Irish Journal of Medical Science (1971 -) (2019) 188:397–403
https://doi.org/10.1007/s11845-018-1842-x

ORIGINAL ARTICLE

Outcomes of transoral laser microsurgery for oropharyngeal squamous cell carcinoma in Ireland and review of the literature on transoral approaches

Robbie S. R. Woods[1] · Lina Geyer[1] · Ana Ionescu[1] · Deirdre Callanan[1] · Patrick Sheahan[1,2]

Received: 22 March 2018 / Accepted: 1 June 2018 / Published online: 21 June 2018

Abstract

Background The optimal treatment for oropharyngeal squamous cell carcinoma (OPSCC) is controversial. There is increasing evidence that, in selected cases, minimally invasive transoral surgery can offer improved functional outcomes, with equivalent oncologic outcomes, compared to chemoradiotherapy.

Aims We report the outcomes of transoral laser microsurgery (TLM) for treatment of OPSCC at our institution.

Methods Patients with OPSCC undergoing TLM at the South Infirmary Victoria University Hospital, Cork, between 2010 and 2016, were identified from an institutional database. Human papillomavirus (HPV) status was determined by p16 immunohistochemistry. Survival outcomes were analysed using the Kaplan-Meier method. Complications following surgery and gastrostomy tube dependence were evaluated.

Results The study cohort consisted of 26 patients, with mean age of 56 years (range 29–71). Primary tumours were located in the tonsil (18), base of tongue (4) and other subsites (4). Seventeen cases were p16-positive. Complications included haemorrhage necessitating return to theatre (1) and aspiration pneumonia (1). Four patients underwent tracheostomy, all of whom were successfully decannulated. One patient underwent gastrostomy tube insertion during postoperative radiotherapy. No patient was gastrostomy dependent at latest follow-up. Twenty-two patients received adjuvant treatment, with radiation alone (21) or chemoradiotherapy (2). Mean follow-up was 27 months. Five-year locoregional control was 92% and disease-specific survival was 81%.

Conclusions In selected patients with OPSCC, TLM offers excellent functional and survival outcomes, and as such offers an alternative approach to chemoradiotherapy as primary treatment. We compare TLM to other transoral approaches and discuss its potential use in the Irish healthcare system.

Keywords Human papillomavirus · Oropharyngeal · Squamous cell carcinoma · Transoral laser microsurgery

Introduction

Treatment paradigms for oropharyngeal squamous cell carcinoma (SCC) continue to evolve, particularly with the emergence of tumours related to human papillomavirus (HPV) over the past 20 years. For early-stage oropharyngeal SCC, definitive radiation and primary surgery have yielded similar rates of local control and survival in retrospective studies, although there are no prospective randomised trials comparing the two approaches. Regarding advanced stage disease, gold standard treatment has mostly involved primary concurrent chemoradiation due to the high morbidity associated with open surgical approaches since the VA and RTOG 91-11 trials.

The emergence of minimally invasive approaches to the oropharynx has enabled reconsideration of surgical resection of oropharyngeal tumours as our understanding of the cancer biology improves. Although there is no doubt that previous major open surgical approaches carried significant risks of posttreatment morbidity and mortality, it is now apparent that use of chemotherapy in conjunction with radiation to the head and neck is also associated with high rates of acute and late

✉ Robbie S. R. Woods
robbiewoods@rcsi.ie

[1] Department of Otolaryngology - Head and Neck Surgery, South Infirmary Victoria University Hospital, Cork, Ireland

[2] Department of Otolaryngology - Head and Neck Surgery, University College Cork, Cork, Ireland

toxicity in the majority of patients, particularly with respect to deglutition, over and above those seen with radiation alone. Additionally, most of the studies included in analysis of organ-sparing treatments took place prior to the demographic and biological shifts in oropharyngeal cancer associated with the current predominance of HPV-related oropharyngeal cancer, and it is not clear if these data apply to HPV disease. In some trials, less than 10% of cases comprised oropharyngeal tumours [1]. Also, where HPV cases were present, these may have skewed the results, and in fact, results for non-HPV cases may be even worse.

There is now definite proof of a distinct subgroup of oropharyngeal SCC characterised by HPV-related tumours that behave differently biologically and demonstrate improved prognosis. These tend to occur in younger, healthier patients that are expected to live longer, and so, there is concern related to the morbidity of chemoradiation. It is possible that the new staging system for p16-positive oropharyngeal tumours, due to begin in January 2018, will allow easier decision making when considering de-intensification of treatment in HPV-related cases. Transoral resections can assist in decision making regarding the need for and dose of adjuvant treatment by altering clinical staging in up to 40% of cases [2], while primary treatment with transoral resection is now an established de-intensification approach.

The drivers for transoral approaches have been the development of technology and adaptation from other fields of surgery as well as concern over the morbidity related to chemoradiation in a growing group of younger, healthier patients. These technologies allows for adequate visualisation and exposure of oropharyngeal tumours while removing the morbidity related to open surgical approaches.

Good performance status and mouth opening are usually required, with up to 6.7% of cases unsuitable due to inadequate exposure [3]. Tumour characteristics which will commonly dissuade from primary surgical intervention include tongue base invasion requiring greater than 50% resection, pterygoid muscle involvement, extension into the parapharyngeal fat abutting the carotid, mandible/maxilla extension or invasion, and prevertebral space involvement [4]. Deep neck invasion and involvement of major blood vessels are particularly important to establish prior to considering transoral approaches, although newer combined transoral-pharyngotomy approaches have been described with good early outcomes [5].

Transoral laser microsurgery (TLM) has been in use for many years with excellent oncologic results and improved functional outcomes [6, 7]. Approaches to the oropharynx, however, have been problematic because of the inability to access tumours while sticking to Halstedian principles of en bloc resection with a margin [8]. Nonetheless, the need for en bloc resection has been challenged and it is now widely accepted that the necessity of avoiding tumour violation is not valid in oropharyngeal cases [9]. Therefore, laser can be used to transect a tumour at its most proximal portion to estimate depth of invasion followed by complete resection of the primary tumour in multiple blocks to achieve a free margin. For large tumours, transection and coring out can be done to reduce size prior to resection of the remaining shell using a series of transtumoural cuts [8]. When piecemeal resections are performed, CO_2 laser works best because it causes minimal tissue fulguration allowing easy identification of tumour-host interface as it is nearly fully absorbed by water.

TLM options have widened to include flexible systems with improved access. This includes the Lumenis flexible laser system that allows the surgeon access by malleable handpieces which make it possible to incise tissue at angles in areas otherwise difficult to reach. As with robotic systems, the laser beam is customisable between cutting, haemostatic and ablative effects.

Methods

The Lumenis laser system was purchased with funding from the Head and Neck Cancer Fund at the South Infirmary Victoria University Hospital in 2010. It is the first equipment purchased in Ireland for dedicated use in oropharyngeal resection. This study is a retrospective review of all patients with oropharyngeal carcinoma undergoing TLM at the South Infirmary Victoria University Hospital in Cork. Tumour resections were performed under microscopic control and using the Feyh-Kastenbauer Weinstein O'Malley transoral robotic surgery (TORS) laryngopharyngoscope (Olympus Medical Systems, Hanoi, Vietnam) to facilitate transoral tumour exposure. Resection was undertaken using an AcuPulse 40WG CO_2 laser (Lumenis, Elstree, UK), with the laser beam directed using FiberLase flexible CO_2 laser fibre (Lumenis). Continuous super-pulse was the laser setting of choice and power settings varied depending on the individual case.

Patients were identified within a prospective database monitoring outcomes of head and neck cancer. HPV status was determined by p16 immunohistochemistry. Data was gathered on gender, age, stage, subsite, other surgery, adjuvant treatment complications, gastrostomy dependence, follow-up, recurrence, and survival. Kaplan-Meier survival analysis was used to evaluate locoregional control and disease-specific survival. For each patient, the disease-specific survival was measured in days from the date of diagnosis to censoring (either the date of the latest follow-up or the date ofdeath by other cause) or death from disease, whichever occurred first. Locoregional control was measured in the same way, but considering date of diagnosis of recurrence instead of death from disease. Statistical analysis was performed using IBM SPSS Statistics version 23.0.0.2 software (IBM Corp., NY, USA).

This study was undertaken in accordance with previously granted ethical approval from the Cork Clinical Research Ethics Committee regarding the head and neck cancer database. All patient data were kept anonymous and encrypted throughout.

Results

Between 2010 and 2016, 26 patients underwent TLM. Clinicopathological data is shown in Table 1. The mean age was 56 years old (range 29–71 years) and 18 patients were male. Regarding oropharyngeal subsite, 18 were tonsillar, 4 were from the tongue base, and there were 2 cases each from the soft palate or posterior oropharyngeal wall.

Table 1 Clinicopathological data of patients undergoing TLM

Characteristic ($N = 25$ unless stated)	Number
Subsite	
Tonsil	18 (69%)
Base of tongue	4 (15%)
Soft palate	2 (8%)
Posterior oropharyngeal wall	2 (8%)
HPV status ($N = 23$)	
p16 positive	17 (71%)
p16 negative	7 (29%)
T stage	
T1	17 (65%)
T2	7 (27%)
T3	2 (8%)
T4	0
N stage	
N0	3 (13%)
N1	5 (21%)
N2a	0
N2b	12 (50%)
N2c	1 (4%)
N3	3 (13%)
Neck dissection	
Yes	24 (92%)
No	2 (8%)
Adjuvant treatment	
None	3 (12%)
Radiation alone	21 (81%)
Chemoradiation	2 (8%)
Complications	
Haemorrhage	1
Aspiration pneumonia	1
Tracheostomy	4
Gastrostomy	0

Immunohistochemistry for p16 was positive in 17 cases. Tumour stage was T1–2 in 24 cases.

In cases where neck dissection was performed, only 13% had negative regional disease. There was one haemorrhage necessitating return to theatre, one lower respiratory tract infection related to aspiration and four tracheostomies, three of which were simultaneous with the primary surgery. No patient was gastrostomy dependent at latest follow-up. Adjuvant treatment was carried out in 23/26 patients (21 with radiation alone and two with chemoradiation).

Mean follow-up was 40 months (range 4–95 months). By Kaplan-Meier estimation, 5-year locoregional control was 92.3% while disease-specific survival was 80.8%. Kaplan-Meier survival curves are shown in Figs. 1 and 2. Regarding recurrence, one patient presented with regional and distant recurrence, one patient presented with local recurrence while three patients suffered distant metastatic disease. One patient died from synchronous lung cancer.

Discussion

Primary chemoradiation treatment often necessitates protracted or permanent non-oral feeding, with high rates of gastrostomy tube dependency reported. However, while it has been suggested that transoral approaches may lead to improved functional outcomes with equivalent or better oncologic outcomes, many of these results are not based on treatment with the more advanced intensity modulated (IMRT) or proton beam radiation techniques, which may show considerably improved functional outcomes compared to traditional external beam radiation [10]. Nonetheless, we have shown that the transoral approach can afford low gastrostomy rates potentially leading to improved quality of life.

Our results are comparable to similar studies in the literature. A large single-centre study in 2016 comprising results on 153 patients demonstrated haemorrhage rates of 2.6%, 3-year locoregional control and disease-specific survival of 89.6 and 91.7%, respectively. In that study, 1-year gastrostomy tube dependency was 1.3%, while in our study, the rate was 0%. This compares unfavourably with data in those treated with primary chemoradiation, where 1-year gastrostomy tube rates are reported at 35% at our institution, similar to rates in other studies [11–13]. With increasing use of IMRT, rates have dropped, but still reach 5% in patients with stage I and II disease [10].

There is currently no high-quality evidence from randomised controlled trials regarding clinical outcomes for patients with oropharyngeal cancer receiving transoral surgery compared with primary chemoradiation. Trials, such as ORATOR, EORTC 1420 and RTOG 1221, are underway to further clarify oncologic and quality of life outcomes of transoral surgery compared to conventional non-surgical

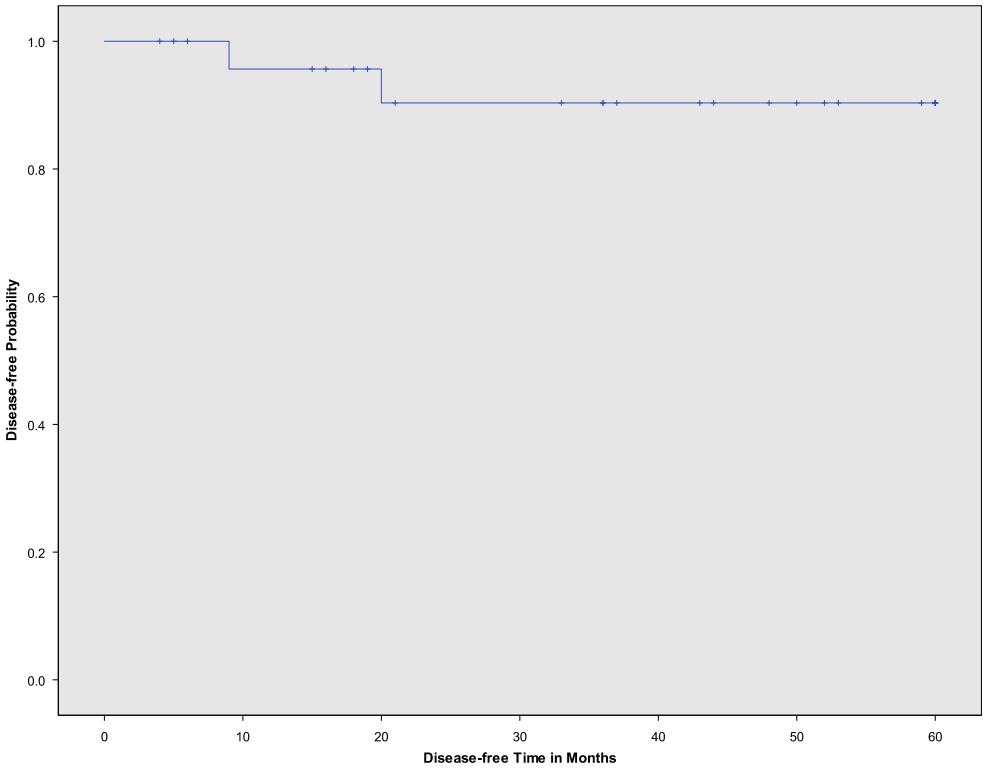

Fig. 1 Kaplan-Meier survival curve for locoregional control

treatments [14, 15]. There is ongoing debate as to the optimal treatment approach for oropharyngeal tumours, but preliminary evidence does suggest that TLM or TORS can offer improved outcomes with reduced morbidity compared to open surgery or chemoradiation, and may even better establish patients suitable for de-escalation, such as in the ADEPT trial. Lacking high-quality evidence to support oncologic superiority of surgery over non-surgical approaches, the decision to

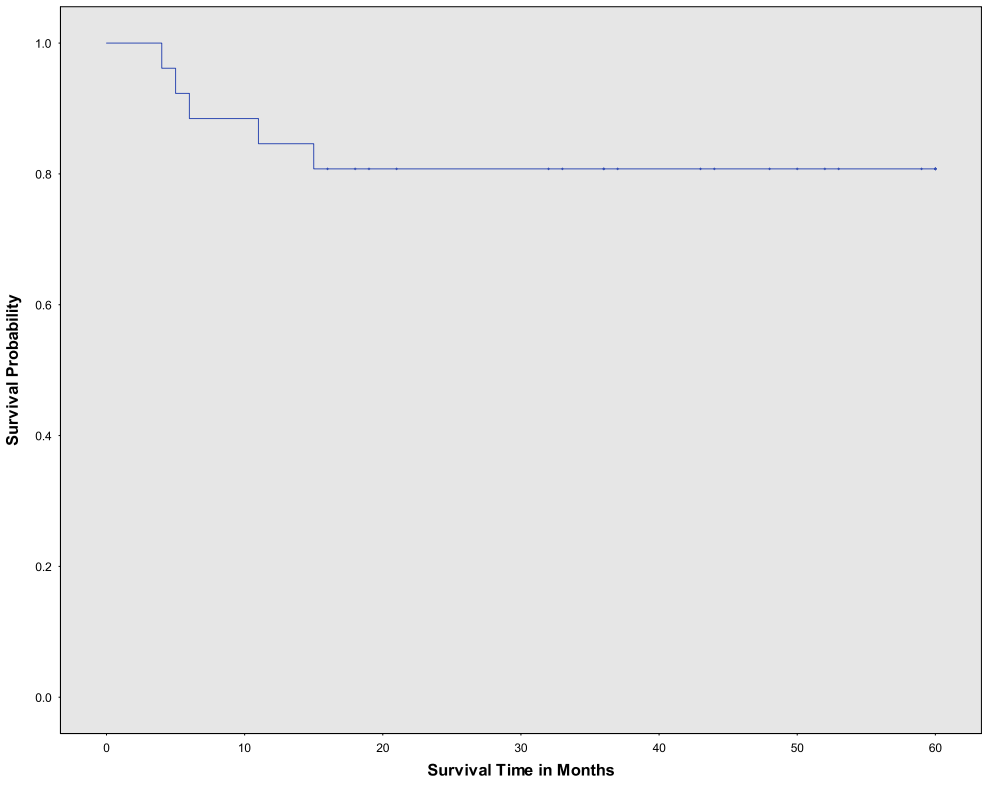

Fig. 2 Kaplan-Meier survival curve for disease-specific survival

use transoral surgery is driven primarily by the need for adequate surgical exposure as well as functional and quality of life considerations, while allowing the patient avoid the morbidity of potentially unnecessary adjuvant therapy [4].

Comparing approaches

Transoral robotic surgery (TORS) has been in use since 2005 [16], and over 1300 reported oropharyngeal cancer resections have been carried out worldwide since its introduction [17]. The most popular system in use for head and neck operations is based on that used in other fields such as urology and gynaecologic oncology, the da Vinci Si HD (Intuitive Surgical, Sunnyvale, CA).

The newer Flex Robotic System (Medrobotics Corp., Raynham, MA) was specifically developed for head and neck surgery and combines the advantages of a flexible endoscope with a robotic system, which supports flexible instruments and cutting devices for transoral surgery [18].

Oncologic outcomes have largely been equivalent between TLM and TORS in the limited data available. Haughey (2011) showed that the 3-year overall survival, disease-specific survival and disease-free survival were 86, 88 and 82%, respectively, with local control rates of 97%, in a series of oropharyngeal cases with a high prevalence of HPV treated with TLM. Seventy-four percent of patients received adjuvant treatment. Importantly, 87% of patients had normal swallowing or episodic dysphagia [19]. Other research has shown oncological and functional results are comparable to any other non-surgical treatment regimen, while the morbidity and complications tend to be lower [20].

Outcomes in TORS are largely similar, such as 89.6% of patients being disease free and an overall survival of 93.8% at mean follow-up of 29 months [21]. A review of the literature in 2012 revealed 2-year overall survival outcomes of 80–90% [22]. Both TLM and TORS can also be successfully used in advanced stage disease and in some cases between 38 and 84% of patients can avoid chemotherapy [4].

Results from both TLM and TORS mostly show improved swallowing, lower gastrostomy rates and higher quality of life measures compared to benchmarks in patients treated with radiation or chemoradiation [23–25]. Although there may be subtle postoperative differences, TORS and TLM are likely to offer similar swallowing outcomes when the impact of just surgery alone is assessed [26]. Outcomes for the new Flex Robotic System are not available as yet; however, it has been established as safe and effective [18, 27].

It is important to note that oncologic outcomes may reflect inherent selection biases when comparing transoral approaches with non-surgical treatment in uncontrolled trials [28]. It must also be recognised that some studies on chemoradiation have reported far less swallowing impairment following particular protocols than were seen in some studies comparing non-surgical with transoral approaches [26].

Training

There is no doubt that all transoral approaches to the oropharynx require specific training, patience and hard-earned experience [29]. Expectedly, higher volume TORS centres have lower positive margin rates and fewer unplanned readmissions [30]. There is inevitably a steep learning curve in whichever transoral approach is used [31]. Nonetheless, it has been suggested that there is an improved ability for trainees to be taught and adopt the technique of TORS when compared with TLM [26]. However, the lack of tactile feedback has also been considered a drawback in relation to TORS in favour of TLM or the Flex Robotic System [32].

Surgical access

There are some distinct differences between transoral approaches. While it has been argued that the visibility of operative microscopy as used for TLM is unparalleled [33], TORS provides benefits over TLM by allowing the surgeon to use two hands to manipulate and resect the tumour with movements in seven degrees of freedom (a range of planes which would be impossible with the human wrist), with the elimination of tremor and potential for enhanced endoscopic images with higher resolution [14]. While retractors that are used for TORS are also now used in TLM, TORS may provide superior visualisation of the tongue base by using angled endoscopes.

Equipment

TLM equipment is mostly well established and, relative to robotic surgery, simpler to maintain. TORS equipment has to a large extent been designed with a view to open cavity surgery. Due to the expense of the equipment, it makes sense to consider multi-purpose use in lower volume centres. The safety profile of robotic instrumentation has been compared to traditional transoral tools with few additional risks identified with the robot [34]. However, there has been traditionally a fundamental design mismatch of the equipment for transoral surgery compared to open cavity surgery, with rigid and relatively bulky robotic arms and a limited number of cutting devices available [18, 33]. The same cannot be said for the new Flex Robotic System, which has been designed specifically for head and neck oncologic surgery [18, 27, 35, 36]. It combines the advantages of a flexible endoscope with a rigid robotic system when at the target area, which supports flexible instruments and cutting devices for transoral surgery. With development in TLM, the Lumenis system can allow bimanual operation in the oropharynx, although TLM still suffers from limitation to line of site access.

Cost

High costs are a significant concern and potential disadvantage of TORS in comparison to other transoral approaches. The expense is almost prohibitive for public healthcare systems, as estimates of buying and installing one robotic system fall between $1–2.5 million with annual maintenance fees of approximately $100,000 added to the individual costs of disposable equipment [17, 37], hence multi-purpose use across a range of departments makes the prospect more viable. The added number of instruments may also increase set-up and operative time adding to the cost burden in comparison with TLM or the Flex Robotic system, which is estimated to cost about $980,000 [38]. The business case for purchasing a robotic system from a head and neck point of view would include a reduction in length of hospital stay and lower rates of tracheostomy and gastrostomy [39]; however, these points would also be valid for TLM and the Flex Robotic System.

Conclusion

The question therefore arises as to which transoral approach to offer patients. There are currently no trials comparing transoral approaches directly, but a protocol for a systematic review was submitted in August 2016 [40]. When considering the evidence to date, despite significant design heterogeneity, it is clear that all approaches can provide similar oncologic outcomes with improved functional outcomes. Clinical trials that include transoral surgery, for example, ECOG 3311, leave the decision to use TORS or TLM to the surgeon, and do not specify criteria for patient selection [41].

There are some clear advantages to TORS compared to TLM, particularly with respect to surgical access and equipment. However, in a publically funded healthcare system, it is not clear that the additional cost of TORS over TLM is justified. The theory behind the FDA-approved Flex Robotic System is extremely promising as it removes some of the perceived disadvantages to TORS and is likely to be significantly cheaper; however, there is insufficient published outcome data to realistically consider it in comparison to TORS or TLM at present.

From 2003 to 2012, there were 789 cases of oropharyngeal tumours in Ireland according to national cancer registry data; however, there were also 687 cases of "other tongue" or "other mouth/pharynx" so the exact incidence is difficult to ascertain. The incidence of oropharyngeal tumours in Ireland is rising in association with increasing HPV-related disease [42]. With the potential for increasing use of transoral approaches in more advanced oropharyngeal disease as well as early stage disease, at least one or two centres offering transoral approaches to the oropharynx in Ireland is warranted. It may be reasonable to consider the use of TORS over TLM if it were to be in an institution where the cost could be spread across multiple departments using the technology.

Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Pignon JP, Maitre A, Bourhis J et al (2007) Meta-Analyses of Chemotherapy in Head and Neck Cancer (MACH-NC): an update. Int J Radiat Oncol Biol Phys 69:S112–S114. https://doi.org/10.1016/j.ijrobp.2007.04.088
2. Walvekar RR, Li RJ, Gooding WE, Gibson MK, Heron D, Johnson JT, Ferris RL (2008) Role of surgery in limited (T1-2, N0-1) cancers of the oropharynx. Laryngoscope 118:2129–2134. https://doi.org/10.1097/MLG.0b013e3181857950
3. Weinstein GS, O'Malley BW Jr, Magnuson JS, Carroll WR, Olsen KD, Daio L, Moore EJ, Holsinger FC (2012) Transoral robotic surgery: a multicenter study to assess feasibility, safety, and surgical margins. Laryngoscope 122:1701–1707. https://doi.org/10.1002/lary.23294
4. Fundakowski CE, Lango M (2016) Considerations in surgical versus non-surgical management of HPV positive oropharyngeal cancer. Cancers Head Neck 1:6. https://doi.org/10.1186/s41199-016-0007-8
5. Sinha P, Pipkorn P, Zenga J, Haughey BH (2017) The hybrid transoral-pharyngotomy approach to oropharyngeal carcinoma: technique and outcome. Ann Otol, Rhinol Laryngol 126:357–364. https://doi.org/10.1177/0003489417691297
6. Ambrosch P, Kron M, Steiner W (1998) Carbon dioxide laser microsurgery for early supraglottic carcinoma. Ann Otol, Rhinol, Laryngol 107:680–688. https://doi.org/10.1177/000348949810700810
7. Steiner W, Ambrosch P, Hess CF et al (2001) Organ preservation by transoral laser microsurgery in piriform sinus carcinoma. Otolaryngol Head Neck Surg : Off J Am Acad Otolaryngol Head Neck Surg 124:58–67. https://doi.org/10.1067/mhn.2001.111597
8. Steiner W, Fierek O, Ambrosch P, Hommerich CP, Kron M (2003) Transoral laser microsurgery for squamous cell carcinoma of the base of the tongue. Arch Otolaryngol Head Neck Surg 129:36–43
9. Robbins KT, Bradford CR, Rodrigo JP, Suárez C, de Bree R, Kowalski LP, Rinaldo A, Silver CE, Lund VJ, Nibu KI, Ferlito A (2016) Removing the taboo on the surgical violation (cut-through) of cancer. JAMA Otolaryngol Head Neck Surg 142:1010–1013. https://doi.org/10.1001/jamaoto.2016.1826
10. Setton J, Lee NY, Riaz N, Huang SH, Waldron J, O'Sullivan B, Zhang Z, Shi W, Rosenthal DI, Hutcheson KA, Garden AS (2015) A multi-institution pooled analysis of gastrostomy tube dependence in patients with oropharyngeal cancer treated with definitive intensity-modulated radiotherapy. Cancer 121:294–301. https://doi.org/10.1002/cncr.29022
11. O'Shea R, Byrne H, Tuckett J et al (2015) Impact of current smoking and alcohol consumption on gastrostomy duration in patients with head and neck cancer undergoing definitive

chemoradiotherapy. JAMA Otolaryngol Head Neck Surg 141:463–469. https://doi.org/10.1001/jamaoto.2015.0279
12. Shiley SG, Hargunani CA, Skoner JM et al (2006) Swallowing function after chemoradiation for advanced stage oropharyngeal cancer. Otolaryngol Head Neck Surg: Off J Am Acad Otolaryngol Head Neck Surg 134:455–459. https://doi.org/10.1016/j.otohns.2005.10.054
13. Paleri V, Patterson J (2010) Use of gastrostomy in head and neck cancer: a systematic review to identify areas for future research. Clin Otolaryngol : Off J ENT-UK; Off J Netherlands Soc Otorhinolaryngol Cervico Fac Surg 35:177–189. https://doi.org/10.1111/j.1749-4486.2010.02128.x
14. Hamilton D, Khan MK, O'Hara J et al (2017) The changing landscape of oropharyngeal cancer management. J Laryngol Otol 131:3–7. https://doi.org/10.1017/S0022215116009178
15. Howard J, Masterson L, Dwivedi RC, Riffat F, Benson R, Jefferies S, Jani P, Tysome JR, Nutting C, Cochrane ENT Group (2016) Minimally invasive surgery versus radiotherapy/chemoradiotherapy for small-volume primary oropharyngeal carcinoma. Cochrane Database Syst Rev 12:CD010963. https://doi.org/10.1002/14651858.CD010963.pub2
16. McLeod IK, Melder PC (2005) Da Vinci robot-assisted excision of a vallecular cyst: a case report. Ear, Nose, Throat J 84:170–172
17. Karateew ED Atlas of head and neck robotic Surgery 1st edition. EDN,
18. Lang S, Mattheis S, Hasskamp P, Lawson G, Güldner C, Mandapathil M, Schuler P, Hoffmann T, Scheithauer M, Remacle M (2017) A European multicenter study evaluating the flex robotic system in transoral robotic surgery. Laryngoscope 127:391–395. https://doi.org/10.1002/lary.26358
19. Haughey BH, Hinni ML, Salassa JR, Hayden RE, Grant DG, Rich JT, Milov S, Lewis JS Jr, Krishna M (2011) Transoral laser microsurgery as primary treatment for advanced-stage oropharyngeal cancer: a United States multicenter study. Head Neck 33:1683–1694. https://doi.org/10.1002/hed.21669
20. Canis M, Martin A, Kron M, Konstantinou A, Ihler F, Wolff HA, Matthias C, Steiner W (2013) Results of transoral laser microsurgery in 102 patients with squamous cell carcinoma of the tonsil. Eur Arch Otorhinolaryngol 270:2299–2306. https://doi.org/10.1007/s00405-012-2335-6
21. Dabas S, Gupta K, Ranjan R, Sharma AK, Shukla H, Dinesh A (2017) Oncological outcome following de-intensification of treatment for stage I and II HPV negative oropharyngeal cancers with transoral robotic surgery (TORS): a prospective trial. Oral Oncol 69:80–83. https://doi.org/10.1016/j.oraloncology.2017.04.010
22. Dowthwaite SA, Franklin JH, Palma DA, Fung K, Yoo J, Nichols AC (2012) The role of transoral robotic surgery in the management of oropharyngeal cancer: a review of the literature. ISRN Oncol 945162:2012–2014. https://doi.org/10.5402/2012/945162
23. Hutcheson KA, Holsinger FC, Kupferman ME, Lewin JS (2015) Functional outcomes after TORS for oropharyngeal cancer: a systematic review. Eur Arch Otorhinolaryngol 272:463–471. https://doi.org/10.1007/s00405-014-2985-7
24. O'Hara J, Cosway B, Muirhead C, Leonard N, Goff D, Patterson J (2015) Transoral laser microsurgery +/− adjuvant therapy versus chemoradiotherapy for stage III and IVA oropharyngeal squamous cell carcinoma: preliminary comparison of early swallowing outcomes. Head Neck 37:1488–1494. https://doi.org/10.1002/hed.23790
25. Genden EM, Kotz T, Tong CC et al (2011) Transoral robotic resection and reconstruction for head and neck cancer. Laryngoscope 121:1668–1674. https://doi.org/10.1002/lary.21845
26. Dawe N, O'Hara J (2017) Swallowing after transoral surgery for oropharyngeal cancer: comparison with primary chemoradiotherapy outcomes. Curr Opin Otolaryngol Head Neck Surg 25:101–107. https://doi.org/10.1097/MOO.0000000000000340
27. Mattheis S, Hasskamp P, Holtmann L, Schäfer C, Geisthoff U, Dominas N, Lang S (2017) Flex robotic system in transoral robotic surgery: the first 40 patients. Head Neck 39:471–475. https://doi.org/10.1002/hed.24611
28. Kao SS, Micklem J, Ofo E, Edwards S, Dhatrak D, Foreman A, Krishnan S, Hodge JC (2017) A comparison of oncological outcomes between transoral surgical and non-surgical treatment protocols in the management of oropharyngeal squamous cell carcinoma. J Laryngol Otol 132:1–7. https://doi.org/10.1017/S0022215117000986
29. Moore EJ, Hinni ML (2013) Critical review: transoral laser microsurgery and robotic-assisted surgery for oropharynx cancer including human papillomavirus-related cancer. Int J Radiat Oncol Biol Phys 85:1163–1167. https://doi.org/10.1016/j.ijrobp.2012.08.033
30. Chen MM, Roman SA, Kraus DH, Sosa JA, Judson BL (2014) Transoral robotic surgery: a population-level analysis. Otolaryngol Head Neck Surg: Off J Am Acad Otolaryngol Head Neck Surg 150:968–975. https://doi.org/10.1177/0194599814525747
31. White HN, Frederick J, Zimmerman T et al (2013) Learning curve for transoral robotic surgery: a 4-year analysis. JAMA Otolaryngol Head Neck Surg 139:564–567. https://doi.org/10.1001/jamaoto.2013.3007
32. Oliveira CM, Nguyen HT, Ferraz AR, Watters K, Rosman B, Rahbar R (2012) Robotic surgery in otolaryngology and head and neck surgery: a review. Minim Invasive Surg 2012:286563. https://doi.org/10.1155/2012/286563
33. Hinni ML, Lott DG (2015) Contemporary Transoral surgery for primary head and neck Cancer. Plural Publishing,
34. Hockstein NG, O'Malley BW, Jr., Weinstein GS (2006) Assessment of intraoperative safety in transoral robotic surgery. Laryngoscope 116:165–168. doi:https://doi.org/10.1097/01.mlg.0000199899.00479.75
35. Funk E, Goldenberg D, Goyal N (2017) Demonstration of transoral robotic supraglottic laryngectomy and total laryngectomy in cadaveric specimens using the Medrobotics Flex System. Head Neck 39:1218–1225. https://doi.org/10.1002/hed.24746
36. Newsome H, Mandapathil M, Koh YW, Duvvuri U (2016) Utility of the highly articulated flex robotic system for head and neck procedures: a cadaveric study. Ann Otol, Rhinol, Laryngol 125:758–763. https://doi.org/10.1177/0003489416653409
37. Shah S, Goldenberg D (2014) Robotic surgery for oropharyngeal cancer. Rambam Maimonides Med J 5:e0014. https://doi.org/10.5041/RMMJ.10148
38. Belfiore M (2016) The robot surgeon of your nightmares can wiggle its way inside you. Bloomberg Businessweek. https://www.bloomberg.com/news/articles/2016-08-25/the-robot-surgeon-of-your-nightmares-can-wiggle-its-way-inside-you
39. Richmon JD, Quon H, Gourin CG (2014) The effect of transoral robotic surgery on short-term outcomes and cost of care after oropharyngeal cancer surgery. Laryngoscope 124:165–171. https://doi.org/10.1002/lary.24358
40. Krishnan SG, Umapathysivam K, Lockwood C et al (2016) Oncological and survival outcomes following transoral robotic surgery versus transoral laser microsurgery for the treatment of oropharyngeal squamous cell carcinoma: a systematic review protocol. JBI Database Systematic Rev Implement Rep 14:90–102. https://doi.org/10.11124/JBISRIR-2016-003061
41. Holsinger FC, Ferris RL (2015) Transoral endoscopic head and neck surgery and its role within the multidisciplinary treatment paradigm of oropharynx cancer: robotics, lasers, and clinical trials. J Clin Oncol : Off J Am Soc Clin Oncol 33:3285–3292. https://doi.org/10.1200/JCO.2015.62.3157
42. Woods RS, Keegan H, White C et al. (2017) Cytokeratin 7 in oropharyngeal squamous cell carcinoma: a junctional biomarker for human papillomavirus-related tumours. Cancer Epidemiol Biomarkers Prev: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. https://doi.org/10.1158/1055-9965.EPI-16-0619