Quality of Life Implications After Transoral Robotic Surgery for Oropharyngeal Cancers

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KEYWORDS

- Quality of life • Functional outcomes • PROMs

KEY POINTS

- Understanding the impact of transoral robotic surgery (TORS) on quality of life of patients requires consideration of functional outcomes and the emotional, psychological, and social construct placed on various symptoms.
- Patients consider swallowing to be the most important outcome after cure and survival. To fully understand a patients' swallowing outcome requires the study of their oral intake, feeding tube dependence, and physical impairment (via videofluoroscopic or endoscopic swallow study), in addition to patient-reported outcome questionnaires.
- Tumor volume, advanced T stage, and adjuvant therapy are major predictors of worse swallowing outcomes after TORS.

INTRODUCTION

As survival for human papillomavirus (HPV)-related oropharyngeal squamous cell carcinomas (HPV-OPSCC) improve, the focus in evaluating treatment strategies and clinical outcomes of patients turns toward their quality of life (QOL). QOL is a multifaceted construct that encompasses a person's physical, psychological, and social health as it relates to a particular disease.[1] It provides clinicians an insight into the patient's perception of the impact that either the disease or treatment has had on their life. Although clinicians' and patients' perception can differ markedly, widespread use of

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various QOL tools and their incorporation into clinical trials as primary or secondary outcomes assists with decision-making processes and the ability to compare anticipated treatment outcomes.

Increasingly then, it is important for clinicians to understand what is being measured, how it is measured, and how QOL data can apply to clinical situations. Indeed, applying QOL results may prove the most challenging, as there is subjectivity and lack of guidance as to how much weight QOL measures should play in clinical decision-making. This is particularly true given (1) the patient's ability to adapt over time such that patient experience in the short term (most easily and frequently measured) may become less relevant as long-term outcomes become clearer; (2) QOL measurements are weighted for survivors who are not dealing with active cancer; and (3) there is little agreed-on standard of analysis and reporting at this time.[2]

QOL is particularly important in the discussion of HPV-OPSCCs. Most of the patients do well and survive after treatment of this condition, and analyzing how each treatment modality affects a patients' perceived state of health and wellbeing is important in deciding the optimal treatment. To fully understand what outcomes are of importance after transoral robotic surgery, we need to first understand the priorities and preferences of patients with HPV-OPSCC.

WHAT ARE THE PRIORITIES FOR PATIENTS WITH OROPHARYNX CANCER?

In a recent prospective trial whereby patients completed surveys before and after treatment, patients with HPV-OPSCC were asked to rank their treatment goals. Patients ranked swallowing right after cure and survival as their top three priorities both before and after treatment.[3] Furthermore, after completion of treatment, a proportion of patients ranked moist mouth within the top 3 priorities.[3] This study brings to light the importance of swallowing outcomes in this patient population, in addition to the detrimental impact that xerostomia can have on patients, so much so that it can change their priorities as they experience new symptoms over time.

MEASURING FUNCTIONAL OUTCOMES

Intimately associated with a patient's QOL is their functional outcome. For patients with oropharyngeal cancer, the swallowing mechanism can be affected by the cancer itself or the cancer treatment. Studies of functional outcomes include various metrics such as the use of feeding tubes, the consistency of ingested food, the risk of aspiration, efficiency of swallow, as well as patient-reported swallowing outcomes.

Perioperative feeding tube use, delivered either through a nasogastric (NG) or gastrostomy (G) tube placement, varies widely (3%–100% and 18%–39%, respectively) based on institutional protocols and varying opinions on prophylactic placement.[4–7] Although the duration of perioperative NG tube placement varies from 2 to 13 days, short-term G-tube placements approach a minimum of 3 months, typically used in the adjuvant therapy period.[8] The decision of feeding tube placement should not be made lightly. G-tube placement is an invasive procedure with a small risk for serious complications and a tremendous impact on the QOL of both the patient and the caregivers due to leakage, soiling, and interference with intimacy and family life. It has even been noted to be one of the worst burdens of treatment.[9–12] Furthermore, a systematic review suggested that feeding route may in fact have unintended consequences, with a greater proportion of patients with swallowing difficulties among those receiving a prophylactic G-tube, even in the long term.[13] Long-term G-tube dependence, defined as greater than a year, ranges from 0% to 10.3% after primary surgical modality with older age, open surgical approaches, resection of more than 25% of the oral tongue, and advance T-stage found to be significant predictors of long-term G-tube dependence.[14,15] It is also worth noting that in one cohort, 10.3% of patients who received TORS followed by adjuvant therapy were G-tube dependent compared with 0.0% in those undergoing TORS alone. Other recent series have mirrored these trends, with long-term tube feeding dependence ranging from 6% to 18.8% for those with advanced stage disease requiring adjuvant treatment.[16,17] Prolonged feeding tube dependence is undoubtedly associated with adjuvant therapy, with 25% to 35% of patients percutaneous endoscopic gastrostomy (PEG)-tube dependent after chemoradiation and 10% after 2 years.[8]

However, the presence or absence of a feeding tube does not fully characterize a patient's swallowing function. In order to further characterize a patient's functional ability, it is important to understand the nature of tube use, such as how frequent patients access feeding tubes and the percentage of their nutritional intake derived from parenteral feeds. The patients' oral intake, including the time to oral intake, and consistency of food ingested provides further insight into functional status. The initiation of oral intake after surgery is closely linked with the perceived safety for swallowing both from an aspiration and from a wound contamination perspective. In addition to swallowing ability and healing, time to oral intake often reflects also the patient's overall condition, including any underlying baseline comorbidities and their pain control. That being said, most case series indicate that oral intake started as early as POD1 after TORS for early staged tumors and varied from 1 to 4 weeks postoperatively depending on the stage of the tumor.[6,18,19] More recently, in the setting of a prospective trial, 92% of patients proceeded to oral intake by discharge and 98% of patients by 1 month, with many requiring compensatory strategies to do so.[20]

Aside from the presence of feeding tube, the placement of a tracheostomy tube was also a commonly reported clinical measure in early studies. As surgeons became more experienced with TORS, placement of tracheostomy tube ranged from 0% to 3.5% at the time of surgery, with permanent tracheostomy tubes exceedingly rare (0.5%).[8,21] With the exception of the recently published ORATOR trial results,[22] contemporary series continue to report low rates of tracheostomy tube placements, occurring more commonly in the setting of complications.[23] Postoperative weight loss is another important functional indicator. A mean weight loss of 4.1% has been reported to occur primarily between POD 1 and 7.[20] Furthermore, case control data reported that surgically treated patients were less likely to experience grade 3 weight loss (per Common Terminology Criteria for Adverse Events) of greater than 5% to 10% of their body weight within 90 days of treatment than nonsurgically treated patients.[24]

Other clinical measures of swallowing include both clinician-rated functional scales such as the Performance Status Scale for Head and Neck Cancer Patients (PSS-HN) and Functional Outcomes Swallowing Score (FOSS) as well as patient-reported outcome (PRO) questionnaires such as the Eating Assessment Tool (EAT-10), MD Anderson Dysphagia Inventory (MDADI), Functional Assessment of Cancer Therapy (FACT), and the Sydney Swallow Questionnaire (SSQ).[25–29] Although there are several PRO measurement tools that capture both function and QOL outcomes, the latter 3 have been more widely used and validated for patients with head and neck cancer specifically.

The strength of the PSS-HN questionnaire is that it captures the normalcy of diet on a 0 to 100 scale, and estimates a patient's ability to tolerate various consistencies of food from liquids (10) to dry foods (60). Although it is a clinician-administered instrument, it explores the patients' comfortability with eating in public and estimates their speech understandability. When the PSS-HN tool was used for TORS patients, the normalcy of diet scores dropped from an unrestricted solid food diet preoperatively

(96.1 ± 17.0) to a range of 25 to 75 points in the 2- to 6-month time frame, before returning back to baseline around the 1-year mark.[5,7] Another clinician-rated scale, the FOSS, distinguishes patients based on the clinician-rated 5-stage scale, ranging from stage 0 = normal function and asymptomatic to stage V = nonoral feeding for all nutrition.[29] In one series, the median FOSS scores at the pre- and 1-month post-TORs interval was 1, which indicated a compensated abnormal swallow function. Patients with a normal pre-TORS FOSS stage generally returned to stage 0 at 1 month.[6]

The EAT-10 questionnaire is a 10-question likert-type PRO survey quantifying various dysphagia symptoms, and although it has primarily been used in evaluating neurologic or benign conditions that affect swallowing, it has recently been validated to correlate with unsafe swallowing in recently treated patients with head and neck cancer, and with postswallow pharyngeal residue on fiberoptic endoscopic evaluation.[30–32] The EAT-10 questionnaire was featured in 2 prospective studies of postoperative (TORS ± adjuvant therapy) patients. One study focused on the evolution of swallowing in the immediate month following surgery, finding that EAT-10 scores significantly increased between POD1 and POD7 but decreased by POD30.[20] When EAT-10 was used in a prospective cohort of patients treated with TORS ± adjuvant therapy, scores were found to significantly worsen in the postoperative period and improve but remain worse than baseline between 6 and 12 months, and for TORS-only patients, there was no difference than baseline scores after 12 months.[23] However, this contrasted with a head and neck–specific QOL eating subscale used in the same study, whereby there continued to be a difference in the TORS-only subgroup beyond 12 months, suggesting EAT-10 may not be as sensitive to changes experienced in this surgical population.

The MDADI is a self-administered 20-item questionnaire, exploring 4 domains of swallowing-related QOL, including global, emotional, functional, and physical subscales, with high scores representing better day-to-day functioning and QOL.[27] Among several studies that used the MDADI tool, composite scores over a year out from surgery ranged from 65.2 to 78.[4,18,33] Furthermore, patients with prolonged feeding tube, higher T-stage tumor, and those who had complications were found to have worse postoperative MDADI scores.[18] Finally, the FACT instrument and SSQ were recently compared with the MDADI, with the FACT-Head and neck cancer–specific questionnaire likely overlapping with the MDADI in collected information.[28]

INSTRUMENTAL SWALLOWING ASSESSMENTS

Although the inventories and questionnaires discussed earlier provide us with the perceived swallowing dysfunction, the exact cause of the dysfunction does not become revealed. More objective data from radiographic or endoscopic swallowing evaluations have not been as frequently reported after TORS. Clinically, speech language pathologists perform fiberoptic endoscopic evaluation of swallowing (FEES) and Modified Barium Swallow (MBS) to characterize oropharyngeal swallowing dysfunction.[34,35] Both studies provide complementary information. With FEES, there is direct endoscopic visualization, which allows for examination of the pharyngeal stage of swallowing including the ability to handle secretions, although the view may be lost during bolus passage as shown in **Fig. 1**.[36] FEES is attractive after TORS to visualize the wound as well as laterality of impairment and physiology such as pharyngeal constriction and velopharyngeal function during swallowing and non-swallowing tasks. The MBS allows for examination of the bolus flow in relation to the surrounding swallowing structure as shown in **Fig. 2** and may be more sensitive

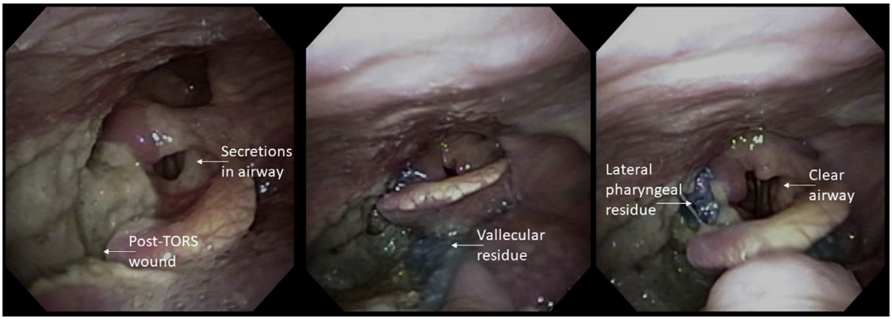

Fig. 1. Fiberoptic Endoscopic Evaluation of Swallowing (FEES). FEES 2 weeks post-TORS for T2 N1 M0 (AJCC 8th edition) HPV-associated squamous cell carcinoma of the right base of tongue with extension to the glossotonsillar fold. Endoscopy (*left image*) reveals tongue base and lateral pharyngectomy wound. After bolus trials, vallecular residue (*middle image*) and lateralized pharyngeal residue (*right image*) are evident along with clear laryngeal airway reflecting dysphagia resulting in inefficient bolus clearance but safe swallowing.

at detecting aspiration but requires the exposure to ionizing radiation.[37,38] MBS may be favored for dynamic views of oral, pharyngeal, and esophageal phases of swallowing and offers more quantitative parameters to characterize pathophysiology of dysphagia.

In order to communicate results of the MBS more universally, the Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) method was developed, which translates MBS-derived assessments into a universal toxicity grade aligning to the common terminology criteria for adverse events (CTCAE) framework that is commonly used in oncology.[39] Scores reflect both the safety and efficiency of a swallow, based on the patterns and interaction of laryngeal penetration/aspiration ratings and pharyngeal residue. This method was recently used to report on a prospective collected cohort

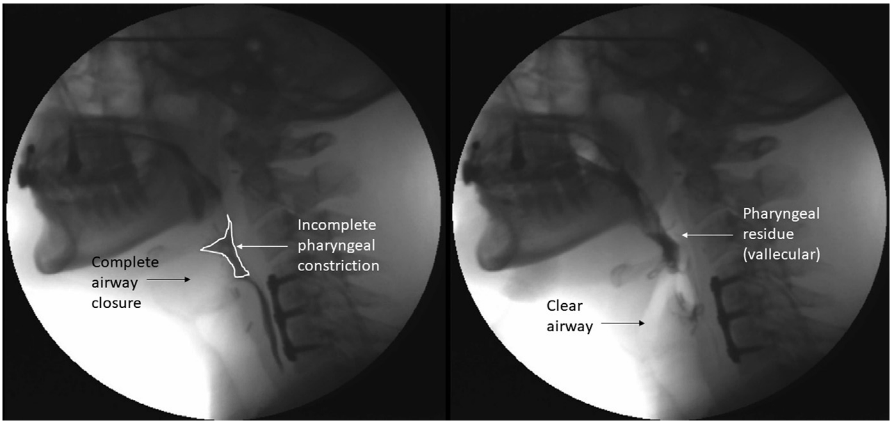

Fig. 2. Modified barium swallow (MBS) study. MBS 4 weeks post-TORS for T1 N2b M0 (AJCC 7th edition) HPV-associated squamous cell carcinoma of the right tonsil. Videofluoroscopy shows incomplete pharyngeal constriction and complete airway closure at peak swallow (*left image*) with vallecular residue and clear airway postswallow (*right image*). Mild dysphagia characterized by inefficient bolus clearance but intact airway protection.

of patients with oropharynx cancer treated with primary surgery, confirming that swallowing acutely worsened after surgery (23% prevalence of moderate to severe dysphagia on average 3 weeks post-TORS), with patients with larger tumor volume predictive of worse swallowing outcomes.[40] Swallowing function improved by 3 to 6 months after TORS, although many remained worse than baseline with up to 13.6% and 13.3% of those requiring adjuvant radiation or chemoradiation respectively, having DIGEST grades greater than or equal to 2 reflective of moderate to severe dysphagia.

QUALITY OF LIFE

Functional outcomes provide a barometer for understanding the degree to which a patient can carry an activity, without the emotional, and psychological importance that patient's may place on the activity. A patient's QOL, however, goes beyond the physical domain and includes the emotional, functional, and social domains. To assess a patient's QOL, a plethora of general and head and neck–specific questionnaires were developed, including the MD Anderson Symptom Inventory Head and Neck (MDASI-HN), University of Washington QoL (UWQOL), Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N), Head and Neck Cancer Inventory, Michigan Head and Neck Quality of Life instrument, European Organization for Research and Treatment of Cancer Core (EORTC) QLQ-C30 as well as QLQ-H&N35, SF-8, SF36 and Health Utilities Index Mark 3 (HUI3), among others.[41] Recent structured reviews outlined the most commonly used questionnaires in head and neck cancer and oropharyngeal cancers as measured by number of publications were the EORTC QLQ-C30/HN-35, UW-QOL, and the MDADI.[41,42] With the plethora of QOL instruments, the National Cancer Institute was tasked with evaluating the various instruments and their suitability for use in multicenter clinical trials. They found that most instruments can adequately assess patient's QOL, with a high degree of reliability and validity, and called for more standardization in their use for clinical trials.[43] Although going in depth with each tool is beyond the scope of this article, the authors highlight the ones that have been used specifically for evaluating patients with OPSCC.

The EORTC QLQ-C30/HN35 is one of the more detailed instruments, containing 2 modules with a 30-question cancer-specific module and an additional 35 questions specific to head and neck cancer (ie, swallowing, senses, speech, and social eating). It takes approximately 7 minutes to complete either module, and each domain is normalized to a scale between 0 to 100, with higher scores reflecting better functional scales but worse for symptom scales.[44] A change of 5 to 10 points reflects a clinically significant change.[45] In a cross-sectional survey of oropharyngeal cancer survivors, with a median of 67 months after treatment, patients treated with surgery alone had less issues with dry mouth, trouble with teeth, and other senses when compared with those treated with radiation.[46]

The UWQOL questionnaire was developed from a surgical perspective, with 15 questions, including 3 generic and 12 domain items that are aggregated into a single composite score between 0 (worse) and 100 (best).[47] A difference of 6 to 7 points indicates a clinically significant change.[48] The UWQOL has been used in 4 studies,[49–52] confirming that those treated with surgery alone had better QOL indexes particularly in the swallowing and diet domains a year out from surgery, and no patient had further deterioration of symptoms after a month. In fact, as many as 74% of surgical patients reported swallowing to be "as well as ever" compared with 32% in the nonsurgical group, although this included transoral laser microsurgery patients.[49]

The MD Anderson Symptom Inventory—Head and Neck Module (MDASI-HN), although not a QOL instrument per say, is a multisymptom survey quantifying the domain of symptom burden. MDASI-HN assesses symptom severity for 11 head and neck cancer–specific items (ie, choking, taste) in addition to 13 cancer symptoms (ie, pain, fatigue, sleep) and 6 interference symptoms (ie, work, relationship).[53] The symptom interference score is considered a QOL surrogate. This tool was recently used to characterize the symptom burden in patients with OPSCC treated surgically versus nonsurgically.[54] Initially, after surgery, patients who underwent surgery alone were significantly worse with regard to their voice, choking, and numbness scores. By 6 months, these scores were similar between the 2 groups, and instead, those who underwent radiation alone had significantly worse dry mouth, mucus, and taste disturbances. For patients treated with a single treatment modality, those who underwent surgery had better MDASI scores than those who underwent radiation at 6 months.[54] It is clear then, that when patients can be treated with surgery alone, this offers them the shortest treatment duration and shorter duration of posttreatment side effects.[55] If multimodality treatment is required, there seems to be similar symptom burden between surgical and nonsurgical cohorts, although nonsurgical cohorts continued to have worse dry mouth and taste disturbances. Use of a multisymptom instrument such as MDASI-HN can help to characterize the trade-off or distinctions in symptom profiles between treatment modalities. At this time, longer term symptom and QOL studies in the late survivorship time frame is lacking in literature, although there are suggestions that certain radiation toxicities may occur years after treatment.[56,57]

HEALTH UTILITIES

QOL measurements can be distilled to a quantified state using health utilities. Health state utilities use numbers to reflect how strongly an individual weighs a particular outcome in the face of uncertainty and are classically derived through various interview techniques such as the Time Trade Off or Standard Gamble methodology.[58,59] When these interview techniques were used to assess whether a healthy person or expert would prefer one treatment over the other, TORS alone was preferred over radiotherapy by both healthy subjects and experts.[60] Even after the addition of adjuvant radiotherapy, subjects still preferred surgery over definitive chemoradiation in paired comparisons but not when trimodality therapy was indicated. These utilities can further be used to perform cost-utility analyses to assist with treatment decision-making. A cost-utility analysis comparing TORS with nonsurgical management for early tumors was found to have a cost savings of $1,366 and an increase of 0.25 quality-adjusted life years compared with nonsurgical management.[61]

Predictors of Quality of Life and Functional Outcomes

In the management of OPSCC, TORS has provided a minimally invasive surgical approach with better functional outcomes and QOL outcomes than traditional open surgical approaches.[62] Furthermore, studies reporting the functional and QOL outcomes have all similarly demonstrated a short-term decrease of either outcome that recovers to near baseline by 6 to 12 months. However, in the treatment of OPSCCs, TORS cannot be considered alone. Upward of 70% of patients will receive either adjuvant radiation or chemoradiation.[8] With the addition of adjuvant therapy, reports have indicated a significant decrease in functional and QOL outcomes at 3 to 6 months that may not fully recover by a year's time.[40,63]

Those who do undergo TORS may receive a lower radiation dose in the adjuvant setting, compared with those treated with definitive chemoradiation. Radiation dose is known to have a logarithmic dose-toxicity scale with 3.4% increase risk of having at least grade 2 dysphagia per increase in gray to the constrictor musculature.[64–66] Indeed, even if trimodality therapy is indicated, there are reports that patients undergoing surgery have better QOL scores than those treated with definitive chemoradiation at 12 months.[4,49,67] Even after stratifying groups by T-stage and subsites, this finding remains significant, but must be interpreted cautiously, as most series are subject to selection bias. Although it is important to acknowledge this, when properly selected, TORS may be able to deliver improved outcomes compared with primary nonsurgical treatment.

Aside from adjuvant therapy, advance T-stage is also an important predictor of postoperative swallowing outcomes. Tumor volume was found to be predictive of swallowing outcomes, with tumor volume greater than 9.35 cm^3 more likely to have worse baseline swallowing dysfunction in addition to ongoing swallowing dysfunction immediately after TORS.[40] Patients with larger tumors were also more likely to have PEG placement.[8]

Despite these excellent outcomes, severe prolonged dysphagia has been reported after transoral resection of oropharynx lesions.[68] Several small case reports have suggested that bilateral glossopharyngeal nerve injury, in addition to injury to the superior pharyngeal constrictor muscles, may have contributed to prolonged swallowing dysfunction.

SUMMARY

TORS has provided an excellent surgical modality for patients with oropharynx cancer, with the potential to minimize the negative impact on functional and QOL outcomes. This is particularly apparent when compared with nonsurgical treatment modalities where studies have demonstrated patients to more readily recover from surgery than radiation or chemoradiation, and in the carefully selected patient, even in the setting of adjuvant therapy. The main predictors of poor functional and QOL outcomes are larger tumors and adjuvant treatment. Therefore, careful selection of patients, particularly those with low-intermediate disease may allow for optimal functional and QOL outcomes.

CLINICS CARE POINTS

- Patients consider swallowing to be the most important outcome after cure and survival.[3] To fully understand a patients' swallowing outcome requires the study of their oral intake, feeding tube dependence, and physical impairment (via videofluoroscopic or endoscopic swallow study), in addition to patient-PRO questionnaires.
- Patients have an acute worsening of swallowing function after TORS, which improves by 3 to 6 months.[20,40]
- Tumor volume, advanced T-stage, and adjuvant therapy are major predictors of worse swallowing outcomes after TORS.[8,40]

DISCLOSURE

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