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Original Research Article

The utility of transoral robotic surgery for oropharyngeal squamous cell carcinoma: functional and perioperative outcomes

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ABSTRACT

Background: To evaluate the functional recovery, oncologic and perioperative outcomes of patients undergoing transoral robotic surgery (TORS) for oropharyngeal squamous cell carcinoma (OPSCC).
Methods: A retrospective cohort study of 103 patients who underwent TORS between 2015 and 2024 was conducted. Patients were stratified into diagnostic-TORS (patients with head and neck cancer of unknown primary origin (HNCUP), n=28) and therapeutic-TORS groups (resection of T1-T2 OPSCC, n=75). The primary outcomes were oropharyngeal function post-TORS. Secondary outcomes related to HNCUP detection, treatment de-intensification, overall survival (OS), and surgical complications.
Results: Immediate oral intake was observed in 90.3% of patients. No patients required long-term gastrostomy feeding. A progressive improvement in diet and fluid levels was observed, with 88.9% of patients achieving a normal diet within 12 months. At 12 months post-TORS, 90.3% of patients recovered their premorbid speech level. HNCUP identification rate was 42.9% with diagnostic-TORS. Five-year OS was 89% (95% CI, 78-94%). Tumours with positive p16 status had significantly improved OS (94% vs. 63%, p=0.001). Although margin status did not demonstrate statistically significant differences in OS (p=0.313), all patients requiring re-excision achieved clear margins, facilitating treatment de-intensification. Post-operative bleeding was observed in 6.8% of patients, with a peri-operative mortality rate of 1.9%.
Conclusions: TORS is effective in oropharyngeal cancer management, delivering excellent functional and survival outcomes. Our study supports the role of TORS in treatment de-intensification. The risk of significant haemorrhagic complications necessitates rigorous perioperative protocols.

Keywords: Transoral robotic surgery, Oropharyngeal squamous cell carcinoma, Head and neck cancer of unknown primary, Oropharyngeal function

INTRODUCTION

Treatment for oropharyngeal squamous cell carcinoma (OPSCC) conventionally involves radiotherapy with or without chemotherapy, while radical surgery is reserved for selective cases. Despite advances in modern radiotherapy techniques and chemotherapy protocols, significant treatment-related morbidities persist. These range from the acute toxicities of mucositis and dysgeusia, to chronic sequelae including xerostomia, speech impairment, dysphagia and osteoradionecrosis.[1] Lip-split mandibulotomy provides necessary access for OPSCC but is invasive and risks facial scarring, mandibular malunion and malocclusion.[2] These debilitating sequelae frequently compromise oropharyngeal function and impair the quality of life in OPSCC survivors.[1,3]

TORS has emerged as a minimally invasive treatment modality with promising oncological outcomes for the

resection of early-stage OPSCC.[4] The enhanced dexterity of double-jointed robotic arms and telescopic three-dimensional visualisation augments access to the oropharynx for targeted tumour ablation, without the need for invasive access procedures.[5] Additionally, TORS has gained recognition for its role in the diagnostic workup of patients with HNCUP. HNCUP accounts for 2-5% of all head and neck malignancies, with the majority of subsequently detected tumours located in the oropharynx.[6] Compared with conventional panendoscopy, TORS offers ipsilateral or bilateral tonsillectomy and tongue base mucosectomy, achieving higher primary tumour detection rates.[7] A key advantage of this approach is the potential to facilitate single-modality treatment and therapeutic de-intensification.[8]

This study aims to review the functional, oncologic and perioperative outcomes of TORS, with an emphasis on its diagnostic and therapeutic applications for the management of OPSCC.

METHODS

Patient selection

A retrospective cohort study was undertaken of consecutive patients who received TORS for the treatment of OPSCC between 2015 and 2024 at the Royal Derby Hospital, United Kingdom. All patients with a minimum of 12 months follow-up were included. Exclusion criteria were applied on patients with distant metastases, previous head and neck cancer treatment, or recurrent disease. Patients were categorised into diagnostic- and therapeutic-TORS groups. HNCUP was defined as absence of an identifiable primary tumour for targeted biopsy on clinical and radiological examination of the upper aerodigestive tract, with a histological diagnosis of squamous cell carcinoma in a cervical lymph node. Radiological examination included contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography-CT (PET-CT). The extent of diagnostic-TORS was determined by the laterality of metastatic cervical lymphadenopathy and findings on pre-operative imaging. TORS-assisted tongue base mucosectomy was performed in cases with suspicious changes within the tongue base on imaging. For ipsilateral glossotonsillar sulcus or tonsil findings, tongue base mucosectomy and ipsilateral tonsillectomy were performed. If both sites were radiologically normal, tongue base mucosectomy with bilateral tonsillectomy were undertaken. The therapeutic-TORS group comprised of patients with biopsy-proven T1-T2 OPSCC, who received TORS-assisted tumour resection with curative intent.

Data collection

Data was collected on patients' gender, age, tumour subsites, p16 status, tumour and nodal classification using the 8th edition of American Joint Committee on Cancer (AJCC) staging system.[9] Treatment factors were recorded on surgical margins, presence of extra-nodal extension (ENE), and if neck dissection and/or adjuvant oncology treatment were undertaken. The primary outcome was the assessment of post-operative oropharyngeal function. Surgical complications, HNCUP detection, treatment de-intensification, and 5-year OS were recorded as secondary outcomes.

Definitions

The p16 immunohistochemistry was utilised as a surrogate marker for tumour human papillomavirus (HPV) status. Surgical margins were classified as clear (≥5 mm), close (>0 mm and <5 mm), or involved (tumour present at the specimen edge). Adjuvant radiotherapy was prescribed following multidisciplinary team discussion for close margins and/or multiple involved lymph nodes, whereas chemoradiotherapy was recommended for involved surgical margins and/or ENE.

Post-operative oropharyngeal function was evaluated via speech and level of oral nutrition. Dietary intake was graded using the international dysphagia diet standardisation initiative (IDDSI) framework (Appendix A) at day 1 post-procedure, and at 1, 6, and 12 months.[10] Speech outcomes were assessed at 12 months by a dedicated speech and language therapist using the Understandability of Speech Scale.[11] OS was calculated from the date of surgery to the date of last follow-up or death.

Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Sciences software (IBM SPSS Statistics version 31.0.10). Kaplan-Meier curves were plotted with a univariate log rank $p<0.05$ (2-tailed) considered statistically significant. Patients with an unidentified primary tumours following diagnostic-TORS were excluded from the OPSCC survival analysis. Subgroup analyses were performed on OPSCC treated with TORS as single-modality treatment.

RESULTS

During study period, 103 patients were included, 28 in diagnostic-TORS and 75 in therapeutic-TORS group.

Diagnostic-TORS

The characteristics of the study population are summarised in Table 1. Tongue base mucosectomy with ipsilateral tonsillectomy was the most common technique performed (50.0%). The primary tumour was identified in 12 patients (42.9%). Diagnostic-TORS yielded no clear margins, while 75.0% of identified tumours had close margins. For the three patients with involved margins, one patient underwent further TORS-assisted re-excision which demonstrated no evidence of residual tumour. Nine

HNCUP patients avoided radiotherapy and underwent TORS as the single treatment modality (32.1%).

Post-operative recovery and functional outcomes

The median duration of post-operative inpatient stay was 2 days (range 1-4 days). All patients in the diagnostic-TORS group were able to commence oral intake at day 1 post-procedure, with 64.3% of patients consuming soft (level 6) diet, and 14.3% of patients consuming normal (level 7) diet (Figure 1). No patients required supplementary nasogastric feeding. The proportion of patients returning to level 7 diet was 53.6% at 1 month, 82.1% at 6 months, and 88.9% at 12 months following surgery. All patients recovered 100% of their premorbid speech function at 12 months.

Therapeutic-TORS

Among 75 patients undergoing therapeutic-TORS surgical margins were clear in 20.0%, close in 44.0%, and involved in 36.0%. Of the 27 patients with involved margins, 55.6% underwent re-excision, and all achieved clear margins at the second procedure. No adjuvant therapy was required for 37.3% of patients. This included the six patients who underwent re-excision, while the other nine re-excision patients had adjuvant radiotherapy due to advanced nodal disease.

Post-operative recovery and functional outcomes

The median duration of post-operative inpatient stay was 4 days (range 1-27 days). At day 1 post-procedure, 10 patients (13.3%) required nasogastric/enteral nutrition (median 15 days; range, 2-45), primarily due to aspiration risk (50.0%). At 1-month post-surgery, 36.9% of patients were consuming normal (level 7) diet, increasing to 68.5% at 6 months and 88.9% at 12 months (Figure 2).

At 12 months, 86.7% of patients had regained 100% of their premorbid speech function, whilst 13.3% of patients achieved 75% of their premorbid speech function.

TORS-related complications

Surgical complications were observed in 7 patients (6.8%). All were post-operative haemorrhage following therapeutic-TORS procedures. Minor bleeding occurred in five patients and was manged with tranexamic acid mouthwash or bedside electrocautery. Major bleeding from the primary surgical site occurred in two patients (1.9%) and was subsequently fatal.

OS outcomes

The median follow-up was 4.7 years (range, 1.1-9.8 years), with 13 deaths (12.6%) during this period. Five-year OS for the 87 patients with OPSCC was 89% (95%CI, 78%-94%). Patients with p16 positive OPSCC exhibited significantly improved 5-year OS, compared to p16 negative tumours (94% vs. 63%, p=0.001) (Figure 3). Based on initial margins, patients with clear margins demonstrated a 5-year OS of 100%, compared with 86% and 88% for close and involved margins, respectively (Figure 4). These differences were not statistically significant (p=0.313). No other tumour or treatment factors were found to be significant predictors of OS (Table 2), precluding multivariate cox-regression analysis.

Subgroup analyses were performed on the 37 patients who underwent TORS as single-modality treatment. Five-year OS was 85% (95%CI, 68%-94%). All these patients underwent neck dissection. The 48.7% had nodal disease, the majority N1 (27.0%), with three patients exhibiting ENE. No patients required nasogastric/enteral nutrition post-operatively.

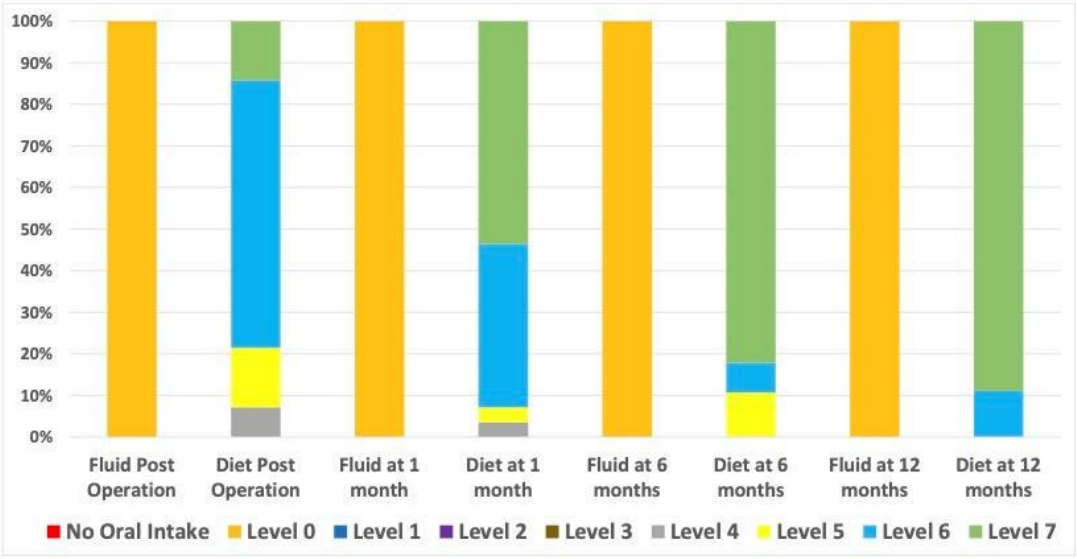

Figure 1: Progressive improvement in diet and fluid levels over 12 months (diagnostic-TORS group, n=28).

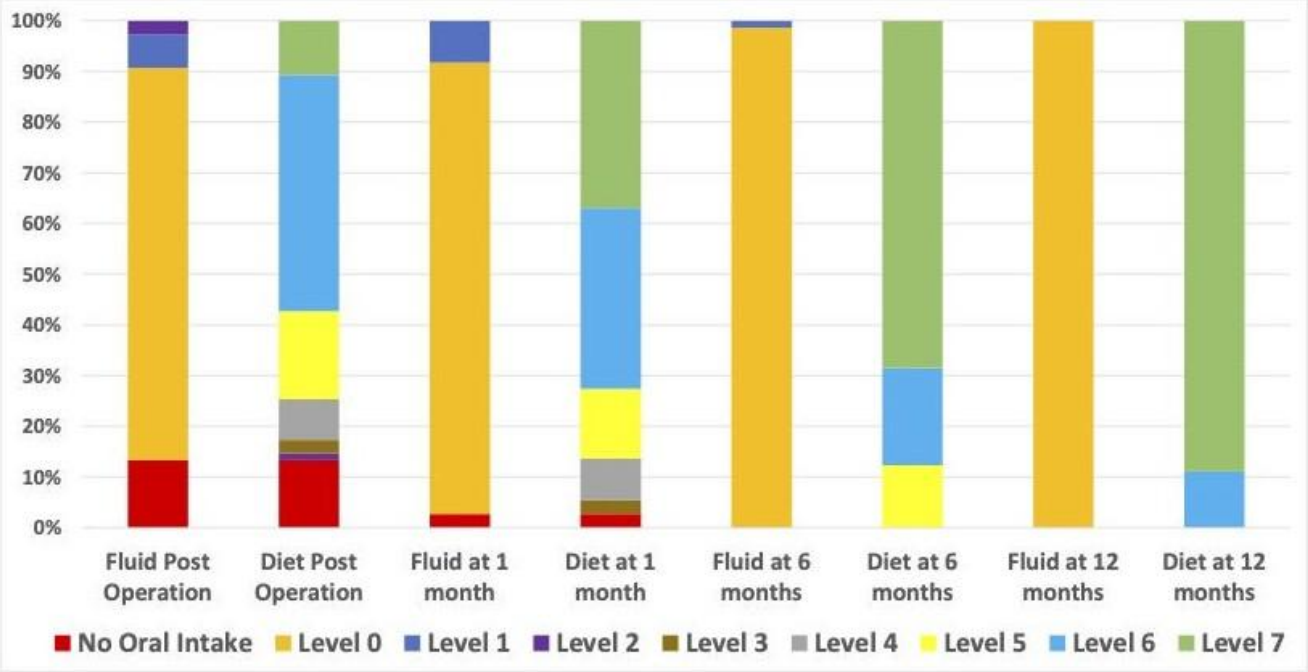

Figure 2: Progressive improvement in diet and fluid levels over 12 months (Therapeutic-TORS group n=75).

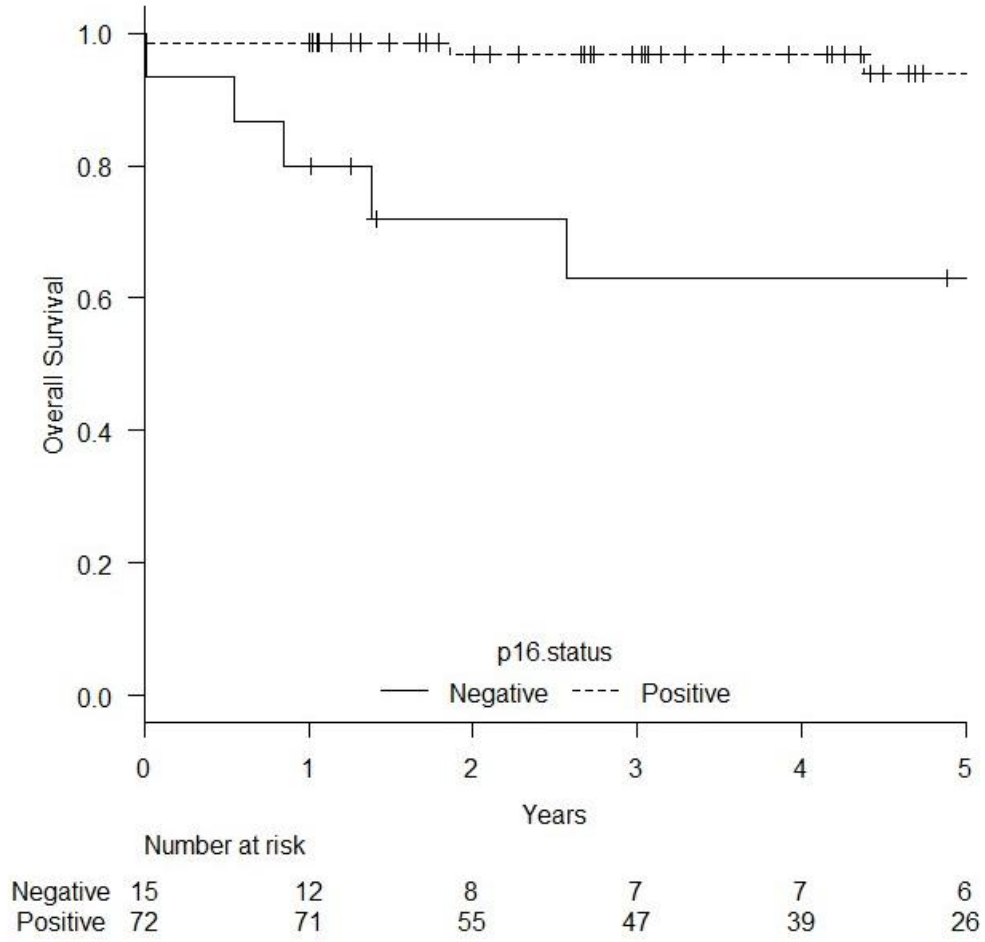

Figure 3: Kaplan-Meier 5-year OS curves for all-cause mortality according to p16 status.

*The Kaplan-Meier survival curve (censored at 5 years) demonstrated that patients with p16 positive OPSCC exhibited significantly improved 5-year OS 94% (95% CI, 82%-98%), compared to p16 negative OPSCC 63% (95% CI, 32%-83%), (p=0.001).

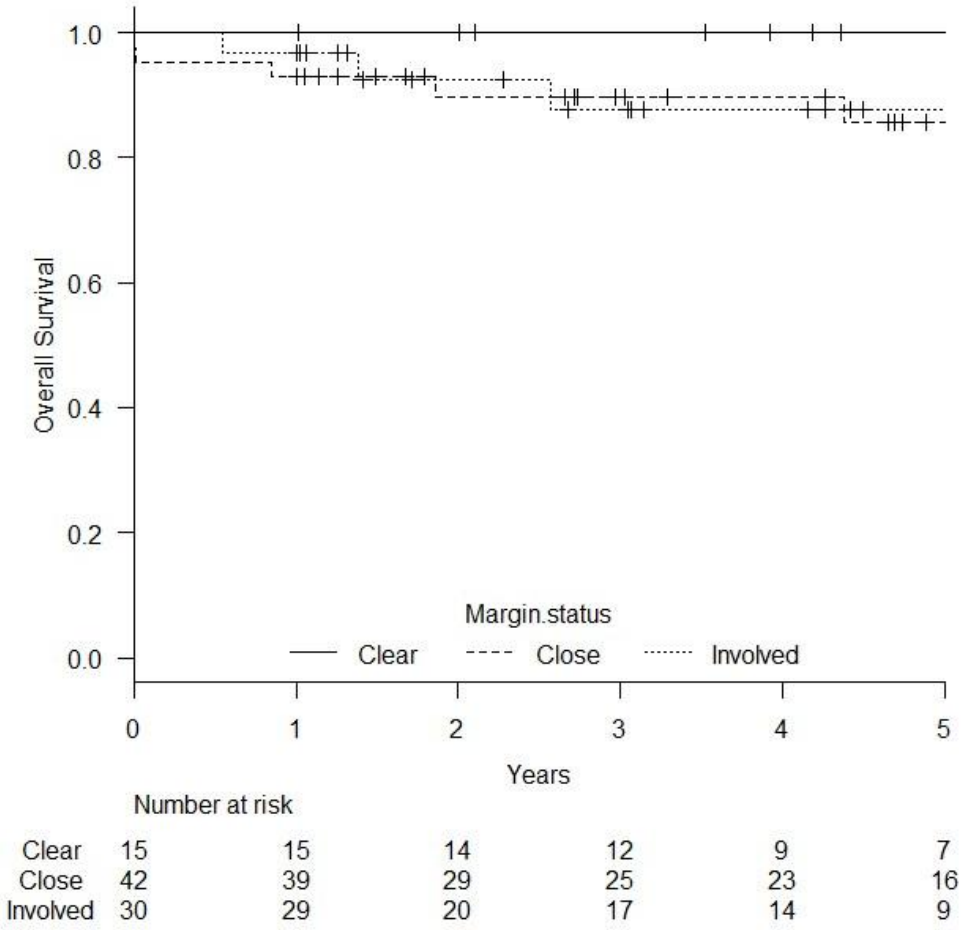

Figure 4: Kaplan-Meier 5-year OS curves for all-cause mortality according to surgical margin status (censored at 5 years).

*The Kaplan-Meier survival curve based on initial margins, demonstrated that patients with clear margins had a 5-year OS of 100% (95% CI, 100%-100%), compared with 86% (95% CI, 68%-94%) for close, and 88% (95% CI, 66%-96%) for involved margins (p=0.313).

Table 1: Demographic characteristics, treatment summary and outcomes of the diagnostic and therapeutic TORS groups.

Diagnostic TORS group, (n=28)			Therapeutic TORS group, (n=75)		
Variables	**N**		**Variables**	**N**	
Gender					
Male	19 (67.9%)		Male	50 (66.7%)	
Female	9 (32.1%)		Female	25 (33.3%)	
Age (in years)					
Median age	59		Median age	61	
Age range	48-78		Age range	41-84	
p16 status					
Positive	21 (75.0%)		Positive	62 (82.7%)	
Negative	7 (25.0%)		Negative	13 (17.3%)	
N-classification	**p16 negative, (n=7)**	**p16 positive, (n=21)**		**p16 negative, (n=13)**	**p16 positive, (n=62)**
N0	0 (0.0%)	0 (0.0%)	N0	8 (61.5%)	14 (22.6%)
N1	4 (57.1%)	19 (90.4%)	N1	2 (15.4 5)	43 (69.4%)
N2	0 (0.0%)	0 (0.0%)	N2	0 (0.0%)	5 (8.06%)
N2a	0 (0.0%)	0 (0.0%)	N2a	0 (0.0%)	0 (0.0%)
N2b	2 (28.6%)	0 (0.0%)	N2b	0 (0.0%)	0 (0.0%)
N2c	1 (14.3%)	1 (4.8%)	N2c	0 (0.0%)	0 (0.0%)
N3	0 (0.0%)	1 (4.8%)	N3	0 (0.0%)	0 (0.0%)
N3a	0 (0.0%)	0 (0.0%)	N3a	0 (0.0%)	0 (0.0%)
N3b	0 (0.0%)	0 (0.0%)	N3b	3 (23.1%)	0 (0.0%)

Continued.

Diagnostic TORS group, (n=28)		Therapeutic TORS group, (n=75)	
TORS diagnostic procedure			
Tongue base mucosectomy	10 (35.7%)		
Tongue base mucosectomy with the ipsilateral tonsillectomy	14 (50.0%)		
Tongue base mucosectomy with bilateral tonsillectomy	4 (14.3%)		
Primary tumour identification			
Identified	12 (42.9%)		
Not identified	16 (57.1%)		
Tumour subsite of identified primary tumour, (n=12)		**Tumour subsite**	
Tonsil	4 (33.3%)	Tonsil	56 (74.7%)
Tongue base	8 (66.7%)	Tongue base	13 (17.3%)
Soft palate	0 (0.0%)	Soft palate	4 (5.3%)
Epiglottis	0 (0.0%)	Epiglottis	2 (2.7%)
T-classification of identified primary tumours, (n=12)		**T-Classification**	
T1	12 (100%)	T1	29 (38.7%)
T2	0 (0.0%)	T2	46 (61.3%)
Surgical margins of identified primary tumours (n=12)		Surgical margins (Initial)	
Clear (≥5 mm)	0 (0.0%)	Clear (≥5 mm)	15 (20.0%)
Close (>0 mm to <5 mm)	9 (75.0%)	Close (>0 mm to <5 mm)	33 (44.0%)
Involved	3 (25.0%)	Involved	27 (36.0%)
Involved surgical margins, (n=3)		**Involved surgical margins, (n=27)**	
Re-excision performed	1 (33.3%)	Re-excision performed	15 (55.6%)
Clear margins after re-excision	1 (100%)	Clear margins after re-excision	15 (100%)
Neck dissection			
Yes	24 (85.7%)	Yes	68 (90.7%)
No	4 (14.3%)	No	7 (9.3%)
ENE			
Yes	10 (35.7%)	Yes	25 (33.3%)
No	18 (64.3%)	No	50 (66.7%)
Adjuvant treatment			
Chemoradiotherapy	11 (39.3%)	Chemoradiotherapy	24 (32.0%)
Radiotherapy	8 (28.6%)	Radiotherapy	23 (30.7%)
No adjuvant therapy	9 (32.1%)	No adjuvant therapy	28 (37.3%)
Duration of inpatient stay			
Median (days)	2	Median (days)	4
Range (days)	1-4	Range (days)	1-27
Oropharyngeal function			
Nasogastric nutrition	0 (0.0%)	Nasogastric nutrition	10 (13.3%)
Median duration of nasogastric nutrition (days)	N/A	Median duration of nasogastric nutrition (days)	15
Range of duration of nasogastric nutrition (days)	N/A	Range of duration of nasogastric nutrition (days)	2-45
Reason for nasogastric nutrition	N/A	Reason for nasogastric nutrition	
Aspiration	N/A	Aspiration	5 (50.0%)
Odynophagia	N/A	Odynophagia	3 (30.0%)
Post-operative bleeding	N/A	Post-operative bleeding	2 (20.0%)
Speech at 12 months			
100% premorbid function	28 (100%)	100% premorbid function	65 (86.7%)
75% premorbid function	0 (0.0%)	75% premorbid function	10 (13.3%)

*N/A not applicable to subgroup.

Table 2: Factors associated with 5-year OS for patients with OPSCC undergoing TORS, (n=87).

Variables	5-year OS rate (%)	Log-rank p value
Overall	89.4 (95% CI, 78-94%)	N/A
Gender		
Male	89.5	0.978
Female	90.0	
Age (in years)		
<60	92.3	0.636
>60	87.5	
p16 Status		
Positive	94.4	0.001
Negative	63.2	
N-classification		
p16 positive, (n=72)		
N0	100	0.197
N1	94.1	
N2	83.3	
N3	100	
p16 positive, (n=15)		
N0	75.0	0.863
N1	50.0	
N2a/b/c	N/A	
N3a/b	66.7	
Subsite of primary tumour		
Tonsil	87.5	0.756
Tongue base	94.1	
Soft Palate	100.0	
Epiglottis	100.0	
T-classification		
T1	90.2	0.943
T2	89.1	
Surgical margins		
Clear (≥5 mm)	100.0	0.313
Close (>0 mm to <5 mm)	85.7	
Involved	87.6	
Neck dissection		
Yes	89.6	0.869
No	90.0	
ENE		
Yes	85.7	0.535
No	91.5	
Adjuvant treatment		
Chemoradiotherapy	86.2	0.767
Radiotherapy	92.6	
No adjuvant therapy	90.3	

*N/A not applicable to subgroup.

DISCUSSION

This study illustrates a single centre's experience using TORS for the management of OPSCC, demonstrating favourable post-operative oropharyngeal function and survival outcomes. Overall, the prognosis for T1-T2 OPSCC resected via TORS appears highly encouraging, especially in patients with p16-positive tumours. Our survival analysis supports the well-established evidence that HPV/p16 status acts as an independent prognostic factor for OPSCC, correlating with significantly improved outcomes.[12]

Compared with primary chemoradiotherapy for OPSCC, Amin et al noted increased short-term dysphagia in TORS patients but decreased risks of short- and long-term gastrostomy tube dependence.[13] In our series, only 9.7% of patients required temporary nasogastric/enteral nutrition, none required long-term gastrostomy feeding, and a progressive improvement in diet was demonstrated over 12 months. Similarly, Lazarus et al noted excellent

functional outcomes following TORS for OPSCC, with all patients on regular diets and with understandable speech at 1-month post-surgery.[14] The minimally invasive nature of TORS additionally facilitates effective recovery, and a short inpatient stay, comparing favourably to radical surgery.[15]

The rate of primary tumour detection in HNCUP is dependent on the diagnostic techniques employed. Panendoscopic examination, with targeted or random biopsies, achieves occult tumour detection rates of 20% to 30%.[7] Van Weert et al has shown the introduction of diagnostic-TORS significantly improves this, yielding an average detection rate of 72%.[16] Our cohort observed a lower detection rate of 42.9%. This may be attributable to the pre-TORS diagnostic workup for HNCUP at our centre. The proportion of patients undergoing tongue base mucosectomy alone, is consistent with other series.[16] However, at our centre, random biopsies of the upper aerodigestive tract and palatine tonsillectomy are not routinely undertaken prior to TORS.[16] Preliminary evidence indicate that the utility of TORS within the diagnostic HNCUP pathway is maximized when preceded by other negative investigations. The American Society of Clinical Oncology published recommendations that tongue base mucosectomy be undertaken when palatine tonsillectomy fails to detect the primary tumour.[7] The systematic review by Farooq et al reported that TORS-assisted tongue base mucosectomy achieves a primary site detection rate of 78% when performed following a negative conventional workup, including PET-CT and palatine tonsillectomy.[17]

Beyond its diagnostic role, TORS enables OPSCC treatment de-intensification. The ECON-ACRIN(E3311) Trial concluded that favourable oncologic and functional outcomes were attained in patients who underwent TORS followed by reduced post-operative radiotherapy.[18] Grewal et al additionally reported reduced treatment-related toxicity from pharyngeal-sparing radiation following diagnostic-TORS in HNCUP.[19] De Almeida et al also demonstrated acceptable disease control with this approach.[8] Although treatment de-intensification was not the primary aim of our study, the 37 patients managed with TORS as single-modality treatment displayed favourable outcomes. Further prospective clinical trials, including the PATHOS trial are currently underway to continue to evaluate the role of TORS in de-intensifying treatment and mitigating long-term morbidity.[20]

The definition of an adequate margin in OPSCC ablation remains controversial due to the proximity of the underlying neurovascular anatomy. The National Comprehensive Cancer Network guideline has suggested a 2 mm margin be considered clear for transorally resected OPSCC.[21] Tucker and Bollig reported a positive margin rate of 16.6% for TORS resected OPSCC, which is comparably lower than the rate of involved margins observed in the current study.[22] Increasing tumour size, tongue base subsite, presence of lympho-vascular invasion and low-volume TORS centres have been associated with increased rates of involved margins.[22,23] Temporal analysis revealed a reduction in our positive margin rate over time, likely reflecting improvements with surgical experience and histopathological evaluation. Although adjuvant therapy may have confounded the impact of margin status on survival in our study, margin involvement is suggested as an important prognostic factor after adjusting for these treatments.[24,25] However, margin distance in HPV-positive OPSCC may not confer the same disease-free or survival advantage, supporting the need for a revised definition of close surgical margins.[25,26]

The overall complication rate in our series was 6.8%, consisting entirely of post-operative haemorrhage. Pinhorn et al found a similar rate of 7.24% for post-operative bleeding following TORS.[27] Perioperative mortality in our cohort was 1.9%, in comparison to 0.6% reported by Davies et al.[28] Notably, both fatalities occurred during the early phase of our TORS program. Following these events, enhanced peri-operative protocols were implemented, that prioritised comprehensive pre-operative anaesthetic evaluation and standardized anticoagulation management. Intraoperatively, it is also standard practice to perform prophylactic transcervical ligation of the lingual, facial, ascending pharyngeal arteries.[29] The systematic review by Stokes et al found large tumours, perioperative anticoagulation, and prior radiation were significantly associated with an increased risk of post-TORS haemorrhage.[30] While transcervical arterial ligation did not reduce the overall incidence of haemorrhage it lead to fewer severe haemorrhages.[30] The improvement in outcomes over time in our series reflects the importance of systematic training and protocol development in optimising patient safety.

Several limitations of this study should be acknowledged. Its retrospective and observational design introduces inherent biases, while the relatively small sample size limits statistical power for subgroup and multivariate analyses. Quality of life was assessed using functional outcomes rather than validated patient-reported indices. Although we postulate that the favourable post-operative oropharyngeal function observed may be attributable to reduced radiation dose following TORS, the absence of detailed radiotherapy planning data precludes a detailed analysis. Interpretation of survival outcomes and implications for treatment de-intensification are further limited by heterogeneity in adjuvant treatment within the cohort.

CONCLUSION

For the management of early-stage OPSCC, TORS demonstrates favourable post-operative oropharyngeal function and survival outcomes. However, TORS is associated with the risk of significant haemorrhagic complications, necessitating rigorous perioperative

protocols. TORS plays a valuable role in primary tumour identification. The true benefit of TORS in treatment de-intensification and its impact on oncologic outcomes continues to be definitively established in prospective trials.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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