Systematic Review of Validated Quality of Life and Swallow Outcomes after Transoral Robotic Surgery

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Abstract

Objective. To systematically review the available evidence on the effects of transoral robotic surgery (TORS) on the post-treatment quality of life (QOL) and swallow function of patients with head and neck cancer.

Data Sources. PubMed and Ovid electronic databases were searched from inception to July 6, 2016. Specific database functions were applied to maximize the search.

Review Methods. Articles in the database were reviewed for inclusion by 2 independent reviewers according to predetermined eligibility criteria. The references of relevant articles were then hand-searched to identify additional manuscripts. For included articles, the study characteristics and relevant data were extracted.

Results. Of 103 articles screened, 20 reporting validated measures of QOL and/or swallow outcomes for 659 patients were eligible for inclusion. Fourteen were observational studies or case series and did not compare the TORS group with another intervention. Two were prospective non-randomized clinical trials that compared outcomes between TORS and primary chemoradiation. Four were cohort studies comparing TORS with other treatment approaches and modalities, including open surgical approaches and transoral laser microsurgery. Overall, most patients who underwent TORS ± adjuvant therapy reported a return to baseline QOL and swallow function by 6 to 12 months posttreatment. Several studies demonstrated superior QOL and swallowing outcomes when compared with primary chemoradiation or open approaches.

Conclusions. Available evidence suggests that patients who undergo TORS for head and neck cancer have good QOL and swallowing outcomes after treatment, but outcomes are dependent on baseline function, T stage, and adjuvant treatment status.

Keywords

head and neck neoplasms, robotics, quality of life, deglutination, oropharyngeal neoplasms

An estimated 64,690 new cases of oral cavity, pharyngeal, and laryngeal cancer will be diagnosed in the United States in 2018, with 13,740 expected deaths.¹ Oropharyngeal cancer in particular has been on the rise, and it is expected to constitute the majority of all head and neck cancers by 2030.² Over the past several decades, chemoradiation therapy (CRT) has been a common treatment for many types of head and neck cancer.³ Despite good oncologic outcomes, this method can result in high toxicities and poor functional outcomes.⁴ Historically, the pharynx and larynx have been poorly accessible sites due to anatomic complexity and proximity to vital structures. Traditional open surgical procedures disrupt the neuromuscular framework of the pharynx, and postradiation tissue fibrosis compromises tissue mobility. Therefore, open surgery and CRT are both associated with significant morbidity, particularly dysphagia.⁵

Advances in treatment over the past decade have led to more widespread use of minimally invasive surgical procedures in the patient population with head and neck cancer. From 2006 to 2007, O’Malley et al and Weinstein et al first described the feasibility and relative safety of transoral robotic surgery (TORS) for select oropharyngeal and supraglottic neoplasms.⁶⁻⁸ TORS has revolutionized the treatment of these areas by improving visibility and adding degrees of freedom to surgical movements, and multiple studies have confirmed feasibility without compromising oncologic outcomes.⁹⁻¹¹ Patients undergoing TORS for oropharyngeal cancer have survival comparable to that of matched patients who received nonsurgical treatment.¹²

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The most important clinical outcome for patients with cancer is survival, but posttreatment quality of life (QOL) and swallowing are also vital outcome parameters from a patient’s perspective and affect how they interact with the world on a daily basis after undergoing treatment. There are limited high-quality data examining QOL and validated swallow outcomes after TORS. The purpose of this article is to systematically review the available evidence on the effects of TORS on posttreatment QOL and swallowing function among patients with head and neck cancer as reported by validated measures of QOL and/or swallow function.

**Methods**

This study did not involve data collection from human participants; therefore, Institutional Review Board approval was not required. The methodology used strictly adhered to the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analyses).

**Search and Selection**

A systematic literature search was undertaken in the PubMed and Ovid databases from inception to July 6, 2016. Terms representing the following concepts were combined as follows “transoral robotic surgery AND quality of life” and “transoral robotic surgery AND dysphagia.” Specific database functions were also applied to maximize the search. Seventy-eight records were identified through the database search. Articles in the database were reviewed for inclusion by 2 independent reviewers (A.C. and A.S.) according to predetermined eligibility criteria. The references of relevant articles were then hand-searched to identify additional eligible articles. A total of 103 records were then screened for relevance and eligibility by the 2 reviewers. Forty-one were excluded secondary to not meeting the predetermined eligibility criteria. Sixty-two articles were then reviewed in full text, and most that were excluded at this stage were done so for lack of a validated measure of QOL or swallowing function. Twenty were found to be eligible for inclusion in our review (Figure 1).

**Study Eligibility Criteria**

Studies published in the English language that included adult patients who underwent TORS for pharyngeal and laryngeal carcinoma and that used a validated measure of QOL and/or swallowing function were eligible for inclusion. Studies in which TORS was performed for indications other than cancer or in patients aged <18 years were excluded. Case reports with less than 10 subjects and review articles were also excluded. All articles were assessed for quality by A.C. and A.S. and the possibility of selection, publication, and other bias was noted. The level of evidence was also
determined with the criteria from the Oxford Center for Evidence-Based Medicine (OCEBM) and Methodological Index for Non-randomized Studies (MINORS).13,14

Data Extraction and Analysis
The full text of the 20 articles was reviewed for the following data points: study methods, sample size, patient demographics (age, sex, smoking status), site and stage of disease, human papillomavirus or p16 status, treatment, follow-up times, and swallowing and QOL outcomes. Data collected demonstrated heterogeneity and were not appropriate for aggregation or meta-analysis.

Results
There were 20 articles reporting validated measures of QOL and/or swallow outcomes for 659 patients that were eligible for inclusion (Table 1). Fourteen of these were observational studies or case series and did not compare TORS with another intervention.15-28 Two studies were prospective nonrandomized clinical trials that compared outcomes between TORS and primary CRT.29,30 Four studies were cohort studies comparing TORS with other treatment approaches and modalities, including traditional surgical approaches and transoral laser microsurgery (TLM).31-34

Population Characteristics
Ten studies examined patients with oropharyngeal cancer; Mercante et al included only T1 and T2 base of tongue carcinomas; and 2 others also limited their study population to T1 or T2 lesions.23,27,28 Five studies evaluated a combination of subsites and stages of head and neck cancer. Two studies evaluated patients with hypopharyngeal cancer, and Park et al evaluated patients with laryngeal cancer who were treated by TORS supraglottic partial laryngectomy.25 Durmus et al reported on patients treated by TORS for carcinoma of unknown origin.17 Hurtuk et al reported on all TORS cases, 88% of which were head and neck squamous cell carcinoma (SCCa).19

Treatment
All studies performed therapeutic or elective neck dissections as indicated, and most were performed at the same time as the TORS, although a few elected to stage these, given concerns of the risk of a through-and-through defect. Two studies included QOL and swallowing outcomes of patients who had undergone TORS without any further adjuvant chemotherapy or radiation therapy.15,23 The remainder of the studies included patients who had received adjuvant therapy for generally accepted indications, such as node positivity, close or positive margins, and adverse pathologic features. Rates of adjuvant therapy were highly variable among studies. Adjuvant radiotherapy (XRT) was delivered in 22% to 100% of cases and adjuvant CRT in 0% to 60%.

Level of Evidence
All studies were evaluated for their levels of evidence per the OCEBM and MINORS criteria.13,14 Based on OCEBM criteria, 2 studies are considered level 3 evidence and the remainder level 4. Based on MINORS criteria, the noncomparative studies were evaluated on 8 parameters and received scores from 6 to 12 (out of 16). The 6 comparative studies were evaluated on all 12 parameters and received scores ranging from 15 to 21 (out of 24; Table 1).

Quality of Life
Five validated measures of QOL were reported by 10 studies: the University of Washington Quality of Life Questionnaire (UW-QOL) in 4 studies,1,5,12,15,21,22,31,32,35 the Head and Neck Cancer Inventory in 3 studies,17,19,36 the Performance Status Scale (PSS) in 2 studies,21,29,37 the Psychosocial Distress questionnaire in 1 study,33 and the SF-8 (Short Form–8; a validated 8-item version of the SF-36) in 1 study.21

When comparisons were made between those who received TORS and those who received open surgery or CRT, the TORS group had higher QOL scores in several categories at various time points.22,29,31-33 Several but not all studies reported the lowest QOL scores at 3 months postoperatively and lower QOL scores in several categories among those who received adjuvant therapy after surgery.17,19,21

Swallowing Function
Four validated measures of swallowing function were reported by 12 studies: the MD Anderson Dysphagia Inventory (MDADI) in 7 studies,16,20,23,27,30,33,34,38 the Functional Outcome Swallowing Scale (a validated measure of oropharyngeal dysphagia) in 3 studies,9,25,32,39 the Swallowing Quality of Life Questionnaire (a validated questionnaire used to detect problems with oropharyngeal dysphagia) in 1 study,28,40 and the Functional Oral Intake Score (FOIS) in 1 study.29,41

When those who received TORS and those who received open surgery or CRT were compared, several studies reported better swallowing outcomes for the TORS group.29,30,33 Sumer et al compared MDADI scores between those who received TORS and those who received TLM and found no significant differences.34 Two studies demonstrated worse swallowing outcomes among those who received adjuvant therapy after TORS.9,16 Supplemental Table S1 (available in the online version of the article) summarizes results from individual studies.

Discussion
The most important clinical outcome for patients with cancer is survival, but posttreatment QOL and swallowing are also vital outcome parameters. Over the past several decades, nonsurgical CRT has been a common treatment for many types of head and neck cancer, and despite good oncologic outcomes, this method results in high toxicities and poor functional outcomes.3,4,42,43 Our review of the available evidence suggests that patients who undergo TORS for head and neck cancer have good QOL and swallowing outcomes after treatment.

Available evidence suggests that TORS alone does not cause long-term disability in swallowing function and QOL once the patient has recovered from the acute postoperative period. However, this is confounded by selection bias in
Table 1. Overview of Studies Including Validated QOL and Swallow Outcomes for Patients with Head and Neck Cancer Treated with TORS.

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Population</th>
<th>Patients, n</th>
<th>QOL or Swallowing Instrument</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moore (2009)24</td>
<td>Oropharyngeal SCCa</td>
<td>45 TORS ± adjuvant therapy</td>
<td>FOSS</td>
<td>4 11 of 16</td>
</tr>
<tr>
<td>Iseli (2009)20</td>
<td>HNSCC</td>
<td>54 TORS ± adjuvant therapy</td>
<td>MDADI</td>
<td>4 10 of 16</td>
</tr>
<tr>
<td>Genden (2011)28</td>
<td>Oropharyngeal, hypopharyngeal, and laryngeal SCCa</td>
<td>56 (30 TORS ± adjuvant therapy vs 26 CRT)</td>
<td>PSS-HN and FOIS</td>
<td>3 19 of 24</td>
</tr>
<tr>
<td>Leonhardt (2011)21</td>
<td>Oropharyngeal carcinoma</td>
<td>38 TORS ± adjuvant therapy</td>
<td>SF-8 and PSS</td>
<td>4 12 of 16</td>
</tr>
<tr>
<td>Hurtuk (2012)19</td>
<td>All indications; 56 (88%) were for HNSCC</td>
<td>64 TORS ± adjuvant therapy</td>
<td>HNCI</td>
<td>4 10 of 16</td>
</tr>
<tr>
<td>Sinclair (2011)27</td>
<td>T1 or T2 oropharyngeal SCCa</td>
<td>42 TORS ± adjuvant therapy</td>
<td>MDADI</td>
<td>4 9 of 16</td>
</tr>
<tr>
<td>Park (2012)26</td>
<td>Hypopharyngeal SCCa</td>
<td>23 TORS ± adjuvant therapy</td>
<td>FOSS</td>
<td>4 11 of 16</td>
</tr>
<tr>
<td>More (2013)30</td>
<td>Stage III or IVa oropharyngeal and supraglottic SCCa</td>
<td>40 (20 TORS ± adjuvant therapy vs 20 CRT)</td>
<td>MDADI</td>
<td>3 21 of 24</td>
</tr>
<tr>
<td>Park (2013)32</td>
<td>Hypopharyngeal cancer</td>
<td>56 (30 TORS ± adjuvant therapy vs 26 open surgery ± adjuvant therapy)</td>
<td>UW-QOL</td>
<td>4 17 of 24</td>
</tr>
<tr>
<td>Sumer (2013)34</td>
<td>Oropharyngeal SCCa</td>
<td>33 (17 TORS ± adjuvant therapy vs 16 TLM ± adjuvant therapy)</td>
<td>MDADI</td>
<td>4 16 of 24</td>
</tr>
<tr>
<td>Dziegielewski (2013)18</td>
<td>Oropharyngeal SCCa</td>
<td>81 TORS ± adjuvant therapy</td>
<td>HNCI</td>
<td>4 10 of 16</td>
</tr>
<tr>
<td>Park (2013)25</td>
<td>Laryngeal SCCa</td>
<td>16 TORS supraglottic partial laryngectomy ± adjuvant therapy</td>
<td>FOSS</td>
<td>4 11 of 16</td>
</tr>
<tr>
<td>Durmus (2014)17</td>
<td>Carcinoma of unknown origin</td>
<td>22 TORS then adjuvant therapy</td>
<td>HNCI</td>
<td>4 10 of 16</td>
</tr>
<tr>
<td>Maxwell (2014)22</td>
<td>HNSCC</td>
<td>177 (105 primary surgery ± adjuvant therapy and 72 primary CRT; 28 of 105 surgical had TORS or TLM)</td>
<td>UW-QOL</td>
<td>4 7 of 16</td>
</tr>
<tr>
<td>de Almeida (2014)16</td>
<td>Oropharyngeal SCCa</td>
<td>92 TORS ± adjuvant therapy but 47 MDADI</td>
<td>MDADI</td>
<td>4 6 of 16</td>
</tr>
<tr>
<td>Chen (2015)31</td>
<td>Oropharyngeal cancer</td>
<td>62 (15 TORS and 16 TLM who received adjuvant therapy vs 31 matched CRT controls)</td>
<td>UW-QOL</td>
<td>4 15 of 24</td>
</tr>
<tr>
<td>Mercante (2015)23</td>
<td>T1 and T2 BOT carcinomas</td>
<td>13 TORS without adjuvant therapy</td>
<td>MDADI</td>
<td>4 12 of 16</td>
</tr>
<tr>
<td>van Loon (2015)28</td>
<td>T1N0 and T2N0 oropharyngeal carcinoma</td>
<td>18 TORS ± adjuvant therapy</td>
<td>SWAL-QOL</td>
<td>4 9 of 16</td>
</tr>
<tr>
<td>Choby (2015)15</td>
<td>Oropharyngeal SCCa</td>
<td>34 TORS without adjuvant therapy</td>
<td>UW-QOL</td>
<td>4 7 of 16</td>
</tr>
<tr>
<td>Slama (2016)13</td>
<td>T1 and T2 carcinomas of the BOT and supraglottis</td>
<td>49 (22 TORS ± adjuvant therapy vs 27 open surgery ± adjuvant therapy)</td>
<td>MDADI and PD</td>
<td>4 15 of 24</td>
</tr>
</tbody>
</table>

Abbreviations: BOT, base of tongue; CRT, chemoradiation; FOIS, Functional Oral Intake Score; FOSS, Functional Outcome Swallowing Scale; HNCI, Head and Neck Cancer Inventory; HNSCC, head and neck squamous cell carcinoma; MDADI, MD Anderson Dysphagia Inventory; MINORS, Methodological Index for Non-randomized Studies; OCEBM, Oxford Center for Evidence-Based Medicine; PD, Psychosocial Distress questionnaire; PSS, Performance Status Scale; PSS-HN, Performance Status Scale for Head and Neck Cancer; QOL, quality of life; SCCa, squamous cell carcinoma; SF-8, Short Form-8; SWAL-QOL, Swallowing Quality of Life Questionnaire; TLM, transoral laser microsurgery; TORS, transoral robotic surgery; UW-QOL, University of Washington Quality of Life Questionnaire.

*Maxwell et al and Chen et al did not differentiate between TLM and TORS and considered them both minimally invasive techniques in their analysis when comparing treatment modalities.
that patients treated with TORS alone without adjuvant therapy have early-stage cancers. There were no significant differences in MDADI scores when preoperative scores were compared with 6- and 12-month postoperative scores among 13 patients with T1 and T2 base of tongue carcinomas treated with TORS without adjuvant therapy.\textsuperscript{23} A study of 34 patients who underwent TORS without adjuvant therapy for oropharyngeal SCCa did not identify any UW-QOL domains that had a significant decrease in QOL during the first year after surgery, in contrast to studies that included patients who received adjuvant therapy.\textsuperscript{15} Results may vary with more advanced disease, as swallowing outcomes are dependent on baseline function and T stage.\textsuperscript{24}

TORS offers the ability to tailor therapy and provide superior swallowing and QOL outcomes even when adjuvant therapy is indicated, further supporting its use. Upon proceeding with TORS, a reasonable topic of discussion and concern is whether the patient would still require adjuvant CRT. This would mean exposure to triple-modality therapy and increased treatment burden. However, the toxicities and morbidity associated with XRT increase with higher radiation doses. Patient who undergo TORS may receive a lower radiation dose in the adjuvant setting than what they would have if they were treated with CRT alone. Several studies reported a decline in QOL and swallow function during treatment with a nadir at the 3-month postoperative time point, correlating with the completion of adjuvant therapy in the form of XRT or CRT.\textsuperscript{17,18,30} Despite this acute decline after treatment, most studies then demonstrated a gradual improvement in QOL and swallowing until an eventual return to baseline for the majority of patients undergoing TORS, even with high rates of adjuvant therapy.\textsuperscript{17,18,30} Gildener-Leapman et al recently reviewed the clinical staging of 76 patients who had undergone TORS and determined that 24 of them would have received primary CRT per National Comprehensive Cancer Network guidelines. Instead, they had TORS first, and only 15 of 24 needed adjuvant CRT; 7 received adjuvant XRT alone; and 2 did not receive any adjuvant therapy. Therefore, they were able to deintensify the adjuvant therapy of 37% of patients who would have received CRT.\textsuperscript{44}

Comparisons between those undergoing primary XRT or CRT and TORS ± adjuvant therapy suggest that patients undergoing TORS have better QOL and swallowing outcomes despite the possible need for adjuvant therapy. Long-term data assessing 12-month posttreatment MDADI results among patients with head and neck cancer treated with XRT or CRT demonstrated continued swallowing deficits, with scores of 73.6 and 68.2 as compared with 86.6 and 77.6 at baseline, respectively.\textsuperscript{42,43} PSS–Head and Neck Cancer and FOIS were compared between 30 patients with head and neck cancer who underwent TORS ± adjuvant therapy (83\% XRT, 47\% CRT) and matched controls who underwent CRT. The TORS group had significantly better scores in the early posttreatment period, and their scores returned to baseline by 9 months; however, the CRT group’s PSS–Head and Neck Cancer diet scores ($P = .03$) and FOISs ($P = .02$) remained lower than baseline 12 months after treatment.\textsuperscript{29} Twenty patients with stage III or IVa oropharyngeal and supraglottic SCCa who were treated with TORS ± adjuvant therapy (100\% XRT, 60\% CRT) were compared with matched controls who underwent CRT. The TORS group had significantly better MDADI scores at 6-month ($P = .004$) and 12-month ($P = .006$) follow-up despite the high rates of adjuvant therapy. When patients were stratified by T stage or subsite, those treated with TORS continued to demonstrate better swallowing outcomes.\textsuperscript{30} Chen et al compared patients with oropharyngeal cancer undergoing transoral surgery (defined as TORS or TLM) with matched controls undergoing CRT, and the transoral surgery group had significantly higher UW-QOL swallowing scores at 1 year posttreatment (91.5 vs 72.1, $P = .01$).\textsuperscript{31} There is inherent selection bias in many of the comparative studies discussed in this systematic review, as patients with more advanced locoregional disease may have not been surgical candidates and were therefore more likely to undergo primary CRT. One needs to be aware of this inherent bias, but we believe that these findings are still meaningful and favor TORS when compared with CRT. More high-quality and larger studies comparing the different treatment modalities are needed.

Hutcheson et al published a systematic review of functional outcomes after TORS for oropharyngeal cancer. They reported overall good swallowing and functional outcomes that are in agreement with our findings, but they included studies reporting only tracheostomy and gastrostomy tube rates, instead of validated measures of swallowing or QOL.\textsuperscript{45} The level of evidence on this topic is limited by a lack of consensus on the optimal assessment of and reporting on swallowing and QOL outcomes after treatment for head and neck cancer and the short amount of time that TORS has been widely available. Most studies in this review had 1 to 2 years of follow-up after treatment, but it would be beneficial to obtain longer-term results, especially since some late toxicities associated with definitive XRT and CRT can occur 5 to 10 years after treatment.\textsuperscript{46} Future studies in this area that stratify preoperative patient factors and disease state (ie, age, human papillomavirus status, smoking status, comorbidities, stage at presentation) will delineate which patient populations will benefit most and have the best outcomes from TORS.

**Conclusions**

Available evidence suggests that patients who undergo TORS ± adjuvant therapy for head and neck cancer have good QOL and swallowing outcomes after treatment, but outcomes are dependent on baseline function, T stage, and adjuvant treatment status. When compared with patients receiving open surgery or CRT, patients undergoing TORS had favorable outcomes with respect to QOL and swallowing function. Further high-quality studies on this topic will be beneficial in delineating which patient populations will benefit most and have the best outcomes from TORS.
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Alexa Castellano, literature review; data extraction and analysis/interpretation; wrote manuscript; Arun Sharma, literature review; data analysis/interpretation; edited/revised manuscript.

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Supplemental Material
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References


