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Chapter 2

American Academy of Otolaryngology—
Head and Neck Surgery Foundation

Head and Neck Cancer

Quality of Life following Chemoradiation Therapy for Head and Neck Cancer

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It is estimated that in 2005 there will be more than 40,000 newly diagnosed cancers of the head and neck, and that this year more than 10,000 patients will die of head and neck cancer (HNC).[1] Despite multiple modalities of treatment such as surgery, radiation, and chemotherapy, head and neck cancers continue to have one of the lowest five-year survival rates.[2]

The treatment algorithms for advanced HNC have changed significantly over the past 10 years. Current treatment protocols for advanced laryngeal cancers usually involve either chemotherapy with radiation (organ preservation) or total laryngectomy (TL) with postoperative radiation. Both treatment modalities have equivalent control rates and are widely used today for advanced laryngeal cancers.[3] Recent data also support the use of chemoradiation (CRT) for HNC in other sites, such as the oropharynx and hypopharynx.[4] As such, an increasing number of HNC patients with primary tumors in the oropharynx and hypopharynx, as well as larynx, are being treated with a CRT protocol rather than the standard surgical resection with postoperative radiation.

Although CRT protocols usually allow preservation of the functional organ, there are still significant acute morbidities, as well as long-term, following CRT. Because of the increasing number of patients with HNC undergoing CRT, there have been numerous studies examining the quality of life (QOL) for such patients during and after their treatment. QOL used as a clinical outcome measurement is often not measured or carefully defined, but rather broadly defined to encompass an individual's perception of his or her emotional, physical, social, and sexual state. Simply, it is the satisfaction and well-being that a patient experiences on a daily basis.[5] QOL issues will differ depending on tumor site, stage, and type of treatment rendered.

QOL Instruments

Quality of life is usually assessed through questionnaires, called instruments. Issues pertaining to quality of life are called domains. The four basic domains are psychological, social, occupational, and physical.[6] Each domain or issue is given a score and, in general, a higher score signifies a better quality of life. Multiple instruments have been utilized to study QOL in head and neck cancer patients, ranging from global (applicable to any disease and containing general physical, social, and psychological questions), to specific head and neck questionnaires, to performance questionnaires that address specific functions such as speech or swallowing.

Commonly used instruments in head and neck cancer patients are the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30

(EORTC-C30), the Head and Neck Core 35 (EORTC-HN35), the Head and Neck Radiotherapy Questionnaire (HNRQ), the University of Michigan Head and Neck Quality of Life Questionnaire, and the University of Washington Head and Neck Disease Specific Measure (UW-QOL).[7]

The University of Washington Quality of Life Instrument, version 4 (UW-QOL, v 4) is a short questionnaire, assessing functional items such as swallowing, pain, and speech. However, psychological issues are not addressed in this instrument. The first section consists of 12 domains that pertain to the degree of quality of life in the categories of pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder function, taste, saliva, mood, and anxiety. The second part of the instrument asks the patients which of the previous issues have been the most important to them in the past seven days. In the final part of the instrument, patients are given three general questions comparing their (1) current health-related quality of life to one month before developing cancer, (2) health-related quality of life during the past seven days, and (3) overall quality of life during the past seven days. Higher scores in each category signify better quality of life. This instrument is simple to use and well-suited for rapid assessment of QOL in HNC patients. A comparison of the UW-QOL with the EORTC QOL C33, the Medical Outcomes Short Form 36, and the EORTC HN35 found that the UW-QOL was a broad measure suitable for low-cost assessment of disease-specific functional status.[8] Because psychological issues are not included in the UW-QOL questionnaires, this limits its usefulness in assessing those issues.

Global questionnaires include the Medical Outcomes Short Form 36, the Karnofsky Performance Index, and the Hospital Anxiety and Depression Scale.[9] The M.D. Anderson Dysphagia Inventory and the Performance Status Scale for Head and Neck Cancer are performance questionnaires addressing specific functions such as swallowing, speech intelligibility, and the ability to eat.[10]

QOL in HNC Patients Prior to Treatment

Patients with head and neck cancer often have multiple medical co-morbidities that will affect their quality of life even prior to undergoing treatment. There is usually a history of heavy smoking and alcohol use. Because of the deleterious effects of smoking, most patients with HNC will also have chronic lung disease. Coronary artery and liver disease are also common in this patient population. A cancer in the upper aerodigestive tract may have an adverse effect on chewing, swallowing, and eating, leading to weight loss and malnutrition. Other chronic illnesses such as hypertension, diabetes, and vascular disease may be present as well. Adverse socioeconomic factors and poor family support also diminish the QOL in HNC patients.

The diagnosis of HNC is often delayed, particularly when the primary site is located in the orophayrnx or hypopharynx. Because of the difficulty in examining such areas and the paucity of symptoms produced, the tumor may not be seen or diagnosed until it reaches significant size, or when a neck metastasis develops. Unfortunately, this means that many patients will present with an advanced stage of HNC at diagnosis, worsening their prognosis and QOL.

Acute Changes during and Immediately Following CRT

Most HNC patients undergoing CRT will receive a platinum-based regimen, such as cisplatin, with or without 5-FU. Patients receiving concurrent chemotherapy with radiation will experience significant mucositis, which may require a break in treatment. Additional acute side effects from CRT include anemia, neutropenia, infectious complications, renal toxicity, ototoxicity, skin changes, fatigue, and weight loss.[11] The mucositis and edema of the aerodigestive tract will lead to varying degrees of dysphagia. Some patients will require placement of a gastrostomy tube (G-tube) for feeding and/or a tracheotomy tube for securing the airway. Because of the many side effects, patients will experience a significant decrease in their overall QOL during treatment. The stress of undergoing chemotherapy and daily radiation treatments also contributes to a generalized depression in many of these patients.

Chronic Changes after CRT

Most of the acute side effects gradually subside after completion of treatment. Studies have shown that, 6 to 12 months after treatment, QOL scores rise to above pretreatment levels.[12] However, most patients report some long-term xerostomia and dysphagia. Because of dry mouth and sticky saliva, only 50 percent of patients in one study were able to resume a normal diet after treatment.[13] Some patients require long-term G-tubes for adequate nutrition. A significant number of patients also reported residual pain even after treatment.[14]

Other long-term side effects after CRT include hoarseness, decreased taste, and difficulty chewing. Further longitudinal studies are needed to determine whether late sequelae following CRT persist or worsen over many years, caused by progressive fibrosis of tissues.

Review of QOL Studies

Many studies have looked at quality-of-life issues for head and neck cancer patients following treatment. Schwartz et al. reviewed the published literature, evaluating the terminology, the design, and the interpretation of quality-of-life measurements in head and neck cancer patients. They specifically examined studies that compared head and neck cancer treatments at a point in time or reported changes over a period of time. They concluded that there were few hypothesis-driven studies, and clinical interpretations of quality-of-life outcomes were often not provided at the conclusion of the studies.[15] Terrell et al. reported on significant clinical predictors in head and neck cancer patients pertaining to quality-of-life issues. The most common predictors of QOL were tracheotomy and gastrostomy tubes, co-morbid conditions, chemotherapy, and neck dissections.[16] Another study evaluated patients with advanced head and neck cancer who underwent CRT on performance and QOL issues. Twelve months after treatment, patient's QOL issues had resolved except for the ability to eat a wide range of food. This data supported the use of intense chemoradiation therapy with minimal impact on QOL issues.[17]

Harrison et al. reported good QOL and oncological outcomes with patients who were treated for cancer of the base of the tongue.[18] Hammerlid and Bjordal et al. examined QOL issues in patients with head and neck cancer. Their studies reported that there were differences in QOL issues depending on the anatomic subsite of the head and neck cancer. They found that tumor stage and site had the most profound impact on individual patients' QOL. Their studies also reported that after one year from end of treatment date, patients returned to their pretreatment QOL state except in the senses, xerostomia, and sexuality.[19] Another study addressed the issue of swallowing after head and neck cancer treatment. The researchers concluded that patients undergoing CRT for oropharyngeal cancer had better functional outcomes related to swallowing than those undergoing surgery with postoperative radiation.[20]

It is often difficult to accurately compare QOL studies of HNC patients in the literature. Many studies examined patients with head and neck cancer in several different subsites, including oral cavity, oropharynx, larynx, and hypopharnyx. Care must be used when comparing QOL outcomes for patients with cancers in the different subsites in the head and neck after treatment. Morton et al. reported that anatomic subsites within head and neck cancer responded differently, and patients ultimately experienced different QOL issues depending on the subsite and treatment received. Organ preservation therapy did not necessarily lead to better QOL outcomes.[21] In addition, many different types of QOL instruments were used in these studies to identify varying domains pertaining to QOL, including mental, sexual, and physical functioning.

Improvement of QOL in Patients Treated with CRT versus Surgery

McDonough et al. compared patients with HNC who underwent CRT versus induction chemotherapy followed by surgery and postoperative radiation. There were significantly higher QOL scores in the nonsurgical group, with lower levels of social distress and avoidance because of better communication abilities and less physical disfigurement.[22] In another study, QOL issues were compared in laryngeal cancer patients who underwent CRT versus total laryngectomy with postoperative radiation (TL+XRT).[23] CRT patients had more problems with chewing, swallowing, and pain, while TL+XRT patients had worse speech and shoulder function. Hanna et al. recently reported that laryngeal cancer patients who underwent CRT had similar QOL scores compared with those who underwent TL+XRT, but functional subscale analysis revealed some differences. CRT patients had greater difficulties with dry mouth, while TL+XRT patients reported more problems with social functioning, sensory disturbances, use of painkillers, and coughing.[24]
Finizia et al. reported similar QOL issues pertaining to psychosocial adjustment and functional ability in patients who underwent CRT and TL+XRT. In the TL+XRT group, a lower level of QOL was reported in those patients who used an electrolarynx.[25] Terrell et al. assessed the QOL outcomes in patients in the Veterans Affairs Laryngeal Cancer Study who underwent CRT and TL+XRT. They reported that the CRT group experienced better QOL outcomes in freedom from pain, lower levels of depression, and less problems with work due to better overall emotional

well-being. Speech scores were similar in both the CRT and the TL+XRT groups.[26] Paleri et al. also assessed the QOL outcomes in patients who underwent CRT and TL+XRT. He reported similar scores between the two groups but a higher trend (better QOL) in the CRT group.[27] Major et al. reported similar QOL outcomes in CRT and TL-XRT patients in the domains of physical functioning, bodily pain, health perception, social functioning, energy/fatigue, and mental health. He reported that the CRT group had a higher QOL in their activities of daily life compared with those undergoing surgery with postoperative radiation.[28]

For laryngeal cancer patients, organ preservation protocols using CRT have the obvious advantage of retaining laryngeal speech. Many total laryngectomy patients undergo speech rehabilitation with the use of an electrolarynx, esophageal speech, or tracheal esophageal puncture. This may explain why in one study some TL patients reported that their speech was the same as always and in another study both TL and CRT patients who retained their larynx showed similar speech scores.[29] In contrast, most CRT patients did not generally receive any speech or swallowing therapy, and this group of patients may potentially benefit from use of intensive therapy in these arenas.
Recently the use of concurrent chemoradiation for organ preservation has been extended to nonlaryngeal sites, including the oropharynx and hypopharnx. Data from these studies confirm the efficacy of CRT for locoregional control of advanced oropharyngeal and hypopharyngeal cancers with acceptable morbidity.[30] Schrader et al. examined a series of patients with hypopharyngeal cancer who

were treated with hyperfractionated radiation therapy and concurrent chemotherapy, and found that late sequelae of treatment were tolerable and did not adversely impact patients' QOL.[31] In the University of Pennsylvania Phase II trial of oropharyngeal cancer patients treated with chemoradiation, organ preservation was attained in 77 percent of the patients and 90 percent did not require permanent tracheotomy or gastrostomy tubes. The eating-in-public and speech understandability scores were not greatly different from patients' pretreatment scores; however, scores for normalcy of diet declined.[32]

There is evidence of benefit from use of amifostine during CRT. This thiol compound protects normal tissues from radiation by binding of the sulfhydryl group with hydroxyl radicals. There is a high concentration of amifostine in the salivary glands after administration, which can decrease the severity of xerostomia after head and neck radiation.[33] Randomized studies demonstrated significant reduction of high-grade xerostomia in patients undergoing CRT for advanced HNC who were receiving amifostine.[34]
Recent advances in radiation therapy techniques such as intensity-modulated radiation therapy (IMRT) also show promise in decreasing the bothersome xerostomia[35]

Conclusion

The efficacy of chemoradiation protocols for locoregional control of advanced head and neck cancer has been demonstrated. HNC patients often have compromised quality of life at the time of diagnosis, even before beginning treatment. Depending on the primary site of the tumor, abnor-

malities in swallowing, chewing, speech, and appearance may occur. Coexisting morbidities such as cardiopulmonary disease, hypertension, diabetes, malnutrition, alcoholism, and poor social support contribute to low QOL.

Treatment with CRT carries significant acute and chronic morbidity. Acute toxicities include mucositis, anemia, neutropenia, renal toxicity, dysphagia, weight loss, fatigue, and depression. Much of the acute toxicity resolves after completion of treatment, and most patients return to pretreatment QOL levels by 6 to 12 months, except for the senses, xerostomia, and sexuality. Other long-term sequelae include continued difficulty with swallowing and chewing, decreased ability to eat a wide range of foods, sticky saliva, and hoarseness. Some patients are unable to eat a normal diet and may even be permanently G-tube dependent.
However, overall, QOL in HNC patients treated with CRT is relatively high, and compares favorably with patients who have undergone surgical resection of their tumor followed by postoperative radiation therapy. HNC patients treated with CRT may benefit from the use of amifostine during treatment. Intensity-modulated radiation therapy techniques may also reduce the incidence of long-term xerostomia. Intensive speech and swallowing therapy may aid in improving these functions following CRT.

Patients and physicians need to understand the differences in sequelae among treatment protocols so that better-informed decisions can be made. Supportive therapy for swallowing and speech function, as well as psychological support, are essential in treatment planning. Future prospective, longitudinal studies are needed to examine QOL issues for patients with advanced HNC.

Quiz

1. The most common acute toxicities associated with chemoradiation for head and neck cancer include all of the following EXCEPT

   a. mucositis
   b. anemia
   c. dysphagia
   d. neck fibrosis
   e. xerostomia

2. Most of the acute toxicities associated with chemoradiation for head and neck cancer resolve

   a. one month following end of treatment.
   b. three months following end of treatment.
   c. one year following end of treatment.
   d. two years following end of treatment.
   e. five years following end of treatment.

3. Chronic sequelae following chemoradiation for head and neck cancer usually include

   a. neutropenia
   b. permanent gastrostomy
   c. permanent tracheotomy
   d. sticky saliva
   e. none of the above

4. The following statement is supported in the literature:

   a. Laryngeal cancer patients who undergo chemoradiation with organ preservation have overall better quality of life than patients who undergo total laryngectomy.
   b. Total laryngectomy patients have worse quality-of-life scores in speech than laryngeal cancer patients who undergo chemoradiation with organ preservation.
   c. Most patients who undergo chemoradiation will require a tracheotomy and gastrostomy tube.
   d. Most patients who undergo chemoradiation are able to return to a normal diet within one year.
   e. Patients who undergo chemoradiation for head and neck cancer have less pain than those who undergo surgery.

5. The following may help to mitigate the adverse effects of chemoradiation treatment in head and neck cancer patients:

   a. amifostine
   b. intensity-modulated radiation therapy
   c. speech therapy
   d. swallowing therapy
   e. all of the above

Correct Answers:

1. d
2. c
3. d
4. a
5. e

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