# Head and Neck Cancer

## Psychological and Psychosocial Effects

Christopher E. Fundakowski
*Editor*

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*This text is both inspired by and dedicated to my patients.*

# Preface

There has been a dramatic shift in the way we talk about, approach, and treat head and neck cancer. In a world where many refer to the "good old days" as a thing of the past, that is not the case in head and neck cancer. The exciting times are right now as we approach cancer care in a way was unimaginable a decade ago. Radically morbid surgery is commonly the exception rather than the rule, and in many cases, the patient has no visible incision, dramatically reduced length of stay, and improved outcome. Reconstructive techniques continue to advance, and great lengths and planning are commonly undertaken by multiple teams before, during, and after surgery to tailor and optimize the function and appearance. Incredibly, free tissue transfers have become the standard of care for many surgical defects, and with the benefit of highly experienced teams, the days of cases running into the early morning hours are few. The administration of radiation has changed where we no longer see the "woody necks" that we used to. Immunotherapy has and will continue to be an exciting area that may prove to completely change the way we approach and think about cancer treatment.

While we commonly focus on survival as a major endpoint in cancer care, it is easy to sidestep the dramatic psychological and psychosocial impact that this diagnosis carries. Patient "outcomes" are much broader than survival. These are commonly complicated issues that take a great deal of time to tease out in a busy clinical setting, surgeons/oncologists commonly lack focused training in these areas, and successful interventions and management of these issues are difficult. Building teams which contain individuals with the appropriate expertise, experience, and availability for these patients is critical.

I have been fortunate to work with many talented head and neck cancer providers given the multidisciplinary nature of our field and am grateful for their input, contributions, and expertise which have made this text possible. The goal of this project was to examine in detail the many areas of impact for the patient who is traveling through the diagnosis and treatment of a head and neck cancer. The reader will be able to explore many of these issues in depth, such as the trends in diagnosis of head and neck cancer, advances and outcomes associated with minimally invasive surgery, long-term quality of life and functional outcomes, issues related to cancer pain, importance and impact of nutrition, how reconstructive advances affect functional outcomes, the impact of cancer recurrence, and financial consequences of cancer diagnosis and treatment.

Fortunately, I would say that our field as a whole understands the importance of these issues and invariably wants nothing but the best for our patients. It is our job now to develop workflows, resources, and a clinical environment that both integrates and places value on all of these facets, knowing that, ultimately, it will impact patient outcomes.

Philadelphia, PA, USA Christopher E. Fundakowski, MD

# Acknowledgments

I would like to thank my wife, Aimee, who somehow has remained supportive and tolerant of my career while being an unbelievable mother and wife and full-time healthcare professional. I also owe the foundation and trajectory of my career to my other two “families,” Miami and Nashville. I am fortunate to have so many gifted clinicians who take part in this project. Thank you again for your time and efforts.

# Contents

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# Chapter 1
# Trends in Head and Neck Cancer

**Elizabeth Cottrill, Erin Reilly, and Orly Coblens**

## Etiology

The most common cancer of the head and neck after cutaneous malignancies of the skin is squamous cell carcinoma of the oral cavity and pharynx. Worldwide, there are over 550,000 new cases of head and neck squamous cell carcinoma (HNSCC) diagnosed and 380,000 deaths each year [1]. There is great heterogeneity in rates of HNSCC by geographic distribution. In some developing countries such as India, HNSCC can be one of the leading causes of death, whereas in developed countries such as the USA, it is rare (<10 per 100,000 individuals) [2]. According to the National Cancer Database, in the USA between 1990 and 2004, there were reported 821,779 head and neck tumors (approximately 55,000 per year) which accounted for 6.5% of all tumors [3]. In the USA, according to the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Result (SEER) database between 2009 and 2015, the 5-year survival rate for oral cavity and pharynx cancers combined was 65.3% with an estimated 53,000 new cases and 10,860 deaths projected for the year 2019 [4].

Traditionally, tobacco and alcohol have been the most important risk factors for HNSCC with heavy smokers experiencing a 5- to 25-fold increased risk of developing HNSCC when compared to nonsmokers [5, 6]. Alcohol has both an independent

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and multiplicative effect on the risk for HNSCC, with a more than 35-fold increase in those who smoke more than two packs of cigarettes and consume more than four alcoholic beverages daily [5]. Cessation of smoking for more than 10 years reduces the risk of cancer development [5]. Other risk factors, such as radiation exposure, immunosuppression, chewing betel nut quid, and poor oral hygiene, have also been reported [7–10]. A minority of patients are predisposed to HNSCC as a result of inherited genomic instability, for example, in Fanconi anemia.

Over the last 20 years, the epidemiology of HNSCC has changed significantly due to the rapidly increasing incidence of human papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (OPSCC) [11]. Even after adjustment for multiple patient-specific factors, patients with HPV-associated OPSCC have improved overall and disease-free survival compared to HPV-negative tumors [12]. Treatment de-escalation trials are therefore currently being conducted to assess whether the survival advantage can be maintained with less therapy since individuals may live many decades with the toxicities associated with radiation treatment [2].

Recurrence of HNSCC and disease-specific deaths often occur within 3 years of diagnosis [13, 14], and patients are often considered cured after 5 years of disease-free survival with only very rare recurrence occurring after this time. However, subsequent malignancies may occur in survivors for a number of reasons including genetic susceptibilities (e.g., cancer syndromes), shared etiologic exposures (smoking, alcohol, and environmental exposures), and mutagenic effects of cancer treatment. The overall cancer rate in head and neck cancer survivors is higher than the general population. After treatment, smoking remains a critical determinant of outcomes, as smokers are at higher risk for treatment failure, disease recurrence, and development of second primaries [15–17].

## Staging of Head and Neck Cancer

Assigning the appropriate clinical and pathologic stage is one of the most important initial tasks for clinicians who diagnose and treat cancer patients. Staging forms the basis for understanding the extent of disease at initial presentation and the long-term prognosis for the patient. It allows for a standardized lexicon to be used when describing malignancies and as such is a useful system for understanding the changing incidence and prevalence of these malignancies on a population level. The American Joint Committee on Cancer (AJCC) has led the efforts to define and revise the staging system in the USA and collaborates with the Union for International Cancer Control (UICC) to maintain a system that is used worldwide. This follows the traditional tumor, lymph node, metastases (TNM) staging paradigm.

Cancers of the head and neck are staged according to their site of origin with seven major sites identified: (1) oral cavity, (2) pharynx, (3) larynx, (4) nasal cavity and paranasal sinuses, (5) thyroid gland, (6) salivary glands, and (7) skin cancers including melanoma. In 2018, the eighth edition of the *AJCC Cancer Staging*

*Manual* was published and the Head and Neck Section introduced significant modifications to the prior edition. The most significant update to the staging system includes the creation of a separate staging algorithm for HPV-associated cancers of the oropharynx which also includes differentiating pathologic staging of high-risk HPV oropharyngeal cancers from clinical staging by exclusively using node number. This separation and different staging criteria distinguishes it from classical OPCSCC and emphasizes the improved prognosis of these cancers [18]. Other major updates include division of cancer of the pharynx into three separate chapters (nasopharynx, oropharynx, and hypopharynx) and the creation of a separate chapter for cutaneous malignancies of the head and neck (non-melanoma and non-Merkel cell). In the new edition, oral cavity cancers have the additional criteria of depth of invasion rather than only size criteria for staging of the primary tumor. Additionally, all sites except nasopharyngeal carcinoma and high-risk HPV-associated OPCSCC include the important parameter of extranodal extension in staging of cervical nodal metastases [18, 19].

## Trends in the USA

In 2009 Cooper et al. published a 10-year update on the trends in head and neck cancers within the National Cancer Database (NCDB) [3]. They found that between 1990 and 2004, 821,779 head and neck tumors (approximately 55,000 per year) were reported to the NCDB and accounted for 6.5% of all tumors [3]. The mucosally derived head and neck cancers were more commonly associated with lower income, whereas thyroid gland carcinomas had the opposite association. Cooper et al. identified a major shift in the distribution of anatomic sites between 1990 and 2004 such that carcinomas arising in the thyroid gland now constitute the largest group of tumors increasing from 17% to 30% and the relative proportion of non-thyroid malignancies has decreased for every anatomic subsite except carcinomas of the oropharynx (which have increased) and carcinomas of the major salivary glands (which have remained stable) [3]. In terms of cancer subtype, Cooper et al. found that squamous cell carcinoma (SCC) continues to constitute the largest histologic group, but the proportion of SCC relative to others has decreased over time [3]. This decrease in SCC correlated with the increase in thyroid carcinoma. The vast majority (89%) of cancers arising from mucosal surfaces of the upper aerodigestive tract (lip, oral cavity, pharynx, and larynx) were SCC [3]. Squamous cell carcinomas accounted for 90.8% of the common head and neck cancers in men and 83.6% in women [3].

Despite changes in staging systems, Cooper et al. found stage I tumors have become more common over time, and they identified associations between the degree of histologic differentiation, histologic type, and stage, specifically noting an association of undifferentiated and poorly differentiated tumors with higher stage at presentation and well-differentiated tumors most frequently associated with stage I disease [3]. When looking at treatment strategies, Cooper et al. found that the most common initial management between 1990 and 2004 continued to be surgery alone (28.3%), surgery combined with irradiation (22.0%), and irradiation alone (15.2%) [3]. They observed a continuing trend toward an increasing use of combined radiotherapy and chemotherapy (increasing from 6.1% of patients treated between 1990 and 1994 to 11.7% between 2000 and 2004) and a corresponding decrease in the use of radiation therapy alone for initial management [3]. This trend was especially evident for laryngeal tumors as part of organ preservation where the use of surgery alone decreased (21.4–17.5%), the use of surgery and radiation therapy decreased (28.9–20.2%), while the use of concurrent radiation therapy with chemotherapy increased (4.4–15.0%) [3].

## Head and Neck Cancer Subsites

### *Oral Cavity*

The oral cavity is comprised of the lips, alveolar ridge, buccal mucosa, retromolar trigone, floor of mouth, and oral tongue. The most common cancer of the oral cavity is SCC, associated mostly with risk factors of alcohol, tobacco, and betel nut quid use. Chaturvedi et al. all reviewed the SEER registry from 1973 to 2004 and found the US incidence of oral cancer was stable until 1982 and has been on the decline since 1983–2004 [20]. Despite this decline there has been an increase in a subset of patients – white women less than 45 years of age. These cases also tend to have a more aggressive cancer [21]. These cancers are often more common populations that are underserved in terms of medical and dental coverage, and in these populations they are difficult to detect and treat at earlier stages [22]. LeHew et al. point out the importance of early detection and intervention for the US population, especially in underserved areas, however early detection has proven to be a difficult parameter to measure in these areas and is largely dependent on access to primary care providers [22]. Treatment for oral cavity cancers, like all head and neck cancers, requires a multimodal approach. The mainstay of treatment for resectable disease involves primary surgery and sometimes postoperative radiation. Spiotto's group in Chicago investigated primary chemoradiation vs surgery followed by radiation and found that for resectable disease surgery should still be the first goal of treatment [23].

### *Oropharynx*

Oropharyngeal carcinoma includes cancers that arise in the palatine tonsils, tongue base (lingual tonsils), soft palate, and pharyngeal walls. The base of the tongue is functionally and anatomically distinct from the oral tongue (anterior 2/3) in that the muscles of the base of the tongue are more involved with swallowing than speech. Base of the tongue dysfunction resulting from tumor, postsurgical resection, or radiation-related effects may result in transient or permanent dysphagia and aspiration. Resection or irradiation of the soft palate may result in velopharyngeal insufficiency, hyper-nasal speech, and Eustachian tube dysfunction. Squamous cell carcinoma is the most common tumor type in this area and makes up over 98% of oropharyngeal cancers (OPSCC). Traditionally, the development of these tumors was most closely related to tobacco and alcohol exposures, but as mentioned previously, over the last 20 years, the epidemiology of OPSCC has changed significantly due to the rapidly increasing incidence of human papillomavirus (HPV)-associated OPSCC [11]. These patients often present with early primary tumor stage, but advanced nodal stage. HPV-associated OPSCC continues to affect men more often than women, and the risk increases with increasing number of sexual partners. In contrast to traditional HNSCC patients, those with HPV-associated OPSCC are more likely to be younger, nonsmokers, of higher socioeconomic status, and Caucasian [24–26]. Even after adjustment for these factors, patients with HPV-associated OPSCC have improved overall and disease-free survival compared to HPV-negative tumors [12]. Treatment de-escalation trials are therefore currently being conducted to assess whether the survival advantage can be maintained with less therapy since individuals may live many decades with the toxicities associated with radiation treatment [2].

Louie et al. found that the most common HNC in 1995 was from the larynx, in 2011 the oral cavity, and their group projects that in 2025 the oropharynx, accounting for 35% of the new HNC cases [27]. They also point out that of those, 50% will likely be under the age of 60 [27]. Therefore, the long-term morbidities and treatment-related side effects are important to consider, especially when it comes to dysphagia and aspiration. Studies point out that despite increased stage of these patients at time of diagnosis, their prognosis with treatment was much better [28]. Therefore, it has been proposed and investigated to de-intensify treatment in order to decrease the long-term side effects. The De-ESCALaTE HPV trial was completed from 2012 to 2016 using immunotherapy (cetuximab) over standard platinum-based chemotherapy (cisplatin). While it showed that the overall side effect profile was similar for both arms, the overall locoregional control and 2-year overall survival was decreased for the cetuximab group. Therefore, it continues to be recommended that treatment include radiotherapy and platinum-based chemotherapy [29].

Another recent advancement in the treatment of OPSCC is the development of transoral robotic surgery (TORS). Prior to TORS, surgical intervention for the oropharynx presented significant morbidity, often requiring jaw-split, tracheostomy, severe dysphagia necessitating a gastrotomy tube, as well as prolonged operative length [30, 31]. TORS offers a standardized en bloc resection for oropharyngeal malignancies. The outcomes for patients that have undergone TORS result in decreased postoperative radiation and decreased gastrostomy tube dependence [32].

In the USA there are currently three FDA-approved vaccines available against HPV: a bivalent HPV-16/HPV-18 vaccine (Cervarix®, GlaxoSmithKline Biologicals), a quadrivalent HPV-6/HPV-11/HPV-16/HPV-18 vaccine (Gardasil™, Merck Sharp and Dohme), and a nanovalent HPV-6/HPV-11/HPV-16/HPV-18/HPV-31/HPV-33/HPV-45/HPV-52/HPV-58 (Gardasil™). With reference to cervical cancer, prospective clinical trials have demonstrated that premalignant lesions can be prevented by HPV vaccination and detected by screening for HPV infection. Given the success of these vaccines in cervical cancer prevention, it is postulated that vaccination may be similarly successful in preventing head and neck cancer. A double-blinded study by Herrero found 93.3% vaccine efficacy against oral infections with HPV-16/HPV-18 in women in Costa Rica 4 years after receiving vaccination [33, 34]. Another study demonstrated that vaccination with the quadrivalent vaccine induced HPV antibodies in the oral cavity of males that correlated with the level of circulating antibodies [35]. Using the National Health and Nutrition Examination Survey (NHANES), vaccinated adults (age 18–30 years) were found to have a lower prevalence of HPV-6, HPV-11, HPV-16, and HPV-18 compared to unvaccinated adults [36]. Gillison has demonstrated that the prevalence of oral HPV-16/HPV-18/HPV-6/HPV-11 was significantly reduced in vaccinated versus unvaccinated individuals (0.11% vs 1.61%) [20]. It has yet to be determined whether HPV vaccination and decreased oral HPV infections will prevent the development of OPSCC or other HNSCC; however, in response to mounting evidence, in 2016 the American Head and Neck Society published a position statement which concludes, "based on the observed link between HPV infection and the majority of OPSCC and the safety and efficacy shown of the currently available HPV vaccines in preventing HPV infection, The American Head and Neck Society strongly encourages HPV vaccination of both boys and girls for prevention of OPSCC and anogenital cancers" [37].

## *Larynx and Hypopharynx*

Hypopharyngeal and laryngeal cancers commonly present with symptoms of hoarseness, dysphagia, dyspnea, and swallowing dysfunction. They are more common in men versus women. The most significant risk factors for development of laryngeal cancer are tobacco and alcohol usage which work synergistically [38]. With the decline in tobacco use, there has been a decline in incidence of laryngeal cancers; however the full effects of the increasingly popular marijuana and vaping are still to be determined. Rates for new laryngeal cancer cases have been falling on average 2.4% each year over the last 10 years with 4.7 cases per 100,000 persons in 1992 to 2.4 cases per 100,000 persons in 2016 in the USA [39]. Death rates have been falling on average 2.2% each year over 2007–2016. Five-year survival rate for patients presenting with localized disease is 77%, but significantly worse for those presenting with regional nodal metastases (44.7%) or distant metastases (33.3%) [39]. Multidisciplinary workup and treatment is pivotal, and for laryngeal cancer in particular, the input from speech pathologists and dietitian is helpful in guiding treatment option and posttreatment rehabilitation.

For all stages of laryngeal cancer, the function and preservation of laryngeal functions is paramount in determining the treatment. Early-stage tumors are usually treated with transoral laser microsurgery/endoscopic resections or very narrow field radiation. There are also open laryngeal conservation options that depend on the integrity of the cricoid cartilage. These are the supraglottic, supracricoid, and vertical partial laryngectomies [40–42]. The success of these surgeries is dependent on well-planned preoperative workup (including pulmonary function) and counseling [43, 44].

For advanced-stage laryngeal cancers, data from the VA and RTOG 91-11 studied induction chemotherapy followed by concurrent chemoradiation versus concurrent chemoradiation alone [45]. For many years since these studies in the 1990s, concurrent chemotherapy and radiation had become the mainstay of treatment with the option for salvage laryngectomy in case of locoregional recurrence [46]. Given the decrease in overall survival for patients with laryngeal cancer, institutions have begun to show benefit of primary laryngectomy again [47].

## *Sinonasal Malignancies*

Malignancies of the nasal cavity and paranasal sinuses account for less than 3% of all cancers of the upper aerodigestive tract. The incidence has remained stable over time, and tumors of epithelial origin predominate, most commonly squamous cell carcinoma followed by adenocarcinoma. Less frequent pathologies include esthesioneuroblastoma, mucosal melanoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, and sinonasal undifferentiated carcinoma (SNUC) [48]. Unlike other cancers of the head and neck, sinonasal malignancies are not associated with tobacco or alcohol use. Instead, wood dust and nickel are known risk factors, and HPV has recently been suggested to play a role in the malignant transformation of inverted papillomas.

Most patients present with nonspecific symptoms that mimic inflammatory sinus disease, such as nasal obstruction, epistaxis, or facial pain, often leading to a delay in diagnosis and advanced stage of disease. Despite this, the rate of regional or distant metastasis at the time of diagnosis is less than 10%. The most commonly involved subsite is the nasal cavity, followed by the maxillary sinus. More advanced disease at presentation leads to potential difficulty in determining the exact site of origin or attachment point. A unified staging system was not developed until 2003 by the American Joint Committee on Cancer (AJCC), and currently the ethmoid sinus and nasal cavity are bundled together, while the maxillary sinus is staged separately. In the most recent eighth edition guidelines, the T staging remains unchanged, but the modification for nodal staging also applies to cancers of the sinonasal tract.

Given the infrequency and diverse pathology of nasal tumors, survival and treatment analyses are limited. However, multimodality therapy is the standard approach. Surgical excision is the mainstay, with postoperative radiotherapy often considered. High-grade pathologies, such as esthesioneuroblastoma and sinonasal undifferentiated carcinoma, will require adjuvant treatment even after a successful resection. The development of the endoscopic technique has resulted in a shift of the surgical approach from the standard open craniofacial method. Several studies have found that disease control was at least equal comparing endoscopic to open but that endoscopic had better overall functional and cosmetic outcomes [49].

The anatomy of the sinonasal cavity is unique in its proximity to vital structures like the orbit and skull base, both of which are frequently involved by sinonasal malignancies. The main objective with skull base involvement is reconstruction and restoration of the water-tight seal between the intracranial and sinonasal cavity. The nasoseptal flap was discovered in 2006 and has become the vascularized tissue of choice since. The challenge with the orbit is whether to preserve the eye or not. While orbital exenteration results in functional, aesthetic, and psychological losses, radiation toxicity to the globe is not benign either. A recent trend toward orbital preservation in cases of periorbita or fat invasion has shown similar survival and local control compared to exenteration [50]. Induction chemotherapy has also been employed to reduce tumor volume and help preserve the eye; however it has not been shown to improve overall survival [51]. Advances in targeted immunotherapy are promising, especially for squamous cell carcinoma of the head and neck as well as mucosal melanoma. The preliminary data is encouraging, and it is likely that targeted therapy will gain widespread use in sinonasal malignancies [52].

## *Nasopharyngeal Carcinoma*

Nasopharyngeal carcinoma (NPC) has distinct epidemiologic and biologic factors that differentiate it from other head and neck cancers. It is endemic to areas of Southeast Asia and Northern Africa, as high as 25 cases per 100,000, compared to only 1 case per 100,000 in North America and Europe. Over the past few decades, the incidence has decreased worldwide but most significantly in those endemic locations. This is thought to be attributed to the reduced consumption of salt-preserved fish in the Chinese diet, a known risk factor for the development of NPC [53]. Epstein-Barr virus (EBV) is also a known etiologic cause of NPC. The pathogenesis is thought to be related to a latent infection that combined with a genetic predisposition leads to malignant transformation. EBV is not only useful for initial diagnosis, especially for an unknown primary tumor, but can also be employed as a biomarker for monitoring recurrence [54]. HPV has recently been suggested to play a role in NPC that is EBV-negative and is associated with a poorer prognosis; however the data on this is scarce.

The World Health Organization (WHO) revised the classification of NPC in 2005, defined by the following histologic subtypes: (1) keratinizing squamous cell carcinoma, (2a) non-keratinizing differentiated carcinoma, (2b) non-keratinizing undifferentiated carcinoma, and (3) basaloid squamous cell carcinoma. Group 2 is predominately EBV-positive, and specifically 2b is the most common subtype, found primarily in endemic areas. NPC can also be characterized by TNM staging, of which it is important to note that the N staging differs from other head and neck sites. N1 represents any unilateral cervical metastasis less than 6 cm and above the supraclavicular fossa, N2 is the same but bilateral, N3a is greater than 6 cm, and N3b is within or below the supraclavicular fossa.

The nasopharynx is a difficult location to access surgically, and clear margins are often difficult to obtain. For this reason, surgery is often reserved for salvage or recurrent cases. Nasopharyngeal carcinoma is radiosensitive and thus, the primary modality of treatment is radiation. Early-stage disease can often be treated with radiotherapy alone and survival rates remain high, around 90%. Locally advanced disease (i.e., stages II–IV) requires chemotherapy, most commonly in the form of concurrent chemoradiotherapy with or without adjuvant chemotherapy. Cervical metastases are common and have been reported to be present at the time of diagnosis 80–90% of the time. Neck disease is often treated with radiation as well, with a neck dissection performed only for persistent disease. Immunotherapy directed against EBV has recently been explored and the results of early clinical trials are promising; however further studies are needed to determine their exact role [55].

## *Thyroid Cancer*

Thyroid cancer is generally grouped separately from head and neck cancer in epidemiologic studies and represents 3.1% of all new cancer cases in the USA. The diagnosis of thyroid cancer has increased dramatically over the past 40 years with incidence rising on average 3% per year for the last 10 years making it now the 12th most common cancer in the USA [56]. Unlike many other cancers in the head and neck region, thyroid cancer is more common in women and among those with a family history of thyroid cancer. The number of new cases of thyroid cancer was 14.5 per 100,000 men and women per year based on 2011–2015 cases with a median age at diagnosis of 51 years [56]. Overall 5-year survival for thyroid cancer is excellent at 98.2% and is highest for patients with localized disease (99.9% 5-year survival) and those with only regional metastases (98.2% 5-year survival) [56]. The 5-year survival rate for those with distant metastases (all types) is 56.2%, and the percent of thyroid cancer deaths is highest among people aged 75–84 [56].

There are six types of thyroid carcinoma: papillary (84%), follicular (2%), Hürthle cell (2%), medullary (4%), poorly differentiated (6%), and anaplastic (1%) [57]. The behaviors of these different types are drastically varied, ranging from quite indolent papillary thyroid cancers to rapidly fatal anaplastic thyroid cancers. Staging for differentiated thyroid cancer is the only staging system for a head and neck cancer which incorporates patient age. While the basic TNM staging system was retained, the eighth edition downstages a significant number of patients by raising the age cutoff from 45 years to 55 years of age at diagnosis and by removing regional nodal metastases and microscopic extrathyroidal extension from T3 disease [58].

Fine needle biopsy and cytopathological testing is used to discriminate between benign and malignant tumors; however it is inconclusive in approximately 20–30% of cases [59]. Multiple molecular diagnostic methods have therefore arisen within the past two decades with the intent of narrowing the differential diagnosis. Afirma, a proprietary gene-expression classifier with a high negative predictive value, is designed to identify benign nodules among those with inconclusive results on cytopathological testing (a rule-out test) [60, 61]. Alternatively, next-generation sequencing of a panel of oncogenes and tumor-suppressor genes identifies nodules with mutations that have been associated with thyroid cancer, with high positive and negative predictive values (a rule-in test) [62]. Other tests using microRNA have more recently become available. These tests aim to reduce unnecessary surgery, although their reliability in various clinical-practice settings remains to be definitively established.

The majority of the apparent increase in thyroid cancer has been in papillary thyroid carcinoma (PTC) and is generally accepted to be largely due to greater detection of <1 cm papillary thyroid microcarcinomas (PTMCs) [57, 63, 64]. However, there has also been an observed rise in larger PTC, indicating a true increase in incidence (1.1% annually since 1994 and 2.9% annually for patients with advanced-stage PTC) [65, 63]. Additionally, while overall mortality from PTC remains very low, there has been an increase in mortality rates over the past 30 years [56]. Some authors have suggested that attribution bias and treatment-related deaths may explain this slight increase in mortality [64]. However, treatment-related deaths remain extremely rare (<1%), and attribution bias may not explain why mortality has only increased among patients with PTC, rather than medullary, poorly differentiated, or anaplastic thyroid cancers which are more aggressive [65, 66, 7]. Despite the increasing incidence of small (T1) primary tumors, >25% of PTC patients nevertheless present with regional metastasis at the time of their diagnosis, including PTMC [67]. Although in younger patients (<55 years old) nodal metastasis does not portend a worsened survival, greater numbers of lymph node metastases do entail greater risks of both locoregional tumor persistence and recurrence in PTC [67, 68].

Along with the observed trends in incidence, there has been significant change in trends with regard to disease treatment. The mainstay of thyroid cancer treatment is surgical thyroidectomy; however the extent of surgery has shifted recently with the option for hemithyroidectomy rather than total thyroidectomy for T1 and T2 differentiated thyroid cancers without extrathyroidal extension [69]. Additionally, prophylactic central neck dissection may be appropriately avoided for noninvasive, node-negative T1 and T2 PTC and for many follicular carcinomas [69]. Total thyroidectomy with resection of involved lymph node compartments is the recommended treatment for tumors larger than 4 cm [69]. According to the literature, as many as 12% of patients who undergo thyroid surgery may have postoperative complications including hematoma, hypoparathyroidism, or recurrent laryngeal nerve damage [70]. Although it is not yet a common practice across the USA, several centers around the globe have implemented algorithms for active surveillance of selected small PTCs, and recent studies suggest that PTMCs often remain stable for years and can be safely followed with serial ultrasonography every 6–12 months [71, 72]. In landmark Japanese studies establishing the safety of active surveillance for PTMC, only 10–15% of patients experienced tumor growth, usually within 5 years [71]. In the USA, Tuttle et al. had very similar findings for patients undergoing active surveillance for <1.5 cm nodules with Bethesda V or VI cytopathology and no clinical or radiographic evidence of extrathyroidal extension or regional metastases [72]. This study re-demonstrated that only 10–15% of tumors <1.5 cm showed growth greater than 3 mm during 5 years of active surveillance which was independently associated with younger age at diagnosis [72]. It has been reiterated throughout the literature that proper patient selection is the key to successful management of active surveillance protocols.

With the incidence of thyroid cancer on the rise with the potential for a corresponding increase in thyroid surgeries [64, 73–75], it is arguably more important than ever to seek high-volume thyroid surgeons both to reduce the risk of postoperative morbidity and also to engage with a provider knowledgeable about and comfortable with the option of active surveillance for select patients. While it has been recognized for decades that surgeons with a high-volume thyroid caseload have lower incidences of postoperative complications including recurrent laryngeal nerve injury and postoperative hypocalcemia [76–79], in the USA, the majority of thyroid surgery continues to be performed by low-volume thyroid surgeons (three or fewer cases per year) [77, 78, 80]. Recently, this trend may be reversing. Loyo et al. found that from 1993 to 2008, thyroidectomy cases increased and that cases performed by high-volume surgeons increased from 12% between 1993 and 2000 to 25% between 2001and 2008, whereas cases performed by very-low-volume surgeons decreased from 51% to 34% ($P < 0.001$) [81]. The authors also found that high-volume surgeons had a lower incidence of recurrent laryngeal nerve injury (OR 5 0.7, P 5 .024), hypocalcemia (OR 5 0.7, P 5 .002), and in-hospital death (OR 5 0.3, P 5 .004) [81].

Anaplastic thyroid carcinomas (ATCs) are rare (1–2%), highly aggressive, undifferentiated tumors, and patients diagnosed with ATC have a median survival of 5–12 months and a 1-year overall survival of 20–40% [82–84]. They are among the most lethal cancers and all are considered stage IV at diagnosis. Despite multimodality therapy, including surgery, external beam radiation, and systemic chemotherapy, response rates to standard systemic therapies and long-term outcomes remain dismal [85] with no curative options for patients who have exhausted locoregional therapies. Well-differentiated PTC precedes or coexists with approximately 50% of ATCs [86], and recent molecular profiling studies have identified that between 20% and 50% of ATC harbor activating B-Raf kinase (BRAF) V600 mutations, possible therapeutic targets [87–90]. Very recent data suggests that in a subset of ATC with BRAF V600E mutations, the combined use of dabrafenib (BRAF inhibitor) plus trametinib (MEK inhibitor) is demonstrated to have robust clinical activity exceeding any other nonsurgical treatment option to date and the chemotherapy regimen was well tolerated [91–93]. These findings represent an exciting therapeutic advance for a rare, but devastating, cancer.

## *Salivary Gland Malignancy*

Salivary gland malignancies are comprised of a histologically and pathophysiologically heterogeneous group of cancers. The major salivary glands include the paired parotid glands, submandibular glands, and sublingual glands. There are generally several hundred minor salivary glands which are a few millimeters in size and are located throughout the oral cavity along the hard palate and oral mucosa [94]. The incidence of salivary gland cancer is 1.3 in 100,000 representing less than 9% of all head and neck cancers, and the majority of these present within the parotid gland [95]. The overall 5-year survival is 71.9% [95].

Because the salivary glands are comprised of various cell types, the cancers which arise in the salivary glands are diverse. Using the World Health Organization 2005 classification, Boukheris et al. found the most commonly diagnosed major salivary gland malignancies were mucoepidermoid carcinoma (2.85 per 1,000,000 person years), followed by metastatic squamous cell carcinoma, acinic cell carcinoma, adenoid cystic carcinoma, and adenocarcinoma not otherwise specified [96]. More rare histologic types (less than 1 per 1,000,000 person years) include carcinoma ex pleomorphic adenoma, epithelial-myoepithelial carcinoma, lymphoepithelial carcinoma, salivary duct carcinoma, basal cell carcinoma, oncocytic carcinoma, and other even more rare subtypes. Men are 50% more likely to develop salivary gland cancer than women [96]. These salivary gland carcinomas are not strongly linked to tobacco and alcohol exposure; however exposure to ionizing radiation, including iodine-131, external beam radiation, nuclear event, and dental radiographs, has been shown to increase risk [97–101]. Other risk factors include exposure to silica dust, kerosene, nickel, chromium, asbestos, and cement dust [102, 103].

Staging of salivary gland malignancies is based on primary tumor size, cervical nodal metastases, and distant metastases. Several cancers also will have a pathologic grade which indirectly describes their behavior and therefore is considered in treatment algorithms. In most circumstances, the treatment of salivary gland malignancies is surgical. Extent of surgery for benign parotid tumors is controversial; however for malignant tumors it is more straightforward and is generally dictated by the location and size of the primary tumor. The function of the facial nerve should always be evaluated prior to surgery and preserved if it is not directly involved with the tumor. If facial nerve invasion is suspected prior to surgery, reconstructive options should be discussed with the patient and reconstructive surgeon especially with regard to eye protection. When cancerous pathology is diagnosed by needle biopsy prior to surgery, lymph node dissection will often accompany extirpation of the tumor. There are some authors who have advocated for the use of sentinel lymph node biopsy in clinically and radiographically N0 patients, but this has not yet become a popular practice. In rare circumstances, primary radiation may be in the best interest of patients who are not good surgical candidates. Adjuvant radiation, however, has been found to significantly decrease risk of recurrence in patients with perineural invasion, lymphovascular invasion, extraparenchymal extension, or positive surgical margins, regional nodal metastases, and advanced T-stage tumors [104].

## Conclusion

Despite trends in many developed countries toward decreasing rates of tobacco exposure, recent trends in malignancies of the head and neck region reveal drastic increases in the incidences of HPV-associated oropharyngeal cancer and papillary thyroid cancer. Concurrently, novel treatment strategies have arisen including surgical approaches like TORS for OPSCC that considerably minimize postoperative morbidity and active surveillance for very small PTC. Additionally, the use of adjuvant therapies such as radiation, chemotherapy, and radioactive iodine are being examined to determine if de-escalation of therapy will allow for less treatment-associated morbidity while maintaining excellent survival for select patients. While overall mortality from head and neck cancer is low, there is considerable treatment-associated morbidity which is both cosmetic and functional. The organs with which we communicate both verbally and nonverbally with the world around us and with which we experience the world through taste, smell, and sight can be compromised both by tumors themselves and treatment-related side effects. Mortality is therefore not the only measure upon which we should focus our efforts when treating head and neck cancer patients and developing new treatments.

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# Chapter 2
# Treatment-Related Patient Outcomes for Head and Neck Cancer

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Cancers of the head and neck represent a wide variety of malignancies originating from the upper aerodigestive tract. These include cancers of the nasal cavity, paranasal sinuses, nasopharynx, oral cavity, oropharynx, larynx, and salivary glands. Head and neck cancers represent 3% of all malignancies with approximately 60,000 new cases annually [1]. There has been an overall decrease in the incidence of head and neck cancer; however there is a widely recognized increase in the incidence of human papillomavirus (HPV)-related head and neck cancer [2].

The treatment for head and neck malignancies varies greatly based on the primary site and stage of disease. For example, nasopharyngeal carcinoma is a disease almost entirely within the domain of radiation and medical oncology, with surgery typically reserved only for salvage cases. Conversely, oral cavity cancers are almost universally treated with surgical resection/reconstruction, with radiation and/or chemotherapy used as adjuvant treatments. Similarly, salivary gland cancers are often treated with surgery for locoregional control with or without chemotherapy or radiation. The greatest variability in primary treatment methods exists in the treatment of oropharyngeal and laryngeal malignancies. Cancers of both these sites and the treatment thereof can result in significant deterioration of functional status.

The treatment of oropharyngeal cancers has been marked by several paradigm shifts over the last several decades. Historically, oropharyngeal cancer was a disease treated with conventional open surgical approaches such as lip splits and mandibulotomies. Given these morbid approaches, treatments with reduced morbidity were sought. Harrison et al. compared traditional surgical techniques to primary radiotherapy for oropharyngeal squamous cell carcinoma (SCCa) and demonstrated that surgical patients had significantly worse speech and normalcy of diet [3, 4]. Parsons et al. conducted a review of 51 studies that reported on over 6400 patients who were

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treated for oropharyngeal SCCa. While both surgical and nonsurgical patients had comparable oncologic outcomes, the rate of severe complication was greater than 20% in the surgical group versus 6% in the nonsurgical group [5]. Ultimately, this led to a shift in the treatment from surgery to primary radiation therapy (RT) or chemoradiotherapy (CRT) for oropharyngeal SCCa. In the intervening years, however, oropharyngeal approaches have shifted toward minimally invasive techniques. Transoral laser microsurgery (TLM) and transoral robotic surgery (TORS) have both demonstrated excellent functional and oncologic outcomes [6–8].

The treatment of laryngeal cancers has also proven controversial. Most laryngeal cancers, especially locally advanced tumors, have historically been treated with total laryngectomy as the primary treatment modality. Given the morbidity associated with this, organ preservation techniques have been extensively researched and explored. Landmark reports such as those by the Veterans Affairs Laryngeal Cancer Study Group [9] and Forastiere et al. have demonstrated excellent oncologic outcomes and high rates of larynx preservation with primary nonsurgical treatments [10, 11]. However, recent reports have shown that there has been significant late toxicity associated with CRT regimens for laryngeal cancer [12]. Furthermore, recent reports like that by Carvalho et al. demonstrated that overall survivorship for laryngeal cancer was worse in patients who were diagnosed from 1995 to 1997 versus those that were diagnosed from 1974 to 1976, reflecting potentially worse long-term overall survival with nonsurgical treatments [13]. As such, there has been an increased interest in surgical approaches to laryngeal cancer, namely partial laryngeal surgery and transoral techniques [14–16].

Ultimately, the treatment of cancers of the head and neck will continue to be based upon multiple patient factors including primary site and stage of disease. Primary decision-making continues to be driven by oncologic outcomes. However, for cancers that are amenable to multiple treatment options, other considerations such as toxicities and functional outcomes guide medical decision-making. Thus, an understanding of the available treatment modalities and their outcomes is crucial to the treatment of cancers of the head and neck.

Primary surgical therapy has long been the mainstay of head and neck cancers. While many cancers are now treated with multimodality approaches, surgery remains the primary treatment of choice for many head and neck malignancies.

## Nasal Cavity/Paranasal Sinuses

Cancers of the nasal cavity/paranasal sinuses often present late with extensive tumor. Nodal disease in the neck is also often present at the time of diagnosis. Most cancers of the nasal cavity/paranasal sinuses are treated primarily with surgical resection, either with open craniofacial resections or endoscopic resections. Combined approaches may be employed as well. Nodal disease is treated with adjuvant radiation and chemotherapy. For open approaches, 5-year survival ranges from 27% to 94% for T4 to T1 lesions, respectively [17]. Endoscopic techniques have less survival data as these techniques are more novel. However, recent papers suggest disease-specific survival rates of 87–91% [18, 19].

Endoscopic approaches are being extensively studied as they have the potential to be less disfiguring, allow for improved function, and facilitate more rapid recovery. Farquhar et al. demonstrate that patients undergoing endoscopic surgery had shorter hospital length of stay compared to open approaches [20]. Unfortunately, there is a paucity of literature regarding any benefit in functional outcome or postoperative quality of life that compares endoscopic versus open approaches. There is also a lack of any prospective head-to-head studies comparing open versus endoscopic techniques.

## Nasopharyngeal Cancer

Much like cancers of the nasal cavity/paranasal sinuses, nasopharyngeal cancers often present late with extensive local and regional tumor burden. These cancers are almost exclusively treated with primary CRT. Surgery continues to have a very limited role in the treatment of these cancers and is typically reserved for salvage cases. Overall outcomes depend significantly on initial stage, with 5-year overall survival of roughly 70% for patients with stage III and IV disease. Overall survival is often reported to be above 80% in patients who present with early-stage cancers [21, 22].

Major advances in the treatment of nasopharyngeal cancer have centered around the advent of newer radiation-based technologies. Notably, the advent of intensity-modulated radiation therapy (IMRT) has allowed for reduction of radiation dose to normal tissues while maintaining or increasing radiation delivery to tumors. Several studies have shown that IMRT results in significantly superior functional outcomes. In a review by Tribius et al., IMRT was associated with superior overall quality of life, swallowing, speech, senses, pain, and cognitive/emotional well-being compared with conventional radiation [23].

## Oral Cavity Cancers

Mucosal malignancies of the oral cavity are subclassified based on subsite: lips, oral tongue, floor of mouth, buccal mucosa, upper and lower alveolar ridges, and retromolar trigone. Primary radiation therapy for oral cavity malignancies is associated with significant toxicity such as mucositis, xerostomia, and dysphagia. Late toxicities include osteoradionecrosis. As such, unless unresectable, primary treatment of these cancers typically involves en-bloc surgical resection, neck dissection for nodal disease, and reconstruction. Historically, the treatment of these cancers has been disfiguring and debilitating. However, advances in reconstructive techniques, notably microvascular free tissue transfer, have resulted in improved cosmetic and functional outcomes [24]. Additionally, reconstruction with vascularized tissue helps facilitate postoperative radiation therapy when indicated.

Successful treatment of oral cavity cancers depends significantly on local disease control. Overall survival is significantly impacted by stage at presentation and the depth of invasion. Overall survival at 5 years for patients with oral cavity squamous cell carcinoma ranges from 27% to 59.2% for stages 4 through 1 cancers, respectively. Shaha et al. demonstrated that patients with depth of invasion of less than 2 mm had a 95% 5-year overall survival, while overall survival dropped to 65% in patients with depth of invasion greater than 9 mm [25].

Functional outcomes in patients with head and neck cancer are significantly impacted by the quality of reconstruction. Advances in microvascular free tissue transfer have resulted in significant improvements in speech and swallow. Urken et al. demonstrated that patients with mandibulectomy defects that were reconstructed with free tissue transfer had significantly improved normalcy of diet and mastication [24]. While free tissue reconstruction does improve the chance of optimizing functional outcome, these operations are not without significant risk and cost [26], and as such, a thorough discussion between the patient and his/her surgeon is necessary to enable informed decision-making.

## Oropharyngeal Cancers

Historically, cancers of the oropharynx have been challenging to treat surgically given the poor access to the oropharynx. Surgical approaches that centered around lip-split mandibulotomies were unsurprisingly morbid. Work by Harrison et al. demonstrated that primary RT (with or without chemotherapy) had oncologic outcomes comparable to conventional surgical techniques [3]. Parsons et al. reported on a retrospective review of nearly 1200 patients, comparing primary radiotherapy versus primary surgery. In this highly cited review, they demonstrated significantly higher rates of serious complications in surgical patients. Ultimately, this data resulted in a paradigm shift toward primary RT for oropharyngeal cancers. However, there is still a paucity of updated randomized trials directly comparing surgery to RT or concurrent CRT. At this point in time, management is largely institution-specific, where patient management is unfortunately based primarily on retrospective data. With this in mind, there is an appeal to organ preservation therapy in order to avoid the associated morbidity and complications associated with surgery while maintaining similar survival outcomes.

### *Primary Chemotherapy/Radiation Therapy*

Chemotherapy and radiation are not without their own risks and morbidities, ranging from dysphagia, fibrosis, and xerostomia to nephrotoxicity and severe hematologic toxicity. In an attempt to abate the effects of treatment on quality of life, IMRT has been more recently implemented to allow more precise treatment delivery and improve the side effect profile [27]. Meta-analyses have shown that concurrent chemotherapy may have a survival benefit but at the expense of a significant increase in acute and late radiation toxicity [12, 28].

Current treatment practices are typically determined by a patient's oncologic stage. Typically, patients with early-stage disease are treated with single modality therapy, while advanced stage disease is treated with multiple modality therapy. This can be either surgery with postoperative RT or upfront CRT. Primary nonsurgical treatment consists of a radiation course of 60–70 Gray (Gy) delivered to the primary site and neck over 6–7 weeks [29]. These patients typically undergo a posttreatment positron emission tomography-computed tomography (PET-CT) scan to assess treatment response after 2–3 months. Patients with baseline N2 or N3 disease who show persistent disease on PET-CT typically undergo salvage neck dissection.

Prospective, randomized trials comparing RT with concurrent CRT have been conducted [30–32]. These have demonstrated the efficacy of concurrent CRT over primary RT for advanced disease. These studies found no difference in metastatic disease between CRT and RT. Apart from these few prospective studies, the bulk of recent literature on oropharyngeal carcinoma with respect to chemotherapy and radiation has been in the form of large retrospective reviews and nonrandomized trials. These and other studies have shown that posttreatment toxicity is globally worse in patients who receive CRT. Studies have looked at IMRT specifically and have demonstrated overall survival ranging from 70% to 100% and 3-year disease-free survival rates of 65–88% [29, 33–39]. In these studies, unsurprisingly, higher T stage and overall stage was associated with worse overall and disease-free survival. Smoking was associated with significantly poorer overall survival [33]. Tonsillar primaries were shown to have improved overall survival [34].

In the comparison of surgical therapy to CRT, functional outcomes become the keystone of discussion. Patients treated with IMRT have a risk for tracheotomy dependence ranging from 0.1% to 4.5% [40]. Long-term feeding tube dependence for IMRT patients ranged from 0% to 18%, with a high rate of feeding tube dependence needed within the first few months of radiation treatment [41, 42]. Multiple studies have also shown that long-term quality of life measures, using the MD Anderson Dysphagia Inventory (MDADI), are worse in patients treated with CRT [43, 44].

A large confounder in the discussion of outcomes of oropharyngeal cancer is HPV status. This subset of patients has demonstrated favorable response regardless of treatment modality, with significantly improved overall survival and disease-free survival [34, 45–48]. HPV-positive patients are twice as likely to show complete tumor response when treated with CRT compared to those that are HPV-negative [45]. Additionally Straetmans et al. demonstrated that the prognostic value of nodal disease burden is of less value in HPV-positive disease [49]. HPV-related OPSCC has now been established as a novel disease with a separate staging system. As such, new studies are needed focusing primarily on HPV-related disease. Current studies are now focusing on comparing the differences between HPV-positive and HPV-negative patients and the ability to potentially de-escalate therapy for HPV-positive patients. Unfortunately, older studies that have not been stratified for HPV status can no longer apply meaningful conclusions with regards to CRT and surgical outcomes.

## *Primary Surgery*

The increased adoption of minimally invasive, transoral techniques has been a major breakthrough in the surgical treatment of oropharyngeal cancers. TLM and TORS in particular are now being used with increasing frequency. As previously discussed, increased awareness of the role of HPV in the pathogenesis of OPSCC has also affected clinical decision-making. It is now well recognized that HPV-associated cancer is biologically distinct and typically less aggressive than the typical head and neck cancer seen in smokers and drinkers. Thus, with the overall improvement in oncologic outcomes seen given the increased proportion of patients with HPV-related disease, the focus has increasingly shifted toward functional outcomes.

Primary surgical techniques such as TORS and TLM have both demonstrated excellent oncologic results. Disease-specific survival at 2 years for patients who are treated with transoral surgical methods for HPV-related OPSCC ranges from 88% to 98% [50, 51]. The range of locoregional recurrence reported in the literature ranges from 0% to 7% [50, 51]. These reports also demonstrate low rates of distant metastasis, ranging from 1.6% to 6%. However, once again it is important to note that these outcomes are significantly worse for HPV-negative disease. In their multicenter report on TLM, Haughey et al. reported on 2-year disease-free survival of 50% in HPV-negative patients compared to 85% disease-free survival in HPV-positive patients [51].

Reported functional outcomes for patients undergoing transoral surgery have been favorable. Lee et al. compared TORS to conventional surgical techniques and demonstrated that patients who were treated robotically had significantly better functional outcomes as measured by MDADI score, tracheostomy rate, and duration of nasogastric tube dependence [52]. Furthermore, Hinni and Haughey report a 0% rate of permanent tracheostomy in patients treated with TLM [6]. Several studies have reported on long-term gastrostomy tube rates in patients treated with primary transoral surgical techniques. Rich et al. reported a 3.4% rate of gastrostomy tube dependence in patients treated with TLM [53]. Rates of gastrostomy dependence in patients undergoing TORS range from 0% to 7% [7].

The treatment of oropharyngeal cancer is dictated largely by stage at the time of presentation and is very institution-specific. HPV status is also an increasingly important part of selecting the primary treatment modality. Given the introduction of a new HPV-specific staging system, more studies are critically needed that enable comparison of primary surgical and nonsurgical techniques, especially ones that take into account the various de-escalation methodologies.

## Laryngeal Cancers

Historically, cancers of the larynx were treated with total laryngectomy. While oncologic outcomes were sound, this operation is disfiguring and morbid. It results in a permanent stoma and significant speech disability. Similar to much of head and neck surgery, clothing cannot hide scars or other sequelae from treatment. Therefore, unsurprisingly there has been an aggressive pursuit for organ preservation techniques. Large, randomized trials such as the work done by the Veterans Affairs (VA) group and subsequent other groups demonstrated the oncologic efficacy of chemotherapy and radiation [9]. Additionally, these studies revealed that a sizable fraction of patients could maintain a functional larynx after treatment. As such, nonsurgical therapy has become the preferred modality of treatment for select patients.

Recent studies have demonstrated that laryngeal cancer survivorship however has decreased over the last several decades [54–56]. This has forced a re-evaluation of current treatment strategies for laryngeal cancers. There have been several groups that have published several promising studies describing various surgical attempts at organ preservation. Transoral and transcervical partial laryngectomy techniques have been reported with promising oncologic and functional outcomes, particularly in early-stage cancers.

### *Primary Chemo/Radiation Therapy*

RT laid its foundation in the treatment of head and neck cancers with a landmark randomized control trial in 1991. The VA Laryngeal Cancer Study showed that laryngeal preservation with induction chemotherapy followed by RT was possible with satisfactory survival [9]. The VA trial would pave the way for further organ preservation studies, with the prior gold standard of laryngectomy becoming increasingly reserved for surgical salvage.

The VA study's primary treatment modality was the role of induction chemotherapy in addition to radiation. A follow-up study, the RTOG 91–11, demonstrated the increased effectiveness of concurrent CRT in locoregional control and organ preservation. An additional keystone was laid here, supporting the theory of concurrent chemotherapy with 5-FU or cisplatin functioning as a radiosensitizing agent. The RTOG trial showed overall survival of the comparison arms to be equivalent; however, locoregional control with concurrent CRT was 78%, with 2-year laryngeal preservation of 88%. This was significantly improved compared to the other arms [10]. Longer-term follow-up studies showed however that 16% of the CRT group required eventual salvage laryngectomy [57]. While patients with T4 tumors or pre-treatment laryngopharyngeal dysfunction were shown to be poor candidate for organ preservation due to poor oncologic outcomes and increased risk of late radiation toxicities [55, 58], the VA study and the RTOG 91–11 trial established the standard for modern organ preservation therapy.

Modern treatment of laryngeal cancer is typically separated based on oncologic stage. For early-stage glottic tumors, radiation therapy in addition to organ-preserving surgery is the mainstay of treatment. Management decisions center around voice, swallowing, local control, and overall survival. Prior studies have shown that the rates of each are comparable [59–61]. Cure rates for single modality radiation therapy have been reported to be from 71% to 95% [62]. Studies focusing on survival have also shown no difference in surgical versus radiation groups, when controlling for T-stage [63, 64].

For early-stage supraglottic tumors, single modality RT can be employed with acceptable local control rates of between 75% and 100% for T1 tumors and laryngeal preservation in 80% of patients [65]. Unfortunately, treatment of early supraglottic cancers with RT has been associated with significant recurrence rates up to 29% [61, 66, 67]. Successful control has also been linked to tumor volume [68].

Additional studies attempted to improve the effectiveness of CRT by adding induction chemotherapy. The GORTEC 2000–2001 study tested the effect of adding docetaxel to the existing cisplatin/5-FU regimen. Results showed that induction chemotherapy provided a higher overall response of 80% versus 59%. However, there was no significant difference in overall or 3-year disease-free survival [69]. Further studies demonstrated no overall improvement in overall survival or progression-free survival between the two regimens [70]. Increased resources have been dedicated to tumor biology and the role of biologic markers/therapies in treating laryngeal cancers. There has been some promise shown in the role of cetuximab, but there has yet to be any head-to-head trials comparing its use to the standard of concurrent CRT [71].

It is well known that CRT is associated with a variety of early and late toxicities from mucositis and dysphagia to severe laryngeal dysfunction necessitating tracheotomy. It was found that up to 43% of laryngeal cancer patients treated with CRT manifested late toxicities after 3 years, with risk factors including age and advanced T stage [12]. A long-term analysis of RTOG 91-11 patients found an increase in noncancer deaths in the CRT group, suggesting laryngeal preservation may carry with it an inherent risk of severe late toxicities [11]. These toxicities manifest as long-term dysphagia, weight loss, and gastrostomy and tracheostomy dependence [58]. With an increased focus on quality of life outcomes and morbidity from CRT, an international panel created consensus guidelines for phase III laryngeal preservation trials. They recommended inclusion criteria to be limited to T2/T3 tumors and to exclude patients greater than 70 years old or with laryngeal dysfunction. The guidelines also recommend that laryngoesophageal dysfunction (LED)-free survival be included as an endpoint, where the primary endpoint is local relapse, total or partial laryngectomy, tracheostomy greater than 2 years, or feeding tube dependence greater than 2 years [72].

Ultimately, the goal of organ preservation is long-term oncologic control and functional preservation. Early laryngeal cancers can be successfully treated with RT. For advanced stages, concurrent CRT is the standard organ-preserving modality. While there have been studies attempting to alter this regimen, no head-to-head trials exist to date.

## *Primary Surgical Therapy*

Primary surgical therapy for laryngeal cancer has become increasingly nuanced with various transoral and transcervical techniques for partial laryngectomy. For patients with advanced disease who are unable or unwilling to undergo CRT, total laryngectomy remains the preferred treatment.

The surgical approach to cancers of the larynx is dictated by stage and subsite. For example, early-stage glottic tumors are amenable to open partial laryngectomy techniques, such as vertical partial laryngectomy. Supraglottic cancers often are amenable to supraglottic (horizontal) partial laryngectomies. Local recurrence rates for T1–T3 tumors treated with vertical partial laryngectomy as reported in the literature range from 2% to 26%. Furthermore, functional outcomes from vertical partial laryngectomy have been favorable. While some hoarseness is guaranteed, over 90% of patients in one study returned to normal diet within 1 month of surgery [73]. In a systemic review by Thomas et al. of open partial laryngectomy procedures, they reported 5-year local control rates ranging from 83% to 97% [74]. Functionally, patients who undergo partial laryngectomies typically remain breathy/hoarse. However, rates of dysphagia are low with Castro et al. reporting good MDADI scores in patients who underwent supracricoid laryngectomy, with a median score of 92 [75].

Transoral approaches to malignancies of the larynx were pursued and popularized first by European surgeons. Laser surgery enabled piecemeal resection, and this has permitted the resection of even advanced laryngeal cancers with endoscopic techniques. Hinni et al. reported on 140 patients who were treated with primary TLM for stage III or IV laryngeal cancer [76]. T stage ranged from T2 to T4 for both supraglottic and glottic primary cancers. They reported a 5-year local control rate of 74%, with overall survival rates of 75% and 55% at 2 and 5 years, respectively. Functionally, the larynx was preserved in 92% of patients. The tracheotomy dependence rate was 2% and the feeding tube dependence rate was 7%. Ambrosch et al. also looked at TLM for supraglottic cancer and demonstrated 5-year overall survival of 69% (stage I and II) and 58% (for stage III and IV). Disease-free survival rates were 79% (stage I and II) and 64% (stage III and IV). Functional outcomes were excellent in this report. Larynx preservation was 89%. Additionally, while 13% of patients needed tracheotomy, no patients required permanent tracheostomy. Finally, only two patients were permanently gastrostomy tube-dependent.

Functional outcomes for patients who undergo surgery for laryngeal cancers are highly dependent on stage of cancer and preoperative functional status. Patients with early glottic cancers tend to have good functional outcomes regardless of treatment modality. Patients with early glottic cancers have good functional outcomes regardless of treatment modality, i.e., transoral laser resection versus RT [77, 78]. For patients with advanced disease that refuse or are not candidates for organ preservation therapy, total laryngectomy can be offered. Surgical voice restoration is usually performed at the time of laryngectomy. Several studies have shown that patients who receive primary voice rehabilitation with tracheoesophageal puncture and prosthesis (TEP) can have satisfactory swallow and voice outcomes. Chone et al. demonstrated a voice rehabilitation success rate of 97% with primary TEP [79]. However, it is important to note that the chance of functional rehabilitation decreases sharply in cases of salvage laryngectomy [80].

Ultimately, the treatment of laryngeal cancer is predicated based on subsite and the stage at the time of presentation. Landmark randomized trials done by groups such as the VA Laryngeal Cancer Study group and the RTOG 91-11 trial resulted in a significant paradigm shift, making chemotherapy and radiation the preferred primary treatment modality. However, recent survival trends have demonstrated a recent reduction in overall survival for laryngeal cancer patients [81]. While causality has not, and likely cannot be determined, this decrease in survival overlaps with the increased popularity of nonsurgical treatments for laryngeal cancer. Furthermore, studies such as that by Nair et al. suggest that there may be improved survival in patients who undergo total laryngectomy versus those who undergo organ preservation treatments [82]. While the VA study did directly compare surgery and radiation therapy, overall survival was not an endpoint for this trial. Additionally these studies looked only at laryngeal preservation and not at laryngeal function. Furthermore, partial laryngectomy techniques were not assessed in these trials. As such there is need for new, prospective trials that compare CRT versus modern surgical technique with overall survival and laryngeal function as primary endpoints.

## Salvage Treatments

The standard of care for recurrent and persistent disease after organ-preserving therapy is salvage surgery. The high risk of complications in salvage cases is well documented. Second attempts at organ preservation with radiation-based treatments lead to significant minor and major complications. These include fistula, stenosis, prolonged tracheotomy, and feeding tube dependence [83, 84]. In turn, focus has turned to preventing the complications associated with salvage surgery and radiated soft tissue [85, 86]. Unfortunately, in patients with recurrent disease, long-term survival outcomes tend to be extremely poor. As such, quality of life and function can become the primary drivers of therapy.

Patients with recurrent disease often are still suffering from the acute or late toxicities of their primary treatment, making them poor surgical candidates with a high risk of wound breakdown and nutritional deficiency. The combination of chemotherapy and radiation causes soft tissue fibrosis, scarring, and destruction of the majority of the local blood supply. This can lead to morbidities not directly related to recurrence, such as chondronecrosis and osteoradionecrosis, which further complicates surgical salvage.

Ultimately, surgery remains the standard of care for recurrent disease. A large meta-analysis of salvage surgery showed a 5-year overall survival of 39%, with 37% survival in larynx primaries and 26% in pharynx primaries. Of note, there is an insignificant risk of death (5.2%) from salvage surgery [86]. Overall complications that encompass the broad range of minor and major complications occur in 30–40% of cases [85]. Further analysis of salvage surgical patents found average survival to be 21.5 months, with the stage of recurrence being the only predictor of survival. Quality of life scores were also assessed pre- and postoperatively and showed a similar correlation with decreased quality of life as stage increased: 64%, 65%, 41%, and 39% for Stage I, II, III, and IV, respectively. Neither survival nor quality of life was associated with recurrence site [86].

## *Oropharyngeal Salvage*

As mentioned earlier in this chapter, organ preservation protocols with CRT have been well established for oropharyngeal primaries. Outcome studies of patients undergoing CRT showed that up to a third of patients may end up requiring salvage surgery [87]. Salvage surgery typically results in extensive defects; there is a large consensus that vascularized tissue should be transplanted to the operated bed. Recent data has demonstrated the improved quality of life and functional outcomes of oropharyngeal reconstructions [87].

In a functional assessment of oropharyngeal patients treated with CRT, 82% required feeding tubes at some point during treatment. 1-year posttreatment, 31% of patients still required feeding tubes. A large predictor of functional outcomes after salvage surgery is related to the patient’s preoperative swallow function and must be considered in patients who post-CRT require feeding tubes to maintain adequate nutritional status.

The reconstruction of large salvage resections is especially complex in the oropharynx. The three-dimensional nature of propelling the food bolus means that removal of multiple subsites greatly impacts swallowing outcomes [87]. Free tissue reconstruction after salvage surgery results in improved quality of life, swallow function, and rates of decannulation [88].

In a recent review of oropharyngeal salvage, 3-year overall survival and recurrence-free survival were 42% and 26%, respectively [89, 90]. It was also found that 80% of patients had intelligible speech after surgery, 90% were successfully decannulated long-term, and a majority were able to eat without need for a feeding tube [6].

## *Laryngeal Salvage*

As previously mentioned in this chapter, there are well-established randomized trials supporting the use of concurrent CRT as the mainstay of organ preservation therapy for laryngeal cancers. Long-term follow-up study of those original cohorts showed that 129 patients eventually underwent total laryngectomy, the large majority for recurrence or persistent disease, with 5% of surgeries being performed for a nonfunctional larynx or chondronecrosis. The incidence of complications ranged from 52% to 59%, with up to 30% of patients having pharyngocutaneous fistulas [57]. Locoregional control after salvage surgery for this same cohort was 74–90% depending on the initial treatment arm. This confirmed the role of salvage total laryngectomy as the gold standard regardless of organ preservation therapy. More recent data estimates the 5-year disease-free survival after salvage total laryngectomy to be from 50% to 70% [57, 89, 91].

Reconstruction after salvage total laryngectomy has received significant attention, especially with the advent of free tissue transfer. Multiple large institutional studies have shown the role of free tissue transfer in reducing major wound complications, fistula, and feeding tube dependence [92, 93]. The use of free tissue reconstruction has shown a significant improvement in postoperative swallowing when compared to primary closure, as has the pectoralis major flap [92, 94]. Aggressive speech pathology follow-up allows many salvage patients to achieve acceptable swallowing and speech outcomes. These outcomes further improve with the use of TEP, where up to 85% of patients have intelligible speech [89, 95, 96]. Finally, up to 90% of patients who undergo reconstruction return to normal oral intake postoperatively [97].

## Conclusions

Cancers of the head and neck represent a wide variety of subsites that often result in significant deformity and functional debilitation. The treatment of these tumors often can worsen cosmesis and quality of life by further weakening structures and mechanisms key to normal speech and eating. Treatment of tumors of the upper aerodigestive tract often requires a multidisciplinary approach with surgeons and medical and radiation oncologists involved in treatment. Patients with head and neck cancer are often presented with a variety of treatment modalities based upon the site of the primary lesion and stage of disease. Oncologic control remains the top priority. However, functional outcomes are increasingly being prioritized. The HPV epidemic has added another variable to this calculus. Patients with HPV-related disease tend to be younger patients with excellent oncologic outcomes, as such functional outcomes are particularly important in these patients.

Current treatment algorithms are dictated by relatively few prospective randomized trials. Furthermore, many of these trials are now nearing two decades in age and no longer appropriately represent modern surgical techniques or our current understanding of tumor biology. As such, there is a need for new prospective clinical trials that both assess oncologic and functional outcomes. This is especially true in patients with HPV-related cancers. Several de-escalation trials are underway, and the results from these studies may aid future decision-making. Ultimately, understanding the treatment options and their functional outcomes is of paramount importance in order to enable informed decision-making.

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# Chapter 3
# Quality of Life Implications in Head and Neck Cancer

**Steven M. Sperry and Nitin A. Pagedar**

To the clinician, survival and cancer control are the most relevant outcome measures to cancer treatment. To the patient, much greater variation potentially exists in what are considered the relevant important outcomes. Some outcomes exist only as the patient experiences them and, thus, are not directly observable, but are no less important as a gauge of the impact of treatment. This category of cancer treatment outcomes is summarized broadly as "quality of life."

## Defining Quality of Life

"Quality of life" (QOL) exists as a concept independent of cancer or healthcare issues. The broadest definition of QOL is an assessment of personal well-being, including personal independence and social, religious, family, psychological, and health considerations. Health-related QOL (HRQOL) is a more limited view of QOL, focusing on aspects most related to or likely to be changed by health issues. The World Health Organization defines QOL as the "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. It is a broad ranging concept incorporating in a complex way the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of the environment" [1]. This definition reveals several important features of QOL: subjectivity, multidimensionality, and cultural context.

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Though there are multiple persons who experience and are affected by an individual's state of health, including the patient, family/friends, and healthcare provider, QOL is only viewed through the individual patient's eyes and therefore is subjective to how they perceive it and possibly in contrast to how other affected individuals perceive it.

The multidimensionality of QOL leads to incorporation of numerous domains into an assessment of QOL. This is an artificial compartmentalization, which imposes constraints of a measurement system on a complex and fluid concept. However, this is necessary to allow communication of a concept which is otherwise difficult to consistently express. One approach to assessing multidimensional QOL would be having the patient express a single summary value, which relies on individuals' ability to internally integrate their experience. In an alternative approach, to improve reliability over time and separation of factors, the domains of experience can be designated a priori and assessed with specific questions. This leads to longer lists of questions, which require more time commitment to complete and a greater amount of analysis, and are biased by the decision of what question to ask.

The decision of what domains and questions to use in assessing HRQOL is important and changes given the intention of the assessment and the anticipated disabilities [2]. A *general* instrument might be applicable to any individual, regardless of disease state; examples include the SF-36 or EQ-5D. A *disease-specific* instrument frames questions expected to be sensitive to change for the particular disease; in the context of cancer in general, common instruments include the EORTC QLQ-C30 or FACT-G. Narrowing the disease focus even further, instruments have been developed specifically for cancer in the head and neck. Some of these utilize a general cancer-specific module and then include more specific head and neck cancer sections (e.g., EORTC H&N-35, FACT-H&N). Others are HRQOL instruments developed specifically for the head and neck cancer patient (e.g., UW-QOL, HNCI). A *symptom-specific* instrument or *symptom scale* might be complementary to these, in focusing even further on a specific issue, but not assessing the broader view of HRQOL; examples in the head and neck include the MDADI (dysphagia) or the DSHNC (disfigurement). A comparison of the question content of a variety of the available H&N-specific HRQOL instruments is demonstrated in Table 3.1.

## Measuring Quality of Life

QOL is a subjective concept but can be assessed and measured by HRQOL instruments which are developed within the scientific principles of psychometrics. Designers of an instrument should incorporate important issues recognized from literature and expert opinion but should especially include patient opinions on what is important. Typically, item reduction is required following direct testing in patients, to reduce the questionnaire to a practical length which still retains sensitivity and validity. The actual presentation should be easily readable with clear font and type with adequate spacing and be accessible at a sixth grade reading level.

**Table 3.1** Head and neck quality of life instruments

| | | General QQL | | | | | | | | Voice | Dysphagia | Disfigurement |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Domains | EORTC H&N35 | FACT-H&N v4 | HNQOLQ | HNCI | UWQOL v4 | NDII | AQLQ | H&NS | FSS-SR | LASA for voice quality | MDADI | DSHNC |
| Facial appearance | | | | | | | | | | | | |
| Satisfaction with appearance | × | × | × | × | | | × | | × | | | |
| Noticeable change in | | | | | | | | | | | | |
| Affects self-esteem | | | | × | | | | × | | | | |
| Affects social contact/ activities | | | | | | | | × | | | | |
| Type of H&N surgery | | | | | | | | | | | | |
| Size of disfigurement | | | | | | | | | | | | × |
| Affects facial expression | | | | | | | | | | | | × |
| Distortion of face or neck | | | | | | | | | | | | × |
| Visibility of disfigured area | | | | | | | | | | | | × |
| Speech | | | | | | | | | | | | |
| Voice quality/ understandability | | × | × | × | × | | | × | × | × | | |
| Voice strength/volume | | | × | × | | | | × | | × | | |
| Hoarseness | × | | | × | | | | | | × | | |
| Communication/talking | × | × | × | × | | | × | | | × | | |
| Voice fatigue/loss | | | | | | | | | | × | | |

(continued)

**Table 3.1** (continued)

| | | General QQL | | | | | | | | Voice | Dysphagia | Disfigurement |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Domains | EORTC H&N35 | FACT-H&N v4 | HNQOLQ | HNCI | UWQOL v4 | NDII | AQLQ | H&NS | FSS-SR | LASA for voice quality | MDADI | DSHNC |
| Ability to sing/whistle | | | | | | | | | | × | | |
| Satisfaction with voice | | | | × | | | | | | × | | |
| Swallowing | | | | | | | | | | | | |
| Saliva/dry mouth | × | × | × | × | × | | × | | × | × | | |
| Bad breath | | | | | | | | | | | | |
| Chewing | | | × | × | × | | | | × | | | |
| Problems with teeth/dentures | × | | | × | | | | | | | | |
| Swallowing | × | × | × | × | × | | | × | × | | × | |
| Trismus | × | | × | | | | | | | | | |
| Normalcy of diet quality | | × | | × | | | × | × | | | × | |
| Normalcy of diet quantity | × | × | | × | | | | | | | × | |
| Speed of eating | | | | × | | | | | | | | |
| Appetite | | | | | | | × | | | | | |
| Food enjoyment | × | | | | | | | | | | | |
| Social eating | × | | | | | | × | × | × | | × | |
| Taste | × | | × | | × | | | | × | | | |
| Smell | × | | | | | | | | | | | |
| Others | | | | | | | | | | | | |
| Pain | × | × | × | × | × | | × | × | × | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Respiratory symptoms (breathing/cough) | × | × | | | | | × | | × | | | |
| Shoulder pain/function | | | × | | × | × | × | | × | | | |
| Hearing loss | | | | | | | | | | | | |
| Loss of vision | | | | | | | | | | | | |
| Skin symptoms | | | | | | | | | | | | |
| Smoking and alcohol use | | × | | | | | × | | | | | |
| General QOL | | | | | | | | | | | | |
| Physical/functional/ sexual well-being | × | × | × | × | × | × | × | | × | | × | |
| Social well-being | × | × | | × | | × | × | | | | × | |
| Emotional well-being | × | × | × | | | | × | | | | × | |
| Overall health-related QOL | | | × | × | × | | × | | × | | | |
| Satisfaction with treatment | | × | | | | | | | | | | |
| Life satisfaction | | | | | | | × | | | | | |
| Total | 35 | 39 | 27 | 30 | 14 | 10 | 41 | 13 | 16 | 16 | 20 | 1 |

From Pusic et al. [41], with permission

*EORTC H&N35* European Organization for Research and Treatment of Cancer H&N 35, *FACT-H&N* Functional Assessment of Cancer Therapy Scale – Head and Neck, *HNQOLQ* University of Michigan H&N Quality of Life Questionnaire, *HNCI* Head and Neck Cancer Inventory, *UWQOL* University of Washington Quality of Life Scale, *NDII* Neck Dissection Impairment Index, *AQLQ* Auckland Quality of Life Questionnaire, *H&NS* Head & Neck Survey, *FSS-SR* Functional Status Scale Self-Report, *LASA for Voice Quality* Linear Analog Self-Assessment Scale for Voice Quality, *MDADI* MD Anderson Dysphagia Inventory, *DSHNC* Disfigurement Scale for H&N Cancer

The instrument results can be expressed as an index summary score or as a profile of scores in multiple domains. An index score is convenient but may err in applying standard valuation to each component of well-being, ignoring the personal weight a patient may place on certain domains over others. Some instruments attempt to allow the patient to apply personal weights to certain domains, though this can increase the complexity of the instrument. Other instruments do not attempt to formulate a summary score, but score each of the component domains to generate a profile. In developing the instrument, the investigators evaluate and report reliability (reproducibility across time in absence of change), validity (truthful reflection of reality), and responsiveness (ability to recognize change when present).

The instrument should be utilized with knowledge of the minimal important difference (MID), which is the smallest change in instrument score which represents a truly important change to the patient and not just a trivial variance. This is different from statistical significance; the MID represents a degree of change which a patient would recognize and be aware of. Though each instrument should ideally report this specifically, it has been suggested that a change of 5–10% in score represents the MID for multiple different instruments [3].

The most frequently utilized and thoroughly tested H&N-specific HRQOL instruments are the EORTC QLQ-H&N35, University of Washington QOL questionnaire (UWQOL), the FACT-H&N, and the Head and Neck Cancer Inventory (HNCI) [4, 5].

## *EORTC QLQ-C30/H&N35*

QLQ-C30 is a self-administered, cancer-specific QOL questionnaire consisting of 30 questions; the H&N35 is a module specific for patients with head and neck cancer, adding an additional 35 questions [6]. The QLQ-C30 is organized into five domains: physical, role, cognitive, emotional, and social; three symptom scales: fatigue, pain, nausea, and vomiting; two global scales (global health and QOL); and six single-item questions (dysphagia, appetite loss, sleep disturbance, constipation, diarrhea, and financial impact). The H&N-35 consists of 7 scales, pain, swallowing, senses, speech, social eating, social contact, and sexuality, as well as 11 single items (problems with teeth, problems opening mouth, dry mouth, sticky saliva, cough, feel ill, painkillers, nutritional supplements, feeding tube, lost weight, gained weight). Scores for both instruments are calculated separately for each domain and normalized to a scale of 0–100, with high scores representing better QOL on functional scales or worse symptoms on symptom scales; no summary score is used. Each module takes 7 minutes to complete and is translated into many languages [4]. The minimal clinically important difference in any domain or scale is considered to be 10. Notable items not assessed include shoulder dysfunction and radiation-induced skin changes [7].

### *FACT-H&N*

The self-administered FACT-H&N consists of FACT-G, a cancer-specific QOL questionnaire that includes 27 questions in 4 domains – physical, social/family, emotional, and functional, and a 12-item head and neck cancer-specific module. Each response is rated from 0 to 4 on a Likert index, considering the past 7 days. Scores are calculated separately for each domain, and an unweighted summary score is calculated for the FACT-G and the total FACT-H&N, with a maximum score of 144. The time to completion is 5 minutes.

### *UW-QOL*

The UW-QOL is a self-administered, head and neck cancer-specific scale consisting of 15 questions, including 3 generic questions and 12 domain items that contribute to the composite score. The scale can be scored with a single composite score (0 is worst, 100 is best) or as 2 subscales (socioemotional and physical). Normative values are well established. It is estimated to take 5–10 minutes to complete. The MID is considered to be 7.

### *HNCI*

The HNCI is a self-administered instrument comprising 30 items grouped into four domains: eating, speech, aesthetics, and social disruption. Questions within domains pertain both to respondents' functional status and to their attitude about their function. Time to completion was reported as 7 minutes [8]. Each domain receives a score scaled to 100, and stratification into low (0–30), intermediate (31–69), and high (70–100) categories has been validated; domain score differences of 4, 10, and 14 represent small, intermediate, and large clinically important differences [9]. There is no composite score.

## Quality of Life Over Time

Each individual conceptualizes well-being differently, thus cross-sectional evaluations of HRQOL across a sample are subject to "noise" or apparent differences due to variations in perception of experience. In a longitudinal evaluation, the individual can serve as their own control, eliminating between-subject variation. The values at several time-points can be compared, to categorize for an individual whether

HRQOL has changed or remained stable. A caveat to the use of the individual as their own control is the phenomenon of response shifting. This refers to the potential lack of internal consistency of an individual's perception of their experience. Over time, an individual may alter their valuation of facets of well-being, change the upper and lower limits of measurement based on their experience, or adapt to their circumstances.

Some additional issues with using longitudinal evaluations of HRQOL include incomplete/missing questionnaires and measurement of effect [2]. It is known that a patient's choice to decline to complete a HRQOL instrument is informative, and an assumption that data are missing at random may not be valid. In the same way, healthy patients are more likely to complete all of the time-points in a longitudinal evaluation. The inherent bias in any longitudinal HRQOL study may also be preserved if the study reports HRQOL measurements as mean change for the group: the "survivor" effect overestimates favorable HRQOL because survivors with better outcomes tend to be measured up to the study endpoint [10]. It is preferable to use response analysis to report the HRQOL measurement: a hypothesis with MID should be prespecified, and then each individual categorized according to the criteria (e.g., improved, worsened, stable), and then arms of a study can be compared for the proportion with a certain HRQOL outcome.

### *Baseline*

The baseline assessment does not reflect an individual's normal HRQOL. Because such assessment is made following the onset of H&N cancer and the diagnosis, it should be viewed as reflecting the HRQOL under circumstances of dealing with the disease and prior to further treatment effects. In the general population, norms have been established which demonstrate in general low scores (suggesting minimal problems) for both the QLQ-HN35 scales and single items [11]. Comparing patients with head and neck cancer at diagnosis to age- and gender-matched population norms demonstrates numerically worse scores for all scales and single items for both the QLQ30 and HN35 questionnaires, except in physical functioning and dyspnea. Multiple domains and symptoms reached the level of a clinically significant difference at the baseline of diagnosis (10 points or more): role functioning, emotional functioning, global QOL, fatigue, insomnia, appetite loss, financial difficulty, localized pain, swallowing, social eating, tooth issues, trismus, and thick saliva.

### *During Treatment and First Year Following*

The general pattern for HNC patients is deterioration of HRQOL during treatment, with maximum deterioration at 1 and 2 months after start of treatment; thereafter, they gradually improve [8, 10] (Figs. 3.1 and 3.2). Most scales and single items in

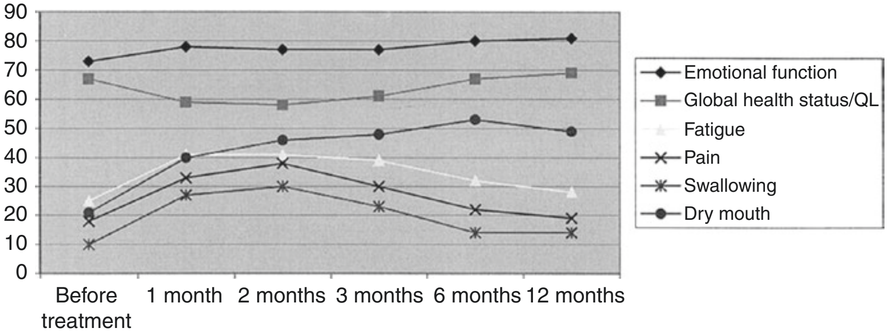
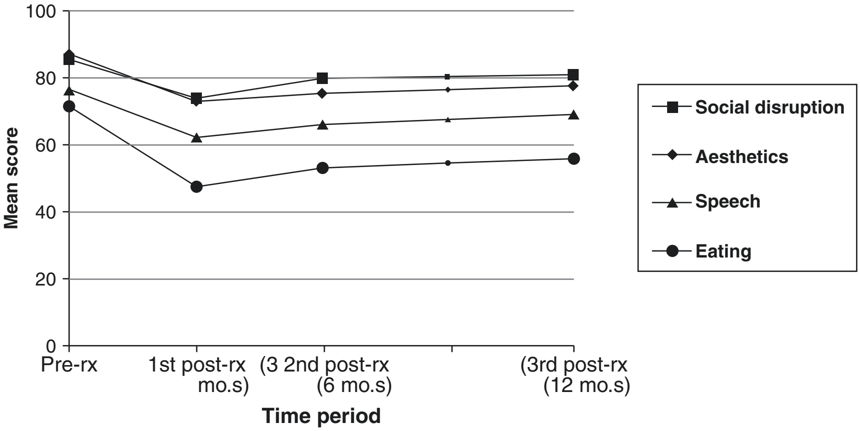


**Fig. 3.1** HNC patient QOL and symptoms over time. (From Bjordal et al. [40], with permission)



| Domain | Pretreatment | 3 mo after treatment | 6 mo after treatment | 12 mo after treatment |
|---|---|---|---|---|
| Social disruption | 85.8 (81.8–89.6) | 74.0 (69.3–78.9) | 80.0 (75.4–84.6) | 81.2 (76.5–85.9) |
| Aesthetics | 87.0 (76.7–97.0) | 73.0 (67.7–78.5) | 75.5 (70.1–80.8) | 78.0 (70.1–80.8) |
| Speech | 76.5 (71.5–81.5) | 62.2 (57.3–67.4) | 66.0 (60.9–71.0) | 69.2 (64.1–74.4) |
| Eating | 71.5 (61.9–81.3) | 47.5 (42.1–53.0) | 53.0 (47.7–58.2) | 56.0 (50.6–61.6) |
| *n* | 176 | 126 | 164 | 178 |

**Fig. 3.2** General pattern for HNC patients is of deterioration of HRQOL during treatment, with maximum deterioration at 1 and 2 months after start of treatment and improvement thereafter. (From Funk et al. [8], with permission)

the QLQ30 and HN35 questionnaires had the worst scores at either 1 or 2 months, with exceptions to this pattern that emotional function was worst at baseline, dyspnea was worst both at 1 and 3 months, and patients had the greatest problems with teeth and dry mouth at 6 months. Of the most common clinically significant deteriorations between diagnosis and 2 months, the largest effects are seen in appetite loss, H&N pain, swallowing, senses, social eating, dry mouth, sticky saliva, and nutritional supplements, while clinically significant deteriorations are also seen in physical functioning, role functioning, social functioning, fatigue, core pain, constipation, speech, sexuality, trismus, feeling ill, painkillers, feeding tube, and weight loss.

Over the rest of the first year, patients generally recover their pretreatment function except for persistent problems with senses, reduced sexual function, and increased dryness in the mouth [10].

In comparing HRQOL during the first year of treatment depending on modality of treatment, Christopher et al. report a trend for patients treated with surgery only to have the highest and stable overall QOL at baseline, 6 months, and 12 months [12]. Post-treatment QOL was lowest in patients treated with chemoradiation, and at 12 months any treatment with radiation had clinically relevant diminished QOL. In another study, Reeve et al. were able to control for relevant clinical and demographic factors and confirmed that receipt of any radiation was independently associated with clinically relevant worsened HRQOL [13].

As opposed to surgical treatment, radiation treatment is associated with xerostomia symptoms, which peak at 6 months; these symptoms are worsened with the addition of chemotherapy [12]. In a study of oral and oropharynx carcinomas, in which all were treated with surgery, the addition of adjuvant radiation was found to significantly affect 3-year HRQOL with more affectation of swallowing functioning and orofacial pain, dry mouth, sticky saliva, less oral opening, sensory disorders, speech problems, and social issues with eating [14]. The patients treated with surgery only had better physical functioning, salivary fluid, taste, and post-operative pain.

Bjordal et al. report that HNC diagnosis at stage III or IV is strongly associated with reduced HRQL, both at baseline and a year later, relative to patients with early-stage disease [10]. Clinically significant differences were seen in QLQ-C30 domains of role functioning, social functioning, appetite loss, and financial difficulties, and QLQ-HN35 areas of pain, social eating, teeth, open mouth, dryness in the mouth, feeling ill, use of painkillers, and use of nutritional supplements.

## *Survivorship*

Many of the cancer-related HRQOL instruments that are available today, though developed to be specific to the H&N site, may not be as applicable for disease-free cancer survivors. These questionnaires include items related to acute and treatment-related symptoms (e.g., vomiting) that are not relevant in the post-treatment period and, conversely, may not assess the issues which are particularly relevant to cancer survivors (e.g., fear of recurrence, return to work). However, there has been some development of HRQOL instruments specifically for survivorship, which include the Cancer Problems in Living Scale (CPILS), Impact of Cancer (IOC/IOCv2), Quality of Life in Adult Cancer Survivors (QLACS), Quality of Life Cancer Survivors (QoL-CS), and Satisfaction with Life Domains Scale for Cancer (SLDS-C). These instruments focus on the psychosocial aspects of survivorship, with relatively little attention to chronic physical effects of cancer and its treatment

[15]. These are useful as generic assessment tools for any type of cancer survivor but therein lack any specific detail relevant to disease site. There is a current effort by the EORTC quality of life group to develop survivorship HRQOL instruments which will capture the whole range of issues relevant to survivors, both in general and with disease-specific modules; this is likely however a long-way off from developing a H&N-specific module for cancer survivors.

Many prospective evaluations of long-term HRQOL in HNC have been published, with some consistent general patterns apparent, though much heterogeneity in the study specifics and data.

Comparing patients surviving head and neck cancer at 3 years after diagnosis to age- and gender-matched population norms demonstrates numerically worse scores for all scales and single items in the QLQ-HN35 questionnaire. Hammerlid et al. report that while no scale from the QLQ-C30 reached a clinically significant difference of >10 points, 6 of the scales from the QLQ-HN35 were clinically significantly different: dry mouth (35 points), trismus (15.8 points), senses (15.0 points), local pain, tooth problems, and sticky saliva [11].

Similarly, at 5 years from diagnosis, compared to age-matched normal population, HNC survivors report problems eating (50%), depressive symptoms (30%), and substantial pain (17%) [16].

Comparing from diagnosis to 8-year follow-up in long-term survivors of HNC using the UW-QOL, Yan et al. found that clinically significant improvement in pain, anxiety, and mood occurred, whereas oral dysfunction (chewing, speech, and taste), shoulder mobility, and appearance were significantly worse at the long-term assessment compared with baseline [17]. Between 1 year and 8 years post-diagnosis, clinically significant improvements are seen in regard to appearance, recreation, speech, saliva, and anxiety, signaling that a nadir and then improvement at long intervals after diagnosis occur in some domains, while patients retain treatment-related dysfunction for the long-term in other domains such as oral function and appearance. This study notably included only oral cavity cancers of generally early stage, with low utilization of free flaps or radiotherapy. Other studies also reflect a general improvement in quality of life after 1 year and in dry mouth, pain, sticky saliva, and role functioning between 1 year and 5 years [18, 19].

Some variations to these results are seen in studies which include other H&N sites than the oral cavity, as well as those which have a higher proportion of advanced stage cancer, which receive free flap reconstruction of defects and also proportionally higher rate of radiation and chemotherapy treatment. These factors seem to have some correlation to worsened long-term HRQOL outcomes [20, 21]. Patients who receive radiotherapy tend to have long-term issues with sticky saliva and xerostomia [18, 19, 22–24]. In the 8–11-year follow-up of advanced oral and oropharyngeal cancers treated with free flap and adjuvant radiation, multiple domains were found significantly to worsen on the QLQ-HN35: emotional functioning, social functioning, swallowing, speech, taste/smell, dry mouth, sticky saliva, and coughing [24].

## Issues Relevant to Particular Disease Sites

There are differences in HRQOL between disease sites of H&N cancer. Bjordal et al. found patients with pharyngeal cancer had the highest overall increase in clinically significant symptom burden over the first year after diagnosis and larynx cancer patients had the least [10]. Differences exist at baseline and then are largest between sites during treatment and shortly after and then diminish but still persist at 12 months (Fig. 3.3).

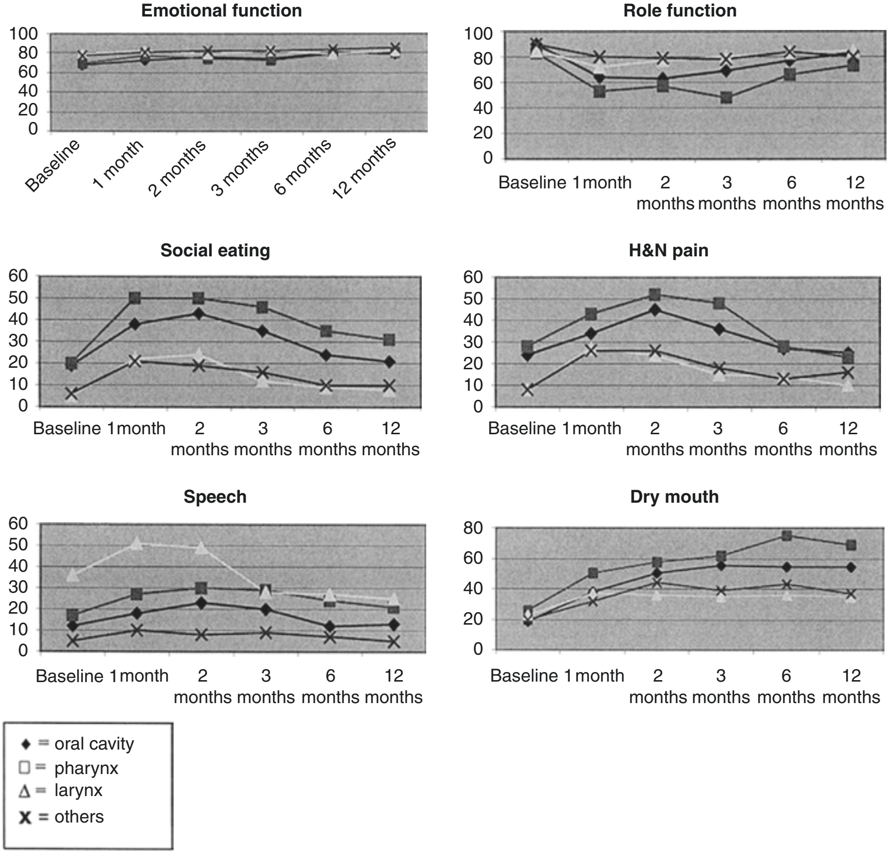


**Fig. 3.3** Differences in HRQOL between disease sites of H&N cancer. (From Ref. [40], with permission)

## *Larynx*

Just at the completion of treatment, patients with larynx cancer report worsened symptoms in appetite loss, sticky saliva, social function, fatigue, nausea, pain, constipation, and nearly all domains from the H&N35 site-specific questionnaire including pain, swallowing, senses, speech, social eating, dry mouth, sticky saliva, coughing, feeling ill, use of painkillers, use of nutritional supplements, use of feeding tube, and weight loss [10]. A limitation of this data is that nearly all of these patients were treated with radiation alone, with very little use of either surgery or chemotherapy. Compared to other H&N sites at 2 months, larynx cancer patients have greater change in coughing and use of painkillers and less change in dry mouth and use of nutritional supplements. At 1 year compared to diagnosis, speech is reported to be significantly improved (and now similar to the pharyngeal cancer scores), and dry mouth was less severe an issue than for other H&N sites. Between 1 and 5 years after diagnosis, these patients report clinically significant deterioration in physical functioning, role functioning, problems with social eating, and dry mouth [25].

Broadly speaking, patients with glottic cancer versus supraglottic cancer report better HRQOL in all domains at diagnosis, except for speech, and at 1 year after diagnosis there was a similar trend for glottic carcinoma patients to have clinically significant better HRQOL in nearly half the domains than supraglottic carcinoma patients [25].

El-Deiry et al. reported a matched-pair study of patients with advanced H&N cancer comparing a group who selected surgery with postoperative radiotherapy with others who selected concurrent chemoradiation [26]. HNCI domain scores between the two groups were not statistically significantly different. Notably, social disruption scores were equivalent, a fact which would likely surprise patients considering laryngectomy or similar operation.

## *Pharynx*

Bjordal et al. found that patients with cancer of the pharynx report a significant increase in symptoms in most domains of the QLQ-C30 and almost all H&N-specific domains of the HN35 at the completion of treatment (2 months from diagnosis) [10]. This study was conducted in the 1990s, and essentially all the patients in this subsite in this study were treated with radiation. Compared with the total group, patients with pharynx cancer more frequently have persistent clinically significant HRQOL issues at 12 months after diagnosis. Clinically significant HRQOL deteriorations are seen in role functioning, senses, social eating, sexuality, and dry mouth, and there was a more frequent use of nutritional supplements, with only changes in senses and sexuality being in common with the rest of the entire cohort of H&N patients.

Compared with surgically treated oral cavity carcinoma patients, surgically treated oropharynx cancer patients have worse overall assessment of QoL, worse physical and emotional functioning, and more symptoms of fatigue and pain at long-term 1- and 3-year follow-up [14]. Compared with surgically treated laryngeal cancer patients at 1 year after diagnosis, surgically treated oropharynx cancer patients have worse oral-associated symptoms such as xerostomia and trismus, while they appear to have better social functioning and better speech and less coughing symptoms [27].

In a comparison of oropharynx cancer patients treated with surgery plus radiation matched to those treated with primary chemoradiation therapy, at 1 year post-treatment similar results were seen on UW-QOL questionnaire for all areas, except swallowing where 74% of the surgical group report swallowing as well as ever versus only 30% of the nonsurgical group [28].

The advent of human papillomavirus (HPV)-associated oropharyngeal cancer and the spread of transoral surgery, and the effects of these seismic shifts on HRQOL, will require ongoing research efforts. With younger patients who have less intense tobacco use histories, HPV-associated cancer may show distinct HRQOL patterns in comparison to those identified the body of literature produced even 10 years ago. HRQOL outcomes after application of transoral robotic surgery (TORS) are under study as well [29].

## *Oral Cavity*

Immediately following treatment at 2 months, the study by Bjordal et al. reports patients with oral cavity cancer appear most affected in the domains of social eating and nutritional supplements [10]. Senses and dry mouth were the only symptoms which negatively persist to a clinically significant extent at 1 year, which is similar for all H&N sites combined. As opposed to other H&N sites, oral cavity patients at 1 year have significant improvement from diagnosis in emotional function, insomnia, use of painkillers, and weight loss.

Most (70%) of long-term oral cavity cancer survivors assessed at 5–10 years reported good or excellent overall quality of life [30]. Half of patients were pain-free, while the other half reported using a painkiller in the last week. The most prevalent problems were dry mouth and sticky saliva in 40% (a similar 40% of patients in this study had received adjuvant radiation treatment after surgery). About 1/3 of patients reported some issue with swallowing solids, sexuality, or teeth.

In comparing oral cavity patients treated with surgery versus with primary chemoradiation, a matched-group comparison demonstrated clinically relevant better overall quality of life in the surgery group, as well as better physical and cognitive functioning, and better swallowing, dry mouth, mouth opening, speech, and sensation [31].

## How to Use This Information in Clinical Practice

HRQOL instruments are widely used and relevant in the conduct of prospective randomized controlled trials. Their widespread use and impact in routine clinical care is lacking. The purpose of including HRQOL in clinical trials is clear, in order to measure important outcomes which inform researchers in comparing different conditions. The motivation to collect and use HRQOL information in routine clinical practice may be less directly obvious. However, asking patients to complete HRQOL as part of a routine visit serves several purposes: provide needed objective measurement of an important health indicator, alert the clinician to potential new issues, and potentially affect long-term trends and overall benefit to the group of current and future patients.

Oncology physicians have three motivations which ground any treatment consideration: to lengthen survival, to decrease or prevent future morbidity, and to improve patient's well-being. The endpoints for assessing the first two considerations are definitive events, while the latter consideration is a multi-factorial subjective concept synonymous with quality of life. Just as a clinician would monitor a blood pressure at each office visit if the patient was being treated for hypertension, if a goal of treatment is to improve well-being then the physician should want some ability to measure this across clinical encounters.

A number of studies have attempted to assess the impact of routine health quality assessment and feedback on patient care, with two systematic reviews identifying 27 RCTs which randomized patients or practitioners to an intervention group which was provided patient-reported health status information compared to a control group of standard routine care [32, 33]. Of 12 studies assessing patient satisfaction, in 7 a favorable difference was seen. Of 22 that assessed process of care, 14 found a difference was identifiable with the intervention. Of 16 studies that assessed a patient outcome, a significant improvement was found in at least 1 outcome in 7 studies. If HRQOL assessment had no associated cost, these mixed outcomes should be enthusiastically viewed, as patients and clinicians would value the information obtained through the questionnaires and possibly these may positively influence process and some outcomes [34]. Of course, the administration and assessment of surveys utilize resources and must be viewed in terms of the net benefit in the health system. However, as patient satisfaction is included in measuring value in today's healthcare markets, the calculus shifts toward increasing utilization of HRQOL assessment in routine clinical care. Use of well-defined instruments along with computer-driven administration decreases the resource utilization as well.

The utility of HRQOL instruments may be different at different points in the patient's experience with cancer. At the initial diagnosis and treatment decision stage, the clinician can use knowledge collected from HRQOL long-term studies to help inform the patient of expected sequelae and outcomes of the treatment options. For many head and neck cancers, several treatment options are often available, without clear evidence supporting one over the other. Patient involvement in the decision-making process is important, and it may be HRQOL expectations which are decisive factors. Evidence from studies of patients deciding how to treat their cancer in the presence of multiple options suggests that the more decisional control they have, the less decisional conflict they experience and the more satisfied they are with the decision-making process [35]. However, more actively involved patients also rate the decision as being more difficult than if they were not in control of the decision. A similar pattern is seen in regards to informational knowledge: men who were more informed and educated about prostate cancer reported less decisional conflict and greater decision-making satisfaction but greater difficulty with the decision-making process.

The downstream effect of having more upfront knowledge of expected HRQOL may be that the patient appraises their actual HRQOL more favorably following treatment [35]. Patients with cancer who expect to experience a given side effect are indeed more likely to experience the side effect. However, by adjusting their value system, they no longer rate the expected side effect as severe a disability. This may be because people tend to overinflate the probability of success when making decisions, and to justify their treatment choice and outcomes following treatment, they bias their information processing and appraisals [36]. The informed and knowledgeable patient who had decisional control will continue to believe 6 months later that they made the best decision under the circumstances and, therefore, may justify their decision by subtly adjusting their reporting of side effect and HRQOL severity.

It can be difficult to present an accurate picture of expected outcomes after treatment to the patient. The outcomes ranked by head and neck cancer patients as the most important priorities include (1) “being cured of my cancer,” (2) “living as long as possible,” (3) “being able to swallow all foods,” and (4) “having no pain” [37]. Though data regarding recurrence and survival rates are often the most focused on by clinicians in counseling sessions with patients, well-developed sources for accurate portrayal of HRQOL issues which are important to patients, such as swallowing and pain, can also be used in treatment planning [38]. One of these, accessible online at http://www.hancsupport.com/wwibl, presents long-term HRQOL results for 1500 head and neck patients (using the UW-QOL questionnaire) organized into 26 different groupings by head and neck site (oral cavity, larynx, etc.) and treatment modality (surgery, radiation, combined, etc.). As no two patients’ experience could ever be guaranteed to be the same, such information presentation as this is effective in demonstrating the range of quality of life domains impacted, the frequency of good and bad results, and the degree of variation and uncertainty possible.

Use of support services and rehabilitation efforts can be guided by monitoring of the HRQOL issues reported by the patient, and rehabilitation efforts can help improve the HRQOL outcomes. In long-term follow-up, the assessment by a physician of moderate to severe hoarseness or mild, moderate, or severe dysphagia is associated with clinically relevant decreases in patient-reported quality of life and functioning [39]. This highlights the importance of swallowing and voice to HRQOL and suggests these as valuable targets for tailoring treatment approaches and rehabilitation efforts, as opposed to other common physical findings, including soft tissue fibrosis and xerostomia, which are not per se associated with changes in patient-reported quality of life [39]. At the time of treatment, the most common needs for supportive care are for a dental hygienist (77%), a physical therapist (73%), a speech therapist (42%), a dietician (38%), and a special diet (62%) [24].

At the point of long-term follow up, the common needs for supportive care are limited to a dental hygienist (46%) and a physical therapist (23%) [24].

## Future Directions

Despite its importance as a measurable outcome of cancer treatment, research on HRQOL in HNC patients is as yet comparatively limited. Several centers around the world have endeavored to measure and report HRQOL outcomes of cohorts of patients, but the absence of repetition of findings, the size of the reported cohorts, the variation in the oncologic and treatment histories of the studied patients, and the nature of QOL measurement combine to make published research findings less settled than we might wish. Continuing research on this outcome assessment in HNC patients is needed. In addition, as treatment choices have migrated over time and across geographic regions, well-designed and comprehensive assessment of HRQOL in HNC patients needs to continue. Certain adverse effects are characteristic of specific treatments (such as xerostomia related to radiation) and are currently included in most HNC-specific HRQOL questionnaires; as new treatments continue to be introduced, such as systemic chemotherapy and immunotherapy, we will need to broaden or change HRQOL domains to follow evolving toxicities – examples include tinnitus and hearing loss, skin changes, and damage to other organs systems.

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# Chapter 4
# Mental Health in Head and Neck Cancer

**Christine Mei and Zoukaa Sargi**

With cancer research continuing to push the boundaries of modern science, new chemotherapeutic agents are being tested and put to use at a growing rate. Clinical treatment plans continue to be refined to capture increasing cure rates and decreasing morbidity and mortality. The quest to find the ultimate "cure for cancer" is well underway. As such, curing the cancer becomes the main goal of patients and their healthcare teams, and consideration of the mental health of patients and caregivers throughout cancer diagnosis, treatment, and survival can sometimes become overshadowed and neglected. Yet, mental health (MH) issues can present aggressively and can threaten outcomes of treatment and overall prognosis of patients. The importance of the emotional, spiritual, and psychological aspects of cancer has led to the development of the field of psycho-oncology in the past 50 years. Psycho-oncologists advocate for the consideration of individual psychological challenges, as well as cultural and linguistic challenges, in the choices of precise treatment for cancer. Many avenues of cancer care support, from adjustment and coping education to novel biobehavioral therapies, are being developed. To truly benefit from the mission of this growing multidimensional discipline and to capitalize on the advances in chemotherapy, radiation, and surgery, it becomes particularly important to conduct a thorough survey of MH in cancer and generate a solid framework to incorporate supportive intervention throughout the course of cancer.

Head and neck cancers (HNCs) are mostly epithelial malignancies of the upper aerodigestive tract and are estimated to cause roughly 380,000 deaths per year worldwide [1]. HNCs are considered one of the most traumatic and distressing types of cancer and carry some of the highest rates of mental disorders and suicide among all cancers [2–5]. The central and prominent location of disfigurement in HNC and its treatment is thought to be one of the major reasons for distress among HNC patients [4, 6, 7]. Further, debilitating changes in basic functions, such as

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speaking and swallowing, greatly impact the mental health and quality of life of HNC patients [8–10]. Demographic and health behavior risk factors related to HNC pathogenesis are also important considerations when considering MH outcomes. The more recent advent of HPV-positive HNC in younger patients, with better prognosis and increased post-cancer life years, represents a unique challenge in HNC mental health. While some resources exist to support MH in HNC, more research and clinical implementation must be done to create efficient individualized MH evaluation and treatment during the process of HNC and its treatment. This chapter aims to summarize the current findings and future directions of MH in HNC.

## Health Behavior Risk Factors and MH in HNC

Special considerations for MH in HNC stem from the major risk factors for HNC. Tobacco use, alcohol use, and human papillomavirus (HPV) infection are all independent major risk factors for the development of head and neck cancers. These three risk factors are strongly tied to individual psychosocial behaviors, socioeconomic status, and cultural context and represent areas for study of both cause and effect of distress in HNC.

### *Tobacco and Alcohol Use*

Tobacco and alcohol use cause HNC due to their cytotoxic and mutagenic effects on the exposed epithelia of the upper aerodigestive tract [11, 12]. Tobacco and alcohol use are nonadaptive coping mechanisms, and their use prior to diagnosis is important to consider as patients undergo the HNC diagnosis and treatment process. The highest rates of tobacco use are associated with American Indian/Alaskan, White, and African-American race, male gender, and low socioeconomic and educational status [13–15]. Personality traits such as extrovertism, neuroticism, and impulsivity have been tied to smokers, with strong evidence of comorbidity between smoking and psychiatric disorders, such as schizophrenia and depression [16]. It is estimated that more than 30% of patients with psychiatric disorders meet criteria for substance abuse or dependence, thought to develop as a reaction to stress [17]. In HNC, tobacco has been found to be a stronger risk factor for HNC than alcohol consumption [18], and studies have focused on progression of tobacco use throughout the HNC process. HNC current or recent smokers presenting for treatment have been found to face increased challenges, being more likely to be unpartnered, unemployed, and lacking insurance and adequate finances [19]. This patient population may also have fewer psychological resources, demonstrating lower religious faith and more fatalistic beliefs [19]. HNC patients presenting for treatment who are current or recent smokers will experience higher symptom burden after treatment [19]. This, along with the additional challenges they face, can put these patients at higher risk for mental health disturbances throughout the HNC process.

Rates of continued smoking after HNC treatment have been reported to be between 29% and 56% [20–24], with the range thought to be due to variation in screening pattern and patient characteristics across studies. Chen et al. (2014) found that 21%, 21%, and 20% of HNC patients treated with radiotherapy were found to be smoking 1, 2, and 3 years posttreatment, respectively, which increased to 32%, 27%, and 25% when including only former smokers [25]. Presence of a preexisting psychiatric condition at initial cancer diagnosis, most commonly a mood disorder, significantly predicted for persistent smoking at follow-up [25]. Further, elevated rates of depression after HNC treatment place patients at increased risk for smoking [26]. Studies show that relapses are common in HNC patients and that patients are more likely to smoke if household members are also smoking, if they held fatalistic beliefs, or if they had completed treatment [27–30]. Patients are more likely to quit if they have a supportive partner, and social isolation, common in HNC, can affect tobacco use [31]. Fear of recurrence is also paradoxically associated with continued tobacco use in HNC survivors [32].

Continued tobacco use can lead to decreased survival, increased risk for recurrence and development of secondary primary tumors, increased treatment toxicity, and heightened depression and distress [33–36]. Though tobacco use is thought of as a stress-relieving mechanism, studies have found that patients who achieve abstinence experience a marked reduction in anxiety compared to those who fail to quit long-term [37]. These findings show that prioritizing control of existing mood disorders, thoroughly executing tobacco cessation programs, and promoting consistent psychological and social support should be considered to prevent adverse outcomes related to tobacco use in HNC patients.

Whites and Native Americans have the highest rates of alcohol use and, thusly, the greatest risk for alcohol use disorders compared to other ethnic groups. Once alcohol dependence occurs, Blacks and Hispanics experience higher rates than Whites of recurrent or persistent dependence, and the consequences of drinking appear to be more profound for Native Americans, Hispanics, and Blacks [38]. Unemployment is associated with heavier alcohol use and higher risk for developing alcohol use disorders [39], and male gender is correlated with higher and heavier alcohol use [40]. Alcoholism development has been associated with neuroticism features and diminished consciousness traits, and alcoholics who present with depressive disorder have more neuroticism indicators and less awareness compared to those without depression [41–43]. Increasing involvement with alcohol increases risk of depression [44], and major depressive disorder is associated with higher risk of alcohol use disorders [45–47]. In HNC, many patients have a history of heavy alcohol consumption [48], with up to half of HNC patients estimated to continue consumption of alcohol after diagnosis [49, 50]. Current problem drinkers in the HNC population have been found to have the worst depressive symptoms and overall quality of life (QOL) compared to social drinkers and nondrinkers [50].

Pinto et al. (2011) found that maintenance or resumption rate of alcohol use was lower than for smoking for HNC patients after treatment [51]. Some studies have shown that there are no significant connections between depression and alcohol consumption or alcohol dependency in patients with head and neck tumors [52, 53], and others have shown better function and symptom scores with alcohol drinking [54]. Still, excessive alcohol consumption was found to be associated with worse QOL [55]. Further, there is still evidence of a pre-diagnosis alcohol dose-dependent increase in risk of dying and a continuous drinking post-diagnosis increase in risk of dying compared to nondrinkers in the HNC population [48]. Along with the known link between alcohol abuse and comorbid mental distress, HNC patients, particularly those with prior alcohol abuse, should be advised to abstain from alcohol. In terms of mental health outcomes in HNC patients, more investigation must be done to understand the relationship between distress and varying levels of alcohol use.

Alcohol and tobacco use exert multiplicative effects when used in conjunction [56] and have been known to act synergistically to increase risk for HNC [57]. Co-occurrence of alcohol use, tobacco use, and depressive symptoms is high in HNC patients, with one recent study showing two or more co-occurring problems in 21% of patients surveyed [58]. Other studies have shown similar findings of significant clustering of smoking, alcohol misuse, and depressive symptoms [53, 59–61]. Further, smoking cessation has been shown to improve alcohol sobriety, indicating that treatment of one recognized comorbidity can improve the others [58, 62]. The effects of concomitant smoking and alcohol use must be more clearly delineated in relation to development of depression and distress in these patients.

## *Human Papillomavirus (HPV) Infection*

HPV is a DNA virus that invades epithelial cells, with high-risk cancer-forming strains showing propensity for increased host genome integration and evasion from host immune defenses [63]. HPV infection is associated with high-risk sexual behaviors, such as greater lifetime number of sexual and oral sex partners, that lead to greater exposure to HPV. Recent evidence shows that HPV-positive and HPV-negative oropharyngeal squamous cell carcinomas (OPSCCs) are two fundamentally distinct diseases with different mechanisms of tumorigenesis, presentation, prognosis, and response to treatment [64]. HPV-positive HNC is seen in younger patients and differs in patient education level, race, and survival rates when compared to HPV-negative HNC, tending to affect white, male, married, educated, and actively employed individuals [65]. The 8th edition of American Joint Committee on Cancer Staging Manual, enacted in January 2018, has subsequently defined separate staging systems for HPV-positive and HPV-negative OPSCC [66]. HPV positivity of OPSCCs has been found to correlate with better response treatment and favorable prognosis – leading to longer survival, with a 2-year survival of 95% and 5-year survival of 79% (as compared to HPV-negative 2-year survival of 62% and 5-year survival of 46%) [67]. As most young patients are expected to survive these cancers, a new set of potential functional conditions, quality of life issues, and mental health considerations will be faced in subsequent life and work years.

Although research dedicated to psychosocial distress in HPV-positive HNC (HPV-HNC) patients is currently scarce, there are reasons to believe these patients are at high risk. HPV-HNCs are primarily oropharyngeal, a tumor location associated with high rates of depression [68, 69]. Patients are also more likely to undergo combined modality treatments that can produce functional defects, symptoms, and disfigurement that will affect MH. HPV-HNCs are known to be sexually transmitted, following specific behavior patterns that may place patients at high risk of distress, including young age at first sexual encounter, high number of partners, and frequency of oral sex and marijuana use [70, 71]. Studies on HPV and cervical cancer can inform some insight on effects of HPV-HNCs on the MH of these patients [69]. HPV-positive women interviewed after repeated HPV testing endorsed increased anxiety, distress, and concern about sexual relationships, as well as shock, confusion, and distress about testing HPV-positive [72, 73]. Emotions were commonly related to sexual transmission concerns, cause of virus, and anxiety about health implications. Concerns about fidelity, past relations, and spousal suspicions may also potentiate stress in a relationship that is already burdened by the strain of cancer [69, 72, 73]. Future exploration into how HPV positivity effects MH of these patients will allow for effective intervention and alleviate further burden on the patient during the HNC process.

## Psychosocial Distress and Psychiatric Illness in HNC

"Psychosocial distress" is a term that is determinedly broad, defined by the National Comprehensive Cancer Network (NCCN) as an "unpleasant emotional experience of a psychological, social, and/or spiritual nature that may interfere with the ability to cope with cancer, its physical symptoms, and its treatment." Psychosocial distress encompasses depression, anxiety, and other psychiatric illnesses and strives to also include other cognitive, behavioral, and emotional components of suffering [74]. The NCCN explains the choice of the word "distress" because it is more accepting, less stigmatizing, and less embarrassing and can be defined and measured by self-report. This term serves as the basis for a wave of inclusion and awareness in cancer care, and tools that measure distress, including the widely used Distress Thermometer (DT), are used to quantify distress as an indicator of suffering. The NCCN has thorough guidelines to follow for distress management in oncology and details an evaluation and treatment process. Using the DT scoring system and thorough clinical and social assessment, patients are stratified into two groups. A score of 4 or more on the DT denoted evidence of moderate to severe distress and warrants referral to mental health services, social work, and, if applicable, chaplaincy care. A score below 4 on the DT warrants first-line treatment by the primary oncology team and continuous evaluation for additional resources if necessary [75]. This workup is for the general cancer population, and workup is explained in broad strokes.

While the NCCN distress workup aims to cast a wide net to capture oncology patients struggling with distress, it is important to also study MH and distress in each cancer population, such as HNC. A recent study reported as high as 51% of HNC patients experienced clinically significant distress [76]. Distress can be generated throughout the HNC cancer process, beginning with diagnosis and extended past completion of primary treatment. Distress can manifest both subclinically and with clinically recognized psychiatric disorders in HNC patients facing the physical, emotional, financial, and spiritual burdens that accompany HNC and its treatment. In this section, we highlight psychiatric components of distress in patients with HNC and summarize findings to serve as a springboard for medical professionals to identify and address HNC patient distress.

## *Depression in HNC*

Psychiatric illness is prominent in HNC as compared to other cancers, with major depressive disorder (MDD) rates as high as 15–50%. Other psychiatric disorders prevalent in HNC include anxiety, post-traumatic stress disorder, and suicide. Depression remains the most highly studied psychiatric disorder in general oncology, as well as in HNC [77, 78]. The DSM-5 diagnostic criteria for major depressive disorder (MDD) are the presence of five or more of the following depressive symptoms during the same 2-week period that represent a change from previous functioning, with one symptom being either depressed mood or loss of interest or pleasure: depressed mood, diminished interest or pleasure in activities, significant weight change without purposely making the change, sleep disturbances, psychomotor changes, fatigue/loss of energy, feelings of worthlessness/guilt, lack of concentration or indecisiveness, and recurrent thoughts of death or suicidal ideation [79]. Diagnosis and treatment of HNC have been associated with physical disfigurement, loss of function, high morbidity, and reduced quality of life, all of which can have a relationship with the causes and effects of depression and other psychiatric illness [80]. HNC patients who are clinically depressed prior to diagnosis and during the HNC process are more likely to have decreased health-related quality of life during and after treatment, prolonged hospital stays, and reduction of self-care abilities. Depressed patients are also less likely to complete treatment plans, and more likely to be more disabled by fatigue and other comorbidities, and to have continued tobacco and alcohol use [80]. Comorbid depressive illness in HNC is independently associated with a 30–40% relative survival disadvantage [78, 80].

Studies have found a multitude of risk factors have been found to correlate with increased development of depression in HNC. Of note, there have been limited studies on biological explanations for depression risks in HNC patients, with studies failing to support a role for certain genetic polymorphisms in serotonin transporter genes [4, 81]. In contrast, sociodemographic, oncologic, treatment, and other patient-related factors can be significant and reliable predictors of depression in HNC patients. Sociodemographic variables associated with higher levels of depression include female sex, White race, Medicaid enrollment, and US Midwest residency. Oncologic predictors include T3 or T4 stage and hypopharyngeal or laryngeal HNC subsites [4]. Functional changes, particularly dysfunction with salivation and problems with eating, have also been shown to be major risk factors for depression in HNC patients [82]. More extensive treatment and tube dependence are also related to higher risk for development of depression in HNC. Chronic pain as a result of HNC treatment have been shown to lead to measurable increases in depression, anxiety, and decreases in quality of life and recreation [83]. Psychological risk factors found to most predict the development of depression in HNC include depressive symptoms, lack of emotional support and social network, avoidant style of coping, and lack of openness to discuss cancer in the family [4, 84, 85]. Further, disengagement/avoidant coping strategies (rather than engagement-focused coping strategies), such as alcohol or tobacco consumption, are common in people with HNC and are associated with poorer survival rates and higher levels of psychological distress [4, 26, 84–86]. This strategy is especially relevant to HNC patients, as cigarette smoking and alcohol use are established risk factors for HNC [87]. Self-blame at diagnosis has also been found to predict depression posttreatment for HNC [84].

Preexisting depression must also be considered in these patients, as depression has been thought to influence cancer development in a number of ways. Depression may weaken the immune system and place individuals at greater risk for disease development. Chronic stressors associated with depression may also cause a decrease in DNA repair enzymes and natural killer cells that are important in apoptosis, permitting malignant cells to grow and multiply [88–90]. Other theories include shared genes and shared behavioral risk factors between depression and cancer [4, 91, 92]. Preoperative depressive symptoms in HNC patients without preexisting psychiatric history have been shown to be high in HNC patients, and increased preoperative depressive symptoms were found to predict increased postoperative levels of depression [93]. HNC patients with moderate to severe preoperative depressive symptoms have significantly decreased postoperative functional performance status, increased narcotic use, decreased completion of adjuvant therapy, and a longer length of hospital stay [80].

Depression rates in HNC can be as high as 40% at diagnosis and have been reported to be as high as 30% 3 years after diagnosis [94, 95]. Peak symptoms of depression in HNC occur 2–3 months after diagnosis [94, 95]. Longitudinal studies have used Mullen's "seasons of survival" concept to show that rates of depression are high in the "acute survival" stage between diagnosis to treatment, peak in the "extended survival" stage from treatment completion through recurrence surveillance period, and decrease throughout "permanent survival" greater than 5 years after treatment to varying reported levels [96]. Depression can be difficult to diagnose and treat in the cancer course [97], as depressive symptoms can mimic side effects of cancer and treatment, including sleep disturbances and lack of energy and appetite [4]. Additionally, patient-reported and reported-to-interviewer rates of depression vary widely, resulting in the large range of estimated prevalence of depression in HNC. Studies that use patient-reported measures often indicate higher rates of depression, which may be important for clinical care teams to consider when screening patients. Screening methods for depression are numerous across all cancers, with multiple questionnaires validated for HNC, including Depression Anxiety and Stress Scale (DASS), Hospital Anxiety and Depression Scale (HADS), and Hamilton Depression Rating Scale (HDRS) [98]. Inpatient and outpatient evaluation of depression is often done concurrently with anxiety using the well-validated HADS questionnaire, a 14-item scale to be completed by the patient that generates ordinal data, with seven items measuring anxiety and seven items measuring depression over the last 7 days. The scale allots 0 (normal) to 21 (severe) per each subscale to generate a composite score of 42 for the instrument [99]. HNC health-related quality of life questionnaires often screen for mood changes as well. One example is the University of Washington – Quality of Life Head and Neck Cancer questionnaire (UW-QOL), an instrument that covers 12 domains that assess the effects of HNC and its treatment. The 12 domains include pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder function, taste, saliva, mood, and anxiety over the period of the last 7 days. The domains are scored on a scale from 0 (worst) to 100 (best) with a composite score of 1200 for the instrument [100]. Regular and thorough administration of depression screening instruments can be included in H&P assessments at visits with HNC clinicians.

Rieke (2016) recently proposed a conceptual model of the pathway to depression among HNC patients [101]. This model highlights factors influencing preexisting depression and factors influencing depression after cancer diagnosis and HNC outcomes, which are categorized into individual-level factors, environmental-level factors, and social/behavioral risk factors. These factors play a nonlinear role in the development of depression in HNC. This model proposes that depression can be both a risk factor for and result of diagnosis of HNC, a concept that points to the necessity of early and longitudinal treatment for full support of patients with HNC. Smith et al. (2017) recently proposed a clinical intervention framework for depression detection and treatment across the "seasons of survival," tracking targets along the HNC process [97]. This framework can be reconciled with DS guidelines to inform longitudinal MH surveillance and treatment. One of the first steps of programs aimed at decreasing depression in HNC patients is the establishment of a multidisciplinary cancer committee with psychosocial representation. In the acute survival phase, patients are faced with existential distress, demoralization, and resignation to terminal prognosis. Patients may have history of psychiatric illness, negative coping styles, and concurrent substance use. All patient factors must be taken into consideration by the multidisciplinary care team to focus on prevention of depression and distress. In this phase, patients should be adequately educated about the HNC illness timeline, effects of all potential treatment modalities, the importance of tobacco and alcohol cessation, and the symptoms of depression. In some cases, prophylactic medications such as SSRIs can be considered. In the extended survival phase after treatment, patients are facing radiation treatment, advanced HNC stage, physical and functional changes, fear of recurrence, fear of disfigurement, and continued substance use. Screening becomes important in this phase of survival, for high index of clinical suspicion of incident depression. Patients should be questioned about any psychiatric symptoms and given regular, validated screening tools. Once patients enter permanent survival, which has been defined as greater than 5 years posttreatment, studies have shown large falling off of incident depression and distress in the HNC process [97]. However, patients in this stage still experience fear of recurrence, other cancers, tube dependence, late effects of HNC treatment, and employment difficulties. In this stage, it is important to focus on treatment of depressive symptoms, by triaging symptoms to appropriately match patients with psychosocial interventions, including medications, psychotherapy, stress reduction tools, sleep hygiene education, or even psychiatric hospitalization.

## *Post-traumatic Stress Disorder in HNC*

Cancer diagnosis and treatment are highly stressful events and can be traumatic for many patients and their partners, and preliminary evidence shows that the changes associated with HNC can make HNC patients particularly susceptible to symptoms of post-traumatic stress disorder (PTSD), a disorder of anxiety [102, 103]. Though markedly less researched than depression, PTSD is an important consideration in HNC. The DSM-5 diagnostic criteria for PTSD include exposure to traumatic event and 1-month duration of post-traumatic stress symptoms of intrusive thoughts or re-experience, avoidance/numbing, negative changes in mood and cognition, increased arousal, and functional problems [79]. A recent survey of HNC survivors and their partners has shown high levels of cancer-related post-traumatic stress symptoms (PTSS) can persist for many years after diagnosis, with 33.4% of patients reporting PTSS and 11.8% meeting PTSD criteria. Further subgroup patient-partner analysis showed 33.3% of patients and 25.7% of partners reporting PTSS, with 33.3% of patients and 25.7% of partners experiencing PTSD [6]. The relationship between coping strategies with diagnosis and development of PTSD in HNC has been of particular interest in HNC patients. Denial, substance use, behavioral disengagement, venting, self-blame, and, interestingly, use of humor at diagnosis were found to be significantly correlated with lower HRQL and higher post-traumatic stress at 6 months after diagnosis [104]. These findings have indicated the routine use of brief coping questionnaires at diagnosis for patients and indicate those identified to have ineffective coping strategies may benefit from targeted psychoeducational interventions that encourage more adaptive strategies, like problem-solving, relaxation, goal setting, communication, and development of social networks. Patients and their caregivers were also investigated to show that 19% of caregivers met PTSD caseness at 6-month follow-up, associated with caregiver perceptions of low treatment benefits, many cancer symptoms in patient, and caregiver avoidant coping techniques [105, 106]. Caregivers were defined in this case as attendance at clinic with patient who had been diagnosed recently and having a close relationship with the patient, such as spouse, family member, close friend, or formal caregiver. Posluszny et al. (2015) showed that caregivers, which included patient's spouse or significant other, experienced higher levels of PTSD caseness (28.6%) than patients themselves (11.9%) around time of diagnosis, which was correlated more strongly to perceived threat of disease than medical variables in patients or caregivers [103]. This indicates that targeted psychoeducational interventions could also be employed in caregivers, which could lead to better physical outcomes and emotional well-being in patients. Caregiver MH in HNC will be further discussed later in this chapter.

## Research in HNC Patient Stress Management and Treatments

Mental health in HNC is specific to the prior psychiatric history, coping strategies, social support, health behaviors, and individual experiences of each patient. Thusly, support and interventions for MH support in HNC should be personalized to the patient, which represents a difficult challenge to HNC clinicians. Management must also cover HNC-related psychosocial stressors like interpersonal concerns, uncertainty, interference with activities, communication, fear of recurrence, stigma concerns about distress, concerns about disease and treatment, existential stressors, financial issues, lack of information, and anticipated negative surgical consequences including appearance and body image. In this section, we highlight findings on interventions for stress management in HNC patients.

### *Pharmaceutical Intervention*

First-line treatment for standalone MDD, anxiety, and PTSD is pharmacotherapy plus psychotherapy [107–112]. Pharmacotherapy includes antidepressants, of which selective serotonin reuptake inhibitors (SSRIs) are suggested for initial treatments due to safety and side effect concerns with other antidepressants and are considered safe for treatment of depression in all cancer patients [4]. SSRIs include citalopram, escitalopram, fluoxetine, paroxetine, and sertraline. Citalopram hydrobromide, an SSRI antidepressant, has been studied in prevention of MDD in HNC. Patients given prophylactic citalopram showed fewer depressive symptoms (17%), and fewer participants became suicidal (0 of 10) compared to a placebo group (50%; 2 of 12) after 12 weeks of the study [113]. Nondepressed patients were also given escitalopram in an RCT, which showed that prophylactic escitalopram reduced risk of developing depression by greater than 50% [114]. These findings may indicate use of prophylactic antidepressants in at-risk HNC patients, though more research must be done to determine exactly which patients would benefit most greatly from prophylactic intervention. Other newer antidepressants such as bupropion, venlafaxine, and mirtazapine are also used in cancer patients [4], though studies have not been done with these medications in HNC patients specifically. Further, there have been no studies to test additional therapies for PTSD (such as prazosin) in HNC, in which case clinicians must weigh benefits to side effect profiles, as well as interaction with chemotherapy medications or other medications the patients are using. Side effects of SSRIs most commonly include sexual dysfunction, drowsiness, weight gain, insomnia, anxiety, and dizziness.

## Cognitive Behavioral Therapy

Clinicians must be vigilant in staying up-to-date on the methods of psychologic and psychiatric interventions, as they can mobilize these therapies to create a holistic treatment approach specific to the patient. Often, psychologic therapy is in the form of cognitive behavioral therapy (CBT). Generally, CBT is a short-term, skills-focused treatment aimed at altering maladaptive emotional responses by changing the patient's thoughts, behaviors, or both [115]. CBT has been shown to be effective for a wide variety of mental health disorders, with a large number of diverse protocols that include exposure therapy and cognitive therapy. Medical and psychological interventions (MPIs) tested have included the primary medical interventions including surgery, chemotherapy, and radiation, along with a psychological package of psychoeducation, relaxation, and CBT. MPIs have been shown to reduce overall stress, as well as components of stress scale-fear, psychosomatic complaints, information deficit, and everyday life restrictions in a cohort of cancer patients that included HNC patients [116]. MPIs were also shown to create significant improvements in quality of life, on physical, role, and emotional functioning scales, and decreased fatigue, pain, insomnia, appetite loss, diarrhea, and constipation of symptoms scales in these patients [116]. Selection and efficacy of psychotherapy methods in HNC are a topic of ongoing research. Kangas et al. (2013) conducted a study comparing early intervention with cognitive behavioral therapy (CBT) or nondirective support counseling (SC) in HNC [117]. Patients received six CBT or SC sessions that ran concurrently with radiotherapy and were evaluated 1, 6, and 12 months posttreatment. While a higher proportion of CBT recipients were diagnosis-free at 1 year, both brief interventions were shown to reduce acute stress and comorbid depression, reducing PTSD, MDD, and anxiety. Krebber et al. (2016) compared stepped care (SC) to care as usual (CAU) stratified by screening with high-scoring HADS HNC patients. SC therapy was comprised of watchful waiting, guided self-help, problem-solving therapy, psychotherapy, and psychotropic medications [118]. Readministration of HADS posttreatment showed that recovery rate better in SC than CAU, and SC showed better outcomes in higher HADS than lower. Another study compared SC to CAU and measured direct nonmedical costs, productivity losses, and health-related quality of life (HR-QOL), finding that mean cumulative costs were lower and mean number of quality-adjusted life years were higher in SC programs compared to CAU [119]. This indicates that SC is highly likely to be cost-effective in HNC. CBT has also been combined with swallowing therapy (CB-EST) for dysphagia, a predictor of distress and poor QOL [120]. Preliminary results showed the CB-EST led to improvements in a swallowing questionnaire (MDADI), general QOL questionnaire (EORTC-QLQH&N35), dietary scale (PSS), and fatigue scores (CFQ-11). However, the complex therapy showed no change in function scales or HADS scores, potentially due to small sample size.

Although HNC patients have been shown to prefer individual one-on-one therapy compared to group or bibliotherapy [121–123], group interventions, including Nucare and Face IT, have been studied and appear effective [124]. Nucare is a nurse-directed CBT that trained patients in problem-solving, relaxation techniques, cognitive coping skills, goal setting, communication, social support, and lifestyle factors [123, 125]. Face IT is another CBT-based intervention that focuses on social skills strategies, exposure to overcome social anxiety, and cognitive restructuring [126]. Another study showed that nurse counselling and after intervention (NUCAI) on depressive symptoms and HR-QOL in HNC patients improved depressive symptoms and several domains of HR-QOL compared to CAU patients [127]. Nurses involved in the study underwent a 1-day extensive training prior to the study. NUCAI was comprised of 12 months of evaluation of current mental status with HADS, discussing current problems and life domains, providing Adjustment to Fear, Threat or Expectation of Recurrence (AFTER), providing general medical assistance and advice, and referring patients to psychological aftercare. Aftercare referrals were to psychiatrist, psychologist or social worker, or rehabilitation and support programs.

In 2013, Semple et al. conducted a meta-analysis of 7 qualifying randomized controlled trials (RCTs) and quasi-RCTs using psychosocial interventions of 542 adults with HNC [128]. Limited by small number of studies, lack of power, and difficulties comparing different types of interventions and outcome measures, this meta-analysis found no significant change in levels of anxiety or depression following intervention. There was insufficient evidence to make any recommendations on psychosocial intervention in HNC. However, other large-scale meta-analyses of general cancer patients have shown that psychological interventions have large effects on depression and anxiety, recommending routine psychological intervention for cancer patients [129]. This points to the importance for further studies that recruit larger numbers of HNC patients, address methodological problems, and lend to study comparability in both measures and outcomes [130].

## *Survivorship Programs*

Survivorship initiatives have begun to recognize the concerns and unmet needs of cancer survivors and their caregivers [124, 131]. These comprehensive initiatives address major physical, emotional, and cognitive disabilities in HNC survivors through interdisciplinary, disease-specific programs. Unmet survivorship needs have been identified in over 50% of general cancer patients [132]. Studies have found up to 68% of HNC patients had unmet survivorship needs, most frequently in the psychological domain [133, 134]. These needs included fears of cancer recurrence, future uncertainty, sadness, and concerns about family and friends [133]. Surveys of HNC survivor caregivers reported managing fears of cancer recurrence was the most common unmet need [134, 135]. HNC-specific survivorship programs include the Princess Margaret Cancer Centre HNC Survivorship Programme, which serves as a resource for complex HNC patients [10]. The American Cancer Society has also released their guidelines for HNC survivorship care, which includes recommendations for surveillance for HNC recurrence, screening and early detection of second primary cancers, assessment and management of physical and psychosocial long-term and late effects of HNC and its treatment, and care coordination and practice implications [136].

## *Effect of Smoking and Alcohol Cessation Programs on Mental Health*

Tobacco and alcohol use are classic risk factors for HNC. These behavioral risk factors are often causes of head and neck cancers and the effects of treatment that also lend to psychosocial distress, indicating that the role of psychosocial intervention at time of diagnosis throughout the disease trajectory is essential for compliance with treatment and healthy coping posttreatment [137]. Comorbidity of smoking, hazardous alcohol use, and presence of a major depressive episode were found to be high (21% for two or more problems) in HNC patients undergoing radiotherapy [58]. Posttreatment abstinence from smoking has been found to be associated with lower levels of depressive symptoms [138]. However, the relationship between continued risky health behaviors and mental health in HNC is not that simple. Early tobacco consumption following treatment has been found to be predictive of psychological distress at 1-year follow-up, indicating smoking itself may be partly responsible for increasing levels of anxiety and depression [139]. Yet, duration of smoking prior to quitting estimated distress, indicating that prolonged abstinence could correlate to a negative affective state [139]. Clinicians, nurses, social workers, and individual and group smoking or alcohol cessation programs are all integral in the process of quitting. One study implemented a nurse-administered smoking, alcohol, and depression treatment intervention program in HNC patients and found that smoking cessation rates significantly improved compared to care as usual. Although alcohol and depression rates improved, there were no significant outcomes on alcohol and depression at 6 months [61]. More research should be done to define the relationship between alcohol and smoking behaviors with depression.

## *Patient Support Groups*

Patients and caregivers may find community support groups helpful with coping with disease and everyday life after treatment, particularly as social support is related to stronger self-efficacy beliefs and better subsequent health-related outcomes [140]. Social networks have been found to enhance coping ability of patients in laryngeal and hypopharyngeal cancers [141]. Prominent HNC support groups include Support for Patients with Oral and Head and Neck Cancer (SPOHNC), which has over 125 chapters across the United States and offers frequent meetings, as well as resources and literature for patients [142]. Support groups also exist for specific patient subsets like throat cancer and laryngectomee patients, such as WebWhispers local groups. Patients can always form support groups within their own home hospitals and clinics, which should be encouraged by clinicians and clinical staff. Online support groups (OSGs) have also been created, including the Head and Neck, and Oral Cancer Support Group through CancerCare.org. Participation in these OSGs may be more suitable for patients who are impaired in speech or have altered facial appearance and feel more comfortable receiving support [143]. One survey of 199 HNC patients found that longer use of HNC-related OSGs was linked to better HR-QOL, an association that was mediated directly by depression and adjustment [143]. Patients with longer OSG use had lower levels of anxiety and depression, lower negative adjustment, higher levels of empowerment processes, and a greater belief that they are capable of performing well [143]. Patients should be offered local support group materials and encouraged to seek support to their comfort level.

### *Other Psychosocial Distress Management Techniques*

Multiple novel distress management techniques have been investigated that may warrant further investigation. In one study, an individualized mindfulness-based stress reduction program was used for HNC patients undergoing radiotherapy, finding that tension-anxiety scores significantly decreased over the course of the study, though depression-dejection scores did not. This study also showed that post-intervention mindfulness had a significant negative relationship with both total distress and subscales of anger-hostility, confusion bewilderment, depression-dejection, and tension-anxiety [144]. Another psychosocial intervention, the Easing and Alleviating Symptoms during Treatment (EASE) program, was tested in a pilot study. EASE is a telephone-based intervention involving ongoing systematic assessment of physical, psychosocial, and functional needs, psychoeducation focused on managing treatment side effects, and coping skills training to facilitate adaptive coping and improving self-care and symptom management. EASE was shown to be acceptable, feasible, and relevant to HNC patients, with patients showing small improvements in cancer-specific distress. New rehabilitation programs have been aimed at improving dysphagia, fatigue, hearing loss, and pain and stiffness associated with HNC. These rehabilitation programs have had promising results on HR-QOL scores [145] and should be tested for effects on distress level due to correlation between functional changes and distress in HNC. A randomized trial of a skin camouflage program was performed in female survivors of HNC and found that the 3-month, 4-session program effectively improved facial disfigurement, depression, fear of social interaction, anxiety of social interaction, and body image in the experimental group compared to the control group [146]. In another study, a tailored hatha yoga program was found to be feasible and potentially efficacious for HNC survivors [147]. Nutrition programs should also be further investigated as malnutrition is a risk factor for depression development in HNC patients [148]. All of these preliminary studies indicate that methods of mindfulness, education, and exercise should be investigated to have a range of validated distress management tools for patients.

## Caregiver and Physician MH in HNC

Cancer patients often require extensive support from caregivers. These caregivers, typically friends and relatives, undergo many emotional and physical challenges and are known to experience deficits in psychological health and functioning. These deficits include emotional distress and depressive and anxious symptoms [149–151]. Rates of emotional distress in HNC caregivers were found to be 20–38%, depending on use of HADS total score or Mental Health Inventory (MHI) [152–154]. HNC caregivers have been found to have poorer psychological health compared to the general population and to HNC patients themselves [155–157]. Sherwood et al. (2007) described a conceptual framework of caregiver well-being that described caregiver psychological health outcomes as a function of both patient disease characteristics (such as stage, time since diagnosis, patient functional status, and patient needs) and caregiver personal characteristics and resources (such as sociodemographic factors and social support) [158]. Caregiver characteristics are thought to impact or moderate the association between patient disease characteristics and caregiver psychological health. In terms of patient disease characteristics, some evidence indicates that greater number of hours spent providing care was associated with poorer psychological health and that the 6-month interval following diagnosis is a time of significant emotional distress among caregivers [152–154]. Caregivers report high levels of fear of recurrence, which has been positively associated with emotional distress among caregivers at 3 and 6 months post-diagnosis [155]. Further, in studies of patient-spouse pairs, patient use of a feeding tube and lower levels of patient energy were found to correlate with higher levels of spousal emotional distress [154]. Caregivers have reported that they would like to have support groups incorporated within the standard of care for patients [159]. Caregiver personal characteristics associated with deficits in psychological health in HNC caregivers have not been well-defined in HNC. Additional research would benefit caregivers by providing distinct targets for caregiver support.

Of note, there is a lack of studies focusing on mental health status of HNC physicians. HNC physicians must manage patient distress and can experience some of the same devastating effects of the events patients must go through. Burnout, mental illness, and suicide have been found to be elevated among physicians, with surgical specialists like otolaryngologists at even higher risk for professional burnout. Burnout has been associated with worse patient outcomes and independently predicts major medical errors. Resident physicians in otolaryngology have been surveyed about well-being, and lower quality of life correlated with more sleepiness, head/neck oncology, and postgraduate year two. Sleepiness and overall well-being improved in senior residency years. Focused interventions using this information could reduce distress associated with lower quality of life [160]. Resident wellness programs, focused on increasing meaning in the clinical work environment, have begun to be implemented at various institutions. These programs include a “time-banking” initiative at the University of Colorado that promotes resident-led patient education for meaningful patient interactions, as well as a comprehensive resident wellness program at the University of Michigan, which focuses on increasing humanization of residents and patients through resident card handouts [161].

## Conclusion

Acknowledging the health behaviors that lead to HNC, as well as the highly impactful location and functional changes from the cancer and treatment, has led to increasing interest in MH in HNC. The distressing aspects of HNC affect patients, their caregivers, and their physicians alike. MH must be a priority from diagnosis through to the end of these patients’ lives. Here we have summarized the known elements of MH in HNC. We have determined that health behaviors, such as tobacco use, alcohol use, and high-risk sexual behaviors that lead to heighten HPV infection risk, play a long-lasting and complex role with distress levels in HNC. Psychiatric illness is one aspect of psychosocial distress that can more easily be studied due to existing clinical frameworks from which to begin investigation, though other elements of distress are more difficult to identify and quantify. We have highlighted advances in stress management for improving MH in these patients, most notably cognitive behavioral therapy-based interventions. This summary has led to the conclusion that the best is yet to come, with the open opportunities to define the mental health challenges in the landscape of HNC, to generate effective and validated treatments, and to pair treatments with patients and their caregivers.

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# Chapter 5
# Disfigurement

**Charissa Kahue, Nolan Bruce Seim, and Kyle Mannion**

## Disfigurement of the Head and Neck and Quality of Life

Due to the highly visible nature of the region of the body in which head and neck cancers exist, special considerations must be made regarding the significance of disfigurement that results from treatment of this area. Body image is defined as a "dynamic perception of one's own bodily appearance, function and sensations, as well as feelings associated with this perception" [1]. Such feelings may arise in response to reactions from others, an additional component of the definition of body image found in Webster's Dictionary [2]. Reactions from others that are negative in nature may trigger psychological distress, in which case body image *disturbance* is present [3].

While the scope of this chapter encompasses disfigurement of the entirety of the head and neck, it is easy to surmise the disproportionate importance of facial disfigurement in this patient population. The face is the recipient of high visual traffic as it is the aesthetic and identity center of the body. Its importance cannot be understated as patient fear of anticipated changes in facial appearance after treatment of head and neck cancer may sometimes outweigh fears of recurrence of the disease itself [4].

A significant contributor to anxiety in the setting of disfigurement is a patient's collection of experiences of public reactions to their physical appearance. The disgust response to abnormal stimuli is a learned behavior acquired early in life (ages 4–8 years) [5, 6], evidenced by frequent appearance-based childhood teasing and bullying [7]. This, combined with unwelcome behaviors (stares, startle reactions, whispering, questions, avoidance) from observers later in life [8], can invoke feelings of rejection or social pain, perceived by the brain similar to physical pain [9].

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## Objective Assessment of Head and Neck Disfigurement

The first observer-based assessment of head and neck disfigurement was proposed by Dropkin in 1983, in which nurses assigned grades of disfigurement severity to photos of artificial deformities from various head and neck cancer surgeries (in order of severity from least to most disfiguring: radical neck dissection, cheek resection with forehead flap, total parotidectomy with facial nerve sacrifice, total laryngectomy, bilateral radical neck dissection, orbital exenteration, hemimandibulectomy with radical neck dissection, nasal amputation, anterior partial mandibulectomy, segmental mandibulectomy with radical neck dissection, orbital exenteration and radical maxillectomy). This study concluded that resections involving the mandible and central face are the most severely disfiguring, serving as a guide for patient counseling prior to reconstructive surgery [10]. This study's shortcomings were noted by Katz et al., who noted that the preceding grading system overgeneralized disfigurement outcomes without consideration of reconstructive techniques, presence of surgical complications, and history of radiation. It was not until 2000 when another system was proposed, this time modeled on four dimensions: (1) size of the disfigured area, (2) degree of face/neck shape distortion, (3) extent of impairment of facial expression, and (4) visibility of the disfigured area. Grading was based on a 9-point Likert scale with scores of 1, 5, and 9 elaborated further: (1) disfigured area/scar small in size, shape of face/neck not distorted, facial expression not affected, disfigurement minimally visible (close range only); (5) disfigured area/scar moderate in size, shape of face/neck somewhat distorted, facial expression somewhat affected, disfigurement moderately visible; and (9) disfigured area/scar large in size, shape of face/neck very distorted, facial expression very affected, disfigurement very visible (from afar). Inter-rater reliability was high (intraclass correlation coefficient 0.91), indicating agreement among the group of raters (consisted of surgeons, a psychiatrist, and research assistant) [11].

## Coping with Disfigurement

Within the facially disfigured population, both women and young patients are disproportionately negatively affected by their disfigurement. In most cultures, women place a higher value on facial attractiveness than their male counterparts [12]. Overall, results are mixed when comparing appearance-related depression and anxiety between men and women. Some studies suggest that women experience these comorbidities more frequently than men [11, 13–15], while others have reported that gender-based differences do not exist [16–19]. In terms of age, individuals affected by disfiguring processes in the head and neck in adolescence and early adulthood experience marked difficulties with adjustment [20, 21].

It can be difficult to predict how individuals will cope with head and neck disfigurement. While it is clear that some patients habituate to change better than others, type and severity of disfigurement in this region of the body have failed to predict acclimation success [22]. A better predictor of psychological distress in these individuals is their perception of how apparent their disfiguring features are to the general public [23]. Some have argued that congenital facial malformations are easier to “adjust” to, given that affected persons have no memories of life without them [24] and that an increased amount of time facilitates adaptation to reactions from the public [25]. People with acquired disfigurement, on the other hand, must learn adjustment measures after accepting changes in their appearance [26]. In general, patients with limited flexibility experience more emotional difficulties related to their appearance, as demonstrated by Shepherd et al. in a burn patient population [27].

Specific interventions to aid in coping strategy development exist. In cases where cosmetic surgery is available, stress related to a specific feature may decrease, but overall body image likely will not [28]. Changing Faces is a charitable organization in the United Kingdom that provides services to individuals “with a visible difference: a mark, scar or condition that makes them look different” [29]. Social skills training for disfigured individuals offered by this organization was shown to increase confidence levels in new environments [30]. This is of particular benefit given that transitional periods in life (new school, job, etc.) are distressing [23] to persons with disfigurement. Perhaps more effective are the presence of patient social support [11, 31] and frank provider discussions on expected outcomes prior to treatment. In a 1979 article discussing emotional management of head and neck cancer, Herzon and Boshier noted “it may be cruel to lead the patient to believe that his or her appearance, even after reconstructive surgery, may not be changed significantly as a result of a major operation. A team member who attempts to ‘spare the family’ by withholding certain information is usually motivated by a desire to spare himself/herself the pain of relating difficult facts, and such attempts are not a kindness to the family” [4].

## Reconstructive Considerations

The greatest determinant of postoperative disfigurement is the patient’s cancer itself, as it will determine the extent of normal tissues that are resected. While the same surgeon may be performing the oncologic and reconstructive portions of a head and neck cancer operation, ideally the reconstruction should not be considered at all while resecting the cancer. This separation of surgical goals ensures that no oncologic corners are cut to ease the reconstructive burden. That being said, there are some factors that the oncologic surgeon can focus on that may lessen future disfigurement and limit the postoperative patient burden. Most of these factors involve surgical techniques that may limit lymphedema or the musculoskeletal impairment postoperatively and will be discussed below. The greatest dilemma for the reconstructive surgeon is the balance of form and function in planning head and neck reconstruction, for the head and face house structures just as functionally important to life as the region is visually important to body image. This balance may slant one way or the other variably (even dramatically so) in different patients with similar surgical defects based on the patients' goals. Unfortunately, as already discussed the ability to accurately predict a given patient's response to physical disfigurement is difficult at best, and aligning with their preoperative goals does not ensure that the patient will be satisfied.

Nevertheless, preoperative counseling becomes crucial to the reconstructive surgeon. First and foremost, the surgeon and patient need to discuss the reality of what tissues will be absent after resection so the patient understands what challenges they will face. With that common understanding, the surgeon and patient can act as a team to prioritize function such as breathing, voice, swallowing, and physical activity/mobility as well as form, in the alteration of their physical appearance. It goes without saying that the ultimate goal is to maximize both physical function and physical appearance; however reconstruction of many defects may require sacrifice of one for the other, and the patient should ideally have the final say in where that effort lies. The impact of nutrition and speech and swallowing impairment will be discussed elsewhere in this book and won't be reiterated here.

Volumes have been written on reconstruction in the context of head and neck cancer, and the surgical considerations in limiting disfigurement cannot be comprehensively addressed in this chapter. Instead, the primary thought processes of the head and neck reconstructive surgeon will be highlighted in the sections below without specific technical details.

## Site-Specific Disfigurement

### *Facial Nerve Palsy*

Paralysis of the facial nerve can result from many causes beyond that of oncologic resection and has thus been studied for decades. The body of literature available on psychosocial consequences of facial paralysis and palsy (described henceforth as FP) is extensive. The face is the primary instrument of nonverbal communication, and any deficit in its function taxes an individual's ability to convey emotions effectively. What is more, in efforts to compensate for lost function, FP patients may be prone to communicate in unconventional ways, sometimes resulting in miscommunication [22]. The reverse scenario carries similar consequences, with observers indicating difficulty with "reading" expressions on FP faces, yielding hesitancy in and shorter exchanges between observers and FP patients [8]. In multiple studies, general observers have perceived paralyzed faces to be negative (even when in repose) and less happy, attractive, trustworthy, and intelligent than normal subjects [32–35].

Concomitant with the stress of physical disfigurement secondary to facial palsy, FP patients may also have other psychological preoccupations related to social faux pas such as oral incompetence leading to drooling or leakage of ingested foods or drinks.

VanSwearingen et al. were among the first to demonstrate that psychological distress stemming from facial palsy significantly predicted social disability in affected patients [36]. Using a variety of quality of life instruments, many subsequent studies have reported the presence of anxiety and depression in patients with FP [33, 35, 37–44] [references for all, including studies w/o control groups] at increased rates relative to subjects with normal facial function. Notably, facial palsy severity does not predict severity of psychological distress.

When disfigurement in the setting of facial palsy exists without a concomitant soft tissue defect (i.e., facial nerve sacrifice in a parotidectomy with primary closure), treatment targeting the impairment is more likely to be successful at correcting the disfigurement. The literature indicates that patients treated for FP, either conservatively with botulinum toxin or more definitively with static or dynamic reanimation surgeries, experience significant improvements in quality of life [45–48]. Comprehensively addressing the surgical management of facial paralysis is beyond of this narrative, but as a general rule, any procedure (whether static or dynamic) is better than flaccid paralysis of the face. Whenever possible primary nerve grafting is preferred, with cross facial nerve grafts or nonanatomic grafts such as the masseteric nerve being of large benefit as well, alone or in conjunction with static procedures. Innervated gracilis free flap is best performed by an experienced team but can have excellent results, particularly when there is no remaining useable facial nerve or facial musculature.

## *Laryngectomy*

Total laryngectomy represents a distinct entity within the realm of surgical head and neck disfigurement. Resultant physical changes from laryngectomy can easily be concealed from the public yet can simultaneously trigger significant psychosocial comorbidities in the affected patient. In general, laypersons tend to be fearful of airway stomas, whether they exist as tracheostomies or formalized laryngectomy stomas due to a lack of understanding of the disease processes that lead to their necessity as well as the communicative limitations they carry. This leads to social isolation of laryngectomees, as patients (women in particular) gravitate toward withdrawal due to a perceived lack of acceptance of their new condition [24]. New laryngectomees frequently develop psychosocial anxiety and depression similar to other patients with head and neck disfigurement. Over time, however, a subset of laryngectomy patients become resolute and/or transformed from their postoperative disfigurement (5 of 11 in a group described by Bickford et al.) [49]. Others, however, will continue to struggle with social stigmata of their stomas.

Studies have demonstrated that women suffer greater adjustment problems after laryngectomy [49, 50] despite men comprising a majority of patients with laryngeal cancer [51]. In some cases, this is attributable to postoperative stress-provoking reactions from strangers – “it is mainly the way people look at you, the way they talk to you" [49]. Another female laryngectomee published an editorial on her experiences, in which expressed:

> The first look in the mirror is devastating. The stoma is located at the base of the neck. It is open and obvious. If there has been additional neck surgery, that side of the neck is sunken and forever after will have a "scrawny" appearance. The immediate problem is to cover the disfigurement and at the same time allow air to get into the lungs….A woman, because most dresses are open at the neckline, must devise attractive measures to cover the stoma. Until this problem is solved, she may find herself a virtual prisoner in her home. Once covered the stoma is not forgotten. It is especially difficult for a woman to learn to accept this permanent disfigurement. The neck is a sensitive, sensuous area of the body [52].

Beyond that of anecdotes, in a retrospective cohort of laryngectomees, women reported significantly lower scores for global health status, quality of life, and functioning in multiple domains (physical, emotional, and social) compared to men [19].

In line with head and neck cancer patients in general, adjustment to life after laryngectomy is improved in the setting of adequate social support structure after surgery [53]. Time also furthers the emotional healing process of laryngectomees [54], with surgery-related stress levels tapering by 1 year postoperatively [19, 55]. While disfiguring sequelae from total laryngectomy is not discounted, it is encouraging to be able to counsel patients on the optimistic expected trajectory of their recovery and adjustment.

As the presence of an end tracheostoma is unavoidable in a laryngectomee, the impact of the reconstructive surgeon on this disfigurement is limited. However, in cases where the pharynx must be reconstructed or when non-radiated soft tissue is desirable, the choice of reconstructive tissues can have a long-term impact. The pectoralis major, as a myocutaneous flap or a myofascial interposition graft, retains an attachment to the origin of its vascular pedicle below the clavicle. This adds an additional deformity in the form of a visible asymmetry between the donor and normal sides of the neck and clavicle areas which can be avoided with free tissue transfer or use of other regional tissue such as the supraclavicular flap that has no muscular component to the pedicle. When the pectoralis muscle is excessively bulky, the superiormost portion of the muscle (proximal to the insertion of the vascular pedicle) may be thinned or even completely resected to limit the evidence of the muscle passing over the clavicle. The more distal portions of the muscle cannot be thinned (in a myocutaneous flap), and thus the large bulk can lead to further deformity of the neck, particularly if the native skin cannot close over this bulk and skin grafting is necessary. As long as the motor innervation of the muscle is transected, some of the muscle volume typically decreases with time or at least softens as fatty replacement of the muscle occurs.

The presence of an open fistula can also have devastating impact on a patient due to the addition of another visible opening as well as potential odor and discharge. While most fistulas are resolved spontaneously or surgically relatively early in the postoperative period, this becomes the patient's earliest conception of the change in their body creating a much more dramatic first impression that is difficult to overcome. In radiated patients, the use of non-radiated tissue for pharyngeal reconstruction or muscle interposition with primary pharyngeal closure may help limit the risk of fistula [56–65]. The body habitus of the patient guides the surgeon to the most suited reconstructive tissues. For example, in a very thin patient, a free latissimus flap is very desirable for post-laryngectomy reconstruction for can be harvested with a cuff of muscle extending past the skin paddle in all directions which will overlay all of the mucosal closure (much like a pectoralis flap, but without the drawbacks above). However, in the obese patient, this flap becomes nearly prohibitive by its bulk, and all other myocutaneous flaps may have the same prohibition, leading the surgeon to use a thinner fasciocutaneous flap such as the radial forearm free flap.

## *Oral Cavity Disfigurement*

The vast majority of head and neck cancer cases are due to mucosal squamous cell carcinoma. A large portion of these cases are due to a lesion of the oral cavity (i.e., lip, tongue, floor of the mouth, buccal and mandibular gingiva). Surgery can leave a large volumetric and surface area defect requiring some type of reconstruction; however, the impact of disfigurement from intraoral defects is not reported well in the literature. Intuitively, the oral cavity is where advances in free flap reconstructive surgery can be most pronounced. With microvascular free tissue transfer, the reconstructive surgeon is able to significantly decrease the potential loss of form and function caused by the tumor. Over the recent decades, expected free flap survival has become >90% and as such has become the standard of care reconstruction for the oral cavity in these advanced cases.

External changes in appearance are common after oral cavity resection and reconstruction. The extent of this change and the potential for disfigurement are related to the primary site of the lesion, reconstructive method, and success and need for adjuvant treatment. The size of the lesion and the pathologic features requiring the need for adjuvant therapy are typically out of the surgeon's hand (except in the case of close or positive margins); however the reconstructive options are diverse and can produce effective long-term quality of life for these patients [66]. Although there are viable primary, secondary, and locoregional options for reconstruction, this specific discussion will cover the role of free flap surgery, which is most commonly used for advanced lesions. Certainly, it is prudent to utilize primary closure, secondary healing, or the use of skin grafts and other local grafts when able to do so without functional consequence however. The goal of reconstruction is to restore form and function. This can be achieved with various levels of success depending on one's ablative defect.

In oral cavity disease, there is more potential for external disfigurement when the mandible is involved. Reconstruction of the mandible almost always requires free flap reconstruction, most commonly utilizing the fibula, scapula, or osteocutaneous radial forearm free flaps. Considerations to improve the cosmetic and functional outcomes include bony height of the flap, bone stock for potential dental implantation, and anterior/posterior and vertical placement of the reconstructed anterior arch.

Patient factors are critical to consider when selecting the donor site for reconstruction, as are factors such as vascular anatomy, history of atherosclerosis, and adjacent mucosal defect and soft tissue required for reconstruction. Careful reconstructive selection; the expanded use of low-profile, titanium mandibular reconstructive plates; and preoperative virtual surgical planning have greatly improved our ability to precisely and durably reconstruct the mandible.

Skin and mucosal cancers of the lip can produce dramatic visual deformity and require special attention by the reconstructive surgeon. Reconstruction of the lip may include primary closure with and without M-plasty for larger lesions, local tissue rearrangement with Abbe and Estlander flaps, more complex locoregional rotations including Bernard-Fries and Karapandzic flaps, as well as free flap reconstruction for total lip defects. All of these reconstructions leave patients with scars and some degree of microstomia. The goal of reconstruction is to limit the sphincter dysfunction and preserve as much size as possible for mouth opening. These patients' functional quality of life after lip surgery depends largely on the size of the primary tumor and the technique used for reconstruction. When able, primary closure, stairstep, and Abbe/Estlander reconstruction should be used over the more involved techniques [67].

## *Dental Reconstruction*

One of the most significant implications of head and neck cancer treatment remains the impact on dental status. Poor dental hygiene is a well-known risk factor for head and neck cancer, and as such, many patients already have poor dentition requiring dental extraction or an already edentulous state. This obviously simplifies dental reconstruction as the use of prosthodontics for denture fabrication gives patients an excellent appearance and ability for improved mastication. For the patient who already has partial or full dentures, the impact is often minimal; however, a patient with intact dentition (however poor) who undergoes significant dental extractions will often have a dramatic change in their self-image. Those head and neck patients who have quality dentition at the time of diagnosis are likely to have their current state of dental health disturbed by surgery and/or radiation therapy. Preoperative dental evaluation remains critical to identify periodontal disease and address this at the time of surgery or at least prior to radiation therapy in order to reduce the risk of osteoradionecrosis of the mandible long-term, as this can lead to severe disfigurement with potential for significant mandibulectomy after the patient has already adjusted to their post-cancer (and post-cancer treatment) physical state.

Patients with cancers of the mandible or maxilla likely require resection of a portion or all of the teeth-bearing bone in that region. Reconstructive options include use of an obturator (maxilla) and locoregional or free flap reconstruction. Currently when significant portions of the mandible or maxilla require resection, free flap reconstruction has become standard of care [68, 69]. The options for free flap reconstructions are vast and dependent on the defect; however when bone is to be reconstructed, the options include the fibula, radial forearm, scapula, and iliac crest osteocutaneous free flaps [70]. Typically for large mandible defects, the fibula and scapula are the flaps of choice; however with improved techniques in bone harvest and radial plating, the osteocutaneous radial forearm flap (OCRFF) has gained popularity in this setting as well [71]. If osseontegrated dental implantation is planned preoperatively, the fibula specifically but also the scapula and iliac crest bone stock offers a better conduit for the implants. Success of dental implantation in the fibula has been widely seen and reported for many years [72–74]. Other bony flaps, such as the scapula and OCRFF, may require modified surgical techniques and/or additional prep work such as bone grafting or augmenting prior to implantation. Techniques such as "double-barreling" can be used to increase the thickness of bony stock for later implantation [75].

For complex defects or when immediate, single-stage dental reconstruction is to be performed, three-dimensional CT planning guides have become commonly used with great success. Using the patient's preoperative imaging, custom plates and cutting guides can be utilized to reconstruct the mandible or maxilla and even perform dental implantation at the time of primary reconstruction. This technique has gained popularity due to the efficiency of single-stage surgery, accuracy of the custom planning guides and plates, and the ability to fabricate the neo-mandible during the ablative portion of the case while still vascularized in the lower extremity [76, 77].

## *Amputations: Orbital Exenteration, Rhinectomy, Auriculectomy, and Maxillectomy*

Removal of sensory end organs such as the eye, nose, and ear and maxillectomy are among the more severely disfiguring head and neck cancer resections performed [10]. Expected psychosocial distress from resulting aesthetic and functional outcomes ensues and must be prepared to be addressed.

The body of literature regarding quality of life after eye amputation is sparse; however two studies found that individuals who underwent removal of the eye with or without exenteration suffered social detriments from the procedure. Forty percent of individuals in a study by Coday et al. reported these outcomes, while Rasmussen et al. showed that mean scores in the social functioning domain of the Short-Form 36 quality of life questionnaire were significantly lower for affected patients compared to a general population [78, 79]. Extended periods of time permit greater patient and family acceptance of disfiguring outcomes following many head and neck cancer surgeries; however it seems that the converse may be true after orbital exenteration. A qualitative study consisting of interviews of 12 affected patients reported that half of patients grew more concerned about their appearance as time progressed, as fears surrounding the disease process itself were replaced [80]. This indicates the longevity of aesthetic concerns from removal of an individual's eye. After orbital amputation, there is no surgical recreation of the globe with any realism, and maintenance of the appearance of a globe will require a prosthesis. This is most easily accomplished when the surgical defect is limited to the orbital contents; however when it extends to the sinonasal cavities, the presence of air pressure and mucus can limit the fit of a prosthetic eye, and local or regional tissues should be utilized to isolate the orbit if possible. It is rare for malignancies in the orbit to allow preservation of enough structure to maintain functioning eyelids, but this skin is often useful for relining the orbital defect, and the prosthesis recreates the lids and globe. For isolated upper maxillary/orbital defects, the long pedicle of the osteocutaneous forearm, scapula tip, or serratus/rib free flaps are often of most use, and the bone stock of all are adequate as the bone is non-weight bearing. Alternatively, if there is adequate soft tissue for healing, a large prosthesis can replace a significant portion of the face. As a prosthesis grows in size, the utility of bone-anchored securement points increases, and the placement of these should be considered at the time of primary reconstruction (particularly if the patient is to receive radiation). The patient must be counseled ahead of time that even a perfectly constructed prosthesis is a static device, and the globe will not move and consequently only look symmetric with forward gaze.

Nasal reconstruction is a special entity within head and neck surgery. Unlike the ear and eye, realistic-appearing surgical reconstruction of the nose is well within the capabilities of a talented reconstructive surgeon, even with total rhinectomy. Nasal prostheses also have a very realistic end result with the downside of being removable. This fact alone may guide many patients toward surgical reconstruction of the nose as seeing themselves without one of the most defining features of their face (even if only for brief periods when a prosthesis is removed) may be devastating. The options for treatment of nasal defects are numerous, and each rung of the reconstructive ladder is realistically employable. Consistent with all other subsets of head and neck surgical patients, those who have undergone partial rhinectomy and reconstruction experience poorer nasal self-image compared to controls (23.27 vs. 30.61, Nasal Appearance and Function Evaluation Questionnaire, maximum score 35) [81]. Despite this, multiple studies have reported patient satisfaction with appearance >80% following partial nasal reconstruction [82–84]. Surprisingly, in a survey of 33 patients by Moolenburgh, aesthetic satisfaction after nasal reconstruction was not affected by size of rhinectomy defects (University of Washington Quality of Life Survey) [85]. Their overall satisfaction scores (rated 0–100) were very similar to those from 43 nasal prosthetic patients in a separate study by Becker et al. (84 vs. 83.14) [86]. In the Moolenburgh nasal reconstruction study, patients rated their postoperative appearance notably higher than a panel of five plastic surgeons, indicating high patient satisfaction with surgical reconstruction (4.2 vs. 3.5, $p = 0.031$). There are no large series reporting outcomes after total nasal reconstruction due to the relative infrequency that these procedures are undertaken. The largest series to date reported on nine total rhinectomy patients, seven of whom selected prosthetics over free flap reconstruction [87]. Four of the nine (treatment modality unknown) ultimately required initiation of antidepressants for new depression that began after surgery. The author of this series felt that nasal prostheses were the treatment modality of choice, however a few case reports that present successful paramedian forehead flap and free flap options for total nasal reconstruction [88–90]. Reconstruction of a total nasal defect is a significant task, requiring careful patient selection due to the length of time needed for surgery of this extent.

Auriculectomy, like rhinectomy, defects may be reconstructed using any option on the reconstructive ladder. Prosthetic use in this population is generally well-tolerated, perhaps because of the location of the ear off of the face. In general, auriculectomy patients tend to fare better with regard to psychosocial distress from their surgical defects compared to other head and neck patient groups (Fig. 5.1). In a survey of 23 auricular prosthetic users, only 1 patient reported embarrassment secondary to his/her prosthesis [91]. In another survey of 14 auricular prosthesis users, a mean social functioning score of 90.6 out of 100 was reported [92]. In cases of subtotal auriculectomy, preservation of the helical root when possible allows for decreased visual impact on frontal view as well as maintaining use of non-modified eyewear. While there is extensive literature on auricular reconstruction in cases of microtia, trauma, and other benign disorders, it is more controversial in adults and is rarely undertaken in cases of malignancy. Arora et al. noted that due to a frequent lack of useful surrounding skin and soft tissue and lack of pliable chondral cartilage in acquired auricular defects, surgical results may be inconsistent with decreased patient satisfaction [93]. On the contrary others have advocated for prosthetic use only in the setting of failed autologous reconstruction [94]. In a study by Braun

**Fig. 5.1** Despite preoperative declaration that he would desire a prosthesis after total auriculectomy, this patient, like many others, readily adjusted to the loss of an external ear and never sought prosthesis creation

et al., 45 of 65 reconstructed patients who underwent total auricular reconstruction with porous polyethylene were adults, and overall patient satisfaction was 72.7% (Glasgow Benefit Index) [95]. In another study of adult microtia patients who underwent autologous rib reconstruction, overall patient satisfaction was 90% (author's independent questionnaire) [96]. Taken together, all options for aesthetic rehabilitation following auriculectomy should be considered on an individual basis as no definitive superiority of one approach over another has been determined. Multiple options are available for initial coverage of the skin defect after total or subtotal auriculectomy, and most will depend on the patient's surgical defect and body habitus. Cervical rotation maintains local skin with similar color and appearance, but may not be adequate for some defects. Regional flaps including supraclavicular, submental, pectoralis major, latissimus dorsi, and lower island trapezius flaps are all reasonable options depending on the size of the cutaneous defect and depth of the soft tissue and bone loss. For deeper defects (such as loss of lateral temporal bone, parotid and surrounding tissues), free flaps are ideal, and the thigh, rectus, and lateral arm are excellent donor sites. The lack of a subcutaneous muscular pedicle that is present in the thicker regional flaps is very appealing in that it avoids both the visible bulk of the pedicle causing asymmetry of the neck and the physical tethering of the head to the flap origin site. The additional benefit of perforator-based thigh and rectus flaps is that the long-term appearance can be well predicted at the time of surgery, because there is not a large muscle component that may atrophy. In the obese patient, flaps that are traditionally used for their thinness such as the radial forearm free flap and medial sural artery perforator flap may provide enough bulk. The goal is to have a natural contour to the side of the face and neck if no prosthesis is present, but not so much bulk that it would be prohibitive of prosthesis placement. Placement of bone-anchored abutment for a prosthesis and bone-anchored hearing aid placement can be carried out at the time of oncologic surgery, and preoperative consultation with the prosthetist is of great benefit.

The term "maxillectomy" is a broad one and describes the removal of a portion of the maxilla, but fails to indicate the extent resected. A maxillectomy defect can range from a small portion of the nasal floor/palate with no visible external defect to a large midface resection with devastating disfigurement. All other ablative procedures described in this chapter have no identifiable correlations between defect size and quality of life; however maxillectomy is the exception to the rule [97–99]. Obturator prostheses are popular options for palate defects and seal oroantral fistulas to improve hypernasality and nasal regurgitation of oral contents. When facial skin and/or underlying bone are resected, cosmetic prosthetics may be applied to aid in camouflaging a defect. Surgical reconstructive options include pedicled (i.e., temporalis muscle) and free flaps (i.e., radial forearm with or without bone, anterolateral thigh, scapula, fibula), with selection dependent upon patient factors and defect size, shape, and structure. Obturators carry an excellent record of high patient functional satisfaction [99, 100]. Given that they dwell within the oral cavity, they are easily concealed by their wearers and do not attract significant attention. The obvious additional benefit of restoring normal-appearing dentition cannot be overstated. Cosmetic concerns are noted when an ablation defect involves the midface bony structure and/or skin. Patients emotional struggle is considerably greater in this situation; one described in an interview, "my ward nurse said Frankenstein couldn't have made a worse-looking monster" [101]. In this setting, facial prostheses are particularly useful, with better outcomes noted when adequate residual bone stock is available for abutment placement [102]. When defects are too large to retain a prosthetic alone, free flaps and prosthesis use may be combined to achieve better aesthetic and functional outcomes [103–106]. Only one study to date has compared obturation with free tissue reconstruction quality of life measures that include social-emotional functional domains. Breeze et al. found no significant differences between obturator users and free flap patients when examining social-emotional functional domains in maxillectomy patients of varying defect sizes (University of Washington Quality of Life Questionnaire, $p = 0.929$) [107]. While surgical defects created by maxillectomy can be distressing to those affected, several options for aesthetic rehabilitation exist. With careful discussions with patients about desired vs. anticipated outcomes, coordination of reconstruction using surgery, prosthetic use, or both can be utilized with good aesthetic satisfaction.

It is worth mentioning two studies that have examined prosthesis use among multiple subsites. In the largest study of facial prosthetic users by Dings et al., 52 patients who used orbital, nasal, or auricular prostheses were surveyed regarding satisfaction with their respective devices. Nasal prosthesis wearers noted statistically significant worse self-image compared to the other groups and felt that strangers were able to frequently discern the presence of a prosthesis in social interactions ($p = 0.01$). Overall, while some reported decreased mood (25%) and a negative influence on social activities (13%), patients were satisfied with their devices, evidenced by daily wear of 18, 14, and 14 hours per day for orbital, nasal, and auricular prostheses, respectively. In another study that evaluated 35 wearers of the 3 types of prosthetics, those that used secured implants felt that others noticed their prostheses less often (16 vs. 38% and 95% vs. 75%, respectively) and use of their prostheses decreased self-consciousness compared to those that used adhesive [108].

While ablative surgeries involving the eye, nose, maxilla, and ear carry significant disfiguring potential, their aesthetic rehabilitation options, whether reconstructive, prosthetic, or a combination of the two, provide dramatic benefit and result in comparatively less psychosocial distress when compared to other head and neck resections.

## *Donor Site Morbidity*

Most of this chapter has focused on disfigurement in the head and neck region, while many of the reconstructive methods discussed rely on tissues outside of the head and neck. These various donor sites also contribute to the disfigurement of each patient and may even rival the head and neck disfigurement in the patient's mind. The preoperative discussions mentioned above should incorporate the details of the potential donor sites for reconstructive tissue harvest. The patient's social and vocational activities are a useful guide to knowing which donor sites will be readily visible to the patient alone and those that will be visible to others. It is a rare patient whose radial forearm free flap donor site will not be seen by others, while for many patients a thigh, rectus, pectoralis, or subscapular system donor site may never be seen by anyone outside their own household, and the patient's own perception of these defects becomes paramount. This is illustrated best in considering the pectoralis major donor site in women. The breast plays an important part in the self-image of many women [109], and even if no persons other than the patient will view the scar and asymmetry present, it can have dramatic impact. Some patients recognize this preoperatively and even go so far as to refuse consent for that procedure. In others, modifications such as inframammary crease incisions and modified skin paddle position to blend with that incision may suffice to limit the psychological impact of a change in the breast appearance. At other sites, the difference between primary closure of a donor site and the need for a skin graft may affect the conspicuousness of the donor site, as well as adding an additional scar from skin graft harvest. All of these factors should be discussed with the patient preoperatively.

## *Posttreatment Postural Changes*

Deforming musculoskeletal changes of the neck, shoulders, and chest may occur after surgery and/or radiation. Radical or modified radical neck dissection sacrifice of the sternocleidomastoid (SCM) muscle and/or spinal accessory nerve (CN XI) leads to well-established functional deficits [110, 111]. Visible physical deformities may occur due to resection of muscle, muscle that is present but atrophies secondary to denervation, or fibrosis. In cases where CN XI is sacrificed but the SCM is preserved, changes to the trapezius result in characteristic physical changes including shoulder droop at rest [112], loss of the sloping contour of the shoulder (resembles a right angle) due to trapezius atrophy (Fig. 5.2), and flaring of the scapula due to failure of the trapezius stabilization [113]. Removal of all or part of the SCM muscle is occasionally necessary during neck dissection. Cosmetically, this may result in variable degrees of neck volume loss depending upon the extent of muscle bulk in the contralateral neck and body habitus (may be better concealed in patients with large neck circumferences). While functional changes are beyond the scope of this chapter, SCM fibrosis (whether by resection or denervation) may cause lateral neck extension and head rotation toward the operative side in unilateral cases, potentially resulting in an unnatural resting head position. Cases of bilateral SCM sacrifice or denervation may cause anterior head carriage due to loss of extension of the upper cervical spine and loss of flexion in the lower cervical spine [114, 115].

Radiation fibrosis is a progressive process of sclerosis and can affect any soft tissue structure. Radiation-induced musculoskeletal changes may occur due to direct damage to muscle or secondarily by injury to supplying nerves or blood vessels. In general, this leads muscle to become poorly functional and often aberrantly positioned. Historically, wide-field radiation treatments to the neck and chest in

**Fig. 5.2** Obvious disfigurement is present with primarily musculoskeletal surgery despite very high compliance with postoperative physical therapy in this patient. A myofascial pectoralis flap was used to protect carotid reconstruction after radical neck dissection. In addition to the loss of unilateral neck volume, the shoulder and trapezius asymmetry are clearly evident, as is the donor site defect

Hodgkin lymphoma resulted in characteristic changes including cervical kyphosis, head protrusion, central collapse of the anterior chest, and internal rotation of the humeral head(s) [116]. These changes are also commonly observed in patients irradiated for head and neck cancers [117] and so common to practitioners treating head and neck cancer patients that they may overlook the importance of addressing this impact. This type of disfigurement can contribute to pain syndromes due to strain placed on surrounding shoulder and paraspinal muscles [116] and consequent functional impact as well.

Postural changes resulting from treatment of head and neck cancer may be expected to be more functional than aesthetic in nature, especially when compared against other disfigurements described here. However, in a recent study by Eickmeyer et al., neck dissection patients reported significant differences in subjective disfigurement due to shoulder abduction deficits. This applied even in cases where CN XI was preserved, implying that although they are comparatively smaller disfigurements, postural changes may still have significant negative impact on the patient [118].

The oncologic surgeon plays a greater role in avoidance of these disfigurements than the reconstructive surgeon, as most of the postsurgical fibrosis is due to normal tissues that are removed or dissected. While some normal structures may need to be resected to cure a patient's cancer, this is the only situation where normally functional tissue should be sacrificed. Maintenance of the native neural, vascular, and muscular structures in the neck can be safely achieved in most neck dissections. When additional care is taken to preserve not only the neck musculature, but its investing fascia, the resultant fibrosis and disfigurement secondary to limitation of movement should be minimized. In practice this is difficult to study and to enact surgically. Preservation of the deep neck fascia overlying the splenius capitis, levator scapulae, and scalene muscles is relatively easy to perform (even early in one's surgical training). However, maintaining a fascial layer around the sternocleidomastoid to avoid direct exposure of its muscle fibers and consequent scarring of those fibers may be difficult even for an experienced surgeon at times, particularly in the presence of nodal disease in the neck. Similarly, the preservation of the vessels and fascia around the spinal accessory nerve may well limit transient paresis, but is not a simple prospect when the lymph nodes of levels IIA and IIB are to be comprehensively removed.

Treatment of musculoskeletal changes resulting from surgical and radiation treatment of head and neck cancers is very difficult to complete as fibrosis is an irreversible process. Head repositioning devices are available for pain, but do not reverse disfigurement related to these changes [116]. Prevention of these changes is the best modality and can be accomplished by early exercise programs during radiation/after surgery (in both nerve and muscle-sparing and sacrificing surgeries) [119] and deintensified radiation protocols whenever appropriate [120].

## *Lymphedema*

Lymphedema represents one of the more difficult late toxicities for patients having survived their head and neck cancer (Fig. 5.3). Lymphedema is defined as fibrosis and retained lymph causing edema of the treated soft tissues [121, 122], most commonly observed in survivors having received combined chemotherapy and radiation therapy. From the surgical standpoint, the goal of the oncologic surgeon during neck dissection is the comprehensive removal of the fibrofatty tissue containing the lymph nodes of the neck levels being dissected; an oncologically successful surgery, by definition, should result in lymphedema. This under-recognized and undertreated toxicity results in undesirable chronic swelling as well as color and quality change to the treated skin and underlying tissues. The physical findings of lymphedema are thought to be secondary to accumulation of lymph within interstitial spaces, an

**Fig. 5.3** Extreme lymphedema. This gentleman was referred for a second opinion to discuss potential alternatives to hospice for what was presumed to be extensive cancer recurrence involving the entire tongue and lower lip despite negative biopsies. In reality, the dramatic and progressive facial, lip, and intraoral swelling were lymphedema secondary to prior surgery and radiation. The patient had significant subjective improvement in appearance and quality of life after the first 6 weeks of CDT as well as functional improvement

important target during therapy. Lymphedema has been associated with poorer quality of life, increased function impairment, and increased symptom burden overall [123–126].

For long-term survivors of head and neck cancer, lymphedema can be a chronic condition for the remainder of their lives. Although currently thought of as incurable, there are several strategies to improve symptoms for these patients. Currently, level 1 evidence is lacking to support any single therapy or protocol; however data does support improvement with early identification and timely intervention [127]. The current standard of care treatment is “complete decongestive therapy” (CDT) that involves a combination of manual lymph drainage, compression techniques, exercises, skin care, education, and other related self-care [128, 129]. The goal of this therapy is to manage lymphedema as a chronic condition and to prevent chronic fibrofatty changes to the underlying soft tissues.

Currently, the Oncology Nursing Society’s Putting Evidence into Practice protocol has rated CDT as “recommended for practice” with the highest level of evidence [130]. However, the current data this recommendation is based on comes from extremity/non-head and neck lymphedema. That being said, recent literature in head and neck survivors shows promise with retrospective data showing about two-thirds clinically significant response to CDT [131]. Posttreatment interview of patients has also shown a 90% physical and 70% psychological benefit to lymphedema therapy. Several barriers to treatment were also identified by this study however [127].

Cosmetic and functional improvement with lymphedema can be addressed surgically as well. Techniques such as liposuction, autologous fat transfer or augmentation, and local, regional, and free flap reconstruction can benefit patients as well [132]. Liposuction, particularly in the submental region, can significantly improve patients' self-perception as well as objective scoring of appearance [133]. Similarly augmentation with fat for cosmetic and functional purposes has great utility within the facial soft tissues, neck, parotid bed, and vocal cords in differing circumstances [134–136]. Lastly, lymphatic transfer surgery and flap reconstruction or revision can be used in certain settings; however this remains patient- and case-specific. Over the decades, the progression from radical neck dissection to modified radical neck dissection and subsequently selective neck dissections has lessened the amount of normal lymphatic structures that are sacrificed. If the time comes that sentinel lymph node biopsy is found to be oncologically equivalent to elective neck dissection in clinically N0 patients, the surgical contribution to lymphedema may be greatly eliminated (in those found to be pathologically N0). As neck dissection remains the primary surgical treatment of the neck nodes at this time, the planning of the surgical incision may be the greatest impact the resecting surgeon has on postoperative lymphedema. While the loss of deep lymphatics remains stable, the use of incisions with a primarily vertical orientation may lessen the impact of the subcutaneous venolymphatic drainage on a patient's lymphedema. Even unradiated patients often have supraincisional lymphedema with horizontally oriented scars, presumably from the loss of geotropic flow of lymph and blood.

## Conclusion

The primary goal of head and neck oncologic surgery remains the clearance of malignant disease to prolong disease-free survival. Unfortunately, the success of this objective often results in significant head and neck disfigurement with dramatic impact on a patient's non-oncologic outcomes. Poor aesthetic outcomes may induce marked distress to affected patients, decreasing psychosocial quality of life. In all surgical cases, the surgeon must have thorough and frank discussions with the patient and his/her family on expected defect(s), reconstructive options, and expected outcomes from these. With adequate preparation from counseling and preoperative planning standpoints, disfigurement can hopefully be minimized with optimal oncologic and psychosocial success.

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# Chapter 6
# Impact of Communication and Swallowing Dysfunction

**Barbara Ebersole and Kathleen Moran**

A diagnosis of cancer is a frightening reality fraught with physical, financial, and psychosocial implications for patients and their loved ones. For those diagnosed with advanced head and neck cancer, the likelihood of permanent functional impairment relating to communication and/or swallowing is an additional challenge to confront. At the time of diagnosis and onset of treatment, the primary concern of most patients and care providers is survival. However, treatment advances and the rise of human papilloma virus (HPV)-associated malignancies are leading to prolonged lifespan and increased survival, elevating the importance of functional considerations and quality of life.

Head and neck cancer includes cancers of the oral cavity, nasopharynx, oropharynx, hypopharynx, and larynx. These structures are vital to the ability to communicate and swallow. As we will discuss in this chapter, head and neck tumors and their treatment can have acute and lasting effects on communication and swallowing, potentially impacting quality of life. Quality of life (QOL) is a broad term relating to the complex interplay of a patient's expectations, perceptions of functioning or ability, and satisfaction or happiness. It encompasses the psychosocial and, notably, something referred to as psychological well-being [1]. Psychological well-being is described as being composed of six dimensions: self-acceptance, positive relations with others, autonomy, environmental mastery, purpose in life, and personal growth [2]. Patients who are low-functioning in any of these dimensions prior to diagnosis of their cancer are more likely to experience difficulties in adjusting and adapting to functional changes they may experience during and after treatment, thus experiencing a decline in QOL. However, even patients with a positive sense of well-being

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prior to treatment may experience a reduction in psychological well-being and quality of life as a result of speech and swallowing impairment. Functional impairment that impacts even a single aspect of psychological well-being can have a compounding effect that leads to problems in other aspects of well-being, creating a cycle of psychosocial effect (see Fig. 6.1).

Impaired verbal communication can impact all six aspects of psychological well-being. Verbal communication is at the center of our social/family life and, for most, integral to work as well. It is through verbal communication that most people express their wants, needs, thoughts, and ideas. It is how we connect and relate with others around us. It is our primary mode of expression, thus, deeply connected to identity.

> *"The human voice is the organ of the soul."* – Henry Wadsworth Longfellow

Verbal communication is also necessary for the most mundane of daily activities such as making phone calls, asking for help, answering questions, finding what you need at the store, and ordering in a restaurant. Verbal communication is often the workhorse that gets the "business" of life done.

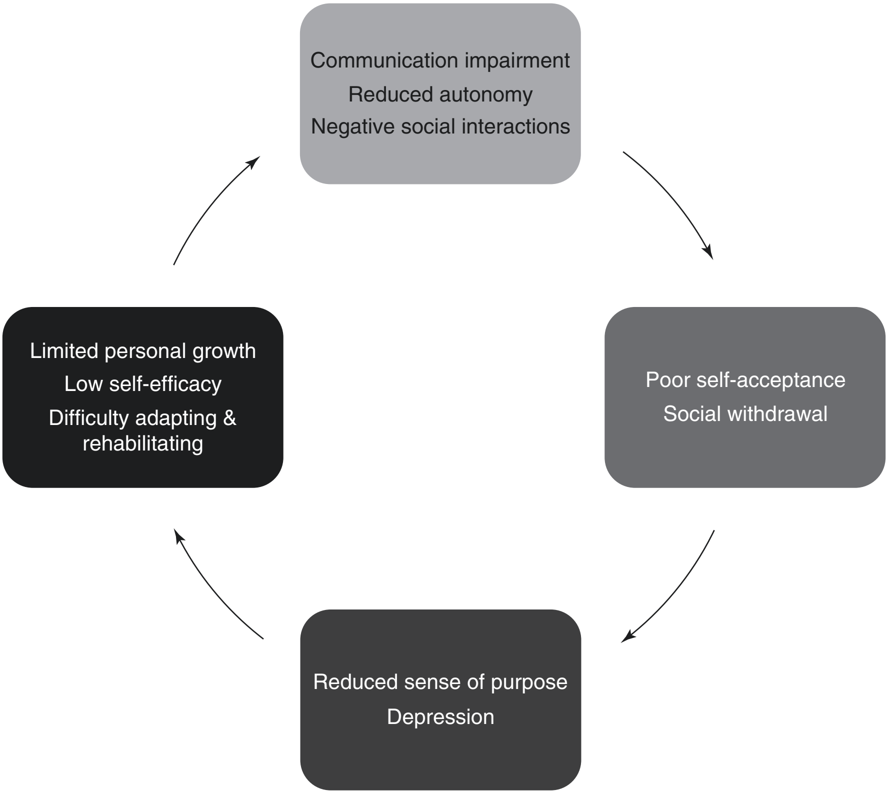

**Fig. 6.1** Cycle of impairment, well-being, and psychosocial effects

Equally fundamental to the quality of our daily lives is the enjoyment we derive from eating and drinking. While, technically, we may eat in order to stay alive, the experience of eating and drinking is a source of pleasure mapped within the reward networks of our pre-frontal cortex [3]. We become hardwired to enjoy and desire certain foods and beverages.

> *"Nothing would be more tiresome than eating and drinking if God had not made them a pleasure as well as a necessity." –Voltaire*

Furthermore, eating is fundamental to social interaction. Holidays, celebrations, and times of mourning often include meals. In fact, it is difficult to imagine a social or family gathering where the sharing of food and beverage is not central to the event. Eating and communicating are fundamental to our autonomy, our sense of self, and to connecting positively with others. Changes in these functions require an ability to cope and adapt on the part of the patient: redefining themselves with respect to where they find pleasure, how they go about getting things

**Table 6.1** Case examples: impact of communication/swallow dysfunction

| Occupational impact | Psychosocial impact |
|---|---|
| 50-year-old male | 70+-year-old female |
| Occupation: Railroad supervisor<br>Needs to be understood on a walkie-talkie<br>s/p RT for vocal fold cancer<br>Has raspy, breathy voice<br>Cannot be heard over walkie-talkie<br>Despite voice therapy and use of amplifier<br>Employer felt safety was at risk<br>Unable to return to work | Long-term survivor of HNC<br>s/p RT for unknown primary<br>She is very active in philanthropic causes Attends frequent cocktail parties<br>Must use sour cream to facilitate eating<br>Embarrassing to ask for<br>Sometimes has to bring her own |
| 40-year-old male | 60-year-old male |
| Occupation: High school math teacher<br>s/p TL for recurrent laryngeal cancer<br>Uses esophageal speech for communication<br>Voice is soft/weak<br>Despite use of an amplifier, unable to be heard in classroom setting<br>Unable to work as a teacher | s/p hemiglossectomy with floor of mouth resection, free flap reconstruction, and post-operative chemo/RT for advanced tongue cancer.<br>Severe dysphagia post-operatively<br>PEG tube dependent<br>His wife feels guilty for eating in front of him and having friends/family over<br>He feels guilty for putting her in that situation |
| 50+-year-old female | 40+ year old male |
| Occupation: SLP, works with stroke patients<br>s/p hemiglossectomy with free flap reconstruction and post-operative chemo/RT for a large tongue cancer<br>Unable to meet occupational speech demand<br>Cannot model precise speech due to dysarthria<br>Unable to return to work | Has two young children at home<br>S/P subtotal glossectomy with free flap reconstruction and post-operative chemo/RT for an advanced tongue cancer<br>Children prefer their mother reading to them at night as they have a difficult time understanding him |

done, and how they connect with others. Table 6.1 provides brief case examples highlighting the impact of communication and swallowing problems on work and psychosocial dynamics.

## Overview of Normal Physiology

### *Communication*

There are many aspects to human communication, with verbal communication (i.e., speech) being our most readily accessed and utilized in everyday life. Speech production is the outcome of two separate neuromotor processes: voice production and articulation. Voice production includes multiple systems: respiratory (lungs), phonatory (larynx), and resonating (upper aerodigestive tract). Voicing begins with the intent to speak, followed by rapid inhalation and then exhalation of air from the lungs. The vocal folds are quickly closed, creating subglottic pressure. When this pressure reaches the minimum necessary threshold, the vocal folds are blown open and begin vibrating. The vocal folds vibrate rapidly (up to 150/second for men, and 230/second for females when speaking normally) and in perfect symmetry. This vibration creates a buzz-like sound which is shaped and amplified (via resonance) as it travels through the cavities of the upper airway (throat, mouth, and sinuses). The voice also creates the supra-segmental features of speech. These include prosody, stress, duration, loudness, intonation, and pitch. Suprasegmentals convey emotions – anger, sadness, and excitement – which are essential to verbal communication. You can change the meaning behind a sentence simply by changing the suprasegmental properties. Any changes in the vocal folds size, shape, or flexibility can affect how they vibrate, altering vocal pitch, intensity, or quality. Changes to the oropharynx or oral cavity can alter resonance, also affecting voice quality or intensity.

We then use our lips, teeth, and tongue to shape those sound waves into words via articulation. Articulation has three primary features used to differentiate phonemes (the individual sounds that make up words): place, manner, and voicing. Place refers to the location where the sound is produced within the vocal tract (e.g., tongue between the teeth, tongue tip to roof of mouth). Manner refers to the way in which the structures contact one another (e.g., stop vs, fricative vs. glide), reflecting the degree of friction and pressure used to create the sound. And finally voicing, which refers to whether the sound is produced with voice or without voice. The differentiating factor between most phonemes is one of these three categories. So, for example, the phoneme /d/ is a voiced, alveolar (tongue tip to alveolar ridge), stop consonant. This is in contrast to the phoneme /t/ which is a voiceless, alveolar, stop consonant. And, it is also in contrast to /z/ which is a voiced, alveolar, sibilant (forcing air through a narrow channel) consonant. Thus, when a person is unable to effectively generate these differentiating phonemic features during articulation, speech becomes difficult to understand as the sounds become less distinguishable (i.e., dysarthria).

### *Swallowing*

Safe and efficient swallowing involves more than 30 nerves and muscles and is dependent on speed, force, and coordination of movements [4]. Swallowing can be characterized as having four stages: oral preparatory, oral propulsive, pharyngeal, and esophageal. The oral preparatory and oral propulsive stages are voluntary. In the oral preparatory stage, food and drink are brought into the mouth and contained within the oral cavity by the lips. The salivary glands are stimulated; saliva is mixed with food as it is chewed, facilitating taste and the creation of a bolus (i.e., a cohesive mass of chewed food or liquid that is ready to be swallowed). The bolus is positioned on the cupped surface of the oral tongue. The oral cavity is sealed anteriorly by the lips and posteriorly by the soft palate and tongue. In the oral propulsive stage, anterior-posterior transfer of the bolus occurs (i.e., lingual stripping wave), with no pocketing or residual of the bolus remaining within the oral cavity. Saliva is an important component of the oral stages as it assists with food breakdown, bolus formation, and oral clearance. Also, adequate jaw range of motion is necessary for biting and rotary mastication.

The pharyngeal stage encompasses two important factors: airway protection (safety) and pharyngeal clearance (efficiency). This stage is involuntary and begins with the bolus head triggering the swallow reflex. The soft palate elevates, closing the nasopharynx, as the tongue base pushes the bolus through the pharynx. The pharyngeal constrictor muscles contract from top to bottom, pushing the bolus downwards. The larynx closes and elevates to prevent aspiration. In rare instances when food or drink enters the laryngeal vestibule, the normal response is a strong cough or throat clear reflex [5].

The esophageal stage is also involuntary. It begins with passage of the bolus through the upper esophageal sphincter (UES). The UES includes the inferior pharyngeal constrictor, the cricopharyngeus, and the cervical esophagus. UES opening is dependent on three factors: neurochemical relaxation of the cricopharyngeus muscle, mechanical forces pulling the UES open (hyolaryngeal excursion), and the driving force of the bolus itself (intrabolus pressure). Once the bolus has entered the esophagus, one to two proximal to distal peristaltic waves move it into the stomach. Clearance should be complete without hold-up, reflux, or regurgitation.

## Risk Factors for Dysfunction and Reduced QOL

Identifying risk factors for physical dysfunction and reduced QOL early may allow care teams to identify and assist those who need increased support during and after their cancer treatment. Communication and swallowing dysfunction is largely dependent on cancer location and stage (size, how advanced the cancer is) as well as the treatment modality employed. At the highest risk for significant dysfunction are those who have advanced tumors of the oral cavity, tongue base, larynx, or hypopharynx. In many cases, communication or swallowing dysfunction is the harbinger of the cancer, triggering work-up and diagnosis. Pre-treatment dysfunction is a reliable predictor of the likelihood for post-treatment dysfunction [4]. Treatment-based risk factors for dysfunction also include multimodality treatment, the intensity of radiation treatment, the specific RT dose to the upper esophageal sphincter, superior pharyngeal constrictors and suprahyoid musculature, and nil per os (NPO) intervals [6–11]. Patient-based factors have also been identified as being associated with increased risk for physical dysfunction; these include active or distant ETOH, living in a rural setting, and advanced age [6–8].

Risk factors for reduced quality of life after HNC treatment include both the presence and severity of physical dysfunction as well as patient-based psychosocial factors. In fact, pre-morbid psychosocial variables may be more influential than physical impairments in predicting reduced QOL [12]. Pre-morbid patient attitudes (e.g., pessimism), coping ability (i.e., poor resilience), mood (e.g., depression), and social support factors influence how a patient conceptualizes and copes with chronic physical impairment after HNC treatment [12, 13]. Those who do not cope well may be less engaged in rehabilitation and less able to adapt. Similarly, the literature reports that as many as 50% of HNC patients present with baseline mild cognitive impairment, and this cognitive impairment is associated with reduced treatment adherence and poorer QOL [14]. Finally, some dimensions of well-being have been found to be age sensitive, making the patient's "stage of life" an important consideration. Autonomy and environmental mastery tend to be more important to younger adults [15–27], while purpose in life and personal growth are more significant for middle-aged and older adults. However, the dimensions of self-acceptance and positive relations with others have been found to be significant components of well-being across all life stages [2].

Over the course of treatment, QOL issues can develop. While clinicians should be sensitive to this, issues surrounding QOL should always be identified by the patient. Patient surveys are useful clinical tools to quickly identify patients with developing functional impairment or QOL issues/concerns. Patient responses on these surveys can be a great springboard for further discussion, intervention, and/or counseling. Table 6.2 lists a variety of validated QOL and functional impairment surveys that may be useful in this population.

## Physical Dysfunction and Their Impact on QOL

### *Dysphonia*

Dysphonia is defined as altered voice quality, pitch, loudness, or vocal effort that impairs communication as assessed by a clinician and/or affects quality of life [37].

Dysphonia typically involves an abnormality in one or more of the following: acoustic-perceptual quality (e.g., roughness, strain, breathiness), vocal intensity (ability to get loud), resonance (hyper/hypo-nasality), and/or vocal endurance. Most

**Table 6.2** Validated functional impairment and quality of life scales

| Scale | # Items | Function | Author |
|---|---|---|---|
| Voice-Related Quality of Life (V-RQOL) | 10 | Voice | Hogikyan and Sethuraman, 1999 [28] |
| Voice handicap Index-10 (VHI-10) | 10 | Voice | Rosen et al. (2004) [29] |
| Quality of Life in the Dysarthric Speaker (QOL-DyS) | 40 | Dysarthria | Piacentini et al. (2011) [30] |
| Swallowing Quality of Life Questionnaire (SWAL-QOL) | 44 | Dysphagia | McHorney et al. (2002) [31] |
| The MD Anderson Dysphagia Inventory- Head and Neck (MDADI-HN) | 20 | Dysphagia | Chen et al. (2001) [32] |
| Eating Assessment Tool (EAT-10) | 10 | Dysphagia | Belafsky et al. (2008) [33] |
| Functional Assessment of Cancer Therapy – Head and Neck (FACT H&N) | 40 | Six subscales: physical, social, family, emotional, functional, and other | List et al. (1996) [34] |
| Vanderbilt Head and Neck Symptom Survey (VHNSS) | 28 | Five subscales: nutrition, pain, voice, swallow, mucous/dry mouth | Murphy et al. (2010) [35] |
| European Organization for Research and Treatment of Cancer Quality of Life – Head and Neck 35 (EORTC QLQ-H&N 35) | 35 | Seven subscales: pain, swallowing, senses, speech, social eating, social contact, sexuality | Bjordal et al. (2016) [36] |

patients who undergo radiation (RT) of the head and neck experience acute dysphonia during treatment. Acute RT-induced dysphonia is typically characterized by a harsh, rough, and strained voice quality resulting from stiff, edematous, and dry vocal folds. Painful voicing (odynophonia) may also be present, limiting verbal communication during treatment. At the peak of treatment, sometimes no sound is able to be produced (aphonia), requiring dependence on others to communicate on the patient's behalf during treatment. These symptoms are usually self-limited, slowly resolving once RT is completed. However, patients with laryngeal cancer are likely to have permanent changes to their voice quality. This often begins prior to treatment, as a result of a glottic malignancy on one or both of the vocal folds. A laryngeal tumor may also invade the recurrent laryngeal nerve, causing impaired motion of a vocal fold (i.e., paralysis or paresis). Vocal fold motion impairment can result in incomplete glottic closure, leading to a breathy, weak (or asthenic) voice quality, poor vocal stamina, and an inability to shout. Treatment of laryngeal cancer may also cause or contribute to voice dysfunction. Vocal fold excision, cordectomy, partial laryngectomy, and/or RT may result in a strained, hoarse, and possibly asthenic voice due to subsequent scarring and/or loss of vocal fold bulk. Finally, in some instances, dysphonia can occur in patients with other cancers of the head and neck. Surgical removal of all or part of the soft palate or maxilla leads to significant changes in vocal resonance and articulatory precision, as the oral cavity now communicates with the nasal cavities. A prosthodontic device (i.e., an obturator; see Fig. 6.2a, b) is typically made to fit the defect and normalize intraoral resonance and pressures. In HNC survivors treated with chemoradiation, lower peripheral cranial nerve palsy can develop years after treatment, leading to global vagus nerve impairment and significant dysphonia.

Dysphonia is widely recognized as leading to negative impacts on QOL. Dysphonic patients experience social, lifestyle, and employment difficulties as a direct consequence of their voice disorder [15, 38, 39]. The psychosocial and QOL impact of dysphonia is determined in large part by the severity of the dysphonia, with those experiencing severe dysphonia most likely to experience impairment and subsequent psychosocial and QOL impacts. However, patients with mild or moderate dysphonia will experience negative impacts if their occupation is contingent on heavy voice use [16]. Similarly, if a patient's wife is hard of hearing, the impact of even a mild reduction in voice volume or clarity could have a detrimental

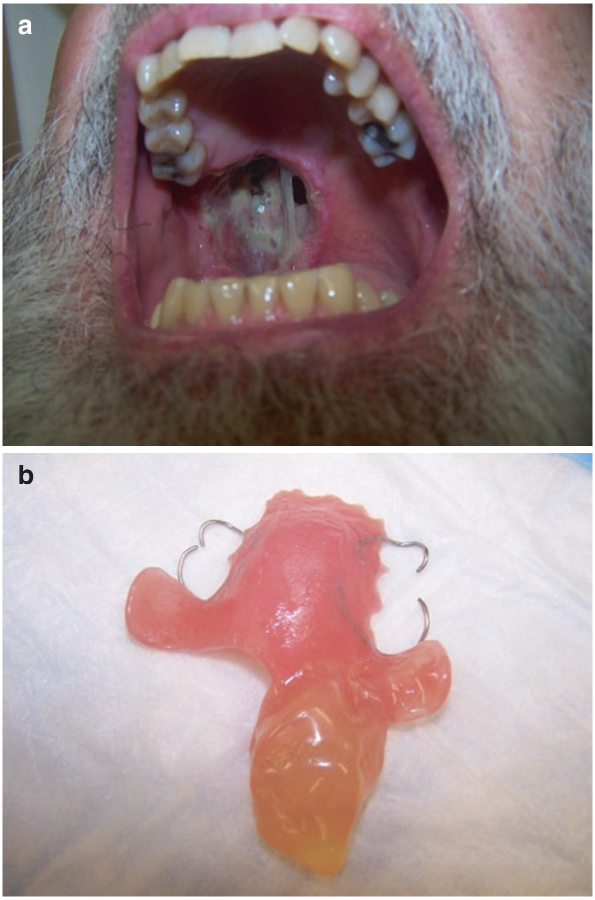

**Fig. 6.2** This defect of the maxilla (**a**) is a result of surgery to remove a maxillary sinus tumor. This defect leads to sound and air pressure leakage out the nose during speech attempts and food and liquid leakage out the nose during eating/drinking. A maxillary obturator (**b**) is made by a prosthodontist. It attaches to the maxilla (via hooking to the teeth in this case) plugging the surgical defect and establishing normal speech and swallowing. The obturator and defect site have to be cleaned/flushed after each meal

impact on his ability to communicate effectively with her, leading to a string of downstream problems in their relationship. Now imagine he is her primary caregiver – the problems compound. Thus, special attention must be given to understanding the voice use/needs and occupational demand in patients at risk for (or with) dysphonia. Both elements (need/use and severity) must be considered in order to understand the psychosocial impact.

## *Total Aphonia*

In very advanced disease, in cases of larynx cancer recurrence (RT failure), or if the larynx becomes completely non-functional (organ failure), the whole larynx is removed (i.e., total laryngectomy). This leads to permanent voice loss (total aphonia) and the need for a permanent tracheostoma (Fig. 6.3). Life can be markedly changed after total laryngectomy (TL). TL requires a form of permanent disfigurement via the creation of a tracheostoma, leading to the potential for feelings of stigma (Fig. 6.4) [17, 18]. Furthermore, patients and their families must adapt to significant changes in pulmonary and respiratory function (e.g., increased coughing and sputum, diminished sense of smell and taste). An alternative sound source must be selected (i.e., alaryngeal voice), resulting in drastic changes to voice quality, as well as a flattening of suprasegmental features (prosody, stress, intonation, and pitch). The overwhelming majority of patients report that loss of voice is the most important QOL factor after TL [19]. In addition, patients report increased feelings of solitude, withdrawal from social conversations and activities, barriers to fulfilling relationships with others, and perceived stigmatization related to their anatomical and functional changes [19].

There are three methods of alaryngeal speech: electrolarynx (EL), esophageal speech, and tracheoesophageal puncture (TEP) with voice prosthesis. All three provide a sound source, which is then shaped by the existing articulators to create

**Fig. 6.3** Pictured is a gentleman following total laryngectomy who now has a tracheostoma. This patient had some difficulties healing immediately after surgery and has some visible scar tissue formation. He also has significant submental lymphedema, altering his appearance. He will require a lot of rehabilitation for his lymphedema and for alaryngeal voice restoration

**Fig. 6.4** This patient is wearing a special filter over her tracheostoma. This filter helps preserve pulmonary function. Learning about and obtaining these devices is a part of the rehabilitation process. Some patients also prefer the appearance of their tracheostoma with this device (rather than an open stoma). These devices are not always covered by insurance and can be costly

speech. The EL is an electronic, battery-operated device with a vibrating head that transmits a buzz-like sound into the throat and/or mouth where it is then shaped into words. The EL is quite easy to learn and a very dependable form of alaryngeal voice. However, the robotic/mechanical sound quality, unwanted attention or perceived stigma, and inability to be hands free (in most situations) may deter people from utilizing this mode of communication.

Esophageal speech (ES) is the most natural of the three forms of alaryngeal voice. The advantages of ES include being hands-free and not requiring a prosthesis or machine; one simply uses their existing anatomy to create speech. ES is generated by using oral and pharyngeal muscles to quickly push air into the cervical esophagus where it is then released in a manner that vibrates the pharyngoesophageal (PE) segment: creating sound. ES speakers report less stress and reduced voice handicap than EL or TEP speakers [20]. However, learning this method of voicing is time-intensive. Also, vocal intensity (volume) may be limited in some patients, which may not be functional or may necessitate the use of a portable amplifier.

Lastly, TEP is a procedure in which a prosthesis, containing a one-way valve, is inserted into the tracheoesophageal wall. This valve allows air from the lungs to enter the esophagus, vibrate the PE segment, and produce sound. The one-way valve also prohibits food/drink from the esophagus to leak into the trachea. As TEP voicing is produced by air coming from the lungs (rather than the oral cavity), TEP speakers can modulate intensity better than ES speakers. TEP voice is also extremely easy to generate. The patient simply takes a breath, occludes the tracheostoma (either with a finger or with a special “hands-free” device that sits atop the stoma), and speaks! The literature supports TEP as providing the best perceptual voice quality, fluency, ease of production, and volume [21–23]. However, as TEP utilizes a prosthetic device seated between the esophagus and the trachea, daily care is required and complications can arise. At best these can be costly and inconvenient for the patient; at worst they can lead to life-threating outcomes (enlarged fistula, aspiration pneumonia, need for a feeding tube). Patient selection is an important factor in optimizing outcomes and limiting risk [24, 25].

Speech-related QOL is lowest immediately after surgery and improves significantly 1 year post-operatively, irrespective of alaryngeal voice method [26]. Also, those who participate in speech therapy tend to report higher QOL when compared to those who do not [27]. Older or retired persons tend to report better QOL following laryngectomy than those in the middle stage of life (where work and financial demands are higher) [40]. Poor or avoidant coping strategies (cognitive and behavioral) are also predictive of poorer QOL in TL patients [41]. Education and counseling is critical in this patient population, as choosing a speech method is a joint decision-making process between the patient and the multidisciplinary team. Furthermore, given the degree of anatomic and physiologic change these patients must adapt to, it is important for clinicians to inquire about and address patients' feelings about these changes. By understanding the patient's psychosocial status and needs, clinicians can facilitate adjustment and help the patient, and their family, develop effective coping strategies.

## *Dysarthria*

Dysarthria is a motor speech disorder associated with disturbances of respiration, laryngeal function, airflow direction, and articulation resulting in difficulties of speech quality and intelligibility [42]. Adequate mobility, sensation, and strength of the articulators are necessary for clear, intelligible speech. Head and neck cancers, surgery, and RT can impact the above and result in dysarthria (Fig. 6.5). Articulation disorders are frequently associated with tumors of the oral cavity, including the lips, floor of mouth, tongue, mandible, buccal mucosa, retromolar trigone, and palate. Dysarthria can be present at diagnosis (pre-treatment) or as the result of surgery and/or RT.

**Fig. 6.5** This woman had a very large tumor of the tongue and anterior floor of mouth requiring subtotal glossectomy with free flap reconstruction. Without a freely mobile anterior tongue, normal articulation is very challenged, particularly for sounds that require the tongue to contact the alveolar ridge or between the teeth

Primary surgery is the typical treatment for oral cavity tumors, with many also undergoing adjuvant RT. Post-operatively, patients may present with reduced intelligibility and clarity secondary to surgical pain/edema, surgical defect, as well as reduced strength, range of motion, and sensation of the articulatory structures. These dysfunctions are highly responsive to rehabilitation, with most patients acquiring intelligible speech. Post-surgical scar contraction, surgical defects, or nerve injury can lead to chronic dysarthria. Dysarthria can also occur as a result of RT and presents differently in the acute vs. chronic stage. During and immediately after RT, the acute effects of RT (mucositis, pain, thick secretions) can result in altered articulation that resolves spontaneously as treatment effects resolve. Chronic RT effects that can influence articulation include fibrotic changes to the articulatory musculature, reduced jaw mobility (trismus), and xerostomia. Patients with xerostomia may find they need to sip water regularly in order to comfortably speak, as their tongue may stick to oral structures during articulation. Very mild changes to sound production can also occur. Severe trismus can affect vowel shaping and reduce the precision of articulatory contacts. Late RT effects include lower cranial nerve palsy (most commonly affecting the hypoglossal nerve and palatal branch of the vagus nerve) resulting in severe dysarthria years after treatment.

Mild-to-moderate dysarthria is most common with patients often having to speak more slowly (with effort) and choose their words more carefully and occasionally having to repeat themselves in order to be understood. These changes can be frustrating and reduce one’s motivation to engage others in conversation. Situations where there is elevated background noise (such as parties, social events, restaurants, concerts) compound these difficulties and may lead to reduced willingness to participate in premorbid social activities. When this occurs, psychological well-being is affected, and a reduction in QOL is likely. Similar to dysphonia, special attention must be given to understanding the speech use/needs and occupational demand in patients at risk for (or with) dysarthria. A salesman in his middle years with a mild dysarthria may experience a decline in QOL equivalent to that of a retired, widower with a moderate dysarthria. Both elements (use and severity) must be considered in order to understand the psychosocial impact.

Severe dysarthria represents speech that is unintelligible in most contexts and typically requires use of an oral prosthetic or alternative communication method. This may be writing, utilization of a communication board, or utilization of a computerized system (i.e., type to talk). Patients with poor coping skills may decline all of these options, becoming further isolated. Supporting these patients can be challenging, as, when counseling is attempted, it can be frustrated by the patient’s difficulty communicating their thoughts and feelings.

## ***Dysphagia***

Dysphagia occurs when someone has difficulty with any one or more of the anatomic or physiologic components of the oral, pharyngeal, or esophageal stages of the swallow [43]. Dysphagia can be present at cancer diagnosis or can be a result of surgery and/or RT. Dysphagia symptoms and severity may progress across survivorship due to progressive fibrosis and/or diminished sensation. HNC treatment can have impacts on all four stages of swallowing: oral preparatory, oral transit, pharyngeal, and esophageal.

Oral stage dysphagia is commonly associated with cancers of the oral cavity including the lips, mandible, tongue, palate, and buccal mucosa (Fig. 6.6). Treatment for HNC can result in loss of dentition, incomplete labial closure, reduced tongue mobility, reduced intraoral sensation, xerostomia, and reduced mouth opening. These dysfunctions can lead to difficulty with bolus containment, formation and transport, and pocketing of foods in the oral cavity. Xerostomia is one of the most common oral stage complaints and occurs as a result of RT. Insufficient saliva can lead to excessive mastication, oral retention of portions of the bolus, and diminished taste and alters the perception of texture.

Pharyngeal stage dysphagia is typically associated with oropharyngeal, laryngeal, and hypopharyngeal tumors. Treatment for HNC can result in poor swallow efficiency (secondary to motor weakness, structural defects, xerostomia or fibrotic stiffness) and reduced swallow safety (secondary to reduced airway protection and/or reduced laryngeal/pharyngeal sensation). At best, these dysfunctions make eating/drinking slow and effortful (e.g., needing to swallow multiple times per bite to clear the pharynx). At worst, they can lead to chronic tracheal aspiration or the need for a feeding tube. The potential for "silent" aspiration (aspiration that does not elicit a cough response) exists in patients who have undergone RT, complicating survivorship, as these patients usually do not recognize that they have dysphagia and so do not report it. For this reason, routine objective instrumental swallow testing (video fluoroscopic swallow study or flexible endoscopic evaluation of swallowing) is necessary for these patients. Chronic aspiration is tolerated in many HNC survivors without complication for many years. This is most true for survivors who are otherwise healthy. However, those who develop complications from chronic aspiration (i.e., chronic aspiration pneumonia) are faced with difficult choices surrounding QOL.

**Fig. 6.6** This gentleman has severe trismus, with maximal mouth opening at less than 10 mm (pictured). As a result, he has difficulty fitting a spoon or fork in his mouth, biting, or chewing. He consumes mostly liquids and some pureed foods. Oral care and oral examination (for recurrence) are also very limited, increasing the risk of dental caries and undetected cancer recurrence

Esophageal dysphagia after HNC treatment is most commonly associated with esophageal stricture. Esophageal stricture can result in food/liquid hold-up above the level of stricture and can result in aspiration, malnutrition, food impaction, and discomfort with eating and drinking. The incidence of esophageal stricture after treatment for HNC has been reported to be between 5% and 24% [44, 45]. That number may be higher with late survivors [46]. Several risk factors have been identified with increased risk of stricture formation: hypopharyngeal and unknown primary tumors, T4 disease, and use of concurrent chemotherapy [47]. The use of a PEG, particularly if the patient is taking nothing by mouth, increases the risk of esophageal stricture, perhaps as a result of disuse of swallow musculature during treatment [48, 49]. Esophageal stricture is generally managed with dilation, although serial dilations are often required and treatment is not always effective.

Dysphagia after advanced HNC typically requires the use of modified food textures (soft and moist), liquid assist for swallowing solids, and slow intake with several swallows needed per bite. Patients may not appear to be having difficulty, but are certainly working harder to consume food. This increased effort, along with changes to taste and appetite, makes eating less enjoyable. When greater dysfunction is present, frequent coughing may occur with meals, a postural strategy may be necessary (e.g., head turn, chin tuck), liquids may need to be thicker, whole food groups may need to be avoided (e.g., dry foods, breads, sandwiches), or anterior leakage may occur (i.e., leakage of food/liquid out the mouth from between the lips) during meals. Those with severe dysphagia often require feeding tubes in order to maintain adequate nutrition. As a result of any or all of these possible changes, the dysfunction is more readily apparent to others and eating/drinking is more likely to be done in private. The experience of eating may lose much of its social and personal capital, becoming simply a means to an end (weight and nutrition). Conversely, some patients are unwilling to sacrifice the pleasure of eating or of sharing food with others socially. They may continue eating without following prescribed measures to prevent aspiration, potentially leading to chronic lung injury or a serious choking event. A choice such as this, to favor QOL over safety/longevity, can lead to strain or even conflict between a patient and his or her family. Family members often want the patient to follow the recommendations made by the healthcare providers in an effort to keep the patient safe and are frustrated by the patient's choice. They may perceive the patient as stubborn or short-sighted when in fact the patient is simply responding to very difficult choices.

Dysphagia is the leading cause of reduced QOL after HNC treatment and is reported in >70% of advanced HNC patients [50]. Dysphagia after HNC treatment has been associated with higher rates of depression in patients [51]. Presence of a feeding tube, penetration/aspiration noted on MBS, and xerostomia were all found to be associated with reduced QOL in dysphagia patients after HNC treatment [52, 53] While the majority of patients report dysphagia, only a minority report satisfaction with the amount of clinical time dedicated to it [54]. This highlights the importance of addressing dysphagia throughout HNC treatment and survivorship. Patients and family members should be counseled regarding the likely impact of dysphagia on their lives. The patient should be encouraged to express how these changes make him or her feel and given an opportunity to clarify what is important to him or her in this context.

## Treatment

This chapter described the effects HNC treatment can have on communication and swallowing function and, subsequently, psychological and psychosocial well-being. Thus, in striving to treat the person, not just the disease, multidisciplinary care is essential. The multidisciplinary care team includes head and neck surgery, plastic surgery, radiation oncology, medical oncology, speech pathology, physical therapy, lymphedema therapy, occupational therapy, social work, psychiatry, psychology, pain management, and nursing. Each member of the team plays a vital role in caring for the patient: treating the disease, the symptoms and effects of the disease and its treatment, and the psychosocial impacts of all of the above.

Speech-language pathologists (SLPs) specialize in the diagnosis and rehabilitation of communication and swallowing disorders and work closely with patients with HNC. SLPs are trained to not only diagnose dysfunction but to identify any resulting impairment that may lead to a reduction in the quality of life. The purpose of rehabilitation is to reduce impairment rather than resolve dysfunction per se. Rehabilitation interventions can be preventative, restorative, compensatory, or palliative in nature. Evaluation and treatment are often lifelong for people with HNC and should begin prior to initiation of cancer treatment. Pre-treatment evaluation can assist in decision making and help predict post-treatment function. Pre-treatment evaluation should include functional assessment of oral motor function, speech, and swallowing. Instrumental swallowing assessment is preferred, particularly for those with cancers of the oropharynx, larynx, or hypopharynx. Screening for cognitive impairment is also very useful. Pre-treatment counseling provides the clinician opportunity to give patients and families realistic expectations for recovery, identify support needs and coping challenges, and reinforce the need for patient engagement in rehabilitation throughout and after their cancer treatment.

Speech/swallowing therapy is usually initiated “prophylactically,” i.e., before initiation of RT and immediately following surgery and/or RT. A treatment plan is developed by the clinician based on input from the patient regarding their goals. Due to the potential for sensory impairment and “silent” aspiration during and after RT, instrumental swallow testing should be utilized in any patient at risk for dysphagia. Treatment of communication and swallowing disorders often include range of motion and strengthening exercises, manual therapies, neuromotor re-education activities (e.g., motor drills), compensatory strategies, and education and counseling related to dysfunction. Long-term survivors of head and neck cancer often face difficult decisions many years after diagnosis, including the need for a feeding tube, tracheostomy, or total laryngectomy for end-stage dysphagia. Education, counseling, and access to all members of the multidisciplinary team throughout survivorship can empower patients to make educated decisions if/when these difficult situations arise.

Support groups can also have a profound impact on patients in all stages of their HNC treatment. Simply connecting and interacting with others who share an understanding of the life-changing effects of their treatment can be empowering. These peer-driven groups offer tremendous information and support for patients and their families. This is portrayed in the patient testimonial excerpts below:

> *"Since meeting with the support group my attitude has changed completely. When I wake up in the morning my first thoughts are: thank you for another day and I am going to make the most of it." – Head and Neck Cancer Support Group member*
>
> *"It made me feel that being alone in this situation was not the loneliest feeling in the world. It made me realize that other people were also going through the feelings I was having, but dealing with them much better than I was. They were living their lives, not just existing." –Laryngectomy Support Group member*

## Conclusion

Head and neck cancer, as well as the treatment for head and neck cancer, can result in communication and swallowing dysfunction throughout survivorship. Determining the impact of these dysfunctions on an individual patient's psychosocial well-being and QOL requires that clinicians understand the degree to which these functions are necessary to the patient's activities of daily living and the patient's baseline ability to cope and adapt with change. Multidisciplinary teams are best positioned to deliver the care necessary to identify and address the impact this disease and its treatment has on a patient's quality of life. Furthermore, the effects of cancer treatment are lifelong – and the medical paradigm should attempt to reflect this.

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# Chapter 7
# The Impact of Nutrition on Patient Outcomes

**Leah Novinger, Lina Nieto, and Avinash V. Mantravadi**

## Introduction

Head and neck cancer patients, of which up to two-thirds are malnourished at the time of diagnosis [1], face unique challenges that can directly affect their outcomes. Physicians tend to overestimate malnutrition and underestimate weight loss in the oncology patient population while patients routinely underestimate the degree of their own malnutrition [2].

Many patients are not psychologically prepared for the effect of treatments on oral intake [3]. Patients interviewed while undergoing treatment for head and neck cancer routinely consider taking an oral diet to be “a full time job” and “a struggle,” often longing “to eat real food” [3]. Many patients view feeding tubes as personal failures and can be subject to widely differing opinions by providers, further complicating their view on this treatment modality [3].

The etiology of malnutrition is frequently multifactorial in head and neck cancer patients. Due to tumor location, tissue loss as a result of surgery, and side effects from adjuvant therapies, mechanical swallowing may be difficult. In addition to dysphagia, patients may experience odynophagia, trismus, globus sensation, and frank aspiration [1]. Poor dentition or tumor bulk may limit mastication. Diet may be constrained by these physical issues but also impacted by alcohol and tobacco

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intake. Over half of patients with head and neck cancer experience depression during treatments, which may further impact nutrition [4].

Malnutrition can be defined as a “subacute or chronic state of nutrition, in which a combination of varying degrees of overnutrition or undernutrition and inflammatory activity have led to a change in body composition and diminished function” [5]. Development of malnutrition has several adverse physical and psychosocial effects including impaired immune response, impaired wound healing, reduced functional status leading to inactivity and inability to work, reduced strength of respiratory muscles, electrolyte disturbances, depression, loss of libido, and poor self-image. In the clinical setting, there are three etiology-based diagnoses for malnutrition and their definitions are based on the presence or absence of inflammatory response. “Starvation-related malnutrition” is defined as chronic starvation without inflammation as seen in anorexia nervosa. “Chronic disease-related malnutrition” refers to chronic inflammation of mild to moderate degree as seen in pancreatic cancer, sarcopenic obesity, and organ failure. “Acute-disease or injury-related malnutrition” refers to disease or injury states with a marked inflammatory response as seen in burns, trauma, and major infection.

## Validated Tests for Malnutrition

The exact prevalence of malnutrition in oncology patients is difficult to assess due to lack of standards for nutrition screening in oncology patients as well as lack of consensus on the validity of these screening tools. However, it is estimated that greater than half of cancer patients experience weight loss at diagnosis. Oncology patients are at risk for malnutrition not only due to the disease process itself but also because of consequences of treatment. It is further estimated that as many as 57% of head and neck cancer patients experience significant weight loss before initiating treatment while between 75% and 80% of patients will experience further weight loss once treatment begins [6].

In order to support a diagnosis of malnutrition, The Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition (ASPEN) have developed clinical characteristics based on energy intake, interpretation of weight loss, body fat loss, muscle mass wasting, fluid accumulation/edema, and reduced grip strength. A minimum of two of these six proposed characteristics must be present to support diagnosis of non-severe (moderate) or severe protein-calorie malnutrition [7].

Malnutrition in the context of acute illness or injury is diagnosed by less than 75% of estimated energy requirement for greater than 7 days (moderate malnutrition) and less than 50% of estimated energy requirement for greater than or equal to 5 days (severe malnutrition). In the context of chronic illness, moderate and severe malnutrition may be diagnosed by less than 75% of estimated energy requirement for greater than or equal to 1 month. Clinicians may estimate energy needs and compare them to estimates of recent intake by obtaining a detailed nutrition history via assessment methods such as food diaries, food frequency questionnaires, and 24-hour dietary recalls. Inadequate intake may then be reported as percentage of estimated energy and protein needs over a defined time period.

Weight change and percent weight loss from baseline are also important indicators of malnutrition. Moderate acute illness or injury-related malnutrition may be diagnosed by percent weight loss of 1–2% in 1 week, 5% in 1 month, and 7.5% in 3 months while severe acute illness or injury-related malnutrition may be diagnosed by greater than 2% weight loss in 1 week, greater than 5% weight loss in 1 month, and greater than 7.5% weight loss in 3 months. In the context of chronic illness, moderate protein-calorie malnutrition may be diagnosed as follows: 5% weight loss in 1 month, 7.5% weight loss in 3 months, 10% weight loss in 6 months, and 20% weight loss in 1 year. Severe chronic illness-related malnutrition is defined as greater than 5% weight loss in 1 month, greater than 7.5% weight loss in 3 months, greater than 10% weight loss in 6 months, and greater than 20% weight loss in 1 year.

A nutrition-focused physical exam will aid in the assessment of moderate to severe subcutaneous fat loss as well as muscle loss. Exam results coupled with percent weight change or reported reduced energy intake may together support a malnutrition diagnosis. Common areas for assessment of fat loss are the orbital region: a hollow look around the eyes characterized by prominent depressions and loose skin may be indicative of the significant fat loss seen in severe protein-calorie malnutrition as compared to the slightly bulged under-eye fat pads one may find in a well-nourished individual. The upper arm region (i.e., triceps and biceps) and the thoracic and lumbar regions (ribs, lower back) are other common exam areas for assessment of fat loss. To assess muscle loss, the temporalis muscle, clavicle region (i.e., pectoralis major, deltoid, trapezius muscles), and anterior thigh soft tissues (quadriceps muscles) are commonly examined. Examples indicative of severe protein-calorie malnutrition may include protruding, prominent clavicles as well as a square appearance of the shoulder to arm joint (deltoid wasting) [8] (Fig. 7.1).

Both the prevalence of malnutrition in oncology patients and the current discrepancies in diagnosis justify the need for validated nutrition assessment and screening tools in clinical practice. Increased use of these screening tools may facilitate diagnosis and result in a more proactive approach in treatment of malnutrition where patients are captured earlier in cancer treatment course when they are only at risk for its development, and nutritional interventions have more significant results (i.e., pre-cachexia). As implied by its name, the scored Patient-Generated Subjective Global Assessment questionnaire (PG-SGA) uses information generated directly by the patient to create an additive score based on prognostic indicators (weight loss, functional status, and nutrition impact symptoms that restrict intake) that define the degree of malnutrition. This further generates a nutritional triage recommendation based on results. The tool's additive score allows for rapid and systematic risk assessment, and repeated assessments/changes in score throughout treatment course allow for continued measure of the effects of nutrition interventions. This makes the PG-SGA a multiuse instrument in that it serves as a nutrition screening tool, assessment tool, interventional triage, and an instrument to measure success of interventions

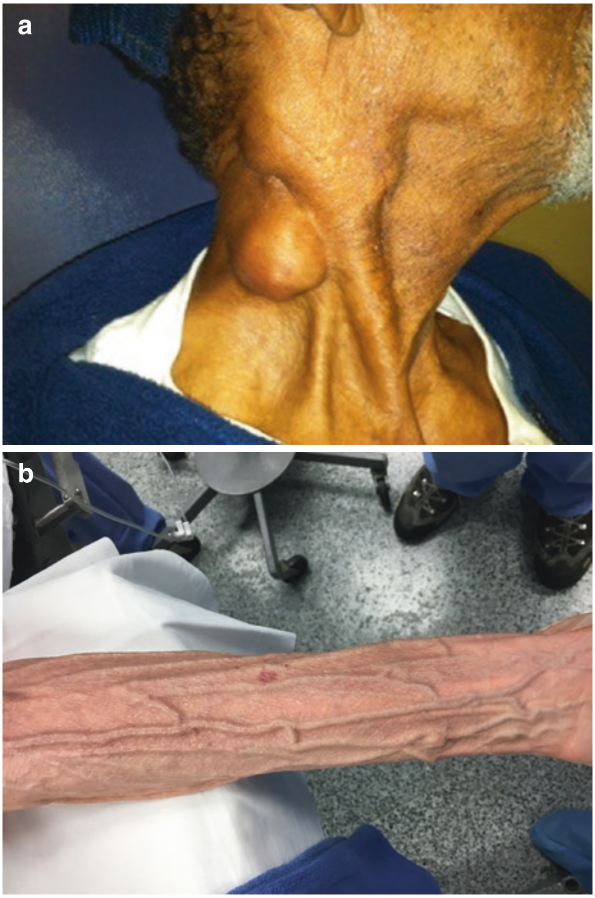
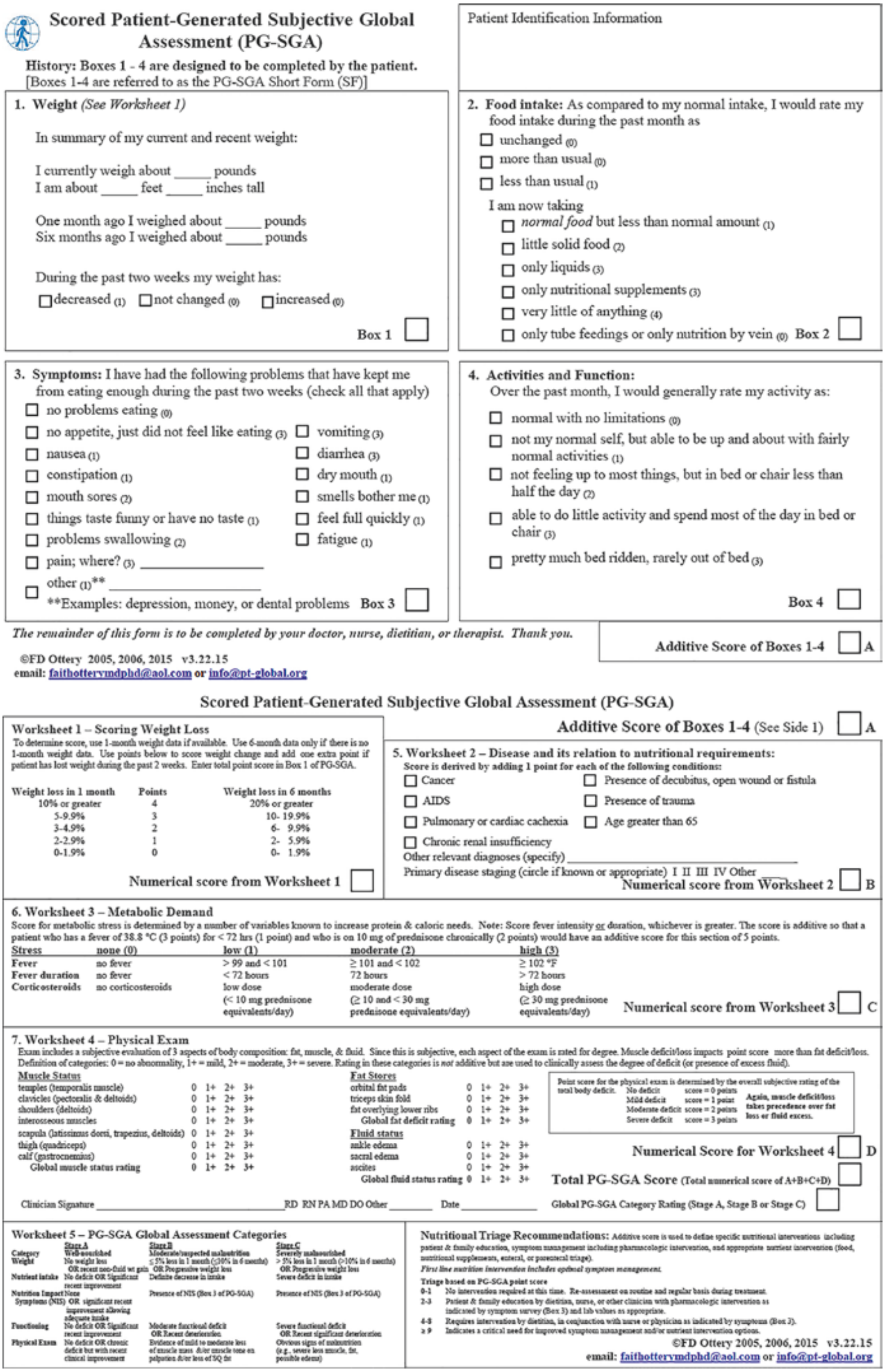


**Fig. 7.1** (**a**) Malnourished appearance, supraclavicular wasting, and prominent clavicle due to high tumor burden in patient with squamous cell carcinoma of the neck. (**b**) Severe malnutrition evidenced by muscle and skin atrophy in right arm/forearm

(Fig. 7.2). It has been applied in a variety of clinical settings for catabolic conditions beside oncology; examples include AIDS patients, geriatric patients, lung transplant patients, and dialysis patients. The Oncology Nutrition Dietetic Practice Group of the Academy of Nutrition and Dietetics has accepted the PG-SGA as the standard for nutrition assessment in the oncology population. Other advantages associated with use of the PG-SGA include involvement of both patient and clinician and its reliance on readily available data. It does not rely on laboratory tests, making it an inexpensive tool.

The first portion of the questionnaire is to be completed by the patient while the second half is completed by the clinician (i.e., doctor, nurse, dietitian, therapist). The four boxes on the first page of the screening tool are organized into the following categories: Weight, Food Intake, Symptoms, and Activities and Function. The fact that the patient independently completes these portions saves clinician time while emphasis on patient involvement empowers him/her to identify the root causes of nutritional issues. Box 1 – Weight History and Box 3 – Symptoms have



**Scored Patient-Generated Subjective Global Assessment (PG-SGA)**

**History: Boxes 1 - 4 are designed to be completed by the patient.**
[Boxes 1-4 are referred to as the PG-SGA Short Form (SF)]

Patient Identification Information

**1. Weight** *(See Worksheet 1)*

In summary of my current and recent weight:

I currently weigh about _____ pounds
I am about _____ feet _____ inches tall

One month ago I weighed about _____ pounds
Six months ago I weighed about _____ pounds

During the past two weeks my weight has:
☐ decreased (1) ☐ not changed (0) ☐ increased (0)

**Box 1** ☐

**2. Food intake:** As compared to my normal intake, I would rate my food intake during the past month as
☐ unchanged (0)
☐ more than usual (0)
☐ less than usual (1)

I am now taking
☐ *normal food* but less than normal amount (1)
☐ little solid food (2)
☐ only liquids (3)
☐ only nutritional supplements (3)
☐ very little of anything (4)
☐ only tube feedings or only nutrition by vein (0)

**Box 2** ☐

**3. Symptoms:** I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply)
☐ no problems eating (0)
☐ no appetite, just did not feel like eating (3)
☐ nausea (1)
☐ constipation (1)
☐ mouth sores (2)
☐ things taste funny or have no taste (1)
☐ problems swallowing (2)
☐ pain; where? (3) ______________
☐ other (1)** ________________
**Examples: depression, money, or dental problems
☐ vomiting (3)
☐ diarrhea (3)
☐ dry mouth (1)
☐ smells bother me (1)
☐ feel full quickly (1)
☐ fatigue (1)

**Box 3** ☐

**4. Activities and Function:**
Over the past month, I would generally rate my activity as:
☐ normal with no limitations (0)
☐ not my normal self, but able to be up and about with fairly normal activities (1)
☐ not feeling up to most things, but in bed or chair less than half the day (2)
☐ able to do little activity and spend most of the day in bed or chair (3)
☐ pretty much bed ridden, rarely out of bed (3)

**Box 4** ☐

*The remainder of this form is to be completed by your doctor, nurse, dietitian, or therapist. Thank you.*

**Additive Score of Boxes 1-4** ☐ **A**

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**Scored Patient-Generated Subjective Global Assessment (PG-SGA)**

**Additive Score of Boxes 1-4** (See Side 1) ☐ **A**

**Worksheet 1 – Scoring Weight Loss**
To determine score, use 1-month weight data if available. Use 6-month data only if there is no 1-month weight data. Use points below to score weight change and add one extra point if patient has lost weight during the past 2 weeks. Enter total point score in Box 1 of PG-SGA.

| Weight loss in 1 month | Points | Weight loss in 6 months |
|---|---|---|
| 10% or greater | 4 | 20% or greater |
| 5-9.9% | 3 | 10- 19.9% |
| 3-4.9% | 2 | 6- 9.9% |
| 2-2.9% | 1 | 2- 5.9% |
| 0-1.9% | 0 | 0- 1.9% |

**Numerical score from Worksheet 1** ☐

**5. Worksheet 2 – Disease and its relation to nutritional requirements:**
**Score is derived by adding 1 point for each of the following conditions:**
☐ Cancer
☐ AIDS
☐ Pulmonary or cardiac cachexia
☐ Chronic renal insufficiency
☐ Presence of decubitus, open wound or fistula
☐ Presence of trauma
☐ Age greater than 65

Other relevant diagnoses (specify) ______________________
Primary disease staging (circle if known or appropriate) I II III IV Other ____

**Numerical score from Worksheet 2** ☐ **B**

**6. Worksheet 3 – Metabolic Demand**
Score for metabolic stress is determined by a number of variables known to increase protein & caloric needs. Note: Score fever intensity or duration, whichever is greater. The score is additive so that a patient who has a fever of 38.8 °C (3 points) for < 72 hrs (1 point) and who is on 10 mg of prednisone chronically (2 points) would have an additive score for this section of 5 points.

| Stress | none (0) | low (1) | moderate (2) | high (3) |
|---|---|---|---|---|
| **Fever** | no fever | > 99 and < 101 | ≥ 101 and < 102 | ≥ 102 °F |
| **Fever duration** | no fever | < 72 hours | 72 hours | > 72 hours |
| **Corticosteroids** | no corticosteroids | low dose<br>(< 10 mg prednisone equivalents/day) | moderate dose<br>(≥ 10 and < 30 mg prednisone equivalents/day) | high dose<br>(≥ 30 mg prednisone equivalents/day) |

**Numerical score from Worksheet 3** ☐ **C**

**7. Worksheet 4 – Physical Exam**
Exam includes a subjective evaluation of 3 aspects of body composition: fat, muscle, & fluid. Since this is subjective, each aspect of the exam is rated for degree. Muscle deficit/loss impacts point score more than fat deficit/loss. Definition of categories: 0 = no abnormality, 1+ = mild, 2+ = moderate, 3+ = severe. Rating in these categories is *not* additive but are used to clinically assess the degree of deficit (or presence of excess fluid).

| Muscle Status | | | | |
|---|---|---|---|---|
| temples (temporalis muscle) | 0 | 1+ | 2+ | 3+ |
| clavicles (pectoralis & deltoids) | 0 | 1+ | 2+ | 3+ |
| shoulders (deltoids) | 0 | 1+ | 2+ | 3+ |
| interosseous muscles | 0 | 1+ | 2+ | 3+ |
| scapula (latissimus dorsi, trapezius, deltoids) | 0 | 1+ | 2+ | 3+ |
| thigh (quadriceps) | 0 | 1+ | 2+ | 3+ |
| calf (gastrocnemius) | 0 | 1+ | 2+ | 3+ |
| Global muscle status rating | 0 | 1+ | 2+ | 3+ |

| Fat Stores | | | | |
|---|---|---|---|---|
| orbital fat pads | 0 | 1+ | 2+ | 3+ |
| triceps skin fold | 0 | 1+ | 2+ | 3+ |
| fat overlying lower ribs | 0 | 1+ | 2+ | 3+ |
| Global fat deficit rating | 0 | 1+ | 2+ | 3+ |
| **Fluid status** | | | | |
| ankle edema | 0 | 1+ | 2+ | 3+ |
| sacral edema | 0 | 1+ | 2+ | 3+ |
| ascites | 0 | 1+ | 2+ | 3+ |
| Global fluid status rating | 0 | 1+ | 2+ | 3+ |

Point score for the physical exam is determined by the overall subjective rating of the total body deficit.

| | | |
|---|---|---|
| No deficit | score = 0 points | |
| Mild deficit | score = 1 point | **Again, muscle deficit/loss takes precedence over fat loss or fluid excess.** |
| Moderate deficit | score = 2 points | |
| Severe deficit | score = 3 points | |

**Numerical Score for Worksheet 4** ☐ **D**

**Total PG-SGA Score** (Total numerical score of A+B+C+D) ☐

Clinician Signature ______________________ RD RN PA MD DO Other ________ Date ____________

Global PG-SGA Category Rating (Stage A, Stage B or Stage C) ☐

**Worksheet 5 – PG-SGA Global Assessment Categories**

| | Stage A | Stage B | Stage C |
|---|---|---|---|
| **Category** | Well-nourished | Moderate/suspected malnutrition | Severely malnourished |
| **Weight** | No weight loss OR recent non-fluid wt gain | ≤ 5% loss in 1 month (≤10% in 6 months) OR Progressive weight loss | > 5% loss in 1 month (>10% in 6 months) OR Progressive weight loss |
| **Nutrient intake** | No deficit OR Significant recent improvement | Definite decrease in intake | Severe deficit in intake |
| **Nutrition Impact Symptoms (NIS)** | None OR significant recent improvement allowing adequate intake | Presence of NIS (Box 3 of PG-SGA) | Presence of NIS (Box 3 of PG-SGA) |
| **Functioning** | No deficit OR Significant recent improvement | Moderate functional deficit OR Recent deterioration | Severe functional deficit OR Recent significant deterioration |
| **Physical Exam** | No deficit OR chronic deficit but with recent clinical improvement | Evidence of mild to moderate loss of muscle mass &/or muscle tone on palpation &/or loss of SQ fat | Obvious signs of malnutrition (e.g., severe loss muscle, fat, possible edema) |

**Nutritional Triage Recommendations:** Additive score is used to define specific nutritional interventions including patient & family education, symptom management including pharmacologic intervention, and appropriate nutrient intervention (food, nutritional supplements, enteral, or parenteral triage).
*First line nutrition intervention includes optimal symptom management.*

**Triage based on PG-SGA point score**

| | |
|---|---|
| 0-1 | No intervention required at this time. Re-assessment on routine and regular basis during treatment. |
| 2-3 | Patient & family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptom survey (Box 3) and lab values as appropriate. |
| 4-8 | Requires intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms (Box 3). |
| ≥ 9 | Indicates a critical need for improved symptom management and/or nutrient intervention options. |

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**Fig. 7.2** Patient-Generated Subjective Global Assessment questionnaire (PG-SGA) additive scores whereas Box 2 – Food Intake and Box 4 – Activities and Function are not additive; the highest point score should be used.

The professional component includes sections covering diagnosis, age, metabolic stress, and physical exam. It also includes a section for scoring of weight loss. Pertinent components of metabolic stress known to either increase energy/protein needs or negatively affect muscle mass and functional status include fever, sepsis, and corticosteroid use. The physical exam component includes subjective assessment of patient fat, muscle, and fluid status and evaluation of degree of deficit with 0 being indicative of no deficit, 1+ indicative of mild deficit, 2+ indicative of moderate deficit, and 3+ indicative of severe deficit.

The Global Assessment, total numerical score, and nutritional triage recommendations follow. The Global Assessment is divided into a grading system where A = well nourished, B = moderately malnourished or suspected malnutrition, and C = severely malnourished. The numerical score is used for development of nutritional triage recommendation. This point score is based on all data gathered from patient to clinician portion of the assessment tool. A score greater than 9 indicates critical need for improved management of nutrition-related symptoms including pharmacologic intervention, nutrition education, and/or nutritional intervention in the form of nutritional supplements or enteral/parenteral intervention. The numerical PG-SGA score and PG-SGA category score are related but serve as independent triage systems. The numerical score provides specific guidelines called Nutritional Triage Recommendations that indicate the level of medical nutrition therapy needed whereas the categorical assessment with A, B, or C rating allows the clinician to have a clear overall picture of the patient's status. Recent data have shown that the PG-SGA has the potential to predict clinical outcomes, including survival rates, postoperative complications, quality of life, and length of stay. Moreover, a recent review demonstrated that the PG-SGA as well as the PG-SGA Short Form (Boxes 1 through 4) encompasses all domains in the current conceptual definitions of malnutrition as proposed by ASPEN (American Society for Parenteral and Enteral Nutrition) and ESPEN (European Society for Clinical Nutrition and Metabolism) [9].

The PG-SGA is available in multiple languages including Portuguese, Danish, Dutch, English, German, Italian, Norwegian, and Thai. The need remains for greater number of high-quality PG-SGA translations as this allows for capture of a wider patient population as well as for international benchmarking [9]. The PG-SGA shows great promise for use in clinical settings, especially in multidisciplinary outpatient clinics where various staff members can be involved in tool distribution and collection of data.

The malnutrition screening tool (MST) is another item used to screen and identify patients who are at risk for malnutrition. It can be used for adults in both the inpatient and outpatient setting, and the two parameters used for nutritional screening are weight loss and reduced appetite. It is a very simple tool to use in that a cutoff score of only two or higher is needed to determine that an individual is at risk, and this score is based off of two questions.

The tool's first prompt asks patients if they have recently lost weight without trying. Answer no is equal to zero points whereas answer unsure or yes is equal to two points. This first question further prompts patients to provide information on the extent of weight loss, that is, greater amount of weight loss is equivalent to a higher point score (0–4 for recent weight loss). Two to 13 pounds is classified as one point, 14–23 pounds is equal to two points, 24–33 pounds equals three points, and 34 pounds or greater represents a maximum of four points. If a patient is unsure exactly how much weight they have lost, this is also a possible answer equal to two points. The final weight loss score is additive based on both the initial question and its prompt.

The second prompt asks if the patient has been eating poorly due to decreased appetite with answer options no and yes and a score of zero to one, respectively. Once this process is complete, the weight loss and appetite scores are added to generate a final MST score that determines risk. A score of zero or one is categorized as not at risk, "eating well with little to no weight loss." An MST score ≥2 is consistent with an at-risk patient, "eating poorly and/or recent weight loss." Recommendation based on this result is formal nutrition assessment and implementation of pertinent nutrition interventions within 24–72 hours depending on the risk. The MST is to be completed within 24 hours of admission and again weekly during same admission. Medical staff, nursing staff, and dietetics staff may all provide and complete the screening tool for patients. Current practices suggest that nursing staff may complete this form as part of an admission personal health history questionnaire, thereby triggering tasks for dietitians who will receive nutrition assessment referrals for any patient with a score of 2 or greater.

As previously mentioned, the malnutrition screening tool's low cutoff score allows for the capture of a large patient pool, reducing the likelihood that malnourished patients are overlooked early in their admission or treatment course. The short format of this screening tool also makes it more realistic for use as a routine inpatient screening tool when compared to the PG-SGA. The fact that it does not require calculations potentially increases compliance of nursing staff with screening practices. A recent study comparing assessment of nutritional status of PG-SGA to the MST at The Royal Marsden Hospital found that the MST had a sensitivity of 66% and a specificity of 83% [10]. However, this tool has been shown to have better sensitivity in the outpatient oncology setting for patients undergoing both radiation and chemotherapy. It was also found to have good sensitivity in older adult residential settings [10].

A possible drawback of this large patient pool and low cutoff score is that dietitians may receive referrals for the wrong reasons despite a fair specificity percentage of 83% (normally nourished patients referred). Patients may misunderstand and respond positively to questions of recent weight loss even though this weight loss may have been purposeful, decreasing available clinician time for those patients who truly do fall into high-risk categories. Moreover, the MSTs short format does not allow for specification between degrees of malnutrition. A score of 2 or higher simply identifies a patient at risk for malnutrition, but further assessment is needed to determine whether the patient is moderately or severely malnourished. The MST could potentially be used to determine which patients require a more extensive nutrition assessment while a form such as the PG-SGA would be appropriate to generate more specific information for treatment [10].

Additional tools that have been utilized for assessment of malnutrition include the Onodera's prognostic nutritional index (O-PNI), which has been shown to predict adverse events associated with radiation therapy in head and neck cancer patients [11].

## Functional Testing

An assessment of overall functional status has been shown to serve as a marker of malnutrition in addition to the other factors discussed earlier. Lower handgrip strength as measured by the handgrip dynamometer has been shown to correlate with higher PG-SGA scores (indicating malnutrition) in adult head and neck and lung cancer patients.

Bioelectrical impedance analysis is a newer method of assessing body composition [12]. It can be used to assess changes in fat and lean mass as well as fluid shifts experienced by patients, particularly in states of acute illness including the perioperative period as well as those brought on by malignancy and during its treatments. This has been well established in the evaluation of GI, lung, and urological cancers and has now been established as an effective tool in the nutritional assessment of head and neck cancer patients. This modality measures body parameters such as resistance, reactance, and fat-free mass index by recording a voltage change in the applied current to soft tissues. While this method does require specialized equipment, it has been shown to document the impact of malnutrition on survival in the head and neck patient population.

## Biomarkers

Biomarkers at all stages of treatment have been popularized recently because they represent an objective indicator for diagnosis, prediction, and response to treatment. Changes in objective predictors of malnutrition such as prealbumin and albumin have not been associated with more frequent adverse events in patients with head and neck cancer undergoing nonsurgical therapy with radiation [11]. Conversely, preoperative hypoalbuminemia (i.e., <3.5 mg/DL) was independently associated with reduced 5-year overall survival, disease-specific survival, and disease-free survival in patients undergoing surgery for head and neck cancer [13]. In one study the risk of poor outcomes was sixfold higher than in patients with normal preoperative albumin [14]. Patients with postoperative complications have a lower preoperative albumin on average than those who do not experience complications [15]. In a study of 233 patients with Stage 3 or 4 head and neck cancer undergoing surgery with free flap reconstruction, postoperative hypoalbuminemia (i.e., <3.5 mg/DL) was independently associated with higher risk of postoperative wound infection [13, 16]. In addition, hypoalbuminemia 2 months after treatment was associated with reduced overall survival, disease-specific survival, and disease-free survival [14].

Micronutrients may impact outcomes as well as studies show that many head and neck cancer patients are deficient [17]. Vitamin D deficiency and insufficiency is common in head and neck cancer patients [18]. Low vitamin D level is associated with increased risk of head and neck cancer, specifically laryngeal and hypopharyngeal subsites, in smokers, and increased rate of recurrence in all patients [19, 20]. In a study of patients undergoing radiation with or without chemotherapy, low vitamin D levels lost twice as much muscle mass than patients with normal levels during treatment [18]. Pre-treatment Vitamin D insufficiency also correlates well with incidence of mucositis [18].

Underlying inflammation that contributes to poor outcomes can be identified in the pre- and perioperative setting with other laboratory studies. In a study of 100 patients undergoing free flap reconstruction for head and neck cancer, postoperative pro-calcitonin, C-reactive protein (CRP), and leukocyte count did not predict poor flap perfusion in the perioperative setting [21]. However, other studies have looked at preoperative CRP and demonstrated a higher risk of complications. Specifically, a preoperative CRP greater than 10 mg/L was associated with greater risk for postoperative complications (odds ratio = 2.01) and was an independent predictor of complications on multivariate regression [15].

CRP and albumin can be combined to calculate a modified Glasgow Prognostic Score (mGPS) [22]. High CRP (>1 mg/dL) and low albumin (<3.5 g/dL) are each a point for a score of 2. High CRP without hypoalbuminemia is a score of 1. Normal CRP and albumin are a score of 0. Patients with an mGPS of 1 or 2 had significantly worse disease-free and overall survival compared to patients with a score of 0 in patients with stage III or IV head and neck cancer [22]. This finding was consistent when even more stringent parameters were used to measure elevated CPR (CPR > 0.3 mg/dL) [23]. mGPS correlated more with 5-year outcomes than tumor or node classification, site, age, or sex [22]. The hazard ratio for high mGPS was 2.4 compared to tumor (T) classification of 1.58 for overall 5-year survival [22]. In patients undergoing concurrent chemoradiation for head and neck cancer, an mGPS of 1 or 2 experienced significantly worse recurrence-free and overall survival compared to patients with an mGPS of 0 with median follow-up time of 39 months [24].

## Enteral Nutrition in Head and Neck Cancer Patients

Enteral nutrition (EN) is a method of feeding that utilizes the gastrointestinal tract to deliver energy and nutrients in a manner which bypasses the oral cavity. Tube feeding refers to liquid food mixture known as formula that delivers macronutrients (protein, carbohydrate, and fats), micronutrients (vitamins and minerals), and free water through a feeding tube into either the stomach or small intestine. A patient may need a feeding tube for several different reasons which result in an inability to maintain volitional intake. Surgery, inability to eat by mouth due to trauma to the head/neck, altered mentation, dysphagia due to stroke, significantly decreased appetite, or respiratory failure that requires mechanical ventilation via endotracheal tube all result in such a scenario. The major advantage of EN over parenteral nutrition is that is maintains the functional integrity of the GI tract. Therefore, candidates for EN support include individuals with functional GI tract whose disease makes oral intake inadequate, impossible, or unsafe due to risk of aspiration. For individuals who cannot maintain volitional intake and who do not have a functional GI tract (i.e., short bowel syndrome, bowel obstruction, intractable vomiting or diarrhea, GI fistula), parenteral nutrition (PN) is used as it bypasses the normal digestive process. PN is intravenous administration of nutrition including protein, carbohydrates, fats, vitamins, minerals, and electrolytes. Compared to EN, it does not preserve the gut's functional integrity, it is more expensive, and is associated with greater infectious complications.

According to the 2002 "Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients," nutrition support should be initiated in patients with inadequate oral intake for a time period of 7–14 days or in patients where inadequate oral intake is expected for 7–14 days [25]. EN is also indicated in the malnourished patient who is expected to be unable to eat for greater than 5–7 days. In the critically ill patient population, early enteral feeding is recommended; this is defined as initiation within 24–48 hours of ICU admission [26]. Early EN in this patient population is associated with more rapid weaning from mechanical ventilation, improved wound healing, decreased length of stay, and reduced complications overall [26]. ASPEN guidelines state that the previously mentioned clinical benefits from EN are derived through achievement of 50–65% of calorie goal during the first week of hospital admission. Although a universal definition for effective delivery of EN has not been established, it is reasonable to define this as an infusion of >90% estimated energy needs [27].

The choice of route of enteral access is based on several different factors including disease, gastrointestinal function, and estimated duration of nutrition support. Options for short-term placement (<4 weeks) include feeding tube placement through the nose or mouth into the stomach or post-pyloric placement into the small bowel (nasogastric tube, orogastric tube, nasoenteric tube). Nasogastric tubes are less invasive but are only used if the estimated time frame of need is <1 month as these feeding tubes are smaller in diameter and more likely to malfunction. They are also susceptible to accidental displacement.

When nutritional support is estimated to last for a period of greater than 4–6 weeks, gastrostomy, gastrojejunostomy, or jejunostomy feeding tubes are utilized. There are also several delivery methods for enteral nutrition that are appropriate for a variety of clinical situations. Tube feeds may be administered either via continuous or cyclical infusion, intermittent drip, or bolus method. Disease status and comorbidities, location of feeding tube tip, and expected tolerance are all factors to consider when determining best delivery method for a patient. Location of care will also play a role in determining delivery method (i.e., critical care unit, ambulatory patient in home setting, etc.). A single method or a combination of methods may be employed.

Continuous infusion via pump (also known as around-the-clock) is the preferred delivery method for patients who are critically ill, intubated, at risk for developing refeeding syndrome, are being fed through a jejunostomy tube (due to lack of stomach reservoir capacity), or those who are unable to tolerate larger formula volumes as seen with bolus or intermittent gravity drip. Cyclic feeding is similar to continuous infusion in that feedings are provided via a pump, but this is delivered in less than a 24-hour period. They are often used at night, for example, for an 8–12 hour timeframe, to provide supplemental nutrition while a patient is asleep.

Intermittent feedings can either be delivered via pump or gravity drip; in this method of feeding enteral nutrition is administered over a period of 20–60 minutes every 3–6 hours. Bolus or gravity drip feedings are similar to meals; they provide a set formula volume at specific time intervals (i.e., three times a day) throughout the day. They are frequently delivered over a short time period (i.e., 240 mL formula administered over a 10 minute period three to six times a day). The advantages of the bolus delivery method are many: they are more physiologic, they are less expensive as no pump is required, and they allow for greater mobility [28]. Outpatients often prefer this modality for home, and it is important to establish tolerance to this feeding method prior to discharge when possible [28].

## Estimating Nutritional Needs

When estimating nutritional needs for patients on EN, many factors are considered such as extent of surgery, disease stage, presence of comorbidities, age, gender, and level of physical activity. General guidelines for "normal" weight patients estimate 25–30 calories per kilogram actual body weight per day and 1.0–1.5 g pro/kg [29]. The needs of a hypermetabolic or malnourished patient, as seen in high tumor burden or poor oral intake, may increase up to 30–35 calories per kilogram per day and 1.5–2.5 g pro/kg/day [29]. The severely malnourished patient at risk of refeeding syndrome generally receives supplementation at 15 calories per kilogram with gradual advancement to full-calorie goal over the following days of hospital admission.

Adjustments to EN may be appropriate over the treatment course. In the setting of poor wound healing, lack of expected weight gain, or unintentional weight loss, EN needs may be re-estimated and increased. While the enteral formula chosen will depend on the factors previously mentioned, standard polymeric formulas of 1.5 calories per milliliter are generally well-tolerated and frequently used. In the postoperative setting, extensive resections may require specialized higher protein formulas for wound healing or standard formulas with high protein modulars (protein powder or liquid protein supplements). Patients with very high calorie needs or those with complaints of early satiety or GI fullness may use 2 calories per milliliter formula for high calorie provision with less volume.

## Perioperative Nutrition

Preoperative nutrition recommendations state that patients with severe nutritional risk should receive appropriate nutrition support for at least 10 days before surgery for improved outcomes even if this means delay of surgery [30].

Weight loss greater than 10% before surgery is associated with increased complications [12]. The peri- and postoperative period represents a critical time period for intervention to improve outcomes. Early postoperative tube feeding defined as within 24 hours is indicated for patients whose surgical excisions make them unable to resume early oral nutrition. High-dose protein and energy provision (30–35 calories per kilogram body weight) are generally appropriate for this population save for special cases such as reduced renal function, etc. The ESPEN Guidelines on Nutrition in Cancer Patients state that optimal nitrogen supply ranges for repletion, and postoperative wound healing ranges between a minimum of 1 g pro/kg of body weight and a target range of 1.2–2.0 g/kg/day to induce protein anabolism. Recommendations for patients with acute or chronic renal failure state that protein provision should not go higher than 1.0–1.2 g pro/kg/day.

## Immunonutrition

Immunonutrition is defined as the potential to modulate the activity of the immune system by interventions with specific nutrients. In this practice, specific nutrient compositions are utilized to modify body inflammatory and immune responses. It is of most interest in the context of critically ill and surgical patients as both of these patient populations tend to have suppressed immune systems and need alternate means of nutrition support through EN or PN. Many enteral nutrition formulas already are made with some combination of these potentially immune-modulating ingredients.

Head and neck cancer patients often are malnourished at the time of diagnosis, and the postoperative period tends to be followed by a period of immunocompromise and immune suppression that results in increased risk of morbidity and mortality. Surgery induces catabolic stress to the body, which stimulates inflammation, depletes nutrient reserves, and thereby impairs the body's normal immune response, increasing the risk for complications after surgery. The rationale of immunonutrition is that using dietary compounds associated with improved immune function during this time frame will reduce negative surgical outcomes such as infection and poor wound healing. Immune-enhanced enteral nutrition formulas that provide basic macronutrients and micronutrients also contain amino acids arginine and glutamine, lipids, that is, omega-3-fatty acids, vitamin E, prebiotics and probiotics, and ribonucleic acids.

At this time, there are no strong evidence-based recommendations or formulas for enteral based immunonutrition [31]. This is attributed to the high degree of variation in ingredients and concentrations by current manufacturers, thereby making it difficult to isolate which of the ingredients mentioned is responsible for the improved immune status and surgical recovery; it is likely that not one single ingredient is responsible but rather the synergistic effect of more than one. The amino acid arginine is a precursor to polyamines and proline, which play important roles in tissue regeneration and wound healing. Omega 3 fatty acids have been associated with attenuation of the inflammatory response.

Strategies and products to deploy immunonutrition remain in their nascent stages without long-term data. The main approach for preoperative nutrition optimization remains the use of standard oral supplements such as Ensure® or Boost®. The standard oral supplements tend to be more accessible for patients due to lower price point and improved taste, thereby resulting in higher rates of compliance among patients. Recent review of the literature found no statistical differences from the standard oral supplement to the immunonutrition supplements. Other studies have shown a trend towards shorter hospital stay and lower infection rates with the use of preoperative immunonutrition. Further research with a larger series must be conducted to clarify better guidelines and recommendations for optimal preoperative nutrition paradigms.

## Other Factors That Contribute to Malnutrition in Head and Neck Cancer Patients

Chemoradiation (CRT) in the treatment of head and neck cancers has known adverse side effects that drastically disturb the patient's nutritional status [32]. Nausea, mucositis, dysphagia, dysgeusia, xerostomia, and thickened saliva are common side effects seen during and after treatment that affect the functional ability to swallow and limit the patient's desire to eat [29]. Over half of the patients were unable to maintain sufficient oral intake during treatment and required enteral feedings. Even for the patients maintaining nutrition completely by mouth, many required supportive care with meals including special preparation or consistency precautions [33].

Mucositis in head and neck cancer patients receiving CRT occurs most often in the oral cavity and/or the pharynx. The Common Terminology Criteria for Adverse Events (CTCAE version 4) rates mucositis from grade 1 with mild symptoms and minimal pain related to inflammation to grade 5 or death. A large percentage of patients will experience some degree of mucositis during treatment. Even grade 1 or 2 can be debilitating to obtaining proper nutrition, especially when compounded with any of the other common side effects. Grade 3 mucositis, which is defined as inflammation and ulceration leading to severe pain interfering with oral intake, is reported to occur in 21–80% of patients [33]. During the seventh and final week of CRT, over half of the patients with oral or pharyngeal mucositis need supportive care with meals through speech pathology or enteral feeding. Of note, patients with T3 or T4 tumors have four times the incidence of grade 3 mucositis than those with T2 tumors [33].

These toxicities typically manifest around week 2 of CRT and peak at week 7, the final week of treatment. Less than a quarter of patients tolerated a full diet by mouth at week 7 [33]. Functional improvement gradually occurs following the final week of treatment. However, over 75% of patients report experiencing dysgeusia 12 weeks post-treatment. A third of these patients have an altered diet secondary to dysgeusia [33]. Dysgeusia is the abnormal taste of food, which can be affected by decreased smell (CTCAE v4). Patients complain of altered taste, unpleasant tastes, or even a loss of taste. The impact of this toxicity on nutrition is profound. Over 95% of head and neck cancer patients receiving CRT experience diet-altering dysgeusia [33]. Symptoms last long after treatment is over, affecting nutrition months following chemoradiation.

Taste can be affected by saliva production because chemical signals cannot reach receptors [34]. Taste and smell can be impacted by smoking, older age, and medications, particularly cyclophosphamide, folic acid antagonists, methotrexate, and platinum agents [34]. Up to 70% of patients with cancer have alterations in taste and smell [34]. The University of Pennsylvania Smell Identification Test can be used to objectively detect smell [34]. Physicians underestimate taste and smell changes in patients undergoing oncologic treatment [34]. Patients frequently describe smell alterations as “rancid” and taste alterations as “bitter, chemical, and nauseating” [34]. Increased or decreased taste and smell sensation are associated with certain chemotherapies and radiation treatments as little as 15–30 Gy and can lead to food aversion [34].

## Prophylactic PEG Tube Placement

Patients with head and neck cancer often require tube feeding due to issues with maintenance of oral intake. Treatment modalities including chemotherapy, radiation, and surgery often exacerbate these issues with side effects including dysphagia, mucositis, stomatitis, nausea, and altered taste. The establishment of a steady source of nutrition that bypasses the oral cavity helps improve functional and nutritional status as well as patient tolerance to treatment. Head and neck cancer patients generally have normal GI function and are candidates for EN.

Prophylactic PEG tube placement prior to initiation of chemotherapy or radiation is likely to lead to reduced incidence of protein-calorie malnutrition [35]. PEG or other gastrostomy tubes are most often used in this population, and post-pyloric feeding tubes are usually only employed in the case of intolerance to gastric feeds. A number of factors have been associated with need for enteral nutrition during radiation treatment including nodal disease, bilateral neck radiation, age, and regional or free flap reconstruction [36].

Caution must be exercised when utilizing EN during treatment to avoid enteral dependence without active effort of swallowing. Patients who are noncompliant with speech and swallow rehabilitation exercises or those with advanced-stage disease are at particular risk as avoidance of activation of the pharyngeal constrictors can worsen atrophy and scarring and lead to a higher likelihood of long-term feeding tube dependence [29]. Furthermore, esophageal stricture may contribute to dysphagia and PEG tube reliance for years after treatment is finished [29].

## Cachexia

Cachexia is a multisystem condition primarily characterized by loss of skeletal muscle mass that may not improve with nutritional support that affects 30% of patients with head and neck cancer at the time of treatment [37]. Cancer cachexia is associated with poorer outcomes, poorer response to treatment, and poor quality of life after diagnosis in head and neck cancer patients [38]. A consensus group defined cancer cachexia as >5% weight loss over 6 months, or >2% weight loss and either body mass index (BMI) <20 kg/m$^2$ or evidence of sarcopenia [39]. As such it remains a clinical diagnosis; however, certain tests can provide an indication as to whether a patient is cachectic.

A cardinal feature of cancer cachexia is muscle wasting. Decreased skeletal muscle fiber size and protein expression in animals with cancer cachexia compared to those without cancer cachexia has been consistently demonstrated [40–42]. Skeletal muscle index can quantify presence of muscle wasting in patients with cancer based on calculations previously described on abdominal computed tomography (CT) imaging of the lumbar spine area [37, 43, 44].

Underlying systemic inflammation is another marker of cancer cachexia. Elevated inflammatory markers in tissue in mice have been demonstrated with cancer cachexia [45]. However, systemic inflammation has not been studied extensively in patients with head and neck cancer and cancer cachexia compared to those without cancer cachexia. However, a recent study demonstrated that the Glasgow Prognostic Score, calculated from albumin and C-reactive protein, correlated with outcomes in head and neck cancer patients with cachexia [22]. In addition, a particular genotype (TNF-α −1031 T/C) associated with the TNF-alpha cytokine may be more frequently found in patients with cachexia [46].

Several treatments are currently undergoing testing in clinical trials, but currently there are no drugs approved for the treatment of cachexia by the Federal Drug Administration [47].

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# Chapter 8
# The Impact of Pain

**Aurora Mirabile**

Head and neck cancer is diagnosed in about 650,000 patients worldwide each year (about 6% of all cancer in the global population) [1]. A diagnosis of head and neck cancer can be physically and emotionally debilitating. The pathology and its treatment can affect the individual's vital and social function (e.g., breathing, eating and speech) with serious effects on psychological and psychosocial life. In fact, given the site of the appearance of the head and neck, the visibility of the disease, and treatment sequelae, head and neck cancer is one of the most psychologically traumatic cancers [2, 3] and one of the worst diseases in terms of physical dysfunction, related distress limit, or disrupt daily behaviors and social activities [4].

Patients adapt to their conditions differently: sometimes requiring little psychological support but other times developing depression and anxiety at varying degrees of severity and becoming socially isolated. The experience of psychological distress, particularly depression (including every step from subclinical depressive symptomatology until clinical depressive disorder), is quite common among cancer patients and may occur throughout the course of illness, often persisting months beyond the conclusion of treatment in cancer survivors [5, 6].

Nevertheless, depression in head and neck cancer patients has been estimated to be more prevalent than in other types of cancer [5], involving at every degree approximately 15–50% of head and neck cancer patients and affecting immunocompetence, treatment adherence, self-care behaviors, socialization, and quality of life [7–9]. Unfortunately, often, depression and other psychological distress go unreported in clinical trials [10].

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## Pain in Patients with Head and Neck Cancer

Pain is one of the most debilitating symptoms of head and neck cancers, and it is present not only during or after treatment but also at the beginning, as one of the first symptoms of the disease presentation, and sometimes could be a signal of recurrence. In fact, at least half of head and neck cancer patients experience moderate to severe pain and almost all experience some degree of pain at presentation and/or during treatment and at the end [11].

Treatment for head and neck cancer is complex and, often, hard to deal with. Patients may undergo surgery, radiation therapy, chemotherapy, or combinations. These treatments are associated with a range of side effects including difficulties with essential functioning such as eating, swallowing, breathing, and speech as well as taste alterations (dysgeusia), hyposalivation (xerostomia), residual pain, and facial disfigurement [12, 13].

All these discomforts confer marked disability, so that almost half of the patients are unable to go back to work for a long time after treatment cessation [14, 15] and sometimes discontinued employment definitively [16, 17].

The evidences suggest that the use of concurrent chemoradiation improves survival rate and locoregional control but at the cost of increasing toxicities, in particular, the severity and the mean incidence of inflammation of oral mucosa (mucositis) and of pain as a result [18].

Nevertheless, the top patients' priority is being cured and living as long as possible with analgesia [19]. On the contrary, only a minority of the reports consider specifically pain due to the oncological management and pharmacological strategy to address it, and treatment outcome is the most reported endpoint in the available studies based on head and neck cancer patients.

Mucositis has a mean incidence of about 90% and may become severe and painful enough to prevent patients from speaking, eating, drinking, or swallowing, leading to poor quality of life and to a higher risk of psychological distress.

Multiple mechanisms are involved as the sequential interactions of all cell and tissue types, and various physiological elements (e.g., tissue factors and cytokines) of the oral mucosa.

It primarily affects the non-keratinized tissues, such as the soft palate, the pharynx, the floor of the mouth, and the lateral borders of the tongue.

Ulcerations and mucosal infections cause pain severe enough to reduce treatment compliance and its efficacy and, consequently, increase [18, 20] disease recurrence and mortality rate [21, 22].

The analgesic strategies employed for oral mucositis pain treatment vary from local to systemic therapies with different mechanisms of action such as opiates, anti-inflammatory drugs, and anticonvulsants employed to manage neuropathic pain [23–25].

There is insufficient evidence from randomized clinical trials to advice on an optimal intervention specifically for head and neck cancer pain. A few studies regard the management of pain on posttreatment adjustment and quality of life but none to address this issue in head and neck cancer patients. MASCC/ISOO Guidelines recommend patient-controlled analgesia with morphine as the treatment of choice for oral mucositis pain [26]. However, despite individualized approaches, pain control is still often not satisfactory both for the patient and health provider in this care setting, in particular, during swallowing [24, 27].

This is the reason why, during chemoradiation, the consequences of suboptimal pain control could affect dysphagia, malnourishment, treatment acceptance, and compliance, ultimately influencing chemotherapy dose intensity or radiotherapy treatment (RT) continuity.

In fact, high incidence of painful swallowing due to mucositis is also associated with reduction of food and liquid intake, worsening of nutritional status, dehydration, renal insufficiency, need for enteral nutrition or intravenous hydration, reduced compliance with cancer treatment, increase of hospital admissions and unscheduled visits, and long-term dysphagia.

Consequently, acute pain mainly due to oral mucositis, to the neck skin inflammation (dermatitis) in the radiation field, and to radiation-induced fibrosis (e.g., costoclavicular or temporomandibular joint disorder, trismus, and neuropathic pain) dramatically impair quality of life and possibly reduce the chances of cure, hesitating in a lower dose intensity of systemic therapy or in radiation treatment breaks [28].

Thirty-nine studies carried out in head and neck cancer patients showed that pain is present in 50% of patients at the diagnosis, 81% during treatment, and 70% after the oncological treatment (Fig. 8.1). In 30% of the patients, the severity of pain during treatment was higher than during the pretreatment period.

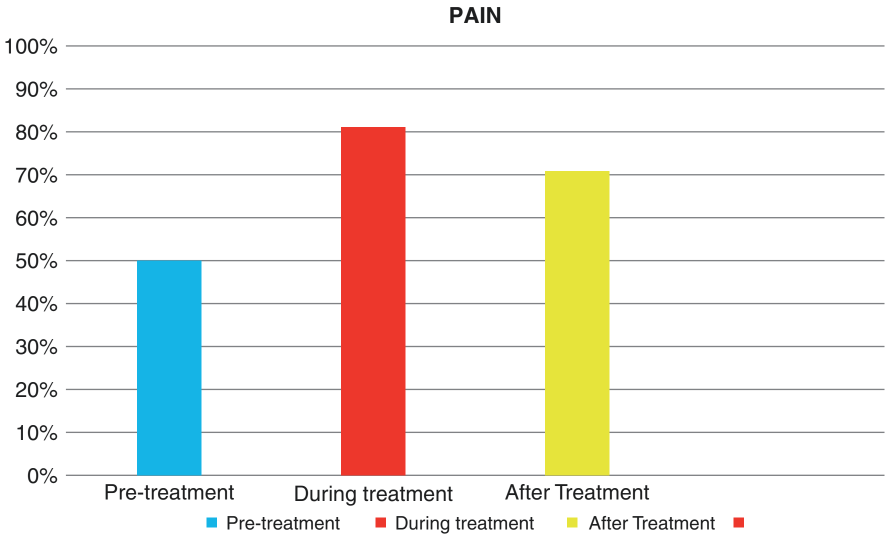

**Fig. 8.1** Percentage of head and neck cancer patients who experienced pain divided in the two periods of treatments

Patients report that mucositis is the most debilitating side effect of their head and neck cancer therapy [29] and, especially, of combining radiation and chemotherapy. Severe acute effects on the mucosa can also result in consequential effects that can chronically impair organ function. Putative risk factors for mucosal sensitivity include aggressive chemoradiation regimens, xerostomia, and active cigarette smoking. Hot, spicy, and acidic food/liquids and dry air can enhance oral pain.

Moreover, mucosal pain may be caused or exacerbated by oral infections; hence, a careful oral exam to rule out infection and to treat it in an easier way is suggested. In fact, basic oral care reduces the frequency and severity of oral mucositis and its associated pain. Pain correlates also with radiation treatment fields, dose, and fractioning. Concomitant chemotherapy or cetuximab results in increased frequency, severity, and duration of mucositis pain.

When making treatment plans, patients' general conditions and their capability to tolerate severe oral pain and high doses of opioids need to be considered. In fact, patients' frailties, age, or severe comorbidities may lead to poor tolerance, considering that the highest peak of RT pain is during the fifth week, and it may not improve earlier than 2–4 weeks after RT, healing in about 2 months [30].

To understand the impact of RT regimens on overall patient well-being, in 2004, Rose-Ped A. et al. [31] interviewed 33 patients who had received RT for head and neck cancer in order to characterize the effects or consequences of RT from the patients' perspectives.

Patients had particularly troublesome or debilitating painful sore throat (20%), followed by mouth sores/pain (18%), and dry mouth (14%) (Fig. 8.2), which cause significant discomfort but most of all serious difficulty to eat, drink, or swallow.

Nearly all patients (90%) reported experiencing dysgeusia, including complete loss of taste (54%), distorted taste (33%), or reduced taste (13%) and about 70% of

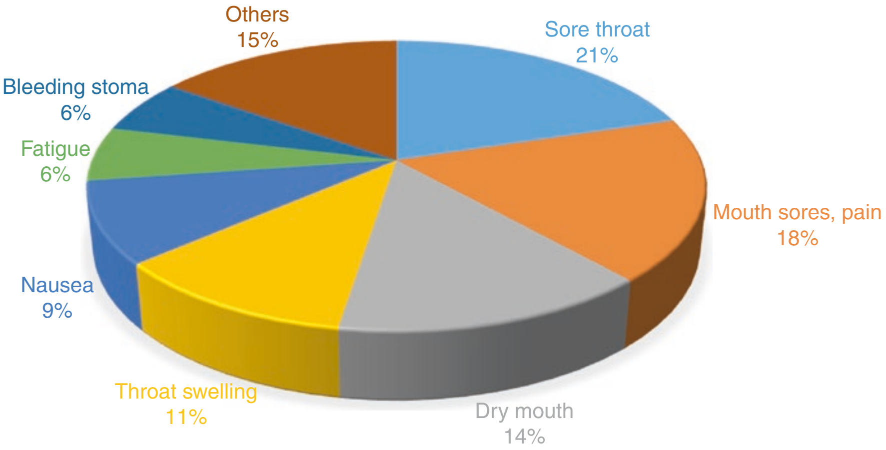

**Fig. 8.2** Single most debilitating side effects

patients reported mouth sores, dry mouth, pain, and irritation too. Hundred percent of oral cavity cancer patients and 86% of pharyngeal cancer patients reported changes in their mouths.

Patients reported that oropharyngeal mucositis developed within approximately 2.5 weeks (range 1–8 weeks) after the start of RT with a healing time ranging from 2 to 24 weeks (mean 8.7 weeks) after completion of RT. Nearly all (92%) patients received supportive care with opioid analgesics, mouthwashes or rinses, and nutritional supplements.

Good oral hygiene and analgesics are the approaches most commonly used to prevent and treat the symptoms associated with oropharyngeal mucositis.

Although optimal management strategies for RT-induced mucositis and its associated complications have not been identified yet, standard oral care protocols are used to prevent or minimize mucositis [31].

Nevertheless, a large number (88%) could not eat or drink or did so with extreme difficulty and reported a significant weight loss (83%), (between 12 and 79 pounds, mean 29 pounds), leading to gastric tube implantation for 29% of patients. Oral pain worsened during the course of RT and persisted after the end of treatments, periods that patients described as the worst part of treatment experiences.

Another study published in 2001 explored the quality of life in 58 head and neck cancer patients during and after radiation treatment. They collected data of physical, emotional, functional, and social aspects at the first week of treatment, at the last week of treatment, and 1 month after treatment with two validated questionnaires: Functional Assessment of Cancer Therapy: Head and Neck (FACT-H&N), a subscale that assesses social and emotional well-being, and the Hospital Anxiety and Depression Scale (HADS).

Results indicated overall increased levels of physical and functional symptoms, head and neck specific concerns, and depression between the first and the last week. However, except for depression, there was some improvement between the last week of treatment and 1 month after although this improvement was not to the pretreatment level. FACT and HADS did not show significant changes across time, suggesting the need of interventions to assist patients when they have completed the radiation treatment course and the need of improvement assessment in some areas of emotional distress [32].

In 2010, Cheng et al. [33] analyzed the incidence of severe oral mucositis associated with cancer therapy, underlining patients' self-reported moderate and severe oral symptoms and quality of life modifications.

This study revealed that patients with severe oral mucositis also suffer from pain and chewing/swallowing difficulties reported as the worst oral functional problems, leading to decreased intake and nutritional deficiencies.

Nevertheless, surprisingly the severity of oral mucositis did not seem to be a significant predictor of oral dysfunction while throat pain was the strongest predictor of chewing, swallowing, and speaking difficulties, suggesting that individuals at increased risk of throat pain were exposed to oral functional impairment.

Pain in the oropharyngeal junction and throat is the most symptomatic and difficult problem to deal with. It may reflect activation of nociceptive receptors at the site of oral mucosal injury to compromise the muscular movement which makes chewing and swallowing difficult and unpleasant.

Early diagnosis and treatment of mucositis as well as an adequate and timely analgesic approach continues to be mandatory to the management of oncological treatments side effects, but even if most of the patients used analgesics and despite the wide use of opioids, pain control continued to be an unmet need. This confirms that oral mucositis need a multidisciplinary approach since it includes sensory and affective dimensions of pain experience [34] as well as a neuropathic component [35].

Moreover, the significant impairment of quality of life resulted from a complex interaction of the extent of oral mucosal injury, the patients' perceptions of pain, and the altered oral functional capacity as confirmed by the literature data in patients who are not being no longer able to eat and enjoy food [36–38].

Therefore, the prevention or reduction of intensity and duration of oral mucositis is important to permit the administration of the full dosage of cancer treatment and, thereby, potentiate the curative or control intent of treatment.

## Mucositis-Induced Pain Management

Currently, mucositis-induced pain management includes the use of topical anesthetics and systemic analgesics even if systemic administration of opioids may be complicated by well-known side effects (e.g., nausea, vomiting, mental clouding, constipation, sedation, and tolerance) which could worsen quality of life.

In head and neck cancer patients, pain due to mucositis may also present as incidental breakthrough pain (BTP), a transitory exacerbation of pain that occurs against a background of stable pain otherwise adequately controlled by opioid therapy with a prevalence of 48% (average of 3.85 episodes per day) [39].

In about a half of head and neck cancer patients, pain is incident, a quarter is spontaneous or due to end of dose failure, while in 5% of the cases the nature of pain could be unknown or mixed (Fig. 8.3). Actually, the majority of pain episodes was associated with some precipitating factor [39].

In this setting, it may arise in response to a predictable stimulus or associated to a precipitating factor (48%) such as swallowing, or it may be related to a specific predictable trigger as incident predictable pain [39, 40] (IP-BTP).

Odynophagia (painful dysphagia or pain with swallowing) due to mucositis can be categorized as incidental and predictable and should be considered as breakthrough pain to be treated with appropriate breakthrough medication dosing.

Preventive administrations of breakthrough pain medication half hour before eating may improve swallow function. Transmucosal intranasal route administration of fentanyl in this setting was judged as the most effective way of administration of analgesics since oral transmucosal administration could be difficult

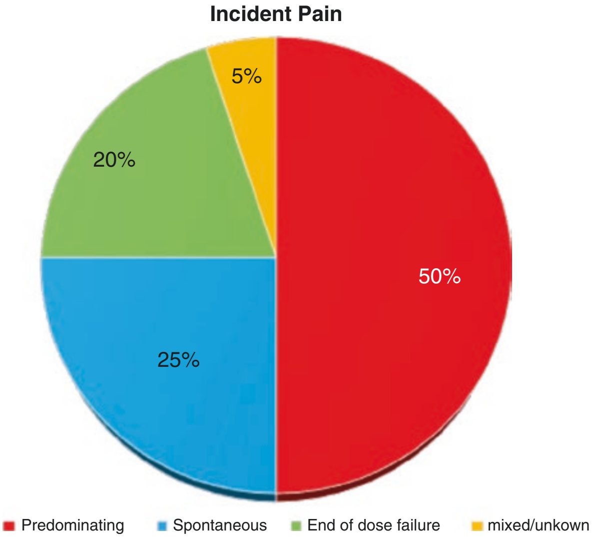

**Fig. 8.3** Different types of incident pain

because of sticky saliva, xerostomia, or oral ulcerations, and irradiated mucosa may have a different absorption of BTP.

There is no standardized treatment protocol for treatment of pain due to mucositis in head and neck cancer with a lack of consensus about the class of drugs, kind of administration, pharmaceutical forms, and side effects of this therapy [24].

Bossi et al. published an experience concerning the feasibility and the activity of fentanyl pectin nasal spray (FPNS) against incidental feeding BTP due to chemoradiation-induced oral and oropharyngeal mucositis in HNC patients [33], showing good activity and acceptable safety of FPNS when administered during concurrent chemoradiation.

This clinical study evidenced the feasibility and the activity of FPNS against incidental feeding BTP due to chemoradiation-induced oral and oropharyngeal mucositis in head and neck cancer patients. The reduction of BTP allows the improvement of swallowing and, potentially, the reduction of a series of mucositis consequences included psychological ones.

Adequate pain control may substantially enhance swallow effort during and after the radiation, minimizing disuse atrophy and fibrosis and optimizing long-term swallow function [41].

Treatment of painful mucositis may benefit also from opioid-based systemic drugs. In fact, an adequate pain regimen should include a fixed and breakthrough medication with an appropriate dose and schedule.

Recent studies have demonstrated that head and neck cancer patients develop neuropathic besides nociceptive pain during their radiotherapy course, suggesting the need to treat both types of pain [42]. Moreover, patients may also experience long-term spontaneous or evoked pain due to epithelial atrophy, neurologic sensitization, and/or neuropathy also due to a chronical recurrent/metastatic disease. Nevertheless, pain could be also expression of a disease recurrence or metastatization.

In fact, neuropathic pain could be also caused by tumor infiltration or due to paraneoplastic or treatment-induced polyneuropathy, and it may be adequately controlled by opioids added to adjuvant drugs [43] because neuropathic pain sometimes poorly responds to narcotics alone [44–47]. Even if high doses of gabapentin have been reported to reduce the need for high total dose of opioids, neuropathic pain control remains a critical item with very frequent failures.

Amitriptyline and gabapentin have been effectively used to treat multiple neuropathic pain syndromes, but only limited data are available in head and neck cancer patient's pain [47–53]. Opiates and gabapentin are believed to interact favorably through a simultaneous decrease in hyperexcitation and increased inhibition of nociception [54, 55]. This effect enhances morphine efficacy and relieves neuropathic pain [54, 56] with a beneficial effect on daily activity, mood, sleep, and quality of life [49, 56]. These data suggest the possibility of satisfactory results, avoiding opioids dose escalations, and reducing the risk of associated adverse side effects, but randomized clinical trials are needed to establish the role of this analgesic combination in this group of cancer patients.

In conclusion, there is a clear need for multidimensional and multidisciplinary pain management algorithms to reduce pain severity and to better manage these symptoms as well as the consequent discomfort (Fig. 8.4) involving palliativists, nurses, physiotherapists, logopedists, and psychologists into patients' care.

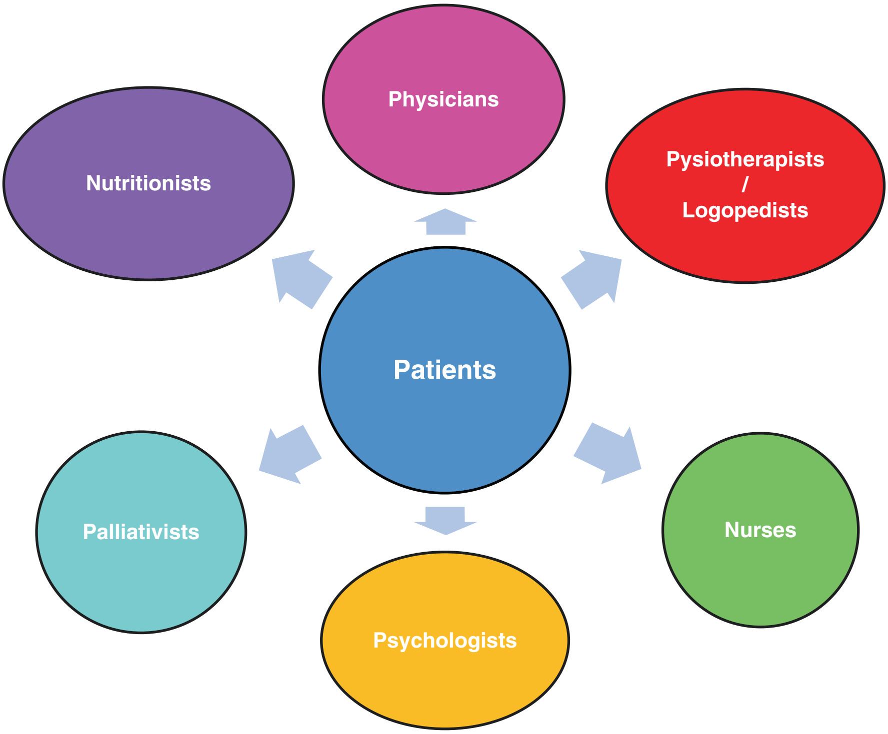

**Fig. 8.4** The multidisciplinary approach to physical and psychological distress of head and neck cancer patients

For this reason, it could be necessary not only to standardize clinical management and treatment according to international guidelines but also to preview psychological support and initiatives to help patients to preserve their quality of life and psychological well-being.

Further research including larger studies with more comprehensive evaluations of pain, quality of life, and psychological distress in head and neck cancer patients is required as an important outcome measure in the evaluation of new preventive and curative interventions to alleviate suffering and to improve the quality of pain and nutritional management.

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# Chapter 9
# Considerations in Advanced and Recurrent Head and Neck Cancer

**Nikhita Jain**

Advanced and recurrent head and neck malignancies contribute to significant mortality and morbidity for patients. Due to difficulty in physical examination, cancers in the oral cavity, oropharynx, and larynx often go undetected in their earlier stages. For this reason, head and neck cancer patients may present with more advanced disease than other cancer patients. As a result, the disease process and its aggressive treatment modalities can impact several aspects of a patient's quality of life.

According to the World Health Organization, health-related quality of life (HR-QOL) encompasses an "individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychosocial state, level of independence, social relationships, and their relationship to salient features of environment" [1]. In simplified terms, HR-QOL can be defined as the multidimensional impact an illness and its treatment have on a patient's perception of his or her physical, psychosocial, and functional capabilities. This chapter will delve into how advanced and recurrent head and neck cancer (HNC) can influence these domains of a patient's life.

## Tools to Measure Quality of Life in Head and Neck Cancer

Assessment of quality of life is challenging in that there are several dimensions influencing a patient's life. Quality of life is largely dependent on a patient's perception of their functional, physical, and psychosocial status before diagnosis and treat-

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ment. Several validated instruments exist to help standardize our understanding of the impact that HNC and its treatment options have on HR-QOL (Table 9.1). These tools can be categorized into five distinct groups [2]:

1. Generalized: identifying the effects that any disease, both chronic and acute, can have on quality of life
2. Disease-specific: describing the impacts of cancer and the perception of cancer on quality of life

**Table 9.1** Quality of life instruments in HNC

| Instrument category | QOL instrument | Brief description |
|---|---|---|
| Generalized | EuroQOL Five Dimensions Questionnaire (EQ-5D) [3] | Questionnaire incorporating five domains – physical, social, mental, symptoms, and health state thermometer |
| | Medical Outcomes Study (MOS) Short Form – 36 (SF 36) [4] | General health questionnaire assessing QOL over the past 4 weeks; eight domains |
| | Sickness Impact Profile (SIP) [5] | Focused on chronic illness; questionnaire addresses psychosocial and physical domain |
| Disease-specific | EORTC Quality of Life Questionnaire (QLQ-C30) [6] | Focused on cancer patients, with domains including overall health, functional status, and symptom impacts |
| | Functional Assessment of Cancer Therapy-General (FACT-G) [7] | Designated for cancer patients; includes four domains – family, physical, emotional, and functional well-being in the past week |
| Site-specific | University of Washington QOL Questionnaire (UWQOL) [8] | Questionnaire specific to head and neck cancer patients with focus on functional status, symptom impact, and overall health. Psychologic domains are also included |
| | EORTC-Head and Neck Quality of Life Questionnaire [9] | Subset of EORTC for head and neck cancer patients, exploring seven domains of QOL, time frame is 1 week |
| | FACT-Head and Neck [10] | Questionnaire assessing how HNC impacts pt's family, physical, emotional, and functional well-being in the past week |
| | MD Anderson Symptom Inventory-Head and Neck (MDASI-HN) [11] | Questionnaire for HNC patients, addressing symptom severity, symptom interference, and treatment-related impacts on QOL |
| | Vanderbilt Head and Neck Symptom Survey (VHNSS) [12] | Detailed questionnaire focusing on how a variety of symptoms impact quality of life in the past week |
| Treatment-specific | UWQOL for surgical patients | UWQOL with additional questions specific to surgical treatment options |
| | Head and Neck Radiotherapy Questionnaire (HNRQ) [13] | Questionnaire focused on symptoms and disabling factors associated with radiation therapy |
| | Quality of Life Radiation Therapy Instrument Head and Neck Module (QOL-RTI/H&N) [14] | Quality of life questionnaire about radiation therapy and its impact on specific assessments like mucous, saliva, taste, cough, and local pain |

**Table 9.1** (continued)

| Instrument category | QOL instrument | Brief description |
|---|---|---|
| Symptom-specific | Liverpool Oral Rehabilitation Questionnaire [15] | QOL questionnaire focusing on oral function and denture satisfaction |
| | Voice-related QOL (V-RQOL) [16] | Questionnaire describing communication-related difficulties associated with compromised voice and/or laryngeal structures |
| | MD Anderson Dysphagia Inventory (MDADI) [17] | Questionnaire includes global, emotional, functional, and physical subscales to describe QOL impacts of dysphagia in HNC patients |
| | Xerostomia Questionnaire (XQ and XQOL) [18] | Questionnaire assessing the physical functioning, psychologic functioning, social functioning, and pain/discomfort in patients with dry mouth |
| | Shoulder Pain and Disability Index (SPADI) [19] | Questionnaire focuses on two domains: pain and disability related to shoulder pathology |

3. Site-specific: evaluating how head and neck cancer influences quality of life
4. Treatment-specific: examining how interventions for HNC affect quality of life
5. Symptom-specific: assessing how specific sequelae of HNC impact quality of life

Together, these instruments seek to measure the various elements of HR-QOL. Given the wide variety of validated questionnaires, a major pitfall of quality of life-driven research is the lack of a “gold standard” tool. Additionally, depending on primary tumor site and stage, patients with HNC can experience a range of different symptoms impacting quality of life. No QOL instrument effectively accounts for such variation. Even treatment-specific or symptom-specific tools will reflect variation in response based on intervention itself. For example, patients who undergo free flap reconstruction may perceive questions on a UWQOL Surgery survey differently than those who undergo local reconstruction. Finally, when studying HR-QOL among patients, it is challenging to account for differences in baseline quality of life. Patients with HNC may have several comorbidities that are largely unrelated to their tumor. Therefore, when choosing a QOL instrument, it is critical that clinicians define their research question and understand the degree of detailed information required to answer that question. Ultimately, tool selection should consider study objective, patient population of interest, and the strengths and weaknesses of the QOL tool itself [3].

## The Psychosocial Impact of Advanced and Recurrent HNC

Evidence suggests that there are specific patient and treatment factors associated with improved psychosocial quality of life scores. For example, males with advanced HNC report higher social and emotional quality of life. Additionally, time since therapy completion is positively correlated with the psychosocial quality of life score. This correlation is stronger when patients report participation in rehabilitative therapy following their cancer treatment. As functional status improves, emotional and social well-being also improves. This section will delve into the various psychosocial factors that should be considered when evaluating quality of life in advanced HNC patients.

## *Self-Esteem and Impacts of Disfigurement*

Oftentimes, high levels of anxiety and increased social isolation are documented in patients with advanced and recurrent HNC. Several studies indicate that these sentiments are linked to a patient's body image [4]. Advanced head and neck tumors are usually quite visible, and depending on location, degree of ulceration, and extent of facial involvement, they significantly influence an individual's self-esteem. In a retrospective study of patients with oral or maxillofacial cancer, most patients admitted to preoperative distress related to fear of disfigurement [5]. About 60% of those patients also reported feeling stigmatized from cancer-related appearance. Local and free flap reconstructions after tumor resection further contribute to perceptions of disfigurement. Interestingly, gender did not impact quality of life scores related to body image and self-esteem. Age was inversely related to body image scores – older individuals plagued with advanced HNC are significantly less impacted by their appearance or disfigurement [4]. In other studies, worsened quality of life scores related to self-esteem and body image were noted in patients with inaccurate preoperative expectations – demonstrating the importance of patient counseling and understanding prior to surgical resection of HNC.

## *Depression and Emotional Coping*

Compared to patients who solely undergo surgery, advanced HNC patients with multimodal treatment or nonsurgical treatment report significantly higher rates of depressive symptoms [6]. Length of posttreatment time is linked to a significant decrease in depressive symptoms; QOL scores associated with depression are about 40% lower for survivors 15 years out from treatment, than for patients only 120 days out from treatment [6]. Emotional coping style also influences overall quality of life among patients with advanced and recurrent HNC. Patients who rely on avoidance strategy endorse poorer overall HR-QOL. Similarly, passive coping styles (associated with closing off to spouses, inexpression of emotion, and more pessimism) contribue to more psychosocial distress for patients and their loved ones [7].

### *Caretakers*

Quality of life scores of caretakers of advanced HNC patients need to be considered as well. As expected, emotional support from spouses and family members bolster HNC patient's perception of personal well-being. Thus, baseline fatigue and health status of caregivers impact the QOL scores of HNC patients. Several studies reveal that caregivers of head and neck cancer patients report poorer mental health than the general population [8, 9]. Distress was most often associated with disruption of daily life schedule because of caretaking, poor coping and communication styles of patients, and presence of feeding tubes [10]. Further, caretakers of advanced cancer patients were at an increased risk of morbidity and mortality, related to an inability to address their own medical needs [11]. Risk factors for caretakers with poorer psychosocial health include providing more hours of care, disrupted social interaction, and disrupted attention of self-care [12].

## The Physical Impact of Advanced and Recurrent HNC

Depending on extent of tumor invasion and treatment option, advanced and recurrent HNC also affects patients' physical capacities. Physical impairment can greatly diminish quality of life. Furthermore, patients with better physical self-efficacy before diagnosis and throughout treatment have been shown to have better survival outcomes [13]. This section will delve into the various physical factors to consider when evaluating quality of life in advanced HNC patients.

### *Disability in Activities of Daily Living*

Pain contributes significantly to disability in activities of daily living (ADLs). Debilitating pain associated with treatment negatively impacts general activity, walking, normal work, sleep quality, and life enjoyment. In a multicenter study, patients with advanced-stage HNC had significantly higher pain scores than those with other types of malignancy, with a greater percentage requiring analgesics during cancer treatment course [14]. The higher prevalence and severity of pain was hypothesized to be due to location of tumors, as most anatomical structures of the head and neck are pain-sensitive and concentrated in a small space [15]. Treatment-related pain may often be neuropathic in nature, attributed to surgical nerve sacrifice, adjacent tissue edema, or local neurotoxicity.

Furthermore, feeding tube dependence and postoperative recovery impair patients' independence in ADLs. Comorbidities and age prior to cancer treatment also affect ability to perform ADLs. Furthermore, treatment modality impacts patients' activity status. Systemic weakness from chemoradiation was found to be very debilitating during treatment course and in the immediate months posttreatment. Interestingly in a study evaluating patient-related outcomes for free flap reconstruction in elderly patients, 75% of subjects denied major limitations to activities of daily living once 32 months out from surgery [16].

### *Deconditioning and Malnutrition*

Oftentimes, advanced and recurrent head and neck cancer causes unintentional weight loss. Chemotherapy and radiation have both been noted to decrease muscle mass among head and neck patients, leading to deficits in mobility and decrease in physical activity [17]. Among advanced HNC patients, more than 50% report sedentary lifestyle with very few participating in light to moderate physical activity. Elderly HNC patients are least likely to partake in physical activities, contributing to worse quality of life and prognosis [18]. Early and consistent physical activity during treatment course has been shown to improve perception of personal well-being and global quality of life among HNC patients [19]. It also contributes to decrease in fatigue, one of the primary distressing QOL-related outcomes reported by patients with HNC [20]. Additionally, malnutrition is common in advanced HNC patients. Malnutrition is attributed to factors like dysphagia, decreased appetite, and malabsorption from disease and treatment; it negatively impacts both HR-QOL and prognosis. Prophylactic feeding tubes and pretreatment nutritional counseling have both been shown to mitigate the severity of malabsorption in cancer patients.

## The Functional Impact of Advanced and Recurrent HNC

When discussing health-related quality of life in HNC patients, functional status contributes significantly to a patient's overall well-being. Head and neck anatomy is integral to functions like chewing, swallowing, and speech production. Shoulder and neck mobility are also crucial for several activities of daily living. Thus, advanced HNC and its treatment modalities can negatively impact patients' functional quality of life in several ways. This section will discuss the various impacts that advanced and recurrent HNC has on a patient's functional quality of life.

### *Dysphagia*

Advanced-stage HNC (stages III–IV) is associated with severe swallowing dysfunction, especially with oral cavity and oropharyngeal tumors [6]. This is not only due to extent of tumor spread into anatomic structures critical in chewing and initiating swallow but also because of the indicated treatment modality. Advanced and recurrent HNC often requires multimodal therapy, and both nonoperative treatment and surgery + adjunctive therapy are linked with worse dysphagia. However, increasing use of transoral robotic surgical resection has demonstrated improvement in dysphagia scores, when compared to standard chemoradiation for advanced oropharyngeal tumors [21]. As with several other symptoms impacting quality of life, dysphagia has also been shown to improve with time since treatment (Fig. 9.1). However, after about 6 years posttreatment, patients do report recurrence and worsening of dysphagia [6]. One option to mitigate these symptoms is swallow rehabilitation therapy. For example, patients with tongue resections who participate in swallow therapy report significantly improved dysphagia scores than patients who did not participate [22].

## *Speech Impairment*

Difficulty with voice and speech is reported most often with oral cavity, oropharyngeal, and laryngeal tumors. Tongue and laryngeal involvement particularly impact a patient's ability to effectively communicate. Patients undergoing partial glossectomy maintain better articulation than those undergoing hemi-glossectomy [23].

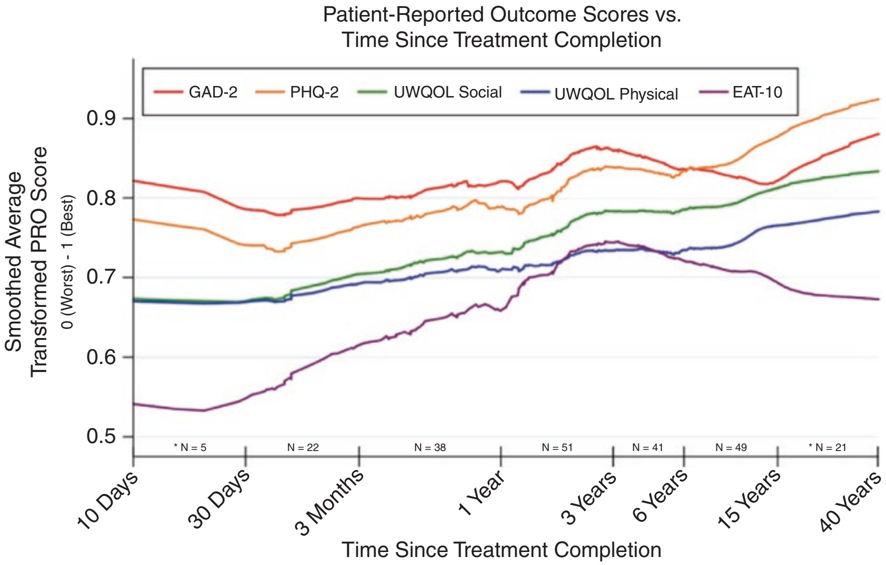

**Fig. 9.1** Patient-related QOL outcomes vs time since treatment completion [22]; EAT-10 = Eating Assessment Tool-10; GAD-2 = Generalized Anxiety Disorder-2; PHQ-2 = Patient Health Questionnaire-2; PRO = patient-reported outcomes; UWQOL physical = University of Washington Quality of Life Physical Subscale; UWQOL social = University of Washington Quality of Life Social-Emotional Subscale. (From Nilsen et al. [6], with permission)

Further, local flap reconstruction of tongue defects is associated with quicker improvement in speech quality than free flap reconstruction. In advanced oropharyngeal cancer, voice changes are often peak within 1 month of therapy; patients report recovery in speech quality by 12–18 months following treatment [24]. However, in a study evaluating speech impairment in stage IV disease treated with concurrent chemotherapy and radiation, over 65% of patients reported late presentation in difficulty with voice, articulation, and speech 10 years following treatment [25].

### *Work-Related Disability*

Advanced head and neck cancer, treated with multimodal treatment or nonsurgical treatment, is also associated with an overall increase in work-related disability. In a multi-site study, 384 patients who worked prior to their diagnosis with HNC were surveyed. Of this sample, more than half of the patients in this study were disabled by their head and neck cancer or treatment [26]. Patients with head and neck cancer who have undergone chemotherapy or neck dissection or have high pain scores are at increased risk for disability from their cancer or their treatment.

Factors contributing to these trends include:

- The need for frequent hospital visits
- Systemic impact of treatment and associated health complications (i.e., immunocompromise, debilitating pain, etc.)
- Impaired neck and shoulder mobility, especially in professions requiring manual labor
- Financial burden of ongoing multimodal treatment

## Tumor-Related Factors and Their Impact on Quality of Life

Inherent variation in quality of life exists depending on tumor site and tumor stage. As one would expect, late-stage tumors (III and IV) are associated with poorer quality of life than early-stage disease. Metastatic disease and recurrent disease often require systemic therapy, which contribute to poorer functional and physical status for patients.

Nasopharyngeal and sinonasal cancers are associated with the least impact on quality of life, with the exception of tumors with orbital involvement. Patients with oropharyngeal cancer reported better HR-QOL scores than those with hypopharyngeal cancer [27]. These differences were often associated with the varying treatment modalities indicated for each tumor site. For example, oropharyngeal and oral cavities significantly impact malnutrition, dysphagia, and generalized weakness [28]; advanced-stage disease in these regions requires chemotherapy and/or radiation. In contrast, late-stage hypopharyngeal and laryngeal tumors more likely impact speech or physical disfigurement, as would be expected with total laryngectomies.

In addition to tumor site and stage, HPV status can impact quality of life for HNC patients. In a large retrospective study comparing QOL, symptom, and functional outcomes of HPV-positive HNC and HPV-negative HNC, patients with HPV-negative cancers reported worse overall quality of life [29]. This is likely because HPV-negative patients are typically older and have more comorbidities at baseline. In the HPV-associated OPC, patients report returning to baseline quality of life or improved quality of life, 1 year after treatment. This was true no matter which treatment modality was utilized.

## Treatment Modalities of HNC and Their Impact on Quality of Life

Treatment modalities of advanced and recurrent disease impact every domain of quality of life among HNC patients. Unfortunately, given the severity of malignancy, multimodal management is often indicated. Most studies indicate that multimodal treatment, while effective in treating HNC cancer, negatively impacts health-related quality of life [6]. There are a variety of QOL domains affected by HNC and its treatment options.

Overall, numbness, difficulty with phonation, and pain were commonly reported adverse effects of surgery. Weight loss, fatigue, and loss of appetite were primarily associated with chemotherapy or radiotherapy. This section will delve deeper into the QOL considerations of each treatment modality.

### *Operative Intervention and Its Impact on QOL*

Early-stage head and neck cancer can often be addressed with curative surgery without long-term costs in quality of life. However, locally advanced disease requires more extensive procedures with significant functional and physical deficits. Common symptoms adversely impacting quality of life in surgical candidates include [6, 30]:

- Disfigurement
- Speech and swallow difficulty
- Lymphedema and fibrosis
- Impaired jaw and/or shoulder mobility
- Postoperative pain

Traditionally, operative intervention has been associated with poorer quality of life outcomes than nonsurgical intervention (chemotherapy and radiation). In the short term, surgery in head and neck subsites like the oropharynx and larynx required invasive approaches for appropriate access. Surgery for locally advanced oropharyngeal cancer previously required open craniofacial defects, associated with poor swallowing function, speech difficulty, and longer hospital stays. Conservative therapy was found to be just as effective in treatment, with fewer quality of life sequelae and less morbidity. However, with the advent of transoral approaches to oral cavity, oropharyngeal, and even thyroid malignancy, recent studies report improved quality of life outcomes with surgery. Compared to patients treated with radiation, patients undergoing surgical resection of oropharyngeal cancer report improved overall quality of life, social functioning, nausea, and financial stress [31]. Furthermore, advances in reconstructive options for head and neck cancer have improved functional status and cosmesis, contributing to better quality of life.

## Neck Dissections

Oftentimes, neck dissection of cervical lymph nodes is indicated for curative treatment of more aggressive HNC. However, a study reported that 48% of their patients undergoing neck dissection were unable to return back to work, because of debilitating shoulder pain from the procedure [32]. The same study concluded that when controlled for other demographic and clinical variables, patients who underwent neck dissection were twice as likely to experience work-related disability than those patients who did not undergo the procedure. Neck dissections have been associated with worse pain scores and decrease in quality of life related to functional status. In radical or modified radical neck dissections, sacrifice of the accessory spinal nerve and/or internal jugular vein can lead to debilitating neck pain and reduced mobility. Lymphedema and scarring associated with the procedure also impacts body image and appearance [30]. With that being said, one study determined that functional status and appearance-associated distress improves for most patients undergoing nerve-sparing neck dissection, when reassessed 2 years postoperatively [33].

## Reconstructive Surgery

Patients offered local reconstruction demonstrate better quality of life score than those who underwent free flap reconstructions, especially for oral cavity and oropharyngeal tumors [23]. QOL domains that are significantly better in local reconstructions included chewing, swallowing, speech, and postoperative pain. Radial forearm free flaps have been found more effective in mitigating these aspects of quality of life, when compared to anterolateral thigh free flaps (ALTFF); this is likely related to less muscle bulk [34]. For example, hemi-glossectomy patients undergoing radial forearm free flap reconstruction demonstrated more understandable speech, improving chewing, and better swallowing than ALTFF patients. Regardless of these initial postoperative differences, patients undergoing both local and free flap reconstructions reported improved general quality of life 1 year after surgery [23]. Postoperative time is associated with improvement in most domains of HR-QOL in surgical HNC patients [6].

### PEG Tube Dependence

Patients with advanced HNC often require a feeding tube to treat nutritional compromise from their disease process and treatment. Studies have demonstrated that prophylactic percutaneous endoscopic gastrostomy (PEG) tubes have reduced morbidity than those placed therapeutically for malnutrition in HNC patients [35]. However, presence of feeding tube is linked with significantly lower quality of life scores among HNC patients [28]. Physical quality of life is impacted by adverse symptoms associated with enteral feeding. Adverse symptoms include nausea, vomiting, diarrhea, reflux symptoms, PEG site infection, and adjacent skin irritation. Such effects also contribute to work-related disability. Furthermore, patients report lower psychosocial QOL, linked to frustration of one's condition, embarrassment of appearance, and inability to partake in social dining.

### Tracheostomy Tube Dependence

Unlike with PEG tubes, tracheostomy tubes are not associated with lower psychosocial QOL scores. Studies report that although tracheostomy tubes interfere with functional quality of life related to activities of daily living, there is no significant distress or anxiety associated with its presence [28]. Further, patients with tracheostomy tubes do not report decreased physical QOL. With a safe airway, patients with advanced HNC are actually able to perform concrete task such as lifting, walking, and carrying better than at baseline.

## *Radiation Therapy and Its Impact on QOL*

Typically, definitive radiation therapy is the treatment modality of choice for early-stage head and neck cancers. However, it is also indicated for locally advanced HNC; specifically, radiation is offered to patients with unresectable tumors or patients who desire nonsurgical organ preservation. The effects of standard radiation therapy in HNC patients are often related to damage to normal structures like salivary glands, oral mucosa, dentition, and musculature. Common symptoms impacting quality of life include xerostomia, painful mucositis, loss of taste, and trismus. Patients treated with radiation therapy report significant problems with oral and nutritional intake, with most common symptoms being xerostomia and decrease in taste [36]. Further, in a study evaluating the impact that radiation therapy had on dysphagia, more than 80% of patients complained of worsened swallow ability immediately after treatment [37]. One year following treatment, these symptoms improved, with only 15% of patients complaining of persistent dysphagia. Concurrent chemotherapy was noted to have worsened dysphagia scores.

### Hyper-Fractionated Radiation

In late-stage head and neck cancer, several studies report a role in hyper-fractionated radiation. This is sometimes utilized in patients who cannot tolerate concomitant chemotherapy due to adverse side effects or recurrent disease unresponsive to chemotherapy. Further, in a meta-analysis comparing survival outcomes in stage III and stage IV head and neck cancers treated with radiation, hyper-fractionated radiation (compared to standard radiation) demonstrated a statistically significant improvement in overall survival at 5 and 10 years posttreatment [38]. However, hyper-fractionated radiation is also associated with worse HR-QOL scores. Patients complained of worse mucositis, neck and throat pain, and nausea 3 months after initiation of radiotherapy [39].

### Hypo-Fractionated Radiation

Advanced HNC may not always be eligible for definitive treatment. Palliative radiation was noted to have less of a cost on quality of life. Unlike fractioned radiotherapy (modality of choice for definitive treatment), hypo-fractionated radiation therapy has been demonstrated to allow for effective palliative control of locally far advanced HNC, with improved QOL scores. This treatment option often involves moderately high treatment doses, with a shorter treatment course and ideally fewer hospital visits [40]. When assessing hypo-fractionated radiation therapy in incurable head and neck cancer, over 60% of patients reported improvement in overall quality of life and pain scores at the end of treatment [41].

## *Chemotherapy and Its Impact on QOL*

Patients with advanced HNC undergo systemic treatment. While chemotherapy is not necessarily curative for HNC on its own, it has been shown to improve survival and cure outcomes when administered in adjunct to radiation therapy. However, chemotherapy toxicity can significantly impact patients' HR-QOL. Adverse effects associated with some of the most common concomitant chemotherapy agents include [42]:

- Nausea/vomiting
- Myelosuppression
- Nephrotoxicity
- Paresthesia
- Tinnitus and hearing loss

Furthermore, patients undergoing chemoradiation report swallow dysfunction and pain; concurrent chemotherapy has been shown to worsen dysphagia scores among patients [37]; however, these symptoms have been shown to improve in 12–24 months following treatment [43]. In addition to impact on functional QOL, chemotherapy impacts physical QOL. Patients with head and neck cancer are more susceptible to opportunistic infection. One study reported that febrile neutropenia occurred in a third of chemotherapy cycles, with severe sepsis or serious infection noted in 46% of episodes [44]. Patients undergoing chemo regimen TPF (docetaxel, cisplatin, and fluorouracil) experienced a higher incidence of febrile neutropenia than those treated with DC (docetaxel, cisplatin).

### Induction Chemotherapy

Sequential chemotherapy administration in the form of induction chemotherapy followed by concurrent chemoradiation is often administered in organ-preserving management [45]. Some studies have noted that induction chemotherapy does not significantly improve survival in advanced head and neck cancer. However, there is evidence supporting induction chemotherapy's role in organ-preserving treatment of laryngeal cancer. Immediately following induction chemotherapy, HNC patients have reported improvement in pain and swallowing-related quality of life for the emotional, functional, and physical domains [46].

### Palliative Chemotherapy

For incurable advanced and recurrent HNC, metronomic chemotherapy is more frequently utilized for palliation. Metronomic chemotherapy involves frequent administrations of low-dose antineoplastic drugs, with an intent to decrease rapid growth of cancer (without tumoricidal intent). One study found oral metronomic therapy consisting of celecoxib daily and methotrexate weekly was associated with improved social and functional QOL scores [47]. Significant improvement was noted in 50% of patients at their 2-month follow-up; 40% of patients continued to report improvement in quality of life in these domains at 6-month follow-up.

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# Chapter 10
# Financial Impact of Cancer Treatment

**Evan M. Graboyes, Avigeet Gupta, and Katherine R. Sterba**

Since President Nixon declared war on cancer in 1971, the United States has seen a tremendous investment into cancer prevention, screening and early detection, diagnosis, treatment, and care delivery with a subsequent increase in survival and decrease in cancer-related morbidity [1]. As a result, there are now more than 15.5 million cancer survivors in the United States [2]. However, concomitant with these scientific advances in cancer treatment and improvements in cancer care delivery has been an exponential increase in the cost of cancer care [3]. Not only is the overall cost of cancer care to the healthcare system increasing, but the proportion of that cost that falls on cancer patients and their families continues to grow [4, 5]. Unfortunately, this trend is expected to worsen over time with the continued developed of targeted and immune-modulating anticancer therapies [6]. In addition, patients continue to increase enrollment in high-deductible plans on the insurance exchanges through the Patient Protection and Affordable Care Act, further increasing the burden of rising cancer care borne by patients [7].

As a result of the convergence between improved oncologic outcomes, increased cost of cancer care, and continued shifting of the burden of the cost of cancer care to the patient, there has been a growing awareness of a phenomenon known as financial toxicity. Financial toxicity is a multidimensional construct comprised of three conceptual domains: (1) material hardship that results from increased out-of-pocket [OOP] costs and lower income, (2) psychological distress resulting from the material hardship, and (3) compensatory coping strategies that families develop in response to the financial cost of cancer and its treatment [8, 9]. The downstream

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impact of financial toxicity is significant and includes altered cancer treatment preferences [10], decreased adherence to cancer treatment [11], increased symptom burden [12], decreased health-related quality of life (HRQOL) [13], and decreased survival [14]. In addition, because financial toxicity disproportionately burdens socioeconomically disadvantaged patients, it is expected to exacerbate disparities in cancer care treatment and outcomes. Understanding the impact of the financial cost of cancer care and its effect on patients and their caregivers is thus of critical importance to patients, clinicians, researchers, and policy makers [15].

This chapter will define financial toxicity following cancer treatment, estimate its incidence in head and neck cancer (HNC) patients, highlight key risk factors, describe various tools for its measurement, and discuss practical considerations for providers vis-à-vis financial toxicity. Knowledge gaps and research opportunities to improve the delivery of patient-centered cancer care that is attentive to the complex issue of financial toxicity will be explored at the conclusion.

## What Is Financial Toxicity

Financial toxicity is a multidimensional construct comprised of three conceptual domains: (1) material hardship that results from increased OOP costs and lower income, (2) psychological distress resulting from the material hardship, and (3) compensatory coping strategies that families develop in response to the financial cost of cancer and its treatment (Fig. 10.1) [8, 9]. The term financial toxicity draws a parallel to the well-known physical toxicity experienced by cancer patients due to treatment side effects [16] although other terms that are sometimes used interchangeably with cancer-related financial toxicity include financial distress, financial hardship, financial burden, and financial impact [9].

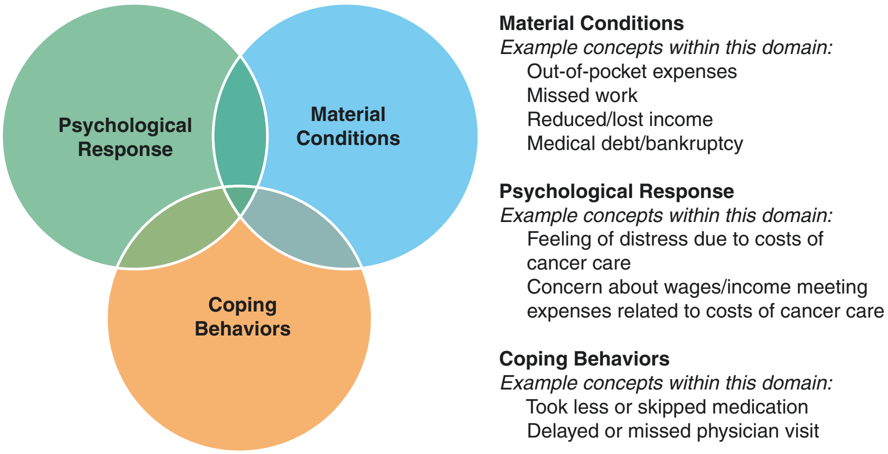


**Fig. 10.1** Domains of financial toxicity. Financial toxicity consists of three separate but potentially overlapping domains: (1) material loss, (2) psychological distress, (3) and compensatory coping behaviors [9]. (From Altice et al. [9], with permission)

For cancer patients, financial distress is a result of the following three costs: (1) the direct (nonreimbursed) OOP medical costs of cancer care, (2) the direct nonmedical costs borne by the patient, and (3) the indirect and opportunity costs associated with cancer treatment [17, 18]. Components of direct OOP cancer costs include insurance premiums and deductibles as well as direct medical costs related to prescription and nonprescription medications, medical professional visits, hospital bills, nutritional services, physical/speech/occupational therapy and other rehabilitative services, home care, and devices and equipment. The direct nonmedical costs that contribute to the cost of cancer care include transportation and lodging for treatment, childcare/elder care, and other supportive services. Indirect and opportunity costs of cancer care include lost income during treatment due to missed workdays from illness and injury as well as future lost earned income from a lack of employment. These indirect costs of cancer care are a critically important factor for patients with HNC as they have the highest rate of disability or quitting work relative to any other cancer [19].

Direct OOP costs, missed workdays, and lost employment due to cancer all contribute to financial toxicity. Finkelstein et al. used the Medical Expenditure Panel Survey to perform a population-based study of the working age population (25–64 years) in the United States from 2000 to 2005 to quantify the impact of a cancer diagnosis on direct OOP costs, missed workdays, and lost employment [18]. They found that the mean annual OOP expenditure was $1170 greater for participants actively treated for cancer relative to those who are not treated for cancer [18]. Compared to those without cancer, cancer patients had a 4.5% relative decrease (and 3.3% absolute decrease) in the odds of employment and missed 22.3 more days of work annually [18]. Between the direct OOP costs and missed workdays, an average household could expect to have their annual medical bill increase from 5% of their annual income to 8% of their annual income [18].

While those being actively treated for cancer face significant financial toxicity from the direct OOP costs of medical care and the lost workdays due to illness, financial toxicity continues for long-term cancer survivors as well. A systematic review by Altice et al. demonstrated that cancer survivors have an annual mean loss in productivity ranging from $380 to $8236 [9]. Of cancer survivors in this review, 12–62% reported that cancer treatment caused them to go into debt and 49% experienced financial distress [9].

## Incidence of Financial Toxicity

The incidence of financial distress among patients with cancer in the United States is quite high [20] with prevalence estimates ranging up to 50% [9]. Cancer-related financial toxicity is especially common in patients with HNC in the United States with cumulative incidence estimates ranging from 40% to 69% [4, 21, 22]. The higher rate of financial toxicity in patients with HNC relative to other types of cancer is likely due to the frequent use of trimodal treatment paradigms in HNC (surgery, radiation, and chemotherapy) combined with a patient population that tends to have a lower socioeconomic status. Interestingly, a study examining financial toxicity in 67 patients with HNC treated with (chemo)radiation in Norway described very low levels of financial difficulties arising from HNC and its treatment [23]. Similarly, only 18% of HNC survivors treated in Canada reported unmet needs about financial support [24]. These data suggest that findings about financial toxicity in HNC patients are probably not generalizable across vastly different healthcare delivery systems (e.g., the United States compared to Norway).

A single institution prospective cohort study of 33 patients with HNC treated with a primary surgical approach with/without adjuvant therapy published in 1989 assessed changes in financial burden over time [21]. Using a nonvalidated patient self-report of financial problems, the authors reported that the incidence of perceived financial difficulties was 9% preoperatively, peaked at 40% at 3 months after treatment, and decreased slightly at 1 year after treatment [21].

In a prospective cohort study of 73 insured patients with locally advanced HNC treated at a single tertiary care academic medical center between May 2013 and November 2014, 69% of patients needed to use at least one financial coping strategy (e.g., borrowing money or using credit, selling possessions or property) within 6 months of treatment [22]. The median OOP cost for this group of patients was $805.93 per month (range $6 to $10,156) and the median indirect cost was $135,271.10 (range $0 to $1,317,882) [22]. The authors suggested that the high OOP costs identified for HNC patients are likely a key contributor to the high incidence of financial distress in patients with HNC [22].

## Risk Factors for Financial Toxicity

Identification of patients at risk for developing financial toxicity using pretreatment, baseline characteristics would theoretically allow for improved multidisciplinary evaluation and prevention through appropriate referrals to financial advisors, patient navigators, and cancer psychologists. Although the incidence of financial toxicity is high for patients with HNC [22], there is a subset of patients who are at exceptionally high risk for financial toxicity. In a prospective cohort study of 73 patients with locally advanced HNC, patients with Medicaid, decreased wealth, higher perceived social isolation, and higher total out-of-pocket costs were independently associated with financial toxicity on multivariable logistic regression analysis [22].

These aforementioned risk factors lead not only to an increased financial stress, but in fact create more barriers in receiving optimal care with an association with medication nonadherence and more missed appointments [22]. This creates an undue cycle of financial toxicity with the initial financial burden of cancer treatment leading to an increased use of cost-coping mechanisms that generates further financial stress and poorer quality of life for patients and their caregivers.

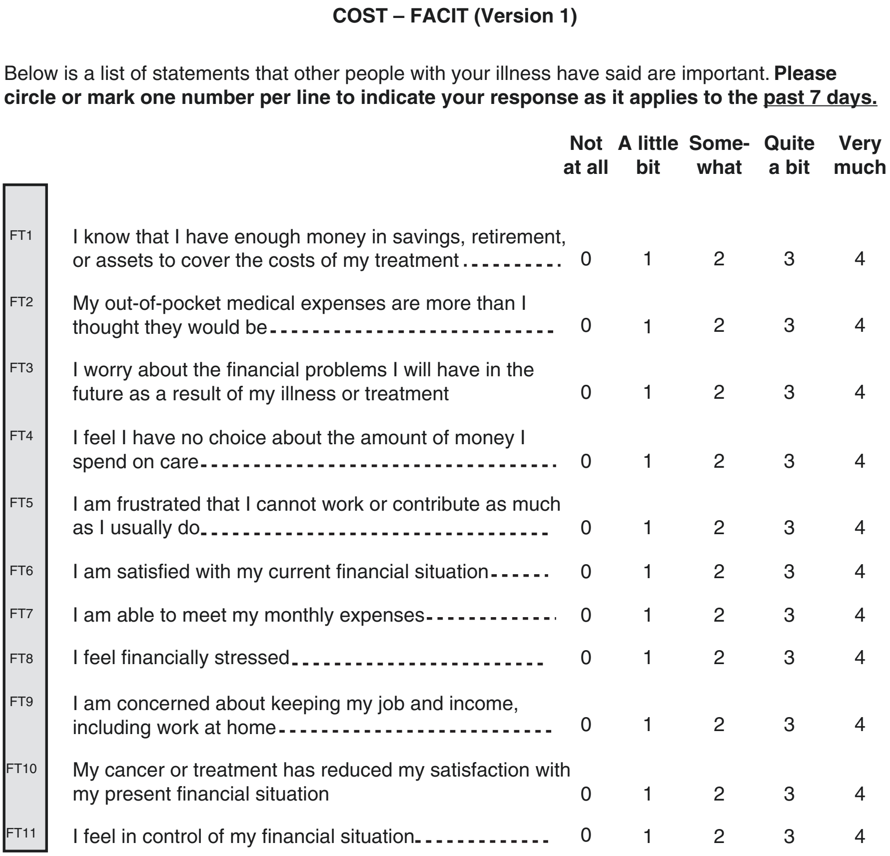
## Tools for Measuring Financial Toxicity

Following the conceptual model of financial toxicity outlined by Altice et al. (Fig. 10.1), measures of financial toxicity can be grouped into three categories: (1) measures of material hardship, (2) measures of psychological distress in response to financial hardship, and (3) measures of compensatory coping behaviors (typically medication nonadherence) [9].

There are a variety of quantitative measures of material hardship resulting from cancer treatment including direct OOP costs, financial burden, productivity loss, medical debt/depletion of assets, and bankruptcy. Financial burden is defined as the ratio of OOP health-related spending to household income [25]. A financial burden of 10–20% or more is considered significant [9, 26]. Quantitative assessment of cancer-related material hardship also includes measures of indirect/opportunity costs. The Work Productivity and Activity Impairment (WPAI) Questionnaire is a validated and reliable tool that measures time missed from work and impairment of work and regular activities due to overall health and symptoms that has been used in oncology patients [27]. Because the indirect costs of cancer care are particularly important for patients with HNC [19, 28], a robust assessment of financial toxicity should include measures of these opportunity costs.

In addition to monetary metrics of financial hardship, comprehensive assessments of financial toxicity should include patient-reported outcome measures (PROMs). Optimizing strategies to deliver patient-centered oncology care is a key priority for major funding, policy making, and regulatory entities [29, 30]. Harnessing patient-reported outcomes (PROs) to deliver patient-centered oncology care results in numerous improved outcomes including better symptom management, enhanced HRQOL, and increased survival [31–33]. Unfortunately, although PROMs have been developed to cover a range of physical and psychosocial aspects of cancer and its treatment, a PRO measure for cancer-related financial toxicity has been lacking until recently [15].

The COmprehensive Score for financial Toxicity (COST) questionnaire is a reliable, validated, single-domain 11-item PRO measure of financial toxicity in patients with cancer that addresses the material and psychological hardship of financial cancer care (Fig. 10.2) [15]. In the original validation study of 233 patients with AJCC Stage IV solid tumors receiving chemotherapy, the COST measure demonstrated appropriate psychometric performance with high internal consistency and test-retest reliability [34]. The COST PRO measure was found to correlate with income and psychosocial distress [34]. In addition, higher levels of financial toxicity (as measured by the COST) were associated with decreased HRQOL, suggesting that the new COST questionnaire is capturing clinically relevant patient-centered outcomes [34]. Although the COST measure is an exciting addition to the PRO armamentarium, it has not been specifically validated in HNC patients. The authors hope that this PRO measure of cancer-related financial toxicity will facilitate continued patient-centered research on the topic to minimize the adverse effects of financial toxicity and its potential to exacerbate existing disparities in cancer care and outcomes [34].



**COST – FACIT (Version 1)**

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

| | | Not at all | A little bit | Some-what | Quite a bit | Very much |
|---|---|---|---|---|---|---|
| FT1 | I know that I have enough money in savings, retirement, or assets to cover the costs of my treatment | 0 | 1 | 2 | 3 | 4 |
| FT2 | My out-of-pocket medical expenses are more than I thought they would be | 0 | 1 | 2 | 3 | 4 |
| FT3 | I worry about the financial problems I will have in the future as a result of my illness or treatment | 0 | 1 | 2 | 3 | 4 |
| FT4 | I feel I have no choice about the amount of money I spend on care | 0 | 1 | 2 | 3 | 4 |
| FT5 | I am frustrated that I cannot work or contribute as much as I usually do | 0 | 1 | 2 | 3 | 4 |
| FT6 | I am satisfied with my current financial situation | 0 | 1 | 2 | 3 | 4 |
| FT7 | I am able to meet my monthly expenses | 0 | 1 | 2 | 3 | 4 |
| FT8 | I feel financially stressed | 0 | 1 | 2 | 3 | 4 |
| FT9 | I am concerned about keeping my job and income, including work at home | 0 | 1 | 2 | 3 | 4 |
| FT10 | My cancer or treatment has reduced my satisfaction with my present financial situation | 0 | 1 | 2 | 3 | 4 |
| FT11 | I feel in control of my financial situation | 0 | 1 | 2 | 3 | 4 |

**Fig. 10.2** The COST measure. The COmprehensive Score for financial Toxicity (COST) – Functional Assessment of Chronic Illness Therapy (FACIT) is a reliable, validated, patient-reported outcome measure of financial toxicity following cancer treatment [34]. (From de Souza et al. [34], with permission)

The InCharge Financial Distress/Financial Well-Being Scale (IFDFW) is another reliable and validated measure of financial toxicity [35]. Although not healthcare specific, it covers material and psychological hardship domains and has been used in numerous prior studies to assess cancer-related financial distress [36–38].

In addition to tools dedicated solely to measuring financial toxicity in cancer patients, questions about financial toxicity of cancer care also frequently embedded in multidomain HRQOL tools. The EORTC/QLQ-C30 is a 30-item reliable and validated multidomain HRQOL measure for oncology patients that addresses financial toxicity through the following single question: "Has your physical condition or medical treatment caused you financial difficulties?" [39] The Cancer Survivors' Unmet Needs Measure (CaSUN) is another tool that has been used to measure financial toxicity in cancer survivors [24]. Among the 35-items in the CaSUN questionnaire is one that assesses the cancer survivor's unmet need regarding financial support [40]. In a study of 158 patients at a quaternary cancer care center using the CaSUN questionnaire, patients who endorsed needing help with financial support as an unmet need did so with moderate to strong strength [24].

## The Impact of Financial Toxicity on Head and Neck Cancer Patients

The downstream impact of financial toxicity on cancer patients is significant as increased levels of financial toxicity are associated with decreased adherence to cancer treatment [11], increased symptom burden [12], decreased HRQOL [13], unmet needs for HNC survivors [41], and decreased survival [14]. To mitigate the adverse effects of financial toxicity, patients employ a variety of cost-coping strategies that mediate the relationship between financial toxicity and worse oncologic and HRQOL outcomes. A flowchart of the economic consequences of cancer treatment and how coping mechanisms lead to worse HRQOL and health outcomes is shown in Fig. 10.3 [6]. Cost-coping strategies have been conceptualized as care altering and lifestyle altering [42]. Examples of care-altering strategies to minimize the burden of cancer-related financial toxicity include not filling a prescription, taking less medication than prescribed, and missing tests, procedures, or appointments [42]. Lifestyle-altering cost-coping strategies include spending personal savings, selling possessions, borrowing money, having other family members work more, spending less on necessities (e.g., food, clothing), and decreasing spending on leisure activities [42].

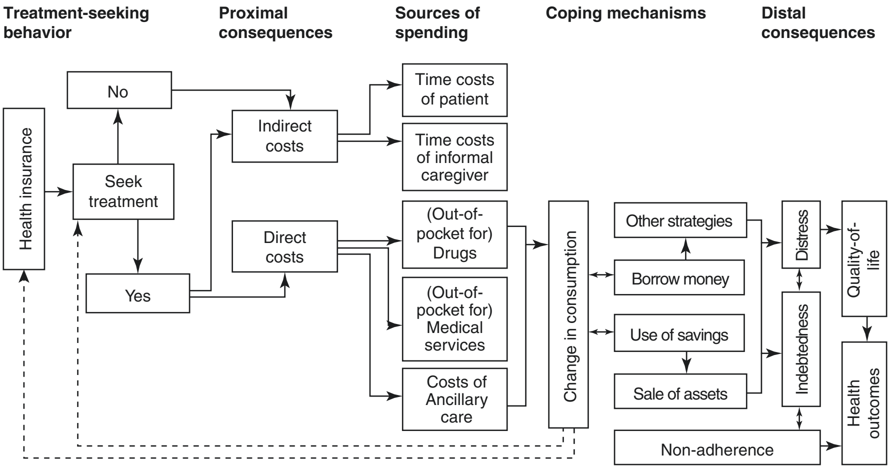


**Fig. 10.3** Flowchart of economic consequences of cancer treatment on the patient and patient coping. (From Carrera et al. [6], with permission)

One of the key downstream impacts of care-altering strategies to mitigate against cancer-related financial toxicity is thus decreased treatment adherence. In a study of insured patients with diverse types of cancer, 20% of patients took less than the prescribed amount of cancer medications, 19% partially filled prescriptions, and 24% did not fill prescriptions at all in an attempt to defray out-of-pocket expenses [43]. Others have documented that higher prescription copayments for aromatase inhibitors are associated with higher rates of nonadherence and nonpersistence in patients with breast cancer [11].

Lifestyle-altering strategies to manage financial toxicity stemming from cancer treatment also significantly contribute to decreased HRQOL. In a sample of patients with locally advanced HNC, 69% of patients reported employing at least one cost-coping strategy within 6 months of treatment initiation [22]. These strategies included using all or a portion of their savings (62% of patients), borrowing money or using credit (42% of patients), selling possessions or property (26% of patients), and having family members work additional hours (23% of patients) [22]. In a different study examining lifestyle-altering behaviors as a consequence of cancer-related financial toxicity, 68% of patients reduced leisure activities, 46% reduced spending on food and clothing, 46% used savings, and 18% sold possessions as a consequence of high OOP cancer care expenses [43]. Other studies have shown that patients suffering from cancer-related financial toxicity are more likely to file for bankruptcy [14]. Furthermore, cross-sectional studies of HNC survivors have demonstrated that financial strain due to cancer is independently associated with unmet needs [41].

In addition to the negative impact that financial toxicity has at the individual patient level, cancer-related financial toxicity also has significant negative implications from a societal perspective. Specifically, as the impact of financial toxicity for cancer patients continues to grow, racial and socioeconomic disparities in cancer care and oncologic outcomes are expected to be exacerbated [34]. In a study of 400 insured cancer patients evaluating stylized cancer treatment scenarios, patients with higher income were more likely to select a treatment due to its perceived impact on survival while lower income patients were more likely to select a treatment due to its perceived impact on cost [10].

## The Impact of Financial Toxicity on Head and Neck Cancer Caregivers

In addition to creating a devastating financial and psychosocial impact on the HNC patient, financial toxicity also impacts family members and caregivers [44]. Data collected from a study of informal cancer caregivers demonstrated that the average time spent caring for cancer patients was 8.3 hours per day for 13.7 months [45]. The estimated cost of caregiving time spent for cancer survivors over a 2-year period after the diagnosis was estimated to be $47,710 [45]. This value was even higher in patients with higher staging and distant or metastatic disease at diagnoses [45]. Informal caregivers spend valuable time with cancer patients and are at risk for making extended employment changes in order to provide the desired level of care [46].

A cross-sectional study of 180 HNC survivor-caregiver dyads revealed that caregivers with reported financial distress had survivors who reported significantly higher fear of cancer recurrence and cancer worry [47]. Financial distress among caregivers causes undue psychosocial concern as well, which may compromise optimal completion of caregiving tasks. A different cross-sectional study of 44 partners of HNC survivors quantified unmet survivorship care needs using the Cancer Survivors' Partners Unmet Needs Survey (CaSPUN). In this study, the authors found that 21% of partners' endorsed needing help finding out about financial support and/or government benefits [48].

In a qualitative study of 31 HNC caregivers, finance-related psychosocial distress was highly prevalent[4]. Caregivers frequently described direct nonmedical costs of HNC treatment (travel for appointments, overnight accommodations) and indirect costs (giving up or significantly reducing paid work to care for family/friends) during the treatment phase [4]. Flexible working arrangements for caregivers, practical community support (e.g., fundraising), private insurance, and access to medical and/or social welfare benefits were all found to mitigate the negative effects of financial toxicity for HNC caregivers [4].

The long-term financial impact of HNC care was particularly distressing to caregivers, but they often attempted to hide the financial situation from the HNC survivor in an attempt to protect him/her from an additional source of worry [4]. As a result of the paucity of attention to the impact of financial toxicity on HNC caregivers, it is not surprising that caregivers of HNC survivors rank “finding out about financial support” as a critical unmet need [49].

## Resources on Financial Toxicity for Patients and Caregivers

Although HNC patients and their caregivers are interested in receiving additional resources about financial toxicity and strategies to manage financial issues, it nevertheless represents an unmet need for many. In a study of 158 HNC survivors treated at a single academic medical center in Toronto, 23% of patients reported being interested-very interested in receiving more resources about managing financial issues after treatment of HNC [24].

There are publicly available resources that can be used to help understand and manage financial toxicity. The National Cancer Institute provides up-to-date information regarding financial toxicity in the form of the Physician Data Query that is beneficial for both the patient [50] and provider [51]. This information summary defines terminology regarding financial distress that is comprehendible at the patient level and discusses risk factors, its effects, and ways to minimize financial toxicity [50].

Financial assistance resources that can be provided to HNC patients and their caregivers include the Head and Neck Cancer Alliance program, The Oral Cancer Foundation, Support for People with Head and Neck Cancer, CancerCare, and The Assistance Fund. These resources allow patients to better understand their financial burdens and also provide an opportunity to communicate with other patients with similar diagnoses and financial stressors. However, the provider should be involved as much as possible in helping patients and their caregivers with this process alongside providing these resources.

## Practical Considerations About Financial Toxicity of Cancer Treatment for Head and Neck Cancer Providers

Although in many cases oncology providers do not discuss the financial toxicity of cancer treatment with patients and caregivers, there is clearly a compelling need to inquire about financial toxicity and engage and support patients and caregivers on this topic [4]. A survey conducted by Jagsi et al. demonstrated that over two-thirds of breast cancer patients that were worried about their finances noted that physicians and their accompanying staff did not help address these issues [52]. Moreover, it was noted that only one-half of medical oncologists and only 15% of surgeons believe that someone in their practices spoke with patients about financial toxicity [52].

Sociodemographic factors also play a role in the doctor-patient relationship and the discussion of financial burden. A study with video-recorded clinical interactions between African American cancer patients and non-African American oncologists revealed that cost discussions occurred in less than half of the encounters (45%) with patients mostly initiating discussion about cost (63%) [53]. Oncologists initiated cost discussions only 36% of times [53], demonstrating that clinicians should become more proactive in cost discussions and understanding of the financial toxicity that affects racial/ethnic minorities.

The management of HNC is a multidisciplinary collaborative effort, and clinicians should be actively engaged and understanding of patient's justified fears of financial distress and its complex interplaying elements (Fig. 10.4). Providers should allow each patient diagnosed with HNC the opportunity to work with patient navigators, psychologists, financial advisors, and other physicians as to best manage medical care with regards to patient autonomy and team collaboration. Discussions of cost with HNC patients and their caregivers need to be further studied and evaluated with multimodal perspectives.

As in other aspects of multidisciplinary HNC care, no single HNC provider can completely manage financial toxicity. A critically important role for HNC surgeons, radiation oncologists, and/or medical oncologists is to help increase awareness that financial toxicity is common following treatment for HNC and that resources exist for its management. Other relevant players to whom referrals should be made to

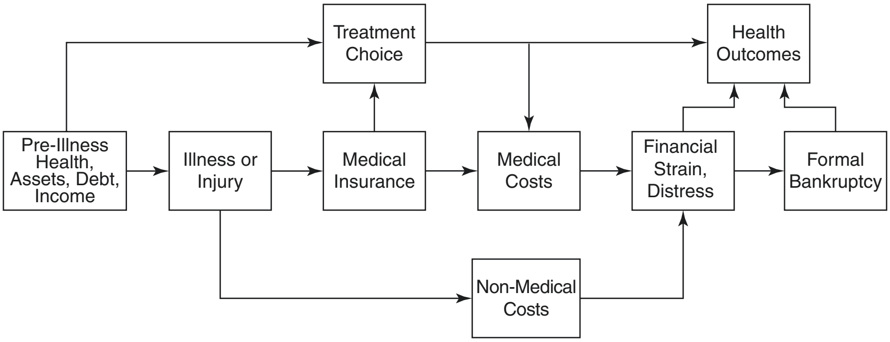


**Fig. 10.4** Conceptual framework relating severe illness, treatment choice, and health and financial outcomes. Cancer and financial strain and distress have a complexity of interplaying elements. (From Board PATE [51], with permission)

assess for and manage financial toxicity include social workers and patient navigators, who may further facilitate engagement with social welfare systems [4].

## Knowledge Gaps and Research Opportunities

With the ever-growing awareness of patient-centered financial toxicity, more literature is becoming available to help clinicians and providers over time. However, further evidence-based research should be conducted to address significant knowledge gaps that preclude the screening, prevention, and treatment of financial toxicity in patients with HNC. One of the major gaps in the area of cancer-related financial toxicity research is inconsistent use of definitions, terms, and measures [9]. The lack of agreed-upon nomenclature and measures precludes identification of targets and development of interventions to prevent and manage financial toxicity in cancer survivors.

Additionally, there should be more transparency and solidarity in the quantification of financial burden to allow investigators to more accurately understand causality. Providers should have all financial resources available at hand based upon a systematic approach to understand and interpret the current types of charitable aid offered to cancer patients.

Research of both patient-level and caregiver-level financial distress is a fundamental pillar in understanding the overall meaning of financial toxicity itself. Adaptation of validated tools to quantify patient-level financial toxicity should be further implemented. Investigators should also take the opportunity to create and develop a validated instrument to quantify the financial burden for caregivers, including informal caregivers.

An overall understanding of the healthcare delivery system as it relates to financial toxicity to patients is also crucial. Providers, patients, and policy makers should value the importance of access to optimal and high-quality cancer treatment in the most efficient manner possible. Questions should be asked regarding which systemic issues are currently present in the healthcare model in order to generate solutions to further advance survival and quality of life and reduce financial toxicity.

There should be implementation of a universal screening tool to determine which patients are at a high risk for financial toxicity, and every patient should have the opportunity to be aware of the possibility of financial burden and the psychosocial impact of cancer at the earliest possible time in the treatment process. In addition, future research should seek to clarify the longitudinal course of financial distress in HNC patients and their caregivers. Only then can the HRQOL of HNC patients further improve as clinicians and patients learn more and more about the patient-centered financial toxicity.

There is much to learn regarding financial toxicity and the root cause of this issue that plagues HNC patients. Providers have a duty to provide the best possible financial resources and further educate themselves for HNC patients who not only suffer from the medical toxicity of cancer but also undue financial toxicity.

## Conclusion

Financial toxicity is particularly common in patients with HNC and represents an unmet need for many patients and their caregivers. The armamentarium of tools to measure and identify financial toxicity, particularly in a patient-centered fashion, continues to grow. There is nevertheless significant future work to be done to develop and implement targeted prevention and treatment strategies for those at highest risk of developing financial toxicity.

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# Chapter 11
# Instruments for Quality of Life and Mental Health Assessment

**Marianne Abouyared, Alizabeth Weber, and Jeffrey J. Houlton**

Head and neck cancer patients have an incredibly high rate of depression, reported at approximately 40%, and possess the highest suicide rates in the cancer community [1, 2]. It is thus extremely important to know which tools are available to screen for depression and quality of life (QOL) difficulties in this population in order to identify at-risk and suffering patients. In addition, head and neck cancer patients may struggle with a disfigured appearance, altered speech and swallowing abilities, social isolation, and high stress/anxiety. Accurately assessing QOL metrics can assist us in improving our patients' well-being and improve treatment outcomes. This chapter will summarize the tools available for assessing quality of life and will provide an organized and concise reference for head and neck surgeons interesting in utilizing these instruments.

Head and neck cancer patients are faced with a very challenging course as they make their way through treatment and recovery. While survival is the primary focus of treatment, once the initial treatment period ends, the patient usually begins to focus on other physical, functional, and social aspects of their life [3]. As more of our patients are surviving their head and neck cancers, quality of life measures become an increasingly important tool in addressing our patients' well-being. Identifying each patient's specific priorities can help tailor our counseling, specialty referrals, and treatment options.

The diversity of cancer subsites in the head and neck leaves each patient with a unique set of challenges. Most will undergo some degree of alteration in their physical appearance, but the oral cavity, pharyngeal, and laryngeal cancer patients have additional insults to speech and swallowing. All of these factors contribute to com-

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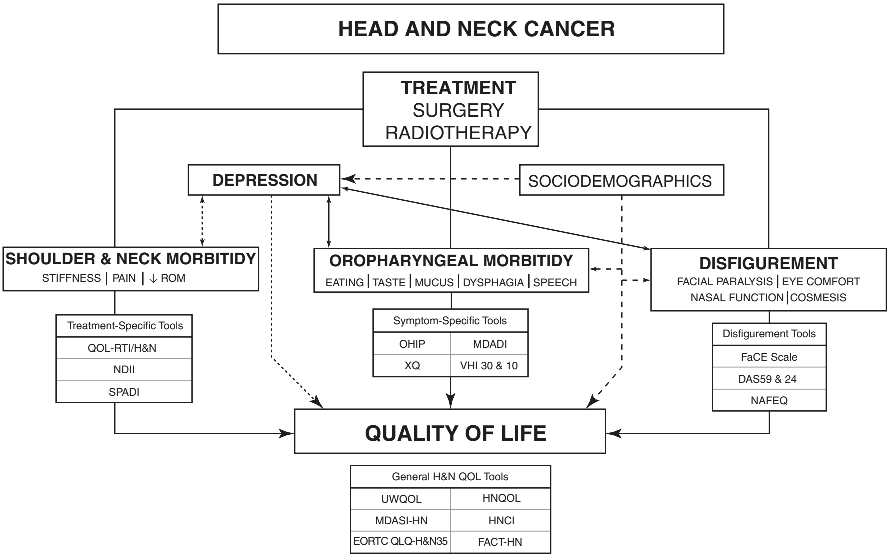

**Fig. 11.1** Head and neck cancer quality of life assessments. QOL-RTI/H&N, Quality of Life-Radiation Therapy Index/Head and Neck; NDII, Neck Dissection Index II; SPADI, Shoulder Pain and Disability Index; OHIP, Oral Health Impact Profile; XQ, Xerostomia Questionnaire; MDADI, MD Anderson Dysphagia Inventory; VHI 30&10, Voice Handicap Index; FaCE Scale, Facial Clinimetric Evaluation Scale; DAS59 and DAS24, Derriford Appearance Scale; NAFEQ, Nasal Appearance and Function Evaluation Questionnaire; EORTC QLQ-H&N35, European Organization for Research and Treatment of Cancer Quality of Life Head and Neck Modules; UWQOL, University of Washington Quality of Life Questionnaire; FACT-HN, Functional Assessment of Cancer Therapy-Head and Neck; HNQOL, Head and Neck Quality of Life Questionnaire; MDASI-HN, MD Anderson Symptom Inventory-Head and Neck Module; HNCI, Head and Neck Cancer Inventory

plex social and emotional sequelae. Figure 11.1 displays the complexity involved in addressing each aspect of a head and neck cancer patient's quality of life.

Thankfully there are many instruments available to assess our patients' overall quality of life, mental health, and functional impairments. The instruments presented here have been widely studied and have been utilized in clinical trials or other high-level studies as important outcome measures. More importantly, these tools are used in the clinical setting to help the clinician focus on improving the patient's quality of life as they enter the survivorship period.

## Importance of Quality of Life Measures for Head and Neck Cancer Patients

The World Health Organization aptly identifies how complex it is to define quality of life and how individualized this can be to each person. They state that "[quality of life] is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationship to salient features in the environment" [4]. With the incredibly high depression and suicide rate in cancer patients, and in head and neck cancer patients specifically, the importance of finding tools to delineate pitfalls in our patients' quality of life cannot be overstated [1, 2].

Our head and neck cancer patients are notably faced with various degrees of disfigurement and altered appearance. They have significant disturbances in their speech and swallowing, which are essential to social interactions and maintaining relationships. Quality of life measures have thus gained acceptance as integral in assessing a head and neck cancer patient's overall well-being. There are dozens of scales, all of which have been studied for their validity, reliability or reproducibility, and sensitivity to changes over time. While there are over 75 tools available for cancer patients of any subtype [5], this chapter will focus on those most commonly used for head and neck cancer patients.

Specific to head and neck cancer, quality of life instruments can be aimed to assess a patient's general well-being versus a more specific symptom-related instrument [6]. Most instruments will assess various domains and combine the results into a single quality of life score; others are validated to provide separate scores for each domain. This may prove to be useful for more targeted therapy. Aside from general quality of life measures, there are also many instruments available to assess each specific symptom a patient may encounter. Some examples are listed in Table 11.1. Most instruments are self-administered by the patient. The most commonly used scoring format is a 5-point Likert-type scale. For example, participants are asked to indicate where they fall from a "strongly agree" to "strongly disagree" range, when asked if they have difficulty swallowing solid foods. The following sections will provide a summary of commonly cited quality of life instruments in the literature, providing the reader a concise and thorough source to reference when selecting which quality of life measure is most appropriate for their patient population.

## Head and Neck-Specific Quality of Life Measures

Each of these measures assesses a variety of dimensions related to head and neck cancer, including, but not limited to, the following: pain, functional performance (speech/swallowing), social well-being, and aesthetics/appearance. In this section we will describe six validated and commonly cited tools that are beneficial to the physician treating a head and neck cancer patient. Table 11.2 summarizes and compares the general format of these six quality of life measures. Each asks the patient to reflect on their feelings and symptoms over a specific time period, which is important to note given that these patients go through a complex healing process and have fluctuating symptoms and concerns during this time.

The two most frequently published questionnaires for assessing overall quality of life in head and neck cancer patients are the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Head and Neck Module (QLQ-H&N35) and the University of Washington Quality of Life (UWQOL)

**Table 11.1** Summary of the most commonly encountered quality of life instruments

| *Head and neck-specific measures* |
|---|
| EORTC QLQ-H&N35 |
| UWQOL |
| FACT-HN |
| HNQOL Questionnaire |
| MDASI-HN |
| HNCI |
| *Treatment-specific measures* |
| QOL Radiation Therapy Index |
| The Neck Dissection Impairment Index |
| Shoulder Pain and Disability Index |
| *Symptom-specific measures* |
| Oral Health Impact Profile |
| Xerostomia Questionnaire |
| MD Anderson Dysphagia Inventory |
| Voice Handicap Index 30 & 10 |
| *Disfigurement-related measures* |
| Facial Clinimetric Evaluation Scale |
| Derriford Appearance Scale 59 & 24 |
| Nasal Appearance and Function Evaluation Questionnaire |

*EORTC QLQ-H&N35* European Organization for Research and Treatment of Cancer Quality of Life Head and Neck Modules, *UWQOL* University of Washington Quality of Life Questionnaire, *FACT-HN* Functional Assessment of Cancer Therapy-Head and Neck, *HNQOL* Head and Neck Quality of Life Questionnaire, *MDASI-HN* MD Anderson Symptom Inventory-Head and Neck Module, *HNCI* Head and Neck Cancer Inventory

**Table 11.2** Head and neck-specific quality of life measures

| | Symptoms evaluated | Time frame assessed |
|---|---|---|
| EORTC QLQ-H&N35 [7] | 7 domains: pain, swallowing, taste/smell, speech, eating in public, social life, sexuality 11 simple items | Past week |
| UWQOL [8] | 12 items: pain, appearance, activity, leisure, swallowing, mastication, speech, shoulder dysfunction, taste, saliva production, mood, anxiety | Past week |
| HNQOL [9] | 4 domains: communication, eating, emotion, pain | Past month |
| HNCI [10] | 4 domains: speech, eating, aesthetics, and social disruption | Past month |
| FACT-HN [12] | 4 domains: physical, social/family, emotional, functional well-being<br>12 simple items related specifically to the head and neck | Past week |
| MDASI-HN [13] | 3 domains: level of symptom severity in general, impact of symptoms on daily life, and specific head and neck symptom severity | Past 24 hours |

questionnaire [6]. Both of these measures provide an overall composite score and assess symptoms specific to head and neck cancer patients. Both ask the patient to reflect on their symptomatology over the last 7 days.

The EORTC QLQ-H&N35 is a 35-item questionnaire with measures specific to pain, swallowing, senses, speech, social eating, social contact, and sexuality. Additional single items are assessed, including pain, dry mouth, and nutritional status. This questionnaire is one of the lengthier available, raising the question of whether patient attention and engagement will effect participation. Validation studies have found the QLQ-H&N35 to be sensitive to radiation exposure and disease site, with radiated patients reporting greater difficulty with pain, swallowing, coughing, dry mouth, and weight loss [7]. Patients with cancer in the oral cavity, oropharynx, hypopharynx, and larynx reported different impairments than those with head and neck cancers in other subsites, with significantly greater difficulty in the swallowing and speech categories. [7]

The UWQOL is a commonly used, concise, 12-question questionnaire that focuses on the patient's sentiments over the last week [8]. Multiple-choice questions are listed regarding the patient's pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder, taste, saliva, mood, and anxiety. The patient is also asked which of those is affecting them the most over the last 7 days (up to 3 may be selected), which can assist the clinician to understand what aspect of a patient's care is most important. The answers are scored with a Likert-type scale, with 0 being no change and 100 being the worst outcome. This tool has been extensively used and has been validated in over 15 languages.

In addition to the EORTC QLQ-H&N35 and the UWQOL, there are other instruments which have been validated to provide separate scores for each domain assessed. Providing these distinct scores per domain can allow the clinician to break down the patient's sentiment on their recovery and quality of life and can help the clinician direct the patient to appropriate resources. These include the Head and Neck Quality of Life (HNQOL) questionnaire, the Head and Neck Cancer Inventory (HNCI), and the Functional Assessment of Cancer Therapy-Head and Neck (FACT-HN). Notably, both the HNQOL and the HNCI assess the patient's symptoms in the last month, while the FACT-HN is focused on the last week of symptoms (Table 11.2). The HNQOL questionnaire measures the patient's score in each of the following domains: communication, pain, eating, and emotion [9]. The HNCI evaluates the following four domains: speech, eating, aesthetics, and social disruption through a 30-item questionnaire [10, 11]. The FACT-HN consists of 27 core items which among them have questions related to 4 domains: physical, social/family, emotional, and functional well-being [12]. There are then an additional 12 items for head and neck-specific symptoms. As with the HNQOL and the HNCI, scores for each domain can be combined or also evaluated separately as subscores.

MD Anderson has also carefully constructed a head and neck-specific questionnaire based on initial focus group meetings with cancer patients and extensive literature review. This head and neck-specific module, called the *MD Anderson Symptom Inventory-Head and Neck Module (MDASI-HN)*, has been tested extensively for internal validity and test-retest reliability and evaluates nine main items: mucus production, difficulty eating, choking/coughing, difficulty with voice or speech, skin pain/rash, taste disturbances, mouth sores, and dental problems [13]. This questionnaire is unique from the others mentioned in that it asks patients to reflect solely on the last 24 hours. Patients are asked to score their symptoms on a scale of 0 (not present) to 10. This tool has been psychometrically validated in seven languages.

In summary, there are many high-quality QOL measures that have been developed to assess the overall well-being/quality of life in head and neck cancer patients. Deciding which instrument to use depends largely on whether the goal is to assess the patient's symptoms in the past day (MDASI-HN), week (EORTC QLQ-HN35, UWQOL, or FACT-HN), or the last month (HNQOL or HNCI). Furthermore, the clinician must decide whether a short inventory will be easier to deliver and for patients to adhere to or whether more extensive data acquisition is desired. Similarly, clinicians should decide whether one composite score will suffice or if it would be more beneficial to break down the patient's quality of life score for each domain, as is validated and possible with the HNQOL, HNCI, and FACT-HN.

## Treatment-Specific Measures

While comprehensive QOL instruments are useful to gauge a patient's overall experience with head and neck cancer, having specific and concise instruments related to issues with treatment allows the care team the ability to quickly summarize well-being. These measures also provide the clinician or researcher an opportunity to compare different treatment modalities and their effects on QOL. Also, more succinct instruments help prevent data gathering fatigue within all facets. Through this section, we will discuss QOL instruments used specifically for those undergoing radiotherapy and neck dissections in an effort to identify areas that may benefit from focused interventions. These are summarized in Table 11.3.

**Table 11.3** Treatment-specific quality of life measures

| | Symptoms evaluated | Time frame assessed |
|---|---|---|
| QOL-RTI/H&N [14, 15] | 25 general items: functional/health, emotional/psychological, family/socioeconomic<br>14 HN-specific items: pain, appearance, speech, chewing and swallowing, mucus and saliva, taste, cough | Past week |
| NDII [19] | 10 items: pain, stiffness, range of motion, functional status, ability to lift objects, work, and carry out recreational activities | Past 4 weeks |
| SPADI [20] | 2 domains: pain, disability (ADLs)<br>13 items | Past 24 hrs |

*QOL-RTI/H&N* Quality of Life-Radiation Therapy Index/Head and Neck, *NDII* Neck Dissection Index II, *SPADI* Shoulder Pain and Disability Index

The *QOL-Radiation Therapy Index (QOL-RTI)* has been used widely for evaluation of QOL changes during radiation therapy in general [14]. An adjunct module designed specifically for the *Head and Neck (QOL-RTI/H&N)* was developed after recognition that radiation to this area causes a unique set of changes, unseen in other areas of radiotherapy [15]. Together, the QOL-RTI/H&N survey is a 39-question assessment, with 14 questions specific to evaluating changes over the previous week in mucous, saliva, eating, taste, speech, cough, and local pain in a Likert-type scale. Studies have shown that the H&N adjunct is more sensitive than general QOL tools to identify critical issues in the head and neck radiotherapy patient [15]. This tool has been validated in multiple languages including Spanish, Chinese, German, and Japanese [16–18]. Combined use of a generalized QOL tool and one that is specific to radiotherapy can help provide a more complete picture about how a patient is tolerating therapy, which could influence future clinical decision-making, provide the patient with targeted treatment to abate their symptoms, and hopefully improve their recovery experience.

The Neck Dissection Impairment Index (NDII) and the Shoulder Pain and Disability Index (SPADI) are two tools we recommend to assess a patient's postoperative morbidity in regard to the neck and shoulder in particular. The NDII evaluates disability after neck dissection in the form of pain, stiffness, range of motion, functional status, and ability to lift objects, work, and carry out recreational activities. It is formatted in a 10-question Likert-type scale and is given in the context of the past 4 weeks [19]. With specific regard to shoulder pathology, the SPADI is a well-cited tool to help to narrow the specific shoulder disability and thus help clinicians and therapists provide a more tailored treatment plan [20]. The SPADI evaluates pain and disability on two separate visual analogue scales, with a total of 13 questions, and focuses on impairments in functional status over no specified time frame. Specifically, these two instruments, the NDII and SPADI, can be used to identify patients who may benefit from focused shoulder therapy and to monitor their progression throughout treatment and rehabilitation.

Assessing the patient's perceived dysfunction following these common treatment modalities is incredibly important to patients. Shoulder dysfunction specifically has been reported to persist following neck dissection and also correlate significantly with overall health-related QOL [21]. Furthermore, shoulder and neck disability after treatment for head and neck cancer has been correlated to have significant impact on almost all domains of QOL including limitations of physical functioning, vitality, pain, general health perception, and general mental health [22]. Consideration of the multiple elements that influence QOL including the large impact of treatment-specific sequelae from radiation or neck dissection is vital to understanding a patient's postoperative health.

## Symptom-Specific Measures

While general head and neck quality of life questionnaires also assess symptoms related to speech and swallowing, having separate symptom-specific QOL measures helps assess one very particular area. These symptom-specific instruments are often used by our speech-language pathology colleagues, most commonly pertaining to dysphagia and voice handicap. The most commonly used symptom-specific instruments are summarized below and in Table 11.4.

Oral health is an important area of well-being related to head and neck cancer patients. A majority of head and neck cancers occur in the oral cavity, and evening treatment of cancers outside of the oral cavity often either directly (through surgery) or indirectly (through the sequelae of radiation or chemotherapy) affects the oral cavity. The *Oral Health Impact Profile (OHIP)* is not specific to head and neck cancer alone, but carefully asks patients, in a series of 14 questions, what difficulties they have faced with their teeth, mouth, or dentures, ranging from speech, oral intake, and general satisfaction with their oral health [23]. Despite it not being originally developed for cancer patients, studies including the OHIP for head and neck cancer patients note a significant decline in quality of life in patients who noted oral impairment [24]. Including dental colleagues and dental assessment in the oncologic approach is thus important both for the patient's physical health and also for their mental well-being.

Xerostomia, or dry mouth, is a symptom closely linked to oral health that is extremely important to independently assess. Countless features pertaining to our cancer patients put them at higher risk for xerostomia, particularly their older age, malnutrition, salivary gland ablation, and exposure to chemotherapy/radiation. Interestingly, it cannot be overlooked, as noted in the theme of this chapter, that head and neck cancer patients may also suffer from pain and depression and may therefore be taking narcotics, antidepressants (from anticholinergic effects), and

**Table 11.4** Symptom-specific quality of life measure

| | Symptoms evaluated | Time frame assessed |
|---|---|---|
| OHIP [23] | 14 items: difficulties w/teeth, mouth, dentures, speech, oral intake, and general satisfaction with oral health | Past month |
| XQ [26] | 8 items: talking, eating, swallowing, speech, and sleep | Past month |
| MDADI [27] | 4 domains: global or subscale: emotional, functional and physical<br>20 items | Past week |
| VHI 30&10 [28, 29] | VHI-30: global or subscale: emotional, functional, and physical<br>VHI-10: Global only<br>30 and 10 items, respectively | Unspecified |

*OHIP* Oral Health Impact Profile, *XQ* Xerostomia Questionnaire, *MDADI* MD Anderson Dysphagia Inventory, *VHI 30&10* Voice Handicap Index other potentially xerogenic drugs, which can further exacerbate the patient's dry mouth [25]. The Xerostomia Questionnaire (XQ) is a quick 8-question self-reported tool that evaluates how dry mouth influences talking, eating, swallowing, speech, and sleep [26]. This is performed on a Likert-type scale with higher values indicating worse xerostomia. Through early identification and treatment of xerostomia, we may lessen this burden and improve our patient's QOL as they recover from their cancer treatment.

Oropharyngeal dysphagia as a sequela from head and neck cancer treatment can be particularly injurious to QOL, nutrition, and overall postoperative well-being. The *MD Anderson Dysphagia Inventory (MDADI)* is a well-validated and reliable tool for clinicians to utilize when evaluating the role of dysphagia on QOL, specifically within head and neck cancer patients. This instrument gauges swallowing dysfunction over the past week through 20 questions, divided into 4 subscales of global, emotional, functional, and physical QOL impairment [27]. In combination with a formal swallowing evaluation, assessment of an individual's perception of their dysphagia and its toll on their QOL can help illuminate areas where treatment may provide benefit. Also, an objective measurement of disease-specific QOL changes may provide a means for demonstrating treatment efficacy and identify room for improvement.

With regard to voice impairment, the patient's own perception of handicap or disability is important to evaluate, because each individual's use of their voice in a social and professional context is unique. Therefore, when considering treatment of a laryngeal pathology or the potential role of speech therapy, an objective measure of perceived impairment can be helpful. There are two well-validated measures to evaluate this: the *Voice Handicap Index 30 (VHI-30)* and an abbreviated version, the *Voice Handicap Index 10 (VHI-10)*, that differ primarily by size, with 30 and 10 questions, respectively [28, 29]. While the VHI-30 is more comprehensive and allows subscale evaluation of voice impairment, the VHI-10 is a quick and global way to examine this metric. Intriguingly, many patients are unaware of the severity of their voice impairment until completing the VHI [28], which emphasizes the importance of identification, especially with regard to our voice's influence in QOL. Therefore, recognition and education about voice handicap may be helpful and motivating to patients throughout their therapy.

## Disfigurement-Related Measures

Aside from functional deficits in speech and swallowing, the head and neck cancer patient's physical appearance is frequently altered. This can drastically change the way an individual thinks about themselves, the way they approach social gatherings, and the way they perceive their own QOL. While the majority of clinicians focus on functional problems such as swallowing, speech, and pain, many head and neck cancer patients endure a significant emotional and psychosocial change while healing from the therapies used to fight their disease. Patients may be hesitant to bring up concerns about their appearance, and therefore, clinician awareness of this impact on QOL is important when evaluating the overall health of head and neck cancer patients [30]. There have been few validated tools for evaluation of disfigurement in the head and neck cancer patient; however there are some instruments available to assess outcomes of facial dysfunction, general appearance, and nasal appearance/function (Table 11.5).

Assessment of facial impairment and disability, particularly related to facial nerve paralysis, has been validated with the *Facial Clinimetric Evaluation (FaCE) Scale*. Through 15 Likert-type questions, the FaCE Scale provides information from the past week about social function, facial comfort, facial movement, oral function, eye comfort, and lacrimal control. This patient-reported tool has been shown to be superior to previous physician-graded scales in regard to assessing facial dysfunction [31]. The *Derriford Appearance Scale 59 (DAS59)* and its shorter version, the *Derriford Appearance Scale 24 (DAS24)*, are tools used to evaluate the role of general appearance on self-esteem, psychosocial activities, and patient awareness/satisfaction [32, 33]. While these may help alert a clinician about potential psychosocial changes or a decline in QOL from appearance changes, neither of these questionnaires are specific to head and neck cancer patients. Additionally, both contain questions that may be unrelated to this population. Lastly, the *Nasal Appearance and Function Evaluation Questionnaire (NAFEQ)* is a useful tool designed for use in the perioperative period following nasal reconstructive surgery. This is a Likert-type survey that dedicates seven questions to airway passage, snoring, olfaction, epistaxis, phonation, and dry mucosa and seven detailed questions related to cosmesis [34]. With 50% of this instrument being directly related to cosmetic concerns, the utility of this tool in the head and neck cancer patient is less applicable.

**Table 11.5** Disfigurement-related quality of life measures

| | Symptoms evaluated | Time frame assessed |
|---|---|---|
| FaCE Scale [31] | 15 items: social function, facial comfort, facial movement, oral function, eye comfort, and lacrimal control | Unspecified |
| DAS59 and DAS24 [32, 33] | 59 items and 24 items, respectively<br>Psychosocial activities, patient awareness/satisfaction, sexual and bodily self-consciousness of appearance | Unspecified |
| NAFEQ [34] | 7 functional items: airway passage, snoring, olfaction, dry mucosa,<br>epistaxis, and phonation<br>7 cosmetic items: overall assessment, item in each part | Unspecified |

*FaCE Scale* Facial Clinimetric Evaluation Scale, *DAS59 and DAS24* Derriford Appearance Scale, *NAFEQ* Nasal Appearance and Function Evaluation Questionnaire

## Conclusions

Caring for head and neck cancer patients requires that we focus not only on curing a patient's cancer but also on treatment-related physical symptoms and psychosocial well-being. As detailed in this chapter, many excellent QOL instruments have been developed and studied. The specific instrument chosen will depend largely on clinician preference and also on what specific metric symptoms and time frame are being captured. By utilizing these quality of life measures, the clinician can assess the complete summary of their patients' care. Identifying if the patient's speech, swallowing, appearance, or general well-being is significantly affected can help the clinician proactively intervene and improve their patients' overall well-being and outcomes.

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# Chapter 12
# Multidisciplinary Care

**Yoseph A. Kram and Eric D. Wirtz**

It is difficult to truly ascertain the effects of psychosocial and psychological distress on patients with head and neck cancer, but in regard to prevalence, studies have shown that it negatively impacts nearly 50% of all patients undergoing treatment for head and neck cancer [1, 2]. Head and neck cancer has been described as being the most “emotionally traumatic” of all cancers due to the primary effect of the cancer and the secondary effects of treatment on the appearance and fundamental functions of those with head and neck cancer [1]. A study published by Shekelle et al. in 1981 showed the presence of depression was associated with a twofold increase in mortality among patients being treated with cancer resulting in a fourfold increase in the rate of suicide in head and neck cancer patients compared with that of the general public or those with other types of cancer [2].

The National Comprehensive Cancer Network (NCCN) recognizes the importance of the multidisciplinary team and support services in head and neck cancer by preempting the management guidelines with a section on this topic: “The management of patients with head and neck cancers is complex. All patients need access to the full range of support services and specialists with expertise in the management of patients with head and neck cancer for optimal treatment and follow-up” [3]. While it is easy to focus solely on the medical and surgical treatment of head and neck cancer, an equally important goal of the multidisciplinary team is early identification and coordinated management of psychological and psychosocial effects of the diagnosis and treatment of head and neck cancer.

Studies in the head and neck cancer scientific literature sometimes use the term “multidisciplinary care” when specifically referencing collaboration between

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physicians and surgeons involved in curative efforts such as surgery, radiation therapy, and chemotherapy. This chapter, and text overall, takes care to include the numerous providers and team members involved in head and neck cancer care and their role in the multidisciplinary team in the management of the psychological and psychosocial effects of head and neck cancer. We will also discuss barriers and strategies on the implementation of the multidisciplinary management of complex cancer care. While the barriers of multidisciplinary care are often great, the synergistic effects of multidisciplinary management produce a combined benefit greater than the sum of the individual parts.

There is abundant literature on head and neck cancer team members' roles and responsibilities and the benefits of including each member in the care of patients; however, there is a paucity of literature on how head and neck cancer teams best function, especially when focused specifically on psychological and psychosocial effects. Despite the nearly universal recognition of the impact of psychologic and psychosocial distress on treatment of head and neck cancer, how it should be treated is less understood. While most authors note the need for multidisciplinary care in treatment of head and neck cancer, fewer recognize the importance of incorporation of psychologic and psychosocial care into the multidisciplinary teams.

This chapter endeavors to present the available evidence for the utilization of multidisciplinary care in head and neck cancer including the psychological and psychosocial effects of head and neck cancer, discuss the roles of each member of the multidisciplinary team, describe barriers that exist within multidisciplinary care, and the strategies that can be utilized to mitigate these barriers.

## Evidence of Benefit

While there are not data to specifically support the use of the multidisciplinary team in the management of the psychological and psychosocial effects of head and neck cancer, there are studies that have retrospectively demonstrated the benefit on the multidisciplinary management of head and neck cancer.

Studies have shown that multidisciplinary team (MDT) care compared to non-MDT care can alter diagnosis, stage, and treatment plan [4], improve late stage survival [5], and improve adherence to clinical quality indicators (CQIs) [6] such as dental assessment, nutritional assessment, PET staging, chemo-radiotherapy for locally advanced disease, and use of adjuvant CRT for high risk disease.

While these data show some benefit of multidisciplinary management of head and neck cancer, there is scant literature discussing the benefit of the multidisciplinary management of head and neck cancer in the treatment of the psychological and psychosocial effects of cancer. However, the importance of multidisciplinary management of the psychological and psychosocial effects of head and neck cancer and its treatment can be deduced from the above data if the need for psychologic and psychosocial care can be demonstrated. The need for high-quality multidisciplinary head and neck cancer care is self-evident as one reviews individual team members' roles and responsibilities and how complex such care can become. One patient in a qualitative review aptly described the effects of lacking coordinated and communicative multidisciplinary care:

> There was no overall communication, there was no one saying, "this is what's going to happen". It was like the plastic surgeon was going to do his bit, the medical oncologist was going to do her bit, the ear nose and throat person was going to do their bit, the maxillofacial person was going to do their bit and so I was just going from specialist to specialist and there was no one telling me what was going to happen. So that was a bit confusing and also a bit unsettling [7].

Up to 49% of patients with cancer meet the diagnostic criteria of depression and patients who develop depression are less likely to complete treatment leading to subsequent increased mortality [8, 9]. It has also been shown that patients who develop depression during treatment of their HN cancer are more likely to have a worse quality of life upon completion of treatment [10]. In addition to these data, there are also numerous studies showing that the treatment of psychological distress can improve treatment adherence, satisfaction with care, and health-related quality of life. Providing interventions such as coping strategies, for example, can improve physical and social functioning, global quality of life, fatigue, sleep disturbance, and depressive symptoms [11]. There are also studies that have shown that individual modalities of head and neck cancer rehabilitation in selected patients can improve quality of life and even survival [12]. Patients should be screened for psychological distress because they may not be an accurate judge of their own level of distress during radiation and therefore do not self-refer for psychological support [13, 14].

Although a large proportion of patients with HN cancer experience clinically significant psychosocial distress, medical professionals frequently fail to recognize this distress. This is particularly concerning given that distress is responsive to treatment, and untreated distress is associated with significantly worse psychosocial and medical outcomes [15].

## Head and Neck Cancer Multidisciplinary Team Members

A comprehensive discussion of the roles and responsibilities of the numerous team members is beyond the scope of this chapter, but these included descriptions introduce the team member with particular attention to relevancy to psychological and psychosocial effects. Examples of typical team member's involvement in multidisciplinary care and management of psychological and psychosocial effects are included. Table 12.1 summarizes training of the team members. Many more types of providers who may participate in the care of patient with head and neck cancer have not been included for the sake of brevity.

Cancer treatment, both surgical and medical (chemotherapy, radiotherapy, immunotherapy), has wide and varying effects on quality of life and long-term psychological outcome. These effects vary on the involved organs, modality of

**Table 12.1** The head and neck cancer multidisciplinary team members and their typical educational degrees and training

| Provider | Typical educational degree and training |
|---|---|
| Head and neck surgeon | Doctor of Medicine (MD)/ Doctor of Osteopathy (DO), Otolaryngology—Head and Neck Surgery Residency, Head and Neck Surgery Fellowship |
| Radiation oncology | MD/DO, Radiation Oncology Residency |
| Medical oncology | MD/DO, Internal Medicine Residency, Hematology/Oncology Fellowship |
| Facial plastic and reconstructive surgery | MD/DO, Otolaryngology—Head and Neck Surgery Residency, Facial Plastic and Reconstructive Surgery Fellowship |
| | General Surgery Residency, Plastic Surgery Fellowship |
| Dentistry/prosthodontics | Doctor of Dental Surgery (DDS)/ Doctor of Medical Dentistry (DMD)<br>Prosthodontics Fellowship |
| Speech-language pathology | Master of Science (MS) |
| Clinical social work | Master of Social Work (MSW) |
| Psychiatry | MD/DO, Psychiatry Residency |
| Clinical psychology | Doctor of Philosophy (PhD) |
| | Doctor of Psychology (PsyD) |
| Nutrition | Registered Dietitian Nutritionist (RND) |
| Primary care/geriatrician | MD/DO: Primary Care Physician |
| | Geriatrics Fellowship |
| | Nurse Practitioner (NP) |
| | Physician Assistant (PA) |
| Palliative care | MD/DO: Residency in various fields, Fellowship in Hospice and Palliative Care |
| | Registered Nurse (RN, LVN/LPN) |

Degrees and training may vary by local, regional, and national accreditation standards

treatment, stage of disease, and also patient-related factors. The decision between surgical and medical treatment of an individual's head and neck cancer is well beyond the scope of this chapter, but cases should optimally involve a multidisciplinary team to assist the patient in the decision-making process.

*Head and neck (HN) surgeons* are physicians involved in nearly every aspect of head and neck cancer and, thus, play a critical role in the assessment and directed treatment of the psychological and psychosocial effects of head and neck cancer. These physicians undergo Otolaryngology—Head and Neck Surgery (OHNS) surgical training, followed by dedicated subspecialty training in Head and Neck Surgery, which is directed toward oncologic and often reconstructive surgery. In some countries, head and neck surgeons initially train in General Surgery prior to dedicated head and neck surgery training. Oral surgeons may also fill this role in some locales. HN surgeons are regarded as the primary experts of head and neck cancer. Screening, biopsy, surgical excision and reconstruction, postoperative aftercare, and surveillance are all physical examples of the roles of head and neck surgeons.

HN surgeons often provide a patient with the initial counseling on head and neck cancer diagnosis and management, including the psychological and psychosocial expectations in this longitudinal process. Irrespective of whether the patient undergoes primary surgical or medical treatment of HN cancer (or multimodality treatment), the treatment course is known to have significant lasting psychological and/or psychosocial effects. While psychological distress often occurs during treatment, it has been shown to be directly linked with quality of life in that those patients with negative physical, social, cognitive, psychological, and emotional issues as well as physical symptoms such as pain, nausea, vomiting, and fatigue negatively affect patients' quality of life [16]. A study by Hung et al. evaluated the effects of surgery on patients' body image score [17]. The study found that radical surgery was the strongest independent predictor of body image score among all patients. The more surgical procedures a patient underwent, the greater correlation with worse posttreatment body image scores. Not only is surgery associated with worse body image score, but it is also known that surgery can negatively affect speech and eating which in turn has been shown to increase body image dissatisfaction compared to those patients who do not have posttreatment difficulty with speech and eating. In turn, patients who undergo primary medical treatment for their HN cancer have been shown to have less impact on body image dissatisfaction compared to those patients who undergo surgical therapy [18].

*Facial plastic and reconstructive surgeons (FPRS)* are physicians who undergo Otolaryngology—Head and Neck Surgery training like head and neck surgeons but then pursue further subspecialty surgical training in this field. In some circumstances, a plastic surgeon, who underwent a General Surgery and Plastic Surgery fellowship pathway, will fill this role. Many head and neck surgeons also receive reconstructive training and participate in this care. FPRS goals are reestablishment of optimal form (aesthetics and structural integrity) and function (speech, swallow, airway protection, among others). Reconstruction can be single-stage with oncologic resection, delayed, or multistaged. Both postoperative aesthetics and function are profoundly intertwined with psychological and psychosocial well-being. Reconstruction following cancer excisions involving the face has a significant aesthetic impact on psychosocial functioning [19].

*Radiation oncology* is a medical field focused on the treatment of cancer through delivery of ionizing radiation. A radiation oncologist will assess and manage radiation side effects as part of the multidisciplinary team and attempts to minimize interruptions related to such therapy side effects as best as possible. They assess candidacy for radiation therapy and discuss optimal strategies in multidisciplinary tumor boards.

During radiation therapy, patients will often experience depressive symptoms [20]. Between 22% and 35% of all radiotherapy outpatients report clinically relevant psychological distress and are at higher risk of developing depression if they receive radiation as their initial therapy compared to those who were treated surgically [21]. In a study from Chen et al., there was a preradiation treatment self-reported anxiety rate of 47% [22]. The median number of total missed treatment days was 11 in patients who reported being "extremely depressed" as compared to 2 days for patients whose pretreatment mood was “neither in a good mood or depressed,” “generally good,” or “excellent.” If patients are actively offered psychological support during radiation therapy between 13% and 41% of the patients will accept a referral for professional support [13, 14, 23]. Given this high level of undetected distress, patients who are undergoing radiation therapy should receive routine screening for psychological distress and be referred for professional support whenever appropriate. It is difficult to ascertain the frequency of which routine screening should be performed. While the American College of Surgeon’s Commission on Cancer requires distress screening to be performed at the minimum frequency of at least once per pivotal medical visit, it is believed that with this infrequency of screening, this may delay or miss an opportunity to care for patients’ who require psychological support. In the study performed by Hess et al., they identified that if patients who are undergoing radiation therapy are screened once every week this would capture 90% of all patients who required psychological support [24]. Radiation oncologists have a role as a member of the multidisciplinary team to screen their patients while undergoing radiation therapy to assess for pretherapy psychological distress or therapy-induced psychological distress and refer them for therapy to not only improve their psychological well-being but also to improve their adherence to therapy and possible chance of survival.

Often known as *hematology/oncology physicians*, medical oncologists focus on nonsurgical and nonradiation based oncologic therapies, especially chemotherapy and immunotherapy. A medical oncologist will assess and manage systemic side effects as part of the multidisciplinary team and also attempts to minimize interruptions related to such therapy side effects as best as possible. Chemotherapy is used either in addition to radiotherapy or can be used prior to curative surgical therapy in head and neck cancer and is indicated for more advanced disease according to NCCN guidelines [3]. The curative potential of existing therapies in head and neck cancer is limited by the morbidity that is associated with therapy. Chemotherapy regimens have included monotherapy and combination therapies of cytotoxic medications such as platinum analogs (cisplatin, carboplatin), 5-FU, antimetabolites (methotrexate), taxanes, and immunotherapy such as cetuximab [25]. Combination chemotherapy and radiotherapy may incur additional toxicity compared to radiotherapy alone including greater mucositis, weight loss, fatigue, and dysphagia. Supportive care for chemoradiation includes erythropoietic agents and granulocyte-colony stimulating factor to counter myelosuppression and antiemetic therapy such as 5-HT3 antagonists [26]. With chemotherapy added to the treatment regimen comes new psychosocial concerns for the patient. For example, an interview-based study of patients receiving chemotherapy from France showed 33% expressed concerns regarding occupations and leisure activities, 32.6% expressing psychological needs, and 30% expressing needs related to interactions with family and friends [27]. Chemotherapy side effects interrelate to psychosocial concerns. Grassi et al. found that in their patient population undergoing chemotherapy that more than half of patients reported nausea (54%) and 14% reported vomiting. This chemotherapy-induced nausea and vomiting were associated with maladaptive coping (i.e., hopelessness-helplessness and anxious preoccupation) and emotional distress with poorer quality of life [28].

HN surgeons, radiation oncologists, and hematology/oncology physicians aim to cure or palliate head and neck cancer directly whereas the following specialists focus on the many other effects of cancer diagnosis, treatment, and surveillance.

*Dentistry and oral surgeons* play a significant role in head and neck cancer management due to the effects of therapy on oral function and hygiene. Regardless of the type of therapy provided for head and neck cancer, treatment often leads to decreased saliva production – the most severe being in those who receive radiation therapy. Hyposalivation not only affects quality of life by causing xerostomia but can also lead to dental demineralization and caries and increased risk of other oral infections such as candidiasis. Oral disease can not only cause pain and decreased oral function but can also negatively impact the psychologic well-being of cancer patients through increased anxiety and depression. These psychologic effects are represented by the fourfold increased risk of suicide in survivors of head and neck cancer [29].

Dentists are key members in the multidisciplinary management of head and neck cancer patients as they are in a position to detect and biopsy oral and oropharyngeal lesions [30]. Once the cancer diagnosis is made, dental providers can positively impact the psychological and psychosocial effects of head and neck cancer through providing continued dental care for these patients to minimize the negative impact of treatment on oral health. As dental extraction is often the result of surgical and/or medical treatment of HN cancer and the fact that patients perceive loss of teeth as a determinant of quality of life and posttreatment depression/anxiety, dental restoration is an important aspect of multidisciplinary management of HN cancer [31]. Similar to plastic and reconstructive surgeons, the goal is restoration of form (dentition) and function (mastication) through veneers, crowns, bridges and other methods.

*Speech-language pathology* (SLP) is an ancillary healthcare field with expertise of communication, including vocalization, and swallowing. The SLP assesses risk factors for aspiration, provides individually tailored swallowing and mastication exercises, and guides the patient as to appropriate texture foods to optimize swallowing [32]. The ability to tolerate oral diet has been shown to affect quality of life and rates of depression in head and neck cancer. A study from Hassanein et al. found that patients with functional oral impairment 6 months after treatment were more likely to have severely depressed emotional states compared to those with normal oral function [33]. It has also been found that patients with trismus following treatment of their head and neck cancer are more likely to have greater levels of depression compared to those with normal interincisal opening [34]. In laryngeal cancer, integrating SLP in both surgical and nonsurgical treatment has psychosocial benefits [35]. Nutrition and SLP services may be closely intertwined in multidisciplinary care; for example, an RCT showed that adding individualized swallowing therapy to individual dietary counseling did not improve food intake but did accelerate swallowing recovery [36]. SLP evaluation and intervention should be initiated prior to treatment if possible. A retrospective cohort study at Johns Hopkins Medical Institutions showed that patients evaluated initially (pretreatment) through the multidisciplinary clinic had more SLP visits during and after treatment than those who did not participate in the multidisciplinary clinic initially (mean = 1.8 vs. 0.2, $P < 0.0001$) [37].

*Clinical social work* is a healthcare profession with special focus on behavioral and bio-psychosocial problems and disorders. This can be performed in patient group settings [38]. Another similar position is the outpatient head and neck oncology nurse coordinator who is dedicated to head and neck oncology coordination and early problem identification [39]. The clinical social worker often focuses on ameliorating the financial, social, and psychological barriers to cancer care. Facilitating support groups, mediating patient-caregiver conflicts, referrals to financial assistance organizations, providing information on spiritual counseling, coordinating transportation to treatment, and providing information about a disease are also possible roles that the clinical social worker can fulfill.

*Psychiatry* is the study and treatment of mental illness, emotional disturbance, and abnormal behavior. Although head and neck cancer is not a psychiatric disorder, secondary effects of head and neck diagnosis and treatment include psychiatric issues such as depression, addiction, and posttraumatic stress disorder (PTSD) [40]. Additionally, psychiatrists often function as or with psychotherapists. Preexisting psychiatric disorders also significantly affect the course of care. The Prevention of Depression in Patients Being Treated for Head and Neck cancer Trial (PROTECT) investigated the use of prophylactic administration of the antidepressant escitalopram oxalate on patients without a baseline diagnosis of depression. This study found that escitalopram oxalate had the ability to prevent the development of depression in patients who were about to begin treatment of their head and neck cancer by greater than 50% [21]. Due to the complex medical histories and medications for treatment and symptom management of head and neck cancer patients, the active involvement of a mental health provider as a member of the MDT is critical.

*Clinical psychology*, conversely, is more focused on the context of distress with non-pharmacologic interventions such as cognitive behavioral therapy and mindfulness [41]. Although limited high-quality evidence exists for psychological interventions improving quality of life for head and neck cancer patients [42], there is evidence that psychological therapy improves emotional, physical, and functional well-being. Given the high prevalence of depression, anxiety, and distress in these patients, it is critical to support the spiritual and psychological well-being of head and neck cancer patients throughout their treatment and recovery.

*Registered dietitians* (RD) are regulated healthcare professionals licensed to manage nutritional problems. Both the nature of head and neck cancer and its oncologic treatments can impact the ability of the body to maintain nutritional status. Nutrition is critical to proper wound healing. RD counseling aims to minimize undesired weight loss, prevent malnutrition, and promote wound healing. RDs may also work to motivate patients with head and neck cancer to maintain oral intake of nutrition, including mindful eating strategies [32].

*Primary care providers*, particularly *geriatricians*, can play a major role in the comprehensive and longitudinal care of older patients with head and neck cancer [43]. These healthcare providers may continue to manage other medical conditions through the course of head and neck cancer care. Studies show that a geriatric assessment prior to initiation of chemotherapy was more helpful in identifying patients at higher risk for chemotherapy-related adverse events than other commonly used measures in oncology practice such as performance status [44]. There is an ongoing trial on the impact of comprehensive geriatric assessment on survival, function, and nutritional status in elderly patients with head and neck cancer: protocol for a multicenter randomized controlled trial (EGeSOR) which will provide valuable insight into the role of the geriatrician [45].

*Palliative care* is medical and nursing care that focuses on providing relief from symptoms, especially pain, and physical and mental stress. Palliative noncurative therapy is focused on management of noncurable disease, including head and neck cancer, but palliative care specialists are also trained to alleviate complex symptomatology at any stage of illness. Hospice care, focusing on communication, collaboration, compassionate caring, comfort, and cultural (spiritual) care, is often closely associated with this field.

## The Tumor Board

The National Cancer Institute defines a tumor board as a treatment planning approach in which a number of physicians who are experts in different specialties (disciplines) review and discuss the medical condition and treatment options of a patient [46]. Although the authors agree with this definition fundamentally, the tumor board is also a prime opportunity for nonphysician members of the care team to provide insight and recommendations into other aspects of the patient's cancer care trajectory. The tumor board should be utilized not only for the discussion of new head and neck cancer patients but also for a discussion of patients with ongoing cancer treatment and patients in the surveillance phase. This is of particular importance to the subject at hand given that much of the psychological and psychosocial of head and neck cancer occur during the treatment and posttreatment phases.

Some members of the multidisciplinary team may attend other tumor boards, such as chest or gastrointestinal, at their institution. It may also be known as Multidisciplinary Team Planning or other similar terms. Institutions may offer Continuing Medical Education (CME) credit for attendance, and survey studies show that providers appreciate these meetings [47]. Nonphysician attendance can better enhance patient care coordination [39].

Shellenberger et al. give an excellent description of the tumor board and its goals: "a dynamic multidisciplinary team planning conference should also be fluid enough to accommodate needs that arise in managing complications during treatment, assessing response to disease, monitoring for recurrence after treatment, and even attending to late effects of treatment" [48].

Tumor board decisions and plans can be enhanced by incorporating input outside the surgeon, radiation oncologist, and oncologist. In particular, a social worker may have particular insight to the psychological, financial, or general barriers that a patient may have to completing therapy. This is an opportune and critical moment to consider the human patient behind the cross-sectional imaging and histopathology. While NCCN evidence-based approaches and practice guidelines are critical considerations, the patient's personal goals of care, which a psychologist or primary care provider may be more longitudinally knowledgeable of, should factor in to decision-making. Tumor boards can also increase education and awareness of head and neck cancer care for students, trainees, and practitioners.

## Multidisciplinary Care Barriers and Strategies

Given the wide array of needs that a patient with head and neck cancer may encounter along the care arc, an approach with multiple specialties providers seems a necessity. However, a distinction may be made between a system with patients receiving care from multiple providers and a system where the multiple providers work together with longitudinal inter-provider feedback. For this reason, interdisciplinary care may be a more apt term [49]. Figure 12.1 illustrates this concept.

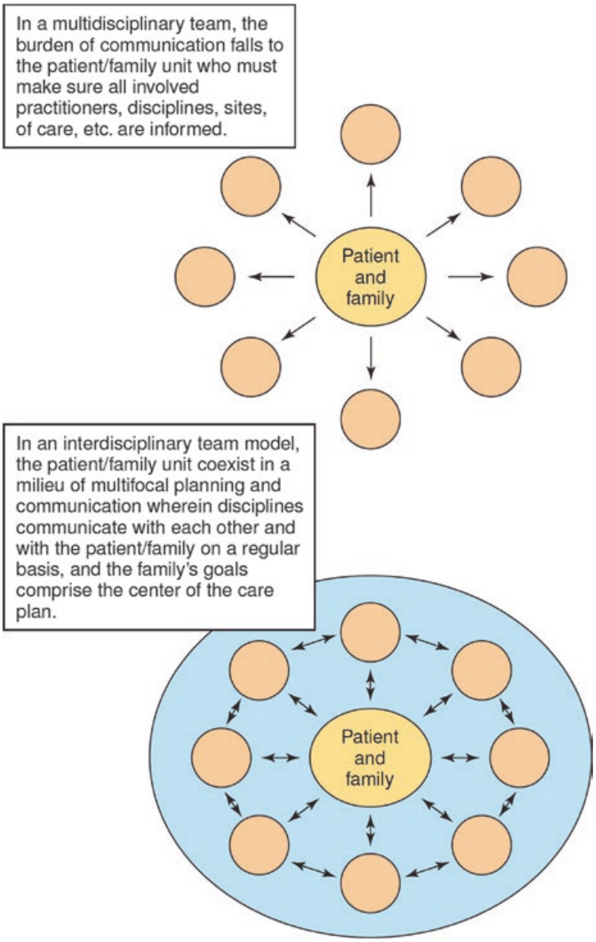

**Fig. 12.1** Distinction between multidisciplinary team and interdisciplinary team models. In an interdisciplinary team model, multiple providers work together with longitudinal inter-provider feedback. (From Street and Blackford [49], with permission)

In a multidisciplinary team, the burden of communication falls to the patient/family unit who must make sure all involved practitioners, disciplines, sites, of care, etc. are informed.

In an interdisciplinary team model, the patient/family unit coexist in a milieu of multifocal planning and communication wherein disciplines communicate with each other and with the patient/family on a regular basis, and the family's goals comprise the center of the care plan.

Every member of the team should attempt to understand each other's roles and responsibilities as well as possible. One general strategy to help in the overall process is the creation of the Head and Neck Oncology Nurse Coordinator whose general role is facilitation of this interdisciplinary process [39]. Figure 12.2 illustrates this coordinator's role. The following discussions of multidisciplinary care barriers and strategies are by no means comprehensive but may be of benefit for providers creating MDTs and navigating team dynamics.

## *Barrier: Recognition of the Need for Another Discipline*

A provider from another discipline cannot help if they are never incorporated into the patient's care. This topic of inclusion is especially relevant to psychological and psychosocial effects of head and neck cancer and its management.

- Lack of screening: Distress screening can help identify barriers to optimal care and recovery. Some studies require patients to express a need prior to psychosocial intervention [38]. Additionally, longitudinal screening across the course of care may be helpful.
- Lack of provider education: Should a given provider lack the knowledge of services that another specialty may offer, then the patient may not be referred for

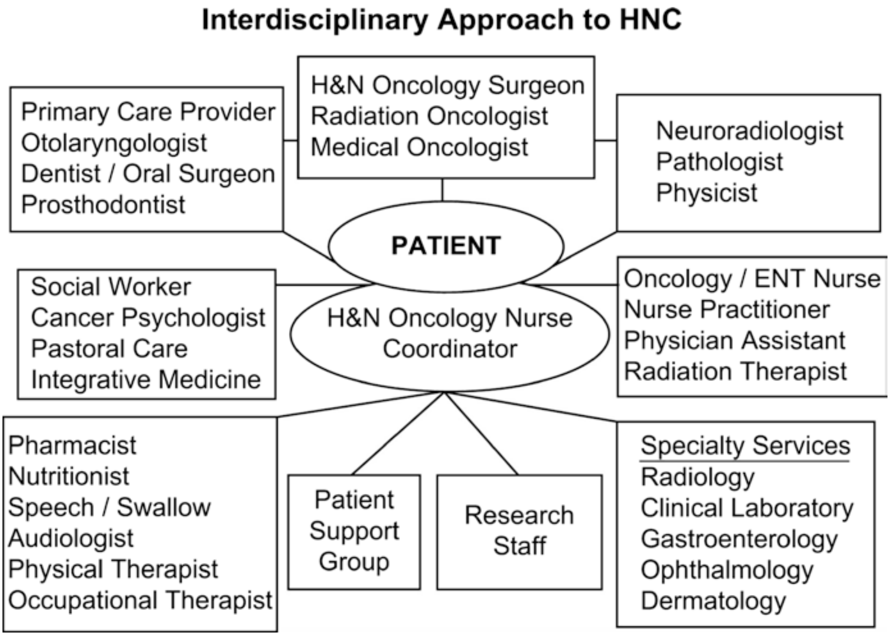

**Fig. 12.2** Facilitation of the interdisciplinary process with a head and neck oncology nurse coordinator. (From Wiederholt et al. [39], with permission)

appropriate care. Palliative care, in particular, is heavily associated with noncurative therapy, but they can be a valuable resource during the course of curative therapy. “Palliative” refers to relieving symptoms without reversing the cause. From this definitional perspective, palliative head and neck cancer care could be considered any supportive care that is not curative or reconstructive in nature. Without clear patient education, a referral to such a specialist could miscommunicate a poorer prognosis and lead to unnecessary psychological distress.

### Strategies

- Automatic consultation with subspecialists based on preset patient and cancer factors. Nutritional assessment, in particular, for any patient requiring a feeding tube is one example of such strategy.
- The measurement of patient-reported outcome measures (PROMs) during and following head and neck cancer management may alert their caregivers to distress and anxiety. Rogers et al. reviewed that head and neck consultants have declined using quality of life questionnaires with reasons cited as lack of resources, unproven value, a time and paper burden, and the misconception that PROMs are a research tool rather than an adjunct to providing patient care and education [50]. PROMs may actually save time if completed prior to the patient encounter and can alert providers to psychosocial issues that may not otherwise arise in discussion.
- Unnecessary referrals and appointments have the potential to add burden to the patient and cost to the healthcare system, and so providers must gauge appropriateness. Stepped care algorithms in head and neck (and lung) cancer patients may be cost-effective tools that spare resources but accommodate severity [51].
- Early training in multidisciplinary care at the undergraduate and graduate medical education levels, such as the UCSF Program for Interprofessional Practice and Education, can introduce concepts and team dynamics that may have been lacking in the past for providers [52, 53].

## *Barrier: Miscommunication*

The topic of communication in oncologic healthcare warrants a textbook in its own right, but a brief discussion is extremely relevant to multidisciplinary head and neck cancer care. Communication settings between providers vary widely in healthcare: face-to-face or telephonic verbal discussions, including the “curbside consults,” postal or facsimile referral correspondence, and the medical record, increasingly electronic, and including both outpatient and inpatient records.

Language and terminology may differ between specialties. The educational pathway for each member varies (see Table 12.1), including their personal and professional backgrounds.

Poor communication with the patient may result in information overload and stress: information presented by different healthcare professionals might not be consistent or could sound divergent if the patient does not fully understand what is being said. Personal, family, and work-related problems that affect financial, social, and emotional well-being might be the primary concerns of the patient and yet might not even be discussed [39]. Patients are not blind to miscommunication. Moore et al. details how inadequate communication can cause stress and confusion about treatment, and conflicting information about treatment contributes to pretreatment anxiety [7].

#### Strategies

- Closed-loop feedback communication with confirmation of comprehension
- Not making assumptions about other caregivers' healthcare literacy, especially in complex subspecialties

### *Barrier: Physical Limitations and Loss to Follow-Up*

The gap between ideal and real-world conditions can diminish head and neck cancer care.

- Gaps in space and time minimize the face-to-face interactions between providers and the patient. This creates opportunities for missed communication. For example, nursing updates may wait while the surgeon operates, or the radiation oncologist may work in a separate campus from the speech-language pathologist.
- Loss to follow-up in cancer may be a result of provider, patient, or external factors.

#### Strategies

- Tumor board conference: Maintain consistent scheduling and ensure that all team members are made aware of changes. Documentation of attendees and case consensuses in a standardized format improves record keeping.
- Inpatient: structured "rounding" with nursing, medical and other staff present. This should take into account daily schedules, such as nursing shift sign-outs and operating room morning start times, among others depending on institutional practices.
- Outpatient: Dual-provider appointments or examinations may be helpful, such as an otolaryngologist performing a nasopharyngoscopy while an SLP observes and interprets.
- Distance between the tertiary care centralized HNC team and the team and locality from which the patient was referred [50]. The clinical nurse, family physi-

cian, otolaryngologist, and dentist are very important to ensure ongoing monitoring and care of late effects of treatment and possible referral to a tertiary care center for further management.
- Some studies describe the psychological effects of awaiting test results (PET scans, pathology reports), but few, if any, describe the psychological effect of awaiting tumor board consensus.
- Maintaining a database of patients with ongoing cancer care at a given institution with contact information and expected dates for follow-up appointments. The Institute of Medicine (IOM) recommends a comprehensive care summary with follow-up plans and ongoing management for patients at primary therapy completion [54].

### *Barrier: Access and Coverage*

- Logistical considerations for the patient such as transportation, child care, housing; employment-related items; and side effects. Radiation treatment, for example, may require patients to attend daily [55].

#### Strategies

- Pivotal role of clinical social worker
- Creation of programs at institutions: Patients living with advanced cancers who underwent the Interprofessional Palliative Rehabilitation Program at the University of Ottawa experienced significant improvement in functioning across several domains. After the initial assessments, the team jointly formulated a tailor-made care plan for each patient. Plans included medical and nursing assessments, physical exercise, and occupational, dietary, and psychosocial interventions. Patients accepted into the 8-week program attended group exercise sessions at a gymnasium in the hospital twice weekly. The gym sessions each accommodated 4–5 patients, supervised by the physiotherapist. Before each gym session, patients were seen by other team members as required, according to need, or as requested by the patient [56]. A similar institutional program was that of McGill University of Montreal [57].

## Conclusion

Multidisciplinary care in the diagnosis and treatment of head and neck cancer represents the standard of care, especially in complex, advanced, and rare cases. Psychological and psychosocial effects arise in nearly every facet of care, and individual members must remain committed to providing every patient with the best chance to achieve personal goals of care and alleviate distress.

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# Chapter 13
# The Role and Importance of the Head and Neck Oncology Nurse Navigator

**Jennifer Jacobs**

For many patients, the worry of having to manage all of their own health care needs after being diagnosed with head and neck cancer is overwhelming. There are many appointments to keep track of and a lot planning, re-arranging, and adapting to a new schedule and routine throughout their treatment. Having another person within the health care team to manage all of that as well as provide additional resources and support makes the transition much easier for the patient. The idea of having someone help navigate patient care originated in 1990 by Dr. Harold P Freeman, a cancer surgeon, and former president of the American Cancer Society. Within his practice of treating patients with breast cancer, he noticed there are many barriers to care that his patient population had to face: lack of transportation, limited financial resources, and even language barriers [1]. Dr. Freeman aimed to develop a way for patients to get through these common issues to receive the care that was needed. Dr. Freeman held mammogram screenings in which he had workers guide patients during the screenings and after if they needed follow up care [1]. Dr. Freeman decided to incorporate this within practice. From allowing another person help navigate patients through the health care system, Dr. Freeman saw his patients' breast cancer survival rates increase from 39% to 70% within 5 years. Through this intervention, the role of nurse navigators soon became a necessity to help all patients manage their cancer treatment efficiently and with ease [1].

Imagine you or a loved one has just been diagnosed with head and neck cancer. What happens next? What does that mean for you or your loved one? Is chemotherapy needed? Surgery, is that an option? What about radiation? What exactly does that consist of? How will speech be affected? Does head and neck cancer affect someone's appearance? How expensive is the treatment? Does insurance cover all treatment costs? How many people survive this type of cancer? Do many people die from this type of cancer? These are examples of possible concerns that patients and

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their families may have. The patient and family member often do not have any idea what their diagnosis means and how their lives will change over the course of treatment [2]. Surely, those concerns can be addressed by the patients' physician and care team. However, helping patients face their diagnosis as well as guide them through their new treatment plan is the primary role of a head and neck oncology nurse navigator [3]. "The nurse navigator responds to questions in a timely manner, explains the rationale behind the planned treatment, and coordinates care across the healthcare continuum. All this can go a long way in reducing a patient's anxiety and enhancing his or her ability to follow through with appointments and prescribed treatment" [1].

Patients can be referred to a head and neck cancer physician through their primary care provider, ear nose and throat doctor, dentist, or can even be self-referred. The initial point of contact for the referral is with the nurse navigator. They make sure that the patient has all the medical records needed for their first visit, including recent biopsies, imaging, blood work, referring doctor's visit note, and anything else that is important to make the first visit go as smooth as possible. When a patient leaves their initial visit the hope is they will have all they need: knowledge as to what the next steps are in their plan of care, what resources are available and, most importantly, someone to contact throughout their journey with head and neck cancer [4].

## Eliminating Barriers

Eliminating barriers to screening, diagnosis, treatment, supportive care, and end of life care is what nurse navigators strive to achieve [5]. One of the many barriers that can hinder a patient's treatment plan and outcome is education. It is vital that a patient comprehends minimally that they have cancer. For many, being diagnosed with cancer is shocking and is very difficult to accept [6]. Simply, if a patient does not understand the basics of what their diagnosis means, they will not be able to fully comply with what is necessary for treatment [4]. They may not understand the complexity of the disease or what is needed for treatment. For instance, if a patient does not understand that smoking cigarettes has a direct correlation with the occurrence and re-occurrence of head and neck cancer, they may not feel it is necessary to try to quit after they are diagnosed. They may believe it is too late. The head and neck nurse navigator will find resources, teach patients the importance of smoking cessation, find local smoking cessation programs that are open for enrollment and ensure they have proper supportive care to quit successfully [4].

Costs and economic issues also play a major part in head and neck treatment. "All patients have financial issues, even if they have insurance" [5]. Types of insurance can fall into four plans including Exclusive Provider Organization (EPO), Health Maintenance Organization (HMO), Point of Service (POS), and Preferred Provider Organization (PPO). EPO's limit a patient to use provider services that is only in their network excluding emergencies. HMO's focus on preventative care and covers health care cost when members receive services within network. Coverage can be limited to members that live or work in their network area [7]. A POS plan keeps out of pocket costs low if a member uses network providers; however, to see a specialist, a referral is needed from the patients' primary care doctor. PPOs are similar to a POS plan, the costs are low when using providers within network, but referrals are not necessary for specialist visits. Members can see providers that are outside the network but will have to pay extra [7]. For patients that have low income or are 65 years or older, they can qualify for Medicare and or Medicaid. Medicare is provided through the United States federal government and is available for people who have low income. Coverage with Medicare can be broken down into four parts: A, B, C, and D. Part A covers inpatient hospital medical services. Part B covers outpatient facility medical services. Part C includes both inpatient and outpatient facility coverage but the member can choose to have a Medicare advantage plan, or Medicare private health plan. This plan offers additional coverage but with additional cost as well. Part D only covers the costs of prescription medications [8]. Patients' financial issues commonly stem from their insurance type. Patients can have a POS type of insurance and require a referral from their primary care provider (PCP) to see a medical oncologist but do not currently have a PCP or have seen their PCP in over 1 year. PCP offices commonly will not provide a referral unless the patient has been recently seen. The facility where a patient may need to have treatment may be out of their insurance plans network. On the other hand, the patient is allowed to see providers out of network but to do not have the means to pay additional fees. Patients may have hospital in-patient based insurance and need supplemental insurance for outpatient services. Majority of treatment planning for head and neck cancer occurs in outpatient facilities. If a patient does not have proper coverage, they are unable to make appointments for the important services related to their cancer diagnosis. When a patient does not have adequate coverage, the next step is to apply for supplemental insurance. The application process from start to finish may take a couple of weeks to months. If the latter, the patient may need emergency coverage in which eligibility varies from state to state. A financial counselor may then be added to the list of supportive care services and referrals to ensure the patient has financial coverage. Consults including radiation, medical oncologist, head and neck surgeons, nutritionist, speech and physical therapist, biopsies, and diagnostic imaging cannot be completed without sufficient insurance coverage. Co-pays can also be an issue for a patient who cannot afford to pay one for each visit. When referrals are on hold, or patients meet resistance with insurance plan requirements that results in delays in diagnosis, delays in treatment, producing a less favorable outcome for the patient [5].

Transportation is another barrier to care which is very difficult for patients to overcome. There are instances in which patients live more than 100 miles away from their treatment center [5]. To drive more than an hour for treatment is often unrealistic and has a direct effect on the patient's quality of life. Often the patients do not drive themselves to appointments. They rely on family, friends, caregivers, or available transport companies. What good are all the supportive care appointments and referrals if a patient is unable to physically get to any of them? The burden of traveling deters diagnosis and timely treatment [9]. “Travel-associated stress was the only non-medical factor that maintained a significant role in heightening overall stress-more so than fear of tumor recurrence or burden of medical expenses” [2]. If traveling for treatment is an issue, the head and neck nurse navigator can assist in finding a means of transportation so that the patient can receive care. Many programs can help provide transportation for cancer patients but may be limited to a certain number of rides or limited to how many miles they can travel. The American Cancer Society has a program called “Road to Recovery” that offers rides to and from treatment for patients diagnosed with cancer and do not have reliable transportation [10]. There are requirements depending on patient eligibility. Caregiver’s may need to assist a patient who cannot walk without help or is under the age of 18 [10]. Additionally, further barriers may arise if the service is fully booked or there are not enough drivers to participate in the programs. When these kinds of issues come up, a social worker can be assigned to help the nurse navigator through these difficult situations.

## Emotional Distress: Patients, Family, and Caretakers

Although education, finances, and transportation are difficult barriers for patients to face when they have head and neck cancer, emotional distress should be considered throughout their entire journey. “More than 90 percent of cancer patients and their families have high levels of distress that are directly related to diagnosis and treatment. Sixty percent of cancer patients and about half of their family members experience significant depression and anxiety” [11]. With all the supportive care referrals, many providers forget that the diagnosis of cancer is tough and difficult to fully foresee the mental toll. Patients are expected to follow through with a list of required appointments and tests to help them when they may just need time to process all the information being pushed on to them and their loved ones [4]. Patients are concerned with survival, worried about the effects of head and neck cancer, and the challenges they will face during and after treatment, for example, possible recurrence, employment status, social support, coping with physical disfigurement, speech, swallow changes, rehabilitation, and physical therapy [2]. Side effects from chemotherapy and radiation such as nausea, vomiting, pain, difficulty swallowing, and tasting foods are also very worrisome for patients [4]. Permanent changes such as tracheostomies, tracheo-esphogeal prosthesis (TEP), or learning how to use an electrolarynx is frightening and discouraging [2]. There are other small nuances that nurse navigators have to work through to make sure patients are well taken care of.

Patients often need diagnostic and staging imaging. Depending on insurance coverage, the testing may need to be authorized by their insurance carrier.

Authorizations although needed, can also delay treatment. Authorizations can take up to 1–14 days. Patients should not have to wait a maximum of 2 weeks for approval. The test has not even been scheduled yet. Depending on the hospital or health care facility, finding an open appointment date and time that is conducive to the patients' schedule can take at most another 2–3 weeks. When a patient encounters these types of financial blocks, treatment can be pushed back up to 1 month or more. Patients want desperately to have a sense of normalcy while being treated for head and neck cancer; however, it is very difficult and can be both mentally and physically draining [4].

## Benefits of Nurse Navigators

With all of these barriers to care for head and neck cancer, how would a nurse navigator manage to accommodate patients' needs and coordinate treatment plans in a timely and efficient manner? This is where the nurse-patient relationship comes into the forefront. Additionally, knowing where to direct the patient for any upcoming supportive care referrals or other specialty physician consults is extremely important. When treating a patient with any type of cancer, their care has to be centered on the patient. This means that the patient needs to develop a rapport with the health care team. Patients should feel listened to, supported, and feel as if their opinions, thoughts, and ideas are relevant regarding their treatment. Patient barriers should be assessed in the beginning of their journey so that they can receive interventions fit for their personal situation [3]. Since nurse navigators are available from the start, during and after treatment, patients tend to develop this relationship with them. "When we meet a new patient and the patient gets our card, that begins our journey together. Whatever follows, we have a wonderful network, and we figure out what they need" [6]. They are engaged and dedicated to making the treatment process as easy as it can be for the patient and their support system. "Throughout my treatments, she was always calling to check on me and she was always there when I was at the hospital for an appointment. She's very comforting" [6]. At times, nurse navigators are a patient's only support system and assist with finding other resources to help and guide patients through this difficult process [4]. Along with being available to support and advocate for their patients, nurse navigators also triage patient symptoms over the phone or during clinic hours. If a patient needs to be seen in clinic, the navigator will get them in. If there is an emergency, the navigator call help the patients decide on the first steps. "Navigators work to keep treatment plans moving forward and agile…we discuss what you can expect, how often you will be here, side effects, what exactly happens during a scan – we're doing all of that nitty gritty. We live in the details" [6].

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# Chapter 14
# In Their Words

**Christopher E. Fundakowski**

## Shanon's Story

It was 9 years ago. I was unusually exhausted and had a sore throat and raspy voice. While rubbing my neck, I felt a lump under the left side of my jaw. It was hard and about the size of a walnut, as I pressed beneath my mandible. At this time I was a dental hygienist of 21 years, nonsmoker, 54 years old. I'll skip the next few months of terrible frustration. As I eventually had to insist on a biopsy, I was diagnosed with head and neck cancer stage 4! Squamous cell carcinoma. I had 35 radiation treatments. Each one consisted of nine individual areas being radiated. I know as I counted every single one in order to survive lying there with my head bolted to a table via a molded mask.

As the weeks passed, my mouth became very dry and sore and my swallowing worsened. I used "magic mouthwash," fentanyl patches, celexa, etc. to attempt some comfort. The first chemotherapy drug caused some permanent hearing loss and tinnitus. Another was more successful. Nausea and vomiting were my sporadic companions and more drugs helped somewhat with that.

By week 4 there was no swallowing. I chewed celery for moisture. Recommended energy beverages made me ill, which was absolutely impossible to explain to those caring for me and loving me. After passing out while showering, I was admitted to the hospital and a feeding tube was inserted. My body appeared to be rejecting this, as I was physically ill following each use. I did eventually benefit from this basic, life-giving nourishment. Thank God. I finished all treatment and returned to my home 3 hours from the hospital. I needed the feeding tube for 7 months and was then able to consume a soft diet.

One "aftereffect" I continue to struggle with is choking. My epiglottis does not function properly due to the radiation. I've not had to seek medical help for this but

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always manage to remove the blockage myself one way or another. A new problem began 18 months ago. I developed pneumonia. Aspiration pneumonia most likely. I've had eight bouts and two hospitalizations since then. This has greatly affected my life. I had to retire recently, at age 63. Pneumonia is debilitating and my body is showing signs of that particular stressor. I keep active and eat a mostly healthy diet to stay as strong as possible.

I usually have a raspy voice. Some days less than others. Even now I often have to explain to restaurant workers that I have swallowing "issues." They are always understanding and accommodating. This, nonetheless, has been frustrating to me on numerous occasions. As is choking in public. I realize I need to eat before going to a party, etc., "just in case." It has made me less eager to attend certain events. I do generally convince myself to go. Living in a small college town tends to mean many people know my situation and think nothing of it. Friends know I'm always up for ice cream!

Interestingly, my mouth still burns if I eat something too salty, peppery, or spicy. I don't drink alcohol. Truly I should not and, also, it still burns. No fun wine tours for me. My health insurance now costs $1400 per month. I have paid thousands of "out-of-pocket" dollars for healthcare. I am a rower of 18 years and thoroughly enjoy this sport. I missed numerous rows this season due to pneumonia. I am able to have a great time with my kids, grandkids, and entire family! I volunteer at church and more. We travel which has been amazing and stressful depending on my health.

As much as the aftereffects of cancer have forever changed my life, I remain forever grateful for each day I am granted. One foot in front of the other. I still take a low dose of celexa, which can't hurt, and am never without my companions of a bottle of water or mouth spray.

My husband feels I am making light of a heavy situation. I must agree. I didn't tell you that two nights ago when I choked on my own homemade chicken noodle soup and had to use the finger technique – I felt so sad and defeated afterward. I forced myself to continue eating. I just recently regained the five pounds I lost in May when I got pneumonia in Rome. Who loses weight in Italy? I do. In June, I was diagnosed with a very tight constricted and fibrotic upper esophageal stricture. I was told it was in need of immediate repair. That surgery has now been pushed back due to my health and the doctor's schedule. Last night as I lay awake hearing the rattling and coughing in my chest, I knew I was again lacking sleep. These setbacks continue sporadically but steadily….

## Pravin's Story

I got diagnosed with cancer 8 years ago after having a routine dental checkup. This was squamous cell cancer of the head and neck. I went through multiple rounds of chemo, radiation, and surgery. Upon each treatment the cancer still persisted in the scans. I was also offered to be on a clinical trial which I took part in it but had to discontinue. Over the last few years, I have not had any changes in my scans, and I am currently not going through any treatment, just regular checkups and pain management.

During the surgery they replaced parts of my jaw and this caused me to have a small hole in my lip. I do not have any movement in the jaw so currently I have a J tube in my stomach (previously it was a G tube – but due to leakage, the doctor suggested we replace it).

I am unable to speak clearly and have to repeat my sentences many times. I have to pronounce words phonetically at times. I have to choose different words or describe things versus saying it directly, had the speech been clear. I have difficulty on the phone to speak to someone. Sometimes the mucus production makes the voice as if I have a cold. I have to clean my mouth before speaking at times especially in the morning. If I am with family, they prefer to speak to me through my family and not myself (impacts me psychologically as why they don't speak to me).

Due to the lip abnormality and oral cavity, I am unable to drink liquids without them spilling out (approximately 60% percent leaks out of my mouth). I have to limit myself drinking or consuming liquids in public as it is not most visually appealing. I usually end up drinking my liquids over a sink or near or in a bathroom. This causes extreme difficulties when I'm traveling or attending family events. I'm only able to drink somewhat thin to medium thin liquids that do not have any pulp as it is difficult for me to clean my mouth and also swallow.

I do not feel as if I belong to the food-and-drink enjoyment part of events. I feel isolated/avoided when I am traveling with groups; this psychologically impacts me as I was always the helpful hand before and people looked up to me. Due to the pain medication, I tend to fall asleep at times even when I am around guests. I feel down at times – depressed at times as well – I don't feel the desire to do anything….

## Rick's Story

The first 24 hours after being diagnosed with cancer was surreal. My wife, family, and my Church Group listened to my thoughts, fears, and concerns. They would attend doctor appointments with me and acted as a second set of ears. They would drive me to my radiation appointments, and they all did their best to cheer me up on the tough days. I found myself feeling depressed when my eating habits were affected and I lost the desire to eat. I lost a large amount of weight in a short amount of time, and this was when people outside of my close circle of family and friends could tell that I was sick. Equally as frustrating was not knowing when my symptoms would get better. I kept hearing that things would get better in another 3 months and then in another 3 months, and when I realized that wasn't the case, I was tremendously disappointed and a little lost. I understand that every individual is different and it is hard to say how one person is going to react to treatment in relation to another, but I would have preferred that my physicians had said "Rick, initial recovery for someone receiving radiation to this area of the body which will affect your oral cavity, is 6–9 months." I believe most patients are like me in that they would want to hear this information upfront so they can prepare themselves mentally as opposed to being "strung along" and not really knowing when they are going to start to feel better/somewhat normal again. Eating was unsatisfying and frustrating at first due to the fact that I simply couldn't taste anything. Now I can eat just about anything, but I would still say that 50% of the food I eat I still struggle to taste as I had before treatment. This whole experience has brought me closer to my wife and family and revealed those individuals in my life who I now know are unconditional friends. I now have more empathy for individuals who are diagnosed with or in the process of fighting any type of cancer.

## Susan's Story

Being diagnosed with cancer was a very numbing experience as I was misdiagnosed first time around. I didn't hear a thing after the words stage 4 cancer passed the provider's lips. My husband and I went to lunch and sat in shock the entire meal. The inability for your brain to comprehend the news is real. I relied on family and friends. You want to be strong for your children so you hide your vulnerability in order to minimize the concern in their lives. My family wrote me beautiful letters of love while I was in the hospital. It was the first thing they gave me when I woke up from surgery. This was both a positive and negative time for my relationships. In hardship people surprise you in many ways. The outpouring from the community was overwhelming. The support from people I had never expected touched my heart. You understand how loved you are. You understand how many people care for your children by the support they received. The inability for some close to me to be emotionally supportive was as equally shocking. There were some eye-opening moments. The diagnosis grew many relationships and minimized others. I felt very anxious being in large settings before I disclosed my diagnosis. The need to keep up a positive front in light of my situation caused great anxiety. I had never experienced this in my life. I remember being at my son's birthday and pretending to be happy and carefree but inside I was in a mild panic. I felt very depressed after surgery as I wanted to return to "normal" life immediately. Having limitations was deeply discouraging. I now have far more compassion for others. I am grateful for my health every day. I am kinder to myself. I love fitness and have put additional emphasis on that as well as my diet. I don't sweat the small stuff and enjoy the little things in life. It has made me a better person. I feel inclined to pay forward all the generosity I was given by friends, family, and neighbors on a daily basis. At the first academic center I visited, I was very unhappy with their "team" and "care plan"… I use those terms very loosely. The need to feel in control and such an emotional time is so important. Within 24 hours of my diagnosis, I began searching for the right providers, team, and treatment plan. Once that was in place, I felt ready to proceed with treatment with great confidence. I can't put my finger on it now, but when I look in the mirror, I feel like there is something different and I am not referring to my scar. The scar is a badge of honor. I see something different in my face.

## Susan's Spouse

There is a lot of mixed feelings and confusion in the beginning. You find yourself trying to console your spouse but also scanning the Internet trying to understand what is going on. We talked to so many doctors because we switched hospitals a few times; you realize that they give cancer diagnoses all day long. As the days continue, you try and comprehend how many people are going through this and it's overwhelming. One doctor was almost robotic about the next steps. It didn't feel right and made us both almost sick to our stomach. The worst is when someone would say, "You have good cancer…." My wife would become incensed! My wife is type A, but I felt very included in all of the discussions about what course of action we were taking. We talked about what direction we wanted to take, etc. I acted as support, information, food shopper, and spokesperson to family and friends when she did not feel like dealing with people. Especially early on when we were unclear and confused, it was important to be there for support. Also the 1 year checkup was nerve racking. The doctors can tell you the odds are good and everything will be fine, but until the results come back, your mind never stops racing and playing out what if scenarios… I would hate to be cliché but once a member of your family gets diagnosed with cancer, it really makes you ignore the small stuff. We have gone on more getaways alone and with the family in the years since diagnosis than we ever did. It really has made me focus on how we want to be as a couple, a family, and how we want to live the rest of our lives out.

# Index

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