefit of relieving one's pain at end of life outweighs the risks of causing death a few moments sooner.

Interventional procedures may be useful for the HNC patient when addressing pain refractory to pharmacological approaches and when there is a desire to decrease the patients' daily opioid intake. Some typical interventional pain procedures used for HNC patients are trigeminal and glossopharyngeal neurolytic blocks, the stellate ganglion block, and placement of an intrathecal pain pump. The decision to insert an intrathecal pain pump is commonly based on HNC patient's prognosis of more than 3 months, and when they are experiencing refractory pain or undesirable side effects from opioids such as severe nausea or constipation [36]. Serial injections with botulinum toxin (Botox) could be used to relieve pain related to muscle spasticity [41].

Medical cannabis was legalized for medical purposes in 29 states as of April 2017. However, at the federal level, marijuana remains a Schedule 1 controlled substance, which means it cannot legally be prescribed under federal law. The role of the endogenous cannabinoid system as a pain and immune system modulator is well known with the cannabinoid receptors CB1 and CB2 being the most researched. Medical marijuana has been studied for neuropathic pain, chemotherapy-induced nausea and vomiting, anorexia, and spasticity. Khelemsky et al. explored the acceptance of medical marijuana for postoperative pain and concluded that patients were more likely to accept it if they were young, had increased pain in the last 24 h, or believed that standard therapies were less effective in controlling pain [43]. Alternatives to smoking, such as using edible or oils or vaporizing, should be encouraged for HNC patients using medical marijuana even though there is not enough data proving a clear relationship between smoking marijuana and the development of cancers of the upper aerodigestive tract.

Conversely, there is evidence suggesting that concomitant use of medical cannabis and opioids may lead to a reduction in opioid doses and opioid-related mortality. Piper et al. [44] found that, after starting medical marijuana, there was a decrease of opioids requirements in 76.7% of the patients who regularly used opioids. The same study showed a decrease of anxiolytics use in 71.8% and sleeping aids in 65.2% in the same patients. Nonetheless, restraint is advised while its use is more thoroughly investigated, so that the opioid epidemic is not replaced by a marijuana epidemic.

There is limited data regarding the benefits of the synthetic cannabinoids for pain relief. Cote et al. showed that Nabilone was no better than placebo for pain relief. A buccal spray of synthetic cannabinoid, Nabiximols, was approved in Canada as a co-analgesic treatment for adults with advanced cancer with moderate-to-severe pain and at the highest tolerated dose of strong opioid therapy. However, Fallon et al. showed no superiority to placebo of this medication in reducing self-reported numerical rating scale (NRS) pain scores in advanced cancer patients [45, 46]. Further research is needed to assess the true benefits and side effects of cannabinoids for treating cancer-related pain [43–52].

15.6 Xerostomia

Xerostomia is a condition typically resulting after radiation in the HNC population and it is caused by the diminished ability to produce saliva. HNC patients may experience a sense of gagging, increased nausea, and even vomiting from the thick and sticky saliva that accumulates in the throat. This condition could also increase the risk for cavities and mouth infections. Patients are encouraged to use saliva substitutes, alcohol-free rinses, to gargle with dilute peroxide solution, consume a low-sucrose diet, and eat moist foods at room temperature. Patients should avoid caffeine, spicy and highly acidic foods, tobacco, and dehydration by drinking fluoridated tap water [53].

15.7 Dysgeusia

Dysgeusia refers to alterations in taste and it is highly prevalent among HNC patients and is dependent upon the radiation dose and volume of the tongue that was irradiated. Bitter taste is most often affected and the effect on sweet taste is largely based on whether the tip of the tongue was in the radiation field [54]. Dietary counseling can be helpful regarding food seasoning, selection, and expanding food choices [53]. Zinc sulfate is a well-tolerated therapy that can improve recovery of taste [55].

15.8 Anorexia/Cachexia

Anorexia/Cachexia is present in about 80% of all cancer patients before death including HNC patients. Families may require additional education about the disease process and the loss of appetite that commonly occurs when patients are actively dying. The importance of not force feeding loved ones should be emphasized to avoid bloating and aspiration, and inadvertently increasing their suffering.

15.9 Nausea and Vomiting

Nausea and vomiting may be triggered by brain or liver metastasis, dysphagia, intestinal motility dysfunctions, pain, anxiety, constipation, or medications. Management of nausea and vomiting includes general measures such as maintaining good oral hygiene, eating smaller volume meals, avoiding food odors. Pharmacotherapeutic measures include prokinetic or neuroleptic agents, benzodiazepines, corticosteroids, 5-hydroxytryptamine (5-HT3) receptor antagonists, and cannabinoids.

15.10 Fatigue

NCCN defines cancer-related fatigue as "a distressing, persistent, subjective sense of physical, emotional or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning [56]." Cancer-related fatigue is more severe, more distressing, and less likely to be relieved by rest compared with the fatigue experienced by healthy individuals.

It is important to recognize fatigue in patients with cancer as it can significantly diminish QOL if left untreated. Fatigue can begin before diagnosis and worsens during treatment and with disease progression [57]. Pain, dysphagia, dyspnea,

chronic infections, or depression can exacerbate HNC-related fatigue. It is important that clinicians evaluate for potentially reversible causes of fatigue (e.g., dehydration, anemia, and dyspnea) [58].

Fatigue can be managed via non-pharmacological treatments and pharmacotherapy. Examples of non-pharmacological treatments include prioritizing expenditure of energy, improving sleep hygiene, creating relaxing bedtime routines (e.g., listening to music, warm baths), establishing daytime routines that include physical exercise, and increasing social and spiritual support systems. Pharmacotherapies traditionally used to treat fatigue include the use of low-dose corticosteroids and central nervous system (CNS) stimulants such as methylphenidate, modafinil, or armodafinil [59]. There is some evidence that methylphenidate may help with fatigue in patients receiving active cancer treatment or post-treatment, but data remain inconclusive for modafinil [60, 61].

15.11 Dyspnea

Patients with HNC should be assessed for dyspnea based on the location and severity of their disease. For these patients, obstruction of airways is more concerning than just the sensation of dyspnea alone. Clinicians should obtain a thorough history to identify signs of obstruction such as a patient's inability to be supine, the presence of tachypnea, stridor on inspiration, and use of accessory muscles. Emergent cases of airway obstruction or other airway distress should be promptly referred to surgery. The inoperable cases may benefit from palliative sedation.

Basic management of dyspnea includes both non-pharmacological and pharmacological measures. Non-pharmacological measures include deep and slow breathing, repositioning, hypnosis, relaxation techniques, aggressive pulmonary toileting, and companionship to reduce spiritual and isolation triggers. Pharmacotherapies used as standard practice in palliative care for management of dyspnea include opioids, benzodiazepines, nebulized agents, and steroids [62].

15.12 Additional Considerations

Tobacco and alcohol use accounts for an estimated 75% of HNC cases [63–65]. Although many HNC patients will quit smoking before or during treatment, 14–60% will relapse [66–70]. Continued smoking is associated with several negative outcomes including increased risk of other smoking-related illnesses (e.g., coronary artery disease), secondary cancers, and primary cancer recurrence [71–73]. In addition, smoking reduces treatment efficacy [74, 75] and worsens treatment side effects [76–79]. One study found that depression was a significant predictor of continued smoking among HNC survivors, surpassing poor QOL and social support [80]. Most cancer institutions have developed smoking cessation programs that incorporate behavioral therapy and pharmacotherapy in accordance with NCCN guidelines.

Consumption of more than three alcoholic drinks per day is associated with an increased risk of HNC [81]. Daily consumption of 50 g of ethanol increases the risk for these cancers 2–3-fold compared to nondrinkers. Moreover, the effects of alcohol and smoking in risk of cancer are synergistic [81, 82].

15.13 Wound Care

HNC patients may experience open, fungating cancer-related wounds causing physical and emotional distress. Such wounds can increase the patients' social isolation when support is needed the most [83]. The malodor commonly results from aerobic and anaerobic bacterial overgrowth, presence of necrotic tissue, and high level of exudates. Wound dressings with alginate, silver, honey, or foam along with wound cleansing with antiseptic solutions or normal saline 0.9% can greatly assist with the reduction of odor. The direct application of antibiotics such as metronidazole gel is recommended over surgical approaches, especially at end of life. Aromatic candles, kitty litter under the bed, plain coffee beans, or vinegar are effective room odor-eliminating methods [83]. Pain management during dressing changes is crucial to ensure compliance and to minimize suffering.

15.14 Communication About Goals of Care and End-of-Life Care

Discussions to establish a patient's goals of care are essential. It is important to assure that therapy aligns with a patient's values and priorities, and is offered in the context of a relationship between the provider, patient, and family. A fundamental principle is to ask the patient and families about their understanding of the illness prior to giving medical updates.

Many communication tools and strategies exist for clinical use. Ariadne Labs in conjunction with Dana–Farber Cancer Institute has developed a Serious Illness Care Program with course offerings, as well as the Serious Illness Conversation Guide to facilitate conversations [84]. VitalTalk is a well-respected communication course developed by national leaders in palliative care [85]. Regardless of the tool used, the goal is to communicate clearly, honestly, and empathically to offer a treatment plan aligned with a patient's goals, values, and priorities.

In the setting of a comfort-focused approach, a signed statement of a patient's wishes (e.g., Out of Hospital DNR form, Physician Orders for Life-Sustaining Treatment (POLST) document specifying Do Not Resuscitate (DNR), Allow Natural Death (AND), or comfort only measures) is important to prevent undesired aggressive treatment such as chest compressions or intubation [86]. The care required for HNC patients can easily overwhelm family and caregivers, predisposing the HNC patient to

Table 15.1 Framework to tactfully introduce the concept of hospice to patients in need of it

Statements about why it may have become necessary	Statements to introduce services encompassed by hospice
• You have expressed a desire to be at home or in a more comfortable environment surrounded by family and friends • It is becoming very difficult for you to travel • I would rather see you conserve your energy for activities more important to you	• What if I could arrange for someone to – Deliver all your medications directly to your home? – Be available 24/7 for any questions and to send someone to your home to help in an emergency? – Provide special equipment free of charge (insurance-dependent) such as a hospital bed, shower chair, commode, and over-bed table? – Help support your family emotionally and spiritually? – Help educate and prepare your family on how to care for you? – Provide someone to be with you so your family could run errands?

die in a hospital setting instead of at home. Early discussion of services offered by hospice may reduce the chances of an unnecessary inpatient death [87].

The use of a home care service, such as home-based palliative care that can transition into hospice care is an ideal option. It is too common for individuals to think the suggestion of hospice involvement implies that they have only a short time to live. Hospice is most effectively discussed when the word "Hospice" is not mentioned until all services are presented. Once the word "Hospice" is uttered, the patient, family, and/or caregiver frequently become anxious and unable to focus on what is being said. An effective method to introduce hospice services involves statements regarding its necessity and then how it may ease the caretaker burden (Table 15.1).

With proper introduction, most patients are amenable to the idea of such support. It is at this time when it may be mentioned that the discussion was regarding hospice. Patients, families, and caregivers can nonetheless be shocked. Discussions about hospice often need to occur in multiple sessions, so families may have time to absorb information, but these conversations should never be abandoned. The healthcare provider must emphasize the positive services hospice can provide and re-enforce that hospice patients live longer and enjoy greater QOL [88–90].

Once hospice is considered an option, the patient and family often meet with area hospice organizations before their services are fully required. This allows time to establish rapport and familiarize the hospice team with the patient's routines and concerns. Early education and referral can eliminate the last-minute panic many families and caregivers experience when they realize they can no longer care for the patient alone. Early referral provides time to develop trust and secure a personality fit between the hospice staff and the patient and family [91].

15.15 End-of-Life Care

Despite all clinical and professional efforts, a patient's condition may continue to decline and comfort care/end-of-life care will need to become the primary focus. The most common cause of death for HNC patients is disease progression that results in physical deterioration, infection, and failure to thrive [1–3, 92]. Tumor growth can cause airway obstruction that can result in aspiration and development of bronchial pneumonia. Ultimately, respiratory failure is one of the most common causes of death for HNC patients [93]. Price et al. found that 48% (n = 20) died from respiratory complications such as failure, pneumonia, airway obstruction, and aspiration [92].

Preparing the patient and family for sudden death events is essential. The possibility of massive hemorrhage due to carotid rupture is rare, but a frightening concern for family. It is unusual for a carotid rupture to occur without prior warning. Frequent leakage or drainage from open neck wounds usually alerts the healthcare provider to this possibility. Precautions such as padding the bed with dark towels and having absorbent pads available to use for compression are recommended [87, 94].

Protecting the airway is another focus that can intimidate family members and unskilled healthcare providers. All should be prepared to address airway obstruction from tumor growth, anatomy shifts, tracheostomy tube displacement, and copious airway secretions necessitating aggressive pulmonary toileting that can suddenly block the airway. A weekly review of care for such emergencies should include insuring accessible and functioning suction equipment and a review of suctioning policy and procedures.

Family members may also need to be educated on the possibility of palliative sedation. This form of deep sedation may become the only option for an HNC patient with a DNR status to prevent further suffering from intractable pain and potentially imminent suffocation [87, 90, 95]. Palliative sedation is ethically acceptable and is defined as the monitored use of medications to induce sedation as a means to control refractory and unendurable symptoms near the EOL. A prospective study with over 500 patients showed that palliative sedation did not hasten death [96]. The acceptance of the term "palliative sedation" over "terminal sedation" has emphasized the difference between management of refractory symptoms at EOL over euthanasia [97].

The CARES tool is an acronym organized pocket reference developed for nurses, which addresses the five most common symptom management needs of the dying and provides recommendations and prompts to effectively care for this unique patient population (Table 15.2).

Table 15.2 CARES tool summary

C	Comfort	– Pain and suffering is the greatest fear for any dying patient and his/her family – Comfort must be provided holistically and should not only focus on pain management but also include reducing anxiety, stress, and interruptions to allow closure – Terminal pain/pain during dying is best managed by around the clock, scheduled or a continuous infusion of opioids and additional doses (boluses) given as needed for breakthrough pain – Discontinue unnecessary tests and activities that will not be treated and will reduce time for closure – There are no dosage limits. Titrate to effect
A	Airway	– Support airways and declining respiratory function – Educate family regarding the normal process of dying and breathing patterns of the dying versus suffering – The use of supplemental oxygen during the dying process is often ineffective but may help to minimize the family's fears of their loved one suffering – Consider use of anticholinergics, anxiolytics, or opioids
R	Restlessness (terminal delirium)	– Nearly, 90% incidence of terminal or restless delirium in actively dying patients [98] – Provide education for the family on methods to minimize agitation and anxiety – Consider the use of anxiolytics or antipsychotics
E	Emotions	– Support the emotional and spiritual management requirements of the dying through conversation, touch, and celebration of the individual's life – Remember every family is unique and grieves differently – Support rituals and assist with obtaining desired clergy or equipment – Your humanity is needed the most now. Always be available
S	Self-care	– Emphasized for the healthcare providers – Address issues of moral distress, burn-out, and compassion fatigue – The need to communicate and seek out personal and professional meaning is encouraged, as is the acceptance of professional grieving, and reframing the sense of failure

Based on B. Freeman (2012) CARES Tool. Published with permission

15.16 Conclusion

HNC patients have unique psychosocial and physical care requirements that must be effectively addressed. The cosmetic disfigurement and/or functional deficits related to this cancer can be demoralizing and may require acute and long-term professional surveillance and assistance in coping. The increased risks of airway obstruction and respiratory infections can greatly impact patient's QOL, and such circumstances can make pain management and issues with anxiety and depression extremely challenging to manage. Collaboration with a supportive care team can provide multidisciplinary assistance to achieve the quality of life that patients ultimately desire.

Acknowledgements A special thank you to Karen Clark, MS of City of Hope for helping to analyze the data and assisting with content edits.

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Survivorship Care Planning and Quality of Life

16

Denice Economou and Virginia Sun

Contents

Abstract

Roughly 436,000 survivors are living with a history of head and neck cancer (HNC), accounting for approximately 3% of all cancer survivors in the United States [1, 2]. With advances in treatment, long-term survival is increasingly common in HNC populations. Despite increasing awareness of survivorship issues, many challenges remain. These include lack of knowledge on late and long-term effects of treatment, and poor integration of survivorship care guidelines into oncology practice. Survivorship care plans (SCPs) are increasingly important for HNC survivors to improve quality of long-term survival.

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E. Maghami and A. S. Ho (eds.), *Multidisciplinary Care of the Head and Neck Cancer Patient*, Cancer Treatment and Research 174,
https://doi.org/10.1007/978-3-319-65421-8_16

Quality survivorship care should focus on management of late and long-term effects of treatment, surveillance for cancer recurrence and second primaries, promotion of healthy lifestyle, and care coordination between providers. This chapter will describe common quality of life (QOL) issues in HNC survivorship, and review the current survivorship care guidelines in HNC.

Keywords
Survivorship · Cancer · Quality of life · Symptoms · Care plans
Late effects

16.1 Definitions of Cancer Survivorship

Cancer survivorship was described in 1985 as "seasons of survival" by Fitzhugh Mullan, a physician and cancer survivor. Mullan described three phases of cancer survival: (1) the acute survival phase that includes diagnosis and treatment; (2) the extended survival that begins at treatment completion; and (3) the permanent survival phase where survivors enter a period of cure [3]. Currently, the most endorsed definition of survivorship is provided by the National Coalition for Cancer Survivorship (NCCS). According to the NCCS, cancer survivorship begins at the time of diagnosis until the end of life; it encompasses a patient's experience of "living with, through, and beyond a cancer diagnosis" and includes family members, friends, and caregivers [4, 5]. In 2013, the American Society of Clinical Oncology (ASCO) adopted a more distinct and functional definition of long-term cancer survivors as "individuals who have successfully completed curative treatment" or "transitioned to maintenance or prophylactic therapy." [6]. For the purposes of this chapter, we will focus on published data, survivorship care planning recommendations, and guidelines for HNC survivors who have completed primary treatment.

16.2 Quality of Life Issues in HNC Survivorship

Ferrell et al. [7] organized a framework of QOL issues for HNC survivors into functional, general physical, psychological, and social well-being domains (Fig. 16.1). QOL assessment in HNC survivors is increasingly important given the growing incidence in younger populations, and the long-term sequelae of multimodality treatments [8]. In general, current evidence suggests that self-reported global health status improves in HNC survivors after treatment completion [9, 10]. However, areas that do not recover to baseline include physical functioning, role functioning, social functioning, fatigue, appetite loss, financial difficulties, speech, and social contact [10]. Predictors of poor

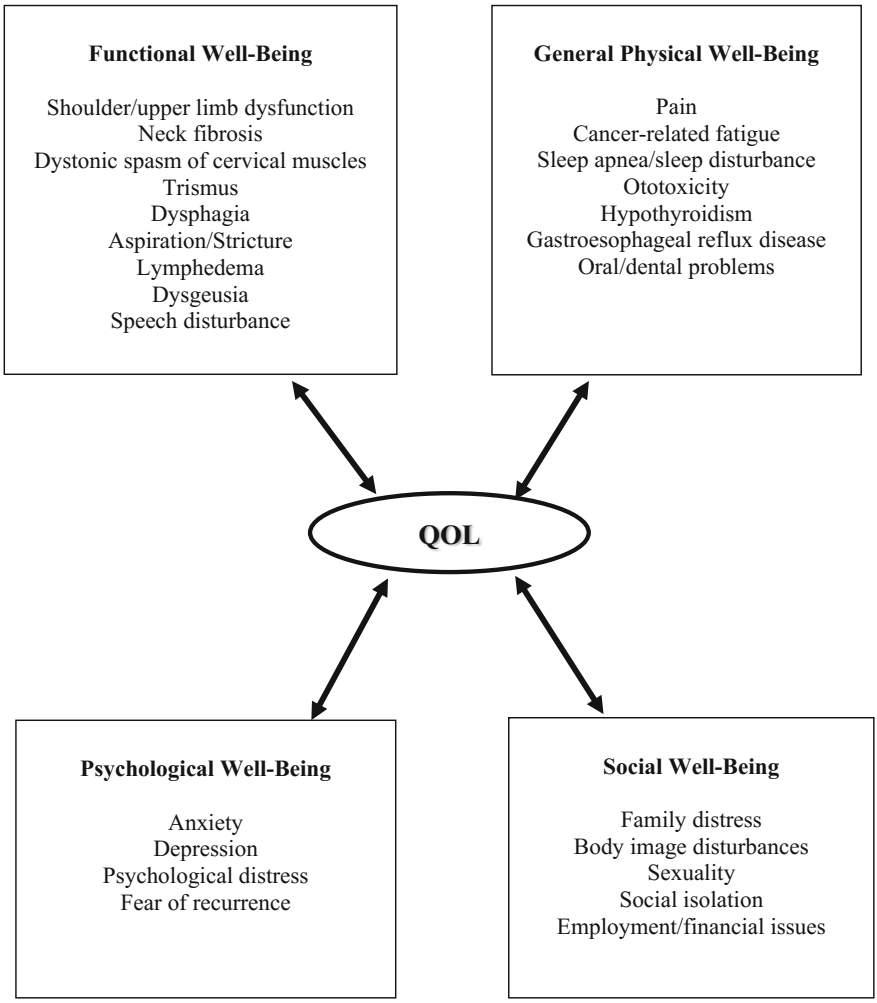

Fig. 16.1 Quality of life (QOL) issues in HNC survivors. Adapted with permission from Ferrell et al. [7]

QOL over time include depressive symptoms, lower socioeconomic status, younger age, multiple comorbidities [9, 11], feeding tube, diagnosis of oral cavity cancer [11], tobacco use, and radiation [12].

16.2.1 Functional Well-Being

The late and long-term functional effects of HNC treatment vary depending on the primary site of disease and treatment regimen [13, 14]. Neuromuscular sequelae

after neck dissection and/or radiation include injury to the spinal accessory nerve (SAN) that may result in shoulder dysfunction and pain. Some degree of SAN electrophysiologic impairment affects all survivors after neck dissection, regardless of extent of surgery (radical, modified, or selective) [15]. Carr et al. reported moderate to severe upper limb dysfunction in 23% of survivors after SAN-conserving selective neck dissection [16]. Shoulder dysfunction and pain are present in up to 70% of survivors after neck dissection [17].

Trismus (inability to fully open the mouth) is a common long-term effect of treatment in oral and oropharyngeal cancer survivors and reported in 28% of cases one year after treatment completion [18, 19]. It has a deleterious impact on QOL as it impacts a survivor's ability to eat, speak, maintain oral hygiene, engage in oral intimacy activities, and other important social aspects of daily living [20]. Approximately 50% of survivors with locally advanced HNC treated with multimodality regimens suffer from chronic dysphagia (difficulty swallowing) [21]. Dysphagia can result in chronic aspiration; more than 50% of cases are subclinical or "silent" with no outward symptoms [22, 23]. Approximately 7% of HNC survivors are at risk for pharyngoesophageal stricture; common symptoms include solid food dysphagia, difficulty belching/vomiting, and pharyngeal sticking [24]. Dysgeusia (altered taste) is more pronounced at 2 months post-radiation, with partial recovery expected over the years [25]. Taste disturbance has a negative effect on QOL and oral intake in HNC survivors [26]. Overall, speech disturbance is relatively rare in HNC survivors but may be more common in oral cavity and larynx cancer survivors. Radiation-induced lower cranial neuropathies may result in delayed speech or voice deterioration [27].

Fibrosis secondary to radiation is a late effect of HNC treatment, and symptoms may take months or years to manifest [28]. Painful dystonic spasm of the cervical muscles is a common manifestation of radiation-induced fibrosis [28]. In nasopharyngeal carcinoma, approximately 11–22% of survivors had neck fibrosis after conventional radiation. The percentage is lower (2.3%) in survivors treated with intensity-modulated radiation therapy (IMRT) [29, 30]. Lymphedema is also a common late effect of HNC treatment. It may develop externally (face, neck, chest) or internally (larynx, pharynx, oral cavity) [2]. Prevalence is reportedly 75% in HNC survivors, with the majority having combined external and internal lymphedema [31].

16.2.2 General Physical Well-Being

Pain is a chronic and persistent symptom in HNC survivors. Cancer-related fatigue (CRF) is common among survivors treated with radiation and chemotherapy [32]. Sleep disturbance secondary to obstructive sleep apnea frequently develops in HNC survivors and may lead to excessive fatigue and daytime drowsiness [2]. Concurrent chemoradiation or lateral skull base surgery or radiation therapy may lead to progressive hearing loss [33, 34]. The reported prevalence of hypothyroidism is 20% at 5 years and higher thereafter [35]. Gastroesophageal reflux disease (GERD) can exacerbate compromised airways, strictures, and aspiration events.

Maintaining oral and dental health is a chronic challenge for HNC survivors [36]. Xerostomia-induced dental caries is one of the most common dental health issues in long-term survivors [37]. Radiation to the oral cavity and salivary glands puts HNC survivors at risk for osteoradionecrosis that can lead to mandible fracture [2].

16.2.3 Psychological and Social Well-Being

HNC survivors are at high risk for anxiety and depression, with prevalence of depressive symptoms around 72% [38, 39]. The most frequently reported reasons for psychological distress in HNC survivors include uncertainty, and interference with activities [40–42]. Because HNC survivors are at risk for recurrence or second primaries, worry and fear are pervasive and long term [43].

Prevalence of body image disturbance and altered self-perception is high in HNC survivors. These concerns result in depressive symptoms, sexuality and intimacy problems, social isolation, and challenges with work and finances [44, 45]. Reported prevalence of body image disturbance is 75%, with 38% avoiding social activities [40, 44].

There is a growing interest in understanding the experience of family caregivers in cancer survivorship [46]. A recent systematic review examined QOL in HNC patient–caregiver dyads [47]. Both HNC patients and partners reported low adjustment for family relationships, work, and social activities [48]. Clinical psychological distress is reportedly 20% for spouses of HNC survivors [49]. Three years after total laryngectomy, over half of spouses (57%) reported high levels of psychological distress [50].

16.3 Planning Survivorship Care in HNC

16.3.1 Overview of Late and Long-Term Effects of Treatment and Disease

Reducing the risk of late and long-term effects should be implemented early in the course of treatment when possible (Table 16.1) [23]. Although there is potential for improvement of acute symptoms, many of the symptoms may increase over time, or not improve at all. Recognizing those at risk for debilitating effects from treatment is essential to preserving QOL for HNC survivors. The growing number of HNC survivors makes it even more critical that healthcare providers work to minimize late functional deficits and restore baseline function.

The 2006 Institute of Medicine (IOM) report established four components of quality survivorship care: (1) Promotion of healthy lifestyles; (2) surveillance for cancer recurrence or second primary cancers; (3) intervention for the consequences of cancer and its treatment; and (4) care coordination that includes communication between survivors, oncology specialists and primary care providers (PCPs) [51].

Table 16.1 Late and long-term effects associated with HNC [23]

Long-term effects secondary to treatment or disease	Symptoms associated with treatment or disease
Airway changes	Obstructive sleep apnea
Voice changes	Hoarseness
Verbal/speaking	Dysarthria
Swallowing	Dysphagia, trismus
Dental/oral changes	Xerostomia, dental decay, mucosal sensitivity
Ototoxicity	Hearing loss, tinnitus
Musculoskeletal changes and deconditioning	Neck and shoulder dysfunction, changes in posture, trismus
Lymphedema, fibrosis	Neck stiffness and pain, neck contour change, skin color and texture changes, trismus, dyspnea
Neurocognitive deficits	Trouble with memory and processing thoughts, fatigue

Care coordination includes the provision of patient-specific treatment summary and survivorship care plan (SCP) to PCPs with information on potential treatment sequelae, instructions for necessary follow-up, and delegation among providers for different aspects of care [51]. The following section describes these components in more detail.

16.3.2 Components of Survivorship Care

16.3.2.1 Prevention of Toxic Exposures and Promotion of Healthy Lifestyles

Prevention in HNC survivors is focused on encouraging tobacco cessation for smokers as smoking decreases their response to treatment and increases mortality [52, 53]. Multiple resources are available to help support tobacco cessation in cancer survivors [54]. Uninsured survivors have been less successful at accessing cessation programs as well as necessary follow-up care [55]. Healthy lifestyle recommendations continue to be important in survivorship. In the adolescent and young adult population, it has been shown that cancer survivors do not practice positive physical activity, healthy diet, reduced alcohol consumption, or smoking cessation when compared to noncancer controls [53, 56].

HNC survivors may benefit from physical activity. In 2010, an update was completed for physical activity trials in cancer survivors and found evidence that increased exercise after cancer treatment improves lymphedema and increases upper extremity strength [57]. The American Cancer Society recommends 150 min of moderate or 75 min of vigorous aerobic exercise per week, plus strength training exercises twice a week [2]. The important message to convey is to keep active and avoid a sedentary lifestyle: “any exercise is better than no exercise.” [2].

Maintaining a healthy diet for HNC survivors is important and a challenge for those with difficulty eating. Dietary recommendations by the ACS Head & Neck

Cancer Survivorship Care Guidelines include much of what is recommended for the general population—vegetables, whole grains, fruits, and low saturated fats [2]. It is emphasized that survivors be seen by a registered dietician or a specialist in nutrition who deals with altered physical function. Health promotion guidelines recommend involvement of a multidisciplinary team of experts in support of patients experiencing difficulty with healthy weight maintenance [2, 58].

16.3.2.2 Cancer Surveillance

The first 3 years are the most significant in surveillance for cancer recurrence [59]. As HNC survivors are also at high risk for second primaries, the continued use of alcohol and nicotine products is contraindicated [60, 61]. One study by Howren and colleagues found that HNC survivors who continue to drink alcohol have a lower survival rate than those who stopped drinking after diagnosis [38].

According to Baxi et al., HNC survivors have comorbidities that place them at increased risk for death when compared to the general population [59]. Second primary cancer occurrence as well as cardiovascular and pulmonary diseases are major causes of death posttreatment for HNC survivors. A Surveillance, Epidemiology, and End Results (SEER) cancer registry study of 13,120 HNSCC deaths found that only 29% of deaths were related to the original HNSCC; 23% of deaths were due to a second primary, 21% to cardiovascular disease, 4% to unspecified cancer, and 23% to all other causes including chronic obstructive pulmonary disease, pneumonia, and influenza [59].

Recommendations for follow-up of HNC survivors are based on risk for relapse of the primary tumor, risk of new secondary cancers, and treatment-related toxicities. The NCCN Guidelines provide a routinely updated recommendation for surveillance time-frames.

16.3.2.3 Monitoring for Late Effects and Delayed Toxicity Associated with Treatments

With the rise of human papilloma virus (HPV) and reduction in tobacco use, there has been a change in the epidemiology of oropharyngeal carcinomas [59]. There is a growing population of younger HNC survivors with fewer comorbidities who live longer and are at risk for late effects and long-term complications of treatments [2]. There needs to be a concerted effort in younger survivors of HPV-associated oropharyngeal cancers who continue to smoke, as their risk for long-term detrimental health effects is much higher [55, 56].

Cervical dystonia, shoulder dysfunction, and trismus would all benefit from referral to rehabilitation professionals who specialize in treatment and management of physical late and long-term effects of HNC [2]. Studies have illustrated the importance of exercise on fatigue and QOL [62–65]. Although more focused research is needed to assess the impact of physical activities on health outcomes, the development of endurance and reduction of fatigue may improve symptoms of decreased body image and depression and improve social interactions for this population [62].

16.3.3 Communication and Coordination of Follow-Up Care

Providing the incredible amount of needed follow-up information that HNC survivors require is a challenge. A shared mechanism among healthcare providers, supportive care providers, survivors, and caregivers is essential. The National Cancer Survivorship Resource Center, a cooperative research group between the American Cancer Society and the George Washington Cancer Institute, has described such systems [66]. Interestingly, survivors sought information from the Internet and peers on topics related to everyday situations but turned to physicians for information on medical diagnosis and recommendations for care [67]. SCPs have been shown to improve understanding of survivorship information for patients and PCPs [68]. Providing a treatment summary and SCP to survivors who have completed initial treatment is especially important in HNC, as their risks for recurrence and secondary cancers are unique to their disease and require focused care and surveillance to improve QOL [23].

Providing SCPs for all survivors completing cancer treatment with curative intent is a requirement for accreditation through the American College of Surgeon's Commission on Cancer (CoC) [69]. The challenge has been the recognition that one model does not fit everyone. Different institutions may adopt different models for different disease types and specific resources vary within settings [70]. Models of survivorship care delivery have been identified by ASCO as part of their compendium of survivorship care resources. Models include the Oncology Specialist Care, Multidisciplinary Survivorship Clinic, Disease/Treatment Specific Survivorship Clinic, General Survivorship Clinic, Consultative Survivorship Clinic, Integrated Survivorship Clinic, Community Generalist Model, and the Shared-Care of Survivor Model [71]. Finding the best option for your setting and resources is the key to providing competent coordinated survivorship care [72]. Access to expert multidisciplinary providers is important in meeting the complex and varied needs of HNC survivors. Collectively, a coordinated process in embracing recommended guidelines for follow-up care is essential to improving QOL for HNC survivors.

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