Original Article

Transoral robotic surgery for patients undergoing total laryngectomy: systematic review of current evidence

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Contributions: (I) Conception and design: S Goel, EH Ooi; (II) Administrative support: All authors; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: S Goel, D Gunasekera; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Background: Transoral robotic surgery (TORS) is an established treatment for oropharyngeal cancer. The use of TORS has extended into performing total laryngectomy (TL) procedures. This systematic review was undertaken to review the feasibility and effectiveness in patients undergoing TORS for TL procedures.

Methods: Databases included were PubMed, Embase and Scopus from their inception till the 8th of October 2023. The search strategy included keywords "total laryngectomy" and "transoral robotic surgery" in combination with boolean operators. Inclusion criteria included adults (>18 years old) undergoing TORS for TL, regardless of indication. Studies that evaluated TORS for multiple procedures were only included if they provided a subset data on patients undergoing TL. All study designs including experimental, analytical observational and descriptive observational were considered, regardless of language or country of publication. Two independent authors screened titles, abstracts, and full texts. Critical appraisal was conducted by same reviewers using the JBI critical appraisal tools prior to data extraction.

Results: The search identified 182 studies with 122 remaining after duplicates removed. Six studies comprising 42 patients were included in final analysis. Five studies were case series and 1 was a cohort study with a subset population of patients undergoing TL. The main indications for TORS TL included primary or recurrent cancers in 78% of cases and a dysfunctional larynx in 22%. A further 10 cases were either dysfunctional larynx or squamous cell carcinoma but a breakdown was not offered for each category. The mean operative time was 261 minutes. The mean nasogastric tube dependent time was 12.26 days. Post-operative fistulas occurred in 23% of cases and 7% requiring conversion to open surgery. Margins were negative in 14 (of 15) cases where margins were reported.

Conclusions: TORS TL offers a feasible minimally invasive treatment option for carefully selected indications. The limited literature identified in this systematic review highlights the indications for this approach and the outcomes with performing this procedure.

Keywords: Transoral robotic surgery (TORS); total laryngectomy (TL); minimally invasive surgery

Received: 25 February 2024; Accepted: 29 May 2024; Published online: 02 August 2024.

doi: 10.21037/ajo-24-19

View this article at: https://dx.doi.org/10.21037/ajo-24-19

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Introduction

Head and neck cancer was the 7th most common cancer worldwide in 2018 (1) with the prevalence of laryngeal cancer amounting to 1.09 million patients worldwide in 2017 (2). Laryngeal cancer occurs more commonly in men compared to women, with rates of 5.8 per 100,000 and 1.2 per 100,000 respectively (3).

The traditional approach to management of advanced laryngeal cancers has evolved over time. Conventionally, these cancers were treated with total or partial laryngectomy procedures with a clinically significant reduction in health-related quality of life outcomes (4). Over the last three decades, there was initially a shift away from these procedures in advanced laryngeal cancers towards organ preservation chemoradiotherapy (5,6). However, there is now a recognition that organ preservation does not necessarily translate to a functional organ with high aspiration and tracheostomy dependency rates. Total laryngectomy (TL) and post-operative radiotherapy have been demonstrated to produce good long-term control and survival rates for advanced laryngeal cancer (7).

The evolution of surgery towards a less invasive approach includes the introduction and adaptation of transoral robotic surgery (TORS) in 2005 by Neil Hockstein and its Food and Drug Administration approval in 2009 (8). TORS has become an established approach for resection in oropharyngeal squamous cell carcinomas (9). It provides minimally invasive access without major tissue disruption through a natural orifice and caters for a three-dimensional view with enhanced freedom in manipulation of surgical instruments. George Lawson then introduced a TORS based approach for TL procedures in 2013 (10). A TORS TL approach aimed to reduce the extent of external dissection in cases of a narrow field TL without neck dissections. As demonstrated with TORS oropharyngectomy experience (11), minimally invasive approaches in head and neck speed up post-operative recovery and reduce time spent in hospital. The benefit of a TORS TL compared to a traditional approach is emerging with a number of publications presenting data on patient selection, indications and outcomes. This systematic review aims to encompass indications, techniques and outcomes of a TORS TL approach. By synthesising available evidence, it aims to provide the most comprehensive review to date of the role of TORS TL on its effectiveness and feasibility. We present this article in accordance with the PRISMA reporting checklist (available at https://www.theajo.com/article/view/10.21037/ajo-24-19/rc).

Methods

Inclusion criteria

Participants

The patient population that will be studied are adults (aged 18 years or older) that underwent TORS for TL procedures. The indication for TL was not considered as an exclusion criterion as the study aimed to capture a comprehensive data set.

Intervention

The review will consider studies that evaluate TORS procedures, specifically in context of TL, regardless of other previous interventions used. Studies that evaluate TORS for TL with or without other adjuvant modalities will also be included. Studies that evaluated TORS for multiple procedures were only included if there was subset data provided for TL patients.

Comparator

The review will consider all studies as long as the population and intervention criteria are met. Examples of comparators may include open approaches, but this is not a requirement for inclusion. There is no formal comparator for inclusion in this systematic review.

Outcomes

Outcome measures will be described in three main categories: functional, oncological and survival. Functional outcomes will include days of dependence on tracheostomy and nasogastric tubes (NGTs) for breathing and feeding respectively. Rates of successful tracheoesophageal punctures (TEPs) or other methods of speech rehabilitation will be included and analysed. Oncological outcomes will include surgical margins post histological analysis and complications of surgery. Examples of complications may include tracheoesophageal fistulas and conversions to open surgery from an initial TORS based approach. If other complications relevant to the study are available, the incidence will be pooled and described as appropriate. Survival outcomes include disease-free survival, defined as the time from intervention to the date of death from the disease, or the recurrence of signs and symptoms from the disease. Overall survival, defined as time from intervention

to the date of death resulting from any cause, will also be considered if available.

Study designs

The review aimed to be comprehensive and hence considered all study designs for inclusion including experimental study designs, quasi-experimental study designs, analytical observational studies and descriptive observational studies. There were no systematic reviews and meta-analyses found on this particular topic. No further limitations were placed on the dates of publication and all countries/health systems and languages were considered.

This review was conducted in accordance with JBI methodology for systematic reviews (12). Ethics approval was not required due to the study being a systematic review of previously published data. There was no registered priori protocol for this study.

Study methods

The aim of the search strategy was to capture all studies available on TORS for TL procedures. It aimed to locate studies published in any language from the inception of databases till the 8th of October 2023. Databases included PubMed, Embase and Scopus with no date restrictions placed. An initial search of PubMed identified keywords in this field by analysis of titles, abstracts, and index terms of relevant studies. Keywords included "total laryngectomy" and synonyms of "transoral robotic surgery". A comprehensive and simple search strategy was developed in conjunction with boolean operators (Appendix 1). Each strategy was amended as required by codings of each database. Once a search was finalised, all identified citations were collated in Endnote 20 (Clarivate Analytics, PA, USA) and duplicates were removed. A reference list was then extracted from Endnote 20 and uploaded into Covidence 2023 (Veritas Health Innovation, Melbourne, Australia) where further duplicates were removed for completeness. Following a pilot, two independent review authors (S.G., D.G.) screened titles and abstracts, then followed by the full text articles for inclusion in this review against the inclusion and exclusion criteria. Disagreements were resolved through discussion and consensus with the consultation of a third author (E.H.O.). The reference lists of all included articles were screened for additional studies.

Eligible studies underwent a risk of bias assessment by two independent reviewers (S.G., D.G.) for methodological quality using JBI critical appraisal tools as appropriate for each study design with results attached (Appendix 2). All studies regardless of the results of methodological quality underwent data extraction.

Data extraction was piloted and extracted using an independently formed tool by two reviewers. The data extracted includes specific details about the study methodology, population demographics, indications for surgery, operative time, hospitalisation time, days of NGT dependence, voice rehabilitation techniques, surgical margins and complications. Effect sizes have been expressed as mean differences for all continuous data that have been extracted. Statistical pooling was not possible and hence, all data has been presented in a narrative format including tables and figures to aid representation. No subgroup analysis was conducted and there were less than 10 studies included in the analysis and hence a funnel plot was not generated to assess publication bias. Heterogeneity was not assessed.

Results

Overview

The search identified a total of 182 studies with 129 remaining after duplicates removed using Endnote 20 (Clarivate Analytics). A further 7 duplicates were found and removed by Covidence 2023 (Veritas Health Innovation) leaving 122 studies for initial screening. Titles and abstracts were screened by two independent reviewers (S.G., D.G.) against the inclusion and exclusion criteria and found 14 studies to be included for full text review. Eight studies were subsequently excluded due to incorrect intervention, outcomes or patient populations (*Figure 1*).

A total of 6 studies were then included for final extraction and analysis (*Table 1*). The quality of evidence was low with 5 studies being case series and 1 study being an analytical cross-sectional study which included a subset data on patients undergoing TORS TL. Studies included were published within years 2013 to 2021 given the recent adaptation of TORS in head and neck units around the world. The total sample size across the 6 studies was 42 patients.

Indications for TORS TL

The main indications for TORS TL included primary or recurrent cancers in 78% and a dysfunctional larynx in 22% (*Table 2*). A further 10 cases were either dysfunctional larynx

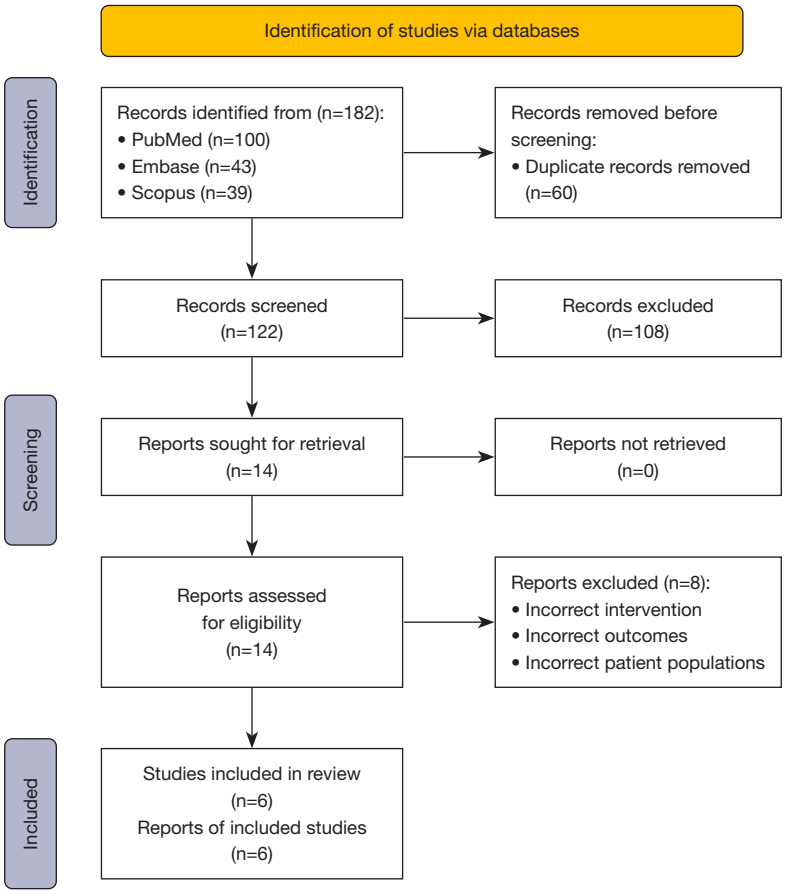

Figure 1 PRISMA of included studies.

Table 1 The characteristics of included studies

Study number	Title	Author	Year	Country/ region	Study design
1	Surgical and oncological outcomes of transoral robotic total laryngectomy: A case series	Hans *et al.*	2021	France	Case series
2	Transoral Robotic Surgery and Geriatric Population: Which Benefit	Hassid *et al.*	2020	Belgium	Analytical cross sectional study
3	Transoral robotic total laryngectomy: report of 3 cases	Dowthwaite *et al.*	2013	Canada	Case series
4	Transoral Robotic Surgery Total Laryngectomy: Evaluation of Functional and Survival Outcomes in a Retrospective Case Series at a Single Institution	Krishnan and Krishnan	2017	Australia	Case series
5	Transoral robotic total laryngectomy	Smith *et al.*	2013	USA	Case series
6	Long-term outcomes of trans-oral robotic surgery-assisted total laryngectomy for recurrent laryngeal cancers	Wang *et al.*	2020	Taiwan	Case series

Table 2 The indications for TL procedures in each included study

Study number	Study	Sample size	Indication for TL
1	Hans *et al.*	10	2 dysfunctional larynx
			3 low grade chondrosarcomas
			5 recurrent laryngeal cancers
2	Hassid *et al.*	10	Dysfunctional larynx
			Squamous cell carcinoma
3	Dowthwaite *et al.*	3	1 low grade chondrosarcoma
			1 squamous cell carcinoma
			1 dysfunctional larynx
4	Krishnan and Krishnan	5	2 dysfunctional larynx
			1 adenoid cystic carcinoma
			1 low grade chondrosarcoma
			1 recurrent laryngeal SCC
5	Smith *et al.*	7	2 dysfunctional larynx
			5 recurrent laryngeal cancers
6	Wang *et al.*	7	7 recurrent laryngeal cancers

TL, total laryngectomy; SCC, squamous cell carcinoma.

or squamous cell carcinoma but a specific breakdown was not offered for each category. Primary cancers undergoing TORS TL included 5 cases of low-grade chondrosarcomas and 1 case of adenoid cystic carcinoma. In 18 cases of salvage TL, all were squamous cell carcinomas and most were previously treated with chemoradiotherapy or radiotherapy alone. Dysfunctional larynx aetiologies included cases of idiopathic bilateral vocal cord palsies, spastic cerebral palsy, cranial nerve palsies secondary to chemoradiotherapy, severe radio-necrosis, intubation related stenosis and chronic aspiration. In these cases, a TL was offered to improve quality of life from a functional perspective.

Operating time

Four studies (13-16) reported similar operating times for TORS TL procedures with a mean of 261 minutes (*Table 3*). Wang *et al.* (2020) (17) reported a mean operating time of 111 minutes which is less than half of all the other reported studies. Differences in technique, approach and the validity of time measurement is unknown. Hospitalisation time was reported by three studies (14-16) with a mean of 22.3 days.

Functional outcomes and long-term follow-up

Main functional outcomes extracted included NGT dependence and voice rehabilitation. The mean NGT dependence time was 12.26 days as reported in five studies (13-17). Krishnan and Krishnan (2017) (16) included three patients who were already dependent on percutaneous gastrostomies for feeding prior to TORS TL procedures. Additionally, Wang *et al.* (2020) (17) reported functional outcome swallowing scale scores of 0 with all patients resuming a normal diet on long-term follow-up. Furthermore, three studies (14-16) reported on voice outcomes with a sample size of 18 patients. Thirteen patients proceeded with primary TEP with no complications. Two patients chose oesophageal voice rehabilitation. One patient underwent electrolarynx placement which failed and subsequently underwent a secondary TEP procedure with recurrent fistulas. The remaining two patients reported were non-verbal prior to TL procedures due to neurological disorders.

Long-term follow-up times varied and were only reported in two studies. Krishnan and Krishnan (2017) (16) reported a 2-year survival of 66% with 4 (of 5) patients alive at time of publication. Wang *et al.* (2020) (17) reported a median follow-up time of 36.1 months with 1 mortality occurring at 19 months and 1 recurrence picked up at 29 months out of the 7 cases. Margins were reported in 15 patients and were negative in 14 (93% clear margins).

Complications

Complication rates were high post TORS TL procedures, occurring in 42% of the patients included in this review. Ten patients suffered pharyngocutaneous fistulas (PCF; 23%). Most studies did not report on further management and outcomes of these fistulas. Where reported, 1 patient suffered recurrent fistulas even after 2 attempts at free flap closures and 1 fistula which healed within 3 weeks post operatively. A further 4 patients suffered long-term stoma stenosis with 2 eventually undergoing curative intervention. There were 3 conversions to open surgery due to inadequate exposure during TORS TL even with extensive cephalad extension of the dissection. Two patients suffered post-operative haemorrhage with returns to theatre. Other complications included local flap inflammation in the initial post-operative period which was successfully managed with antibiotics.

Table 3 Each outcome in the included studies

Study number	Study	Operative time (minutes)	Hospitalisation time (days)	NGT dependent feeding (days)	Voice rehabilitation	Margins	Complications
1	Hans *et al.*	278	13.9	9.3	8 TEP 2 oesophageal voice	5/5 negative	1 PCF 1 haemorrhage
2	Hassid *et al.*	235	32	1	–	–	5 PCF
3	Dowthwaite *et al.*	260	–	1	3 TEP	–	1 return to theatre 1 open conversion
4	Krishnan and Krishnan	272	21	–	1 primary TEP 2 secondary TEP	3/3 negative	1 PCF
5	Smith *et al.*	–	–	–	–	–	2 PCF 2 open conversion
6	Wang *et al.*	111	–	16	–	6/7 negative	4 tracheostoma stenosis

NGT, nasogastric tube; TEP, tracheoesophageal puncture; PCF, pharyngocutaneous fistula.

Discussion

Overall

As TORS becomes an established treatment option for an increasing number of head and neck cancers, most studies focus on this technique for oropharyngeal or supraglottic cancers. This study of 42 patients forms the only known systematic synthesis of evidence on TL procedures using TORS. The procedure details can be summarised in three main steps including cervical dissection, TORS resection and pharyngotomy reconstruction and closure. The main differing point in these was the delivery of the larynx, either through the stoma or the mouth. Dowthwaite *et al.* (2013) (13), Wang *et al.* (2020) (17) and Smith *et al.* (2013) (18) mainly chose to deliver the laryngeal specimens trans-orally whilst Krishnan and Krishnan (2017) (16) moved away from the approach after 1 case. They found delivery through the cervical dissection to result in a smaller neopharyngeal defect to close and hence aiding recovery of these patients. It is important to note that all authors assessed patients for the suitability of TORS based approach by considering history of radiation and assessment with an FK-WO retractor prior to commencing on this pathway.

Functional outcomes

In terms of functional voice rehabilitation, TEP and oesophageal rehabilitation were the most popular choices at 72% and 11% respectively. A systematic review by Maniaci *et al.* (2024) (19) demonstrated a significantly better speech performance post laryngectomy procedures with a voice handicap index of 31.93 versus 35.39 for TEP and oesophageal rehabilitation respectively. This was not correlated with a statistically significant difference in the voice-related quality of life index (P=0.19). One patient who chose electrolarynx for voice rehabilitation underwent a secondary TEP procedure with recurrent fistula formations despite different closure techniques.

Complications

This review shows a total complication incidence of 42% with a TORS based TL approach. Hasan *et al.* (2017) (20) conducted a large systematic review with 3292 patients and showed a similar complication incidence in open salvage TL procedures. The cohort demographics are similar with most of the 42 patients in this review suffering from recurrent laryngeal cancers or dysfunctional larynx which have been previously treated with combinations of chemotherapy and radiotherapy. Hasan *et al.* (2017) (20) demonstrated a pooled incidence of PCF at 28.9% which is comparable to this review at 23.8%. A meta-analysis (21) of TL patients identified multiple risk factors leading to PCF including but not limited to previous chemoradiotherapy, positive surgical margins, hypopharyngeal subsite, supraglottic subsite and advanced primary tumours. This information was unavailable during data collection of studies in this review. Multiple authors have reviewed different techniques

to reduce the incidence of PCF in TL procedures. Paleri *et al.* (2014) (22) demonstrated a one-third reduction in PCF formation with combination use of primary closure with a vascularised pedicle or free flap. Guimarães *et al.* (2016) (23) specifically highlighted the feasibility in using a pectoralis major muscle flap to significantly reduce the incidence by 22% when compared to primary pharyngeal closure. The surgical techniques included in this review only utilised primary pharyngeal closure. Other techniques described in the literature for reduction in the rate of PCFs include stapler assisted pharyngeal closure techniques which have decreased rates of PCFs from 23.4% to 9.5% (24).

Limitations

Although this is the only synthesis of evidence on a TORS for TL approach, it had significant limitations in terms of sample sizes and the quality of the studies included. Most studies were case series and did not describe long-term survival outcomes or follow-up for these patients. This would be important to gauge comparisons with patients undergoing open surgical techniques. The limited number of studies and patient numbers are likely to reflect the small pool of indications for patient selections in this technique. It also reflects on the limited robotic capabilities of most head and neck institutions around the world given the need for high technical expertise and experience in performing this approach. Due to the limited data, all studies chose to report data in narrative format and hence could not be pooled in a meta-analysis. The reported data was heterogeneous in nature and this could be due to the differences in patient selection, procedure techniques and surgeon expertise. Larger and more robust comparative studies are required to undertake a formal meta-analysis to compare to open techniques. Furthermore, Hassid *et al.* (2019) were unable to specify patient characteristics that underwent TORS TL which limited analysis (15). All studies had missing data points in terms of either functional, survival outcomes, and oncological outcomes. It serves as a point of improvement for all studies to report on these three subcategories which are important in analysing effectiveness of interventions, specifically in cases of head and neck cancers.

Conclusions

Transoral robotic TL is emerging as an option in management of patients with recurrent or persistent laryngeal cancers after failed organ preservation therapy, low grade primary malignancies that do not require neck dissections and dysfunctional laryngeal pathologies. There is emerging evidence to support the feasibility of a TORS TL approach but more data and research is required. When compared to open TL technique the post-operative complication rate is equivalent. This systematic review demonstrated only a small number of patients treated with this approach probably due to a reflection of the expertise required in centres to perform TORS TL and the difficulties involved in selecting suitable patients for this approach.

Acknowledgments

This manuscript has been presented as a poster at the ASOHNS ASM 2024 conference.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://www.theajo.com/article/view/10.21037/10.21037/ajo-24-19/rc

Peer Review File: Available at https://www.theajo.com/article/view/10.21037/ajo-24-19/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://www.theajo.com/article/view/10.21037/ajo-24-19/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethics approval was not required due to the study being a systematic review of previously published data.

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doi: 10.21037/ajo-24-19

Cite this article as: Goel S, Gunasekera D, Ooi EH. Transoral robotic surgery for patients undergoing total laryngectomy: systematic review of current evidence. Aust J Otolaryngol 2024;7:34.

Supplementary

Appendix 1 PubMed Search strategy

Table S1 The PubMed search strategy conducted on the 8th October 2023

Search number	Query	Filters	Search Details	Results	Time
1	#1 AND #2		((("transoral"[All Fields] OR "transorally"[All Fields]) AND ("robotic surgical procedures"[MeSH Terms] OR ("robotic"[All Fields] AND "surgical"[All Fields] AND "procedures"[All Fields]) OR "robotic surgical procedures"[All Fields] OR ("robotic"[All Fields] AND "surgery"[All Fields]) OR "robotic surgery"[All Fields])) OR "TORS"[All Fields] OR "robotic surgical procedures"[MeSH Terms]) AND ("Laryngectomy"[MeSH Terms] OR (("total"[All Fields] OR "totaled"[All Fields] OR "totaling"[All Fields] OR "totalled"[All Fields] OR "totalling"[All Fields] OR "totals"[All Fields]) AND ("Laryngectomy"[MeSH Terms] OR "Laryngectomy"[All Fields] OR "laryngectomies"[All Fields]))))	100	22:12:17
2	"Laryngectomy"[Mesh] OR total laryngectomy		"Laryngectomy"[MeSH Terms] OR (("total"[All Fields] OR "totaled"[All Fields] OR "totaling"[All Fields] OR "totalled"[All Fields] OR "totalling"[All Fields] OR "totals"[All Fields]) AND ("Laryngectomy"[MeSH Terms] OR "Laryngectomy"[All Fields] OR "laryngectomies"[All Fields]))	11,561	22:09:22
3	(("transoral"[All Fields] OR "transorally"[All Fields]) AND ("robotic surgical procedures"[MeSH Terms] OR ("robotic"[All Fields] AND "surgical"[All Fields] AND "procedures"[All Fields]) OR "robotic surgical procedures"[All Fields] OR ("robotic"[All Fields] AND "surgery"[All Fields]) OR "robotic surgery"[All Fields])) OR "TORS"[All Fields] OR "robotic surgical procedures"[MeSH Terms]		(("transoral"[All Fields] OR "transorally"[All Fields]) AND ("robotic surgical procedures"[MeSH Terms] OR ("robotic"[All Fields] AND "surgical"[All Fields] AND "procedures"[All Fields]) OR "robotic surgical procedures"[All Fields] OR ("robotic"[All Fields] AND "surgery"[All Fields]) OR "robotic surgery"[All Fields])) OR "TORS"[All Fields] OR "robotic surgical procedures"[MeSH Terms]	17,487	20:58:46

https://dx.doi.org/10.21037/ajo-24-19

Appendix 2 Critical appraisal results

Table S2 Critical appraisal of eligible analytical cross sectional study

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Hassid S, Delcour L, Ambroise J, *et al.* 2020	Y	N	Y	Y	N	N	U	N/A
Cumulative percentage (%)	100.0	0.0	100.0	100.0	0.0	0.0	0.0	0.0

Y, yes; N, No; U, unclear; N/A, not applicable.

Table S3 Critical appraisal of eligible case series

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Dowthwaite S, Nichols AC, Yoo J, *et al.* 2013.	Y	Y	Y	Y	Y	Y	Y	U	Y	N/A
Hans S, Chebib E, Chekkoury-Idrissi Y, *et al.* 2021.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Krishnan G, Krishnan S. 2017.	Y	Y	Y	Y	Y	Y	Y	N	Y	U
Smith RV, Schiff BA, Sarta C, *et al.* 2013.	Y	Y	Y	Y	Y	Y	Y	N	Y	U
Wang CC, Lin WJ, De Virgilio A, *et al.* 2020.	Y	Y	Y	Y	Y	Y	Y	Y	Y	U
Cumulative percentage (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	40.0	100.0	20.0

Y, yes; N, No; U, unclear; N/A, not applicable.

https://dx.doi.org/10.21037/ajo-24-19