A Value Framework in Head and Neck Cancer Care

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OVERVIEW

The care of head and neck squamous cell carcinoma has greatly evolved over the past 30 years. From single modality to a multidisciplinary care, there has also been a concurrent increase in treatment intensity, resulting, at many times, in more zealous regimens that patients must endure. In this article, we apply Porter’s value model as a framework to balance survival, toxicities, cost, and trade-offs from a patient’s perspective in head and neck cancer. This model defines value as the health outcome per dollar achieved. Domains and outcomes that are important to patients, including not only survival or short-term quality of life, but also functional outcomes, recovery, sustainability of recovery, and the lasting consequences of therapy are included in this framework. Other outcomes that are seldom measured in head and neck cancer, such as work disability and financial toxicities, are also included and further discussed. Within this value model and based on evidence, we further discuss de-escalation of care, intensity-modulated radiation therapy, newer surgical methods, and enhancements in the process of care as potential approaches to add value for patients. Finally, we argue that knowing the patient’s preferences is essential in the value discussion, as the attribute that will ultimately provide the most value to the individual patient with head and neck cancer.

In the past 30 years, there have been significant changes in the treatment of squamous cell carcinoma of the head and neck. These changes have been described in a series of reviews in the New England Journal of Medicine. In 1983, combining radiotherapy with chemotherapy still had no proven benefit, and the authors acknowledged, “…patients have tolerated these therapies poorly because of moderate to severe local toxicities that frequently necessitate the interruption of radiotherapy.” In the next 20 years, concurrent chemoradiotherapy was established as the preferred organ-preserving treatment modality, and authors of follow-up reviews emphasized its outcomes: “further improvement in most relevant clinical endpoints—survival rates and the quality of life” should be continuously sought and “[head and neck cancer] remains a disfiguring disease associated with a high mortality rate.” In 2008, with the proven benefit of the targeted agent cetuximab and the relationship of oropharyngeal tumors with human papillomavirus (HPV) brought to light, it was mentioned that “…physicians who are treating patients with locally advanced disease have multiple treatment options. The treatment team should consider the patient’s overall condition and his or her ability to tolerate aggressive therapy.”

These excerpts illustrate the evolution of treatment in head and neck oncology over the past decades: the multimodal treatment approach has led to improvements in survival and locoregional control. However, as we have strived for further improvement in survival, there has been a concurrent increase in treatment intensity, resulting in more zealous regimens that patients must endure. This current multidisciplinary treatment for head and neck cancer also entails resource-intensive care. In a pre-cetuximab and relatively pre-intensity-modulated radiation therapy (IMRT) era, a Surveillance, Epidemiology, and End Results–Medicare analysis estimated the cost of treating elderly patients with head and neck cancer diagnosed in 2004 at $492 million (equivalent to $670 million when adjusted to 2013 dollars) for approximately 15,500 patients.

Therefore, the puzzle of how to account for and balance survival, toxicities, cost, and trade-offs among these outcomes has also been a topic of debate in medicine in recent years, and, surprisingly, not well explored in head and neck oncology. Furthermore, the understanding of the head and neck cancer genome and the possible introduction of additional targeted therapies in the near future may further complicate the equation. In this article, we aim to employ the concepts developed by Porter et al. to delineate a value model in head and neck cancer. This framework may be helpful for the prioritization and ranking of interventions from a patient’s perspective at present and in the future. At the same time, we review potential strategies to improve value in head and neck cancer care.

APPLYING A VALUE FRAMEWORK TO HEAD AND NECK CANCER CARE

Porter et al. proposed aligning stakeholders’ incentives with the concept of value for the patient as an approach for im-
proving the health care system. Value in this context is defined as the health outcome achieved per dollar spent. In this model, the outcomes that are important to patients over the whole cycle of care are included. While these outcomes incorporate measures of survival or short-term quality of life, they also consist of a more complex set of functional outcomes, such as the time to recovery, its sustainability, and the lasting consequences of therapy. Accordingly, the outcomes for any medical condition can be ordered in a three-tiered system, in which the first tier—the most important—represents the health status that is achieved for patients. The second tier is constituted by outcomes related to the recovery process, and the third tier refers to the sustainability of health. Incorporating outcomes that are important for patients is an essential step in defining value. Survival, usually the most important outcome for patients with head and neck cancer, is in the first tier. Still in the first tier are important functional outcomes, such as laryngectomy-free survival, and the preservation of swallowing and speech. Figure 1 depicts the proposed value framework in head and neck cancer care.

Other seldom studied outcomes, measuring time to recovery and sustainability of health, are in the second and third tiers, respectively. The importance of these outcomes should be highlighted in head and neck cancer, as patients undergoing multimodality treatment experience acute and long-term toxicities with the potential to have a debilitating and lasting effect on their functional capacity. For example, data from cross-sectional studies examining work-related disability among patients with head and neck cancer showed that 33% to 52% of patients who were employed at the time of diagnosis were unable to return to work after treatment was completed. Even if they are able to return to work, many patients with head and neck cancer change their jobs after treatment because of physical discomfort and poor health following their cancer treatment. In comparison to other types of cancer, survivors of head and neck cancer have the highest risk of disability or quitting work. These issues become even more important in view of recent changes in the demographics of those afflicted with head and neck cancer. These changes are related to the shift from older patients being diagnosed with tobacco-related head and neck cancers to younger, healthier patients with cancers that are related to HPV. Noteworthy is the fact that although HPV has been associated with more favorable survival outcome (tier 1), tiers 2 and 3 remain poorly studied in this patient population. The importance of measuring return to normal activities, including work, is of paramount importance, as the younger group of HPV-associated patients will similarly leave the workforce during their treatment.

Other outcomes rarely measured are the cost of treatments and their effect on patients’ quality of life. Jacobson et al analyzed administrative claims of patients diagnosed with oral cavity, oropharyngeal, and salivary gland tumors between 2005 and 2007 in the United States. These patients averaged 48.3 days of short-term disability, estimated at a cost of $20,236, compared to $7,829 for a matched comparison group in 2013 dollar values (converted from 2009 values and adjusted for medical inflation). Their out-of-pocket costs were estimated to be on average $3,353 for commercial, and $1,977 for Medicare enrollees. Accordingly, an assessment of German patients with head and neck cancer for priorities revealed the item “I want that all the expenses for cancer treatment, cancer care, and any additional follow-up treatments be covered by my health insurance or by the welfare system” as a top-five priority in 51% of respondents. Going beyond direct treatment-related costs, indirect costs like lost earnings are also important to these patients, as shown in a cohort of Brazilian patients with head and neck cancer, in which 42% of patients reported a significant decrease in household income following treatment. Furthermore, efforts should also be made to develop and validate an instrument to measure this financial toxicity and its impact on a patient’s quality of life.

Conceptually, all the costs involved in the care of an individual patient during the full cycle of care are bundled and compared to outcomes achieved. As stated by Porter et al., “to reduce cost, the best approach is often to spend more on some services to reduce the need for others,” with reductions in cost irrespective to the outcomes being counterproductive. Although decreasing the costs of individual interventions may indeed decrease total costs, the full cycle of care, including, for example, hospitalizations and post-treatment care, should be accounted for.

**POTENTIAL APPROACHES TO INCREASE VALUE IN HEAD AND NECK CANCER CARE**

Within this framework, one can envision several strategies to increase the value for the patient beyond increasing survival...
or decreasing costs. One strategy relates to the association of HPV and oropharyngeal cancers. Several clinical trials showed that the HPV-associated oropharyngeal cancer has a better overall survival after curative intent therapy when compared to HPV-negative disease. Therefore, approaches to de-intensify treatments for this group with the goal of minimizing treatment-related morbidity are underway. For example, the recently completed E1308 study (NCT01084083) investigated the feasibility of reducing radiotherapy intensity in patients with HPV-positive oropharyngeal cancer who had a complete response after three cycles of induction treatment with cisplatin, paclitaxel, and cetuximab. Therefore, the de-escalation of care in a selected group of patients holds the promise to improve functional outcomes while providing similar survival benefit, possibly at a lower total cost because of a less intensive treatment.

Other value approaches may even include strategies that, although not necessarily cheaper or with better survival, also improve outcomes for the patient. For example, a very common late toxicity is xerostomia, where the reduction of saliva leads to persistent dryness of mouth, oral discomfort, dental decay, difficulty in speech, taste alteration, and swallowing dysfunction. In the PARSPORT trial, 94 patients with oropharyngeal cancer were randomly assigned to IMRT or conventional radiotherapy, with a dose of 60 to 65 Gy. Grade 2 or worse xerostomia was significantly less common with IMRT at both 12 and 24 months (38% versus 74%, p = 0.0027 and 29% versus 83%, p < 0.0001, respectively), with no significant differences in other toxicities or in tumor control. IMRT can thus provide value to patients beyond survival.

Novel minimally invasive surgical approaches, namely transoral laser microsurgery (TLM) and transoral robotic surgery (TORS), have also been investigated for head and neck cancers. In a study of 204 patients with advanced oropharyngeal cancer treated with TLM, the 2- and 5-year survival rates were 89% and 78%, respectively. Therefore, the de-escalation of care in a selected group of patients holds the promise to improve functional outcomes while providing similar survival benefit, possibly at a lower total cost because of a less intensive treatment.

However, further validation through well-designed random-
ized trials to identify the precise role compared to other modalities is needed before widespread adoption.

The identification and improvement of care processes that affect outcomes also provide an opportunity to increase value for patients, such as the time to treatment initiation and radiotherapy quality control. Although associated with conflicting results in the literature, largely because of the observational type and the unreliability of randomization in these studies, there has been a suggestion that a significant delay in treatment can lead to worse outcomes, intuitively explained by cancer progression before treatment. Two systematic reviews that investigated the relationship between waiting time before radiotherapy and survival found that treatment delay is a prognostic factor for local recurrence and overall survival. Another care process that has been shown to influence outcome is compliance to radiotherapy planning. As shown in a preplanned secondary analysis of the HeadSTART trial, of the 820 evaluable radiotherapy plans, 208 (25.4%) were noncompliant. Among these cases, 87 (11%) were considered deviations with a predicted major adverse effect on tumor control. The absolute difference at 2-year survival between those who had protocol-compliance plans from the outset and those with major deviations was 20% (70% vs. 50%, respectively). Also remarkable was the finding that among institutions enrolling fewer than five patients in the trial, 29.8% had a deviation predicted to have major adverse effect, compared with 5.4% in institutions enrolling more than 20 patients, suggesting that complex head and neck cancer care should be provided at experienced centers. Combined, these findings demonstrate the value of radiotherapy quality programs as a process that affects outcome of patients. Other improvements in the care process were elegantly described by Corry et al., including the proper documentation of treatment-related deaths and better assessment of late toxicities. In this regard, in a literature review of functional outcomes in head and neck cancer, over 200 methods and tools were identified in a period from 2000 to 2006. This overwhelming number of methods highlights the lack of standard measures, which hinders the comparison of functional outcomes among studies. Future original reports and reviews should shed light on all the domains necessary for each stage of disease. For example, long-term toxicities may have a greater weight on locally advanced and potentially curable disease when compared to the metastatic setting. The opposite may be true for acute toxicities. Therefore, researchers should make an effort to include the collection of these outcomes in their studies.

Finally, it has also been found that a subgroup of patients with HPV-associated disease has a poor prognosis. In a recent retrospective analysis of 505 patients with HPV-associated oropharyngeal cancer treated with radiotherapy alone or concurrent cisplatin and radiotherapy, Sullivan et al. classified these patients into low-risk (T1–3, N0–2C) and high-risk (T4, N3) groups for distant metastases. Within the low-risk HPV-positive cohort, subgroups of patients with N2b (particularly those with more than 10-pack-year tobacco exposure) and N2c were found to have a higher rate of distant relapse when treated with radiotherapy alone (the majority with accelerated radiotherapy schedules) compared with patients treated with concurrent chemoradiotherapy. Furthermore, the proper identification of the patients who are candidates for a possible de-intensiﬁed treatment followed by the validation of this approach in clinical trials means value for the patient with head and neck cancer. In this regard, it is also important to emphasize another process of care: the need of a validated algorithm to properly identify HPV-positive patients through a combination of p16 immunohistochemistry (IHC)/HPV polymerase chain reaction testing or newer accurate HPV detection methods. Unfortunately, the commonly used p16 IHC test lacks speciﬁcity, especially outside the oropharynx, and HPV ISH lacks sensitivity, leading to a signiﬁcant number of misclassiﬁed tumors.

**PERSONALIZING VALUE IN HEAD AND NECK CANCER**

The historic focus on survival has been correctly justiﬁed and centered on the patient. In the late 1990s, a priority scale was developed at The University of Chicago (The Chicago Priority Scale) to evaluate head and neck patients’ preferences before their treatments. Combined, the items “being cured of cancer” and “living as long as possible” were the top priorities in 83% of patients. Most recently, another study assessed German patients for their priorities. Naming their top five priorities among 15 statements, 58% of patients considered, “I want to survive the cancer” as one of their top five priorities. The item, “I want to be able to continue performing all daily life tasks well” was named by 50%. Interestingly, the items, “I want to keep all my body parts” and “I want that the consequences of the cancer not be visible to others” were the least often chosen (11% and 7%, respectively), leading the authors to conclude that “from a patient’s perspective, preservation of function in terms of daily activities, sufﬁcient food intake, or speaking clearly, among others, are more important than mere preservation of anatomic structures.” Although several biases impair the comparison between these two studies, it is interesting to note the contrast between 83% of patients ranking “survival” as their single top priority in 2000, and 58% ranking survival among the top ﬁve in the most recent study. Furthermore, a valid question is whether, by focusing on survival, we are providing value to the 17% of patients in the ﬁrst study or the remaining 42% in the second, based on their preferences. Therefore, the incorporation of patient’s preferences within an established value framework may serve well in the goal of choosing treatment modalities and personalizing value for patients.

Nevertheless, study designs that assess preferences for a speciﬁc treatment or modality over another are also nonexistent in head and neck cancer. For example, Motzer et al. randomly assigned 169 patients with metastatic renal cell carcinoma to either pazopanib or sunitinib for 4 weeks, followed by placebo for 2 weeks and then 4 more weeks of sunitinib. Then, after the 14-day break, the regimens were switched. After 22 weeks, patients were asked to select their
treatment of preference for additional therapy. With similar survival, 70% of patients in the double-blind, cross-over study opted for treatment with pazopanib compared with 22% of the patients preferring treatment with sunitinib (p < 0.001). Further studies of preference elicitation with clear trade-offs among treatment options are thus needed in head and neck cancer, as well as prospective observational studies assessing how patients with head and neck cancers’ preferences change in the continuum of care.

Although this article broadly outlines a framework for value in head and neck cancer care, it is by no means an exhaustive list of outcomes, and it should be seen as the beginning of the conversation on value in head and neck cancer care. Novel treatment regimens, modalities, or technologies can also be analyzed within this framework. As examples, the value of therapy modalities under scrutiny, such as induction chemotherapy and proton radiotherapy in head and neck cancer, should be discussed in terms of health outcome achieved per dollar spent.

Understandably, there is an overwhelming weight given to survival outcomes. However, incremental improvements in survival without regard to functional outcomes or costs should no longer be the status quo. Functional outcomes are at times not properly documented or not even included in studies. In this regard, the use of different methods and tools also impairs the collection and comparison of these data. Efforts should be focused on collecting and defining the outcomes that are important to patients. Discussing among different medical disciplines, with the fundamental input of patients, should define these outcomes. Furthermore, a value framework based on patients’ preferences, aligning physician and other stakeholder incentives with these preferences, may serve well to bring the patient to the forefront of the discussion.

Disclosures of Potential Conflicts of Interest

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References


