Transoral robotic surgery for recurrent cancers of the upper aerodigestive tract- systematic review and meta-analysis

Authors

John Hardman MRCS MSc[1]

Zi Wei Liu FRCS[1]

Grainne Brady MRCSLT MRes[2]

Justin Roe FRCSLT PhD[2, 3]

Cyrus Kerawala FDSRCS FRCS[1]

Francesco Riva MD[1]

Peter Clarke FRCS[1]

Shreerang Bhide FRCR PhD[4]

Dae Kim BDS FRCS PhD[1]

Christopher Nutting FRCP FRCR MD PhD[4]

Kevin Harrington FRCP FRCR PhD[4]

Vinidh Paleri FRCS MS[1]

[1]Department of H&N Surgery, The Royal Marsden Hospital, London, UK
[2]Department of Speech and Language Therapy, The Royal Marsden Hospital, London, UK
[3] Department of Surgery and Cancer, Imperial College London, London, UK
[4] Department of H&N Oncology, The Royal Marsden Hospital, London, UK

Acknowledgements

We are grateful for help with designing conducting the searches from YiWen Hon, Knowledge Resources Manager at the David Adams Library, Royal Marsden NHS Foundation Trust.

Presentations

This work has not yet been presented at any meetings at time of submission.

Conflict of interest statement

The authors declare that there are no conflicts of interest to report.

Funding

No specific funding for this review was obtained.

Correspondence

Vinidh Paleri
Telephone: +44 7899 997 141
Postal address: Department of H&N Surgery, The Royal Marsden Hospital, London SW3 6JJ, UK
Email address: vinidh.paleri@rmh.nhs.uk

Running title

TORS for recurrence (RECUT) systematic review

Key words

Recurrence, cancer, robotics, surgery, H&N

Abstract

148/150 words max

Background

Transoral robotic surgery (TORS) for recurrent head and neck (H&N) cancer is an emerging but relatively infrequent procedure.

Methods

Systematic review and meta-analysis of studies reporting survival data and functional outcomes for patients undergoing TORS for previously treated H&N cancers.

Results

878 records were identified, of which eight were eligible for inclusion, covering 161 cases (range 1-64). The pooled rates were as follows: 2-year overall survival 73.8% (4 studies, range 70.6 to 75.0, 95% confidence intervals (CI) 65.4 to 81.5, [I^2 0.0%, p=1.0]); 2-year disease-free survival 74.8% (4 studies, range 56.2 to 92.0, 95% CI 63.3 to 84.8, [I^2 36.9%, p=0.2]); post-operative haemorrhage 9.3% (4 studies, range 3.3 to 13.3, 95% CI 4.7 to 15.1, [I^2 0.0%, p=0.5]).

Conclusions

Functional and oncological outcomes are favourable, although the follow-up is limited in the literature. Larger cohorts with longer follow up are needed for definitive conclusions to be drawn.

Introduction

Head and neck (H&N) cancer is the 6th most common type of cancer in the world and is increasing in incidence.[1,2] Squamous cell carcinomas (SCC) account for the majority of these tumours, with an increasing number associated with the human papillomavirus (HPV) and a more favourable oncological outcome.[3–5] These HPV-related cancers tend to affect younger patients with fewer comorbidities.[6] As such, there is an increasingly large group of cancer survivors living for many years after their primary treatment.

H&N cancer patients are over 11 times more likely to experience a second head and neck primary cancer than the general population over 20 years of follow-up (standardized incidence ratio 11.2, 95% CI [10.6–11.8]).[7] In addition to second primaries, patients may suffer from residual disease after treatment for their initial primary, identified within a 12 month period, or recurrent disease identified at the same site within 5 years.[8] Commonly, in such cases, radiotherapy will have formed part of the treatment regimen at either the primary site, and/or to the neck, in either a radical or adjuvant capacity. New or recurrent tumours arising within a previously irradiated volume may be considered a homogeneous cohort of patients, for whom re-irradiation rarely forms part of their management, and for whom surgery may be the only hope of locoregional disease control.[9]

Radiotherapy is known to cause detrimental changes in irradiated tissues, reducing healing potential and complicating potential surgery with trismus and altered tissue planes.[10] Options for surgery have traditionally involved transmandibular and transcervical routes.[10] More recently transoral routes have been adopted as endoscopic instruments become more widely available. Transoral Robotic Surgery (TORS) is the latest development in the field which confers significant advantages to the surgeon and to the patient.[9,11,12] For the surgeon, the endoscopic view is three-dimensional and binocular, giving a close objective lens and excellent depth perception. Further, the instruments have wrists which sit within the body cavity, allowing manipulation of the tissues beyond the direct line of sight through the mouth. For the patient, the reduced volume of disrupted tissue and avoidance of mandibulotomy has the potential to reduce functional impairment in the early stages, speed recovery and facilitate better long-term functional outcomes, in addition to reducing complications from delayed healing, including fistula formation, wound dehiscence and osteoradionecrosis.

TORS for recurrent H&N cancer is an emerging technique. As such, individual centres only have a limited experience of operating on such patients. This review aims to collate and assess the contemporary evidence from international centres performing TORS for H&N tumours in an irradiated volume.

Materials and methods

Protocol and registration

This systematic review was conducted in accordance with PRISMA statement.[13] The protocol for this review was preregistered with PROSPERO (CRD42019127609). The following clarifications and deviations were made from the registered protocol: Studies reporting solely on nasopharyngeal carcinoma were excluded; survival data must have been specific for the recurrent cohort, not combined with primary surgery patients; a minimum requirement of 1 year follow-up for survival data was mandated; with cumulative reports, only the most recent publication was included; for the pooled analysis, only publications with cohorts of greater than 10 patients were included; and, finally, a second reviewer was used, as outlined below.

Eligibility criteria

Study characteristics

Types of study to be included

All types of observational and experimental study designs will be eligible for inclusion.

Setting

All countries and health systems will be considered.

Time frame

TORS is a fairly recently developed procedure and so no limitations on date of surgery will be placed.

Report characteristics

Any report date.

All years of publication or presentation will be considered.

English language.

Any publication status, including grey literature.

Participants

Inclusion criteria

Patients with previously treated head and neck cancer.

Aged over 18.

Both sexes.

Undergoing TORS as part of their management for recurrent disease with a therapeutic or palliative intention, ie not diagnostic surgery.

Exclusion criteria

Studies reporting purely on thyroid and nasopharyngeal cancers.

Intervention

TORS.

Comparator

No comparator was chosen.

Outcome measures

Primary outcome

Overall survival (OS) at 2 years.

Secondary outcomes

Disease-free survival (DFS) and disease-specific survival (DSS) at 2 years.

Rates of positive and close surgical resection margins, as reported.

Complications of surgery: fistula and haemorrhage rate.

Functional outcomes, including perioperative and longer-term tracheostomy and gastrostomy usage.

Information sources

Sources to be searched: Databases MEDLINE, PubMed, Cochrane Controlled Register of Trials (CENTRAL).

References of articles from any previous reviews of chosen papers and backward citation check.

Search strategy

Searches were limited to English language entries and were last conducted on 19th September 2019. Search terms for the MEDLINE database are included in supplementary table 1. Briefly, terms related to robotics, H&N anatomic subsites and recurrence.

Data extraction

Selection of studies

The titles and abstracts of all studies were screened independently by two authors (JCH/ZWL). Where necessary, the full texts of articles were obtained. Where there was disagreement for inclusion, these discrepancies were resolved by the senior author (VP). Where abstracts and titles were identified in English language, but the main report was in a foreign language, the main report was translated, and eligibility criteria applied.

Data Extraction and Management

Two reviewers (JCH/ZWL) independently used a pre-piloted data extraction proforma to extract data from the included studies. Raw numbers and percentages were recorded where relevant. Data were entered onto a Microsoft Excel spreadsheet and final approval was ratified by consensus of the first two authors, with discrepancies resolved by the senior author (VP).[14] Data were reported as presented in the articles. The

corresponding authors were contacted on three occasions,[9,15,16] to clarify ambiguous or incomplete survival data, receiving a reply from two.[9,16]

Data items

The data items were chosen to reflect the primary and secondary outcome measures and are detailed in the results tables below.

Data Synthesis

Summary of findings tables are used to present results from the studies. For meta-analyses, only studies with over 10 patients were included. Owing to low numbers and anticipated heterogeneity in the data, sub-group analysis was not felt to be appropriate. A random-effects meta-analysis of the pooled proportions was performed using *metaprop*.[17] Forest plots were generated using the Freeman-Tukey Double Arcsine Transformation to stabilize the variances, the Wilson method was used for 95% confidence intervals.[18,19] Heterogeneity was assessed using the I^2 statistic with p values <0.05 considered statistically significant. Statistical analyses were conducted using Stata *Release 13*, StataCorp LLC, College Station, Texas USA.

Risk of bias

Individual studies

A study-level risk of bias assessment was performed for all included studies. The Cochrane Risk of Bias tool and/or the MINORS tool was used for randomised controlled trials and observational studies, as appropriate.[20] If any other study types had been encountered, then the appropriate bias assessment tool would have been used. Risk of bias of the cumulative evidence also is also commented on.

Results

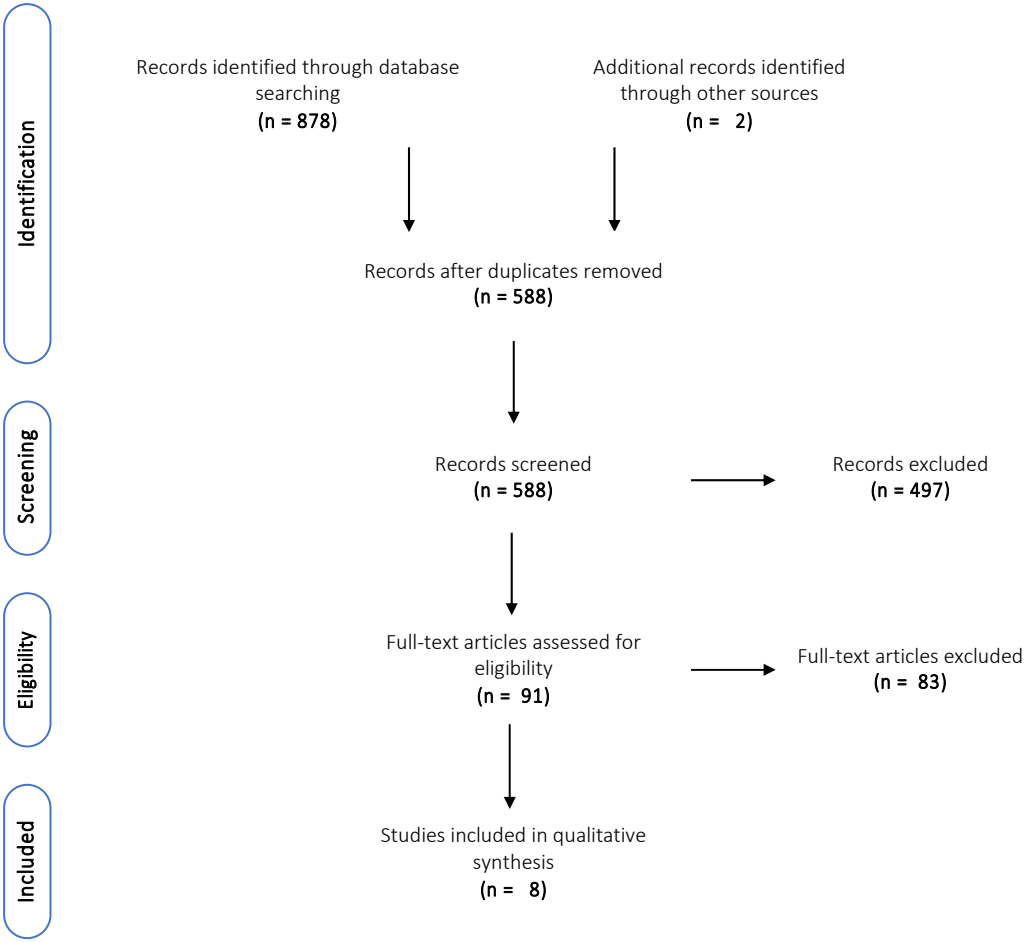

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart with results of the searches, screening and application of eligibility criteria.

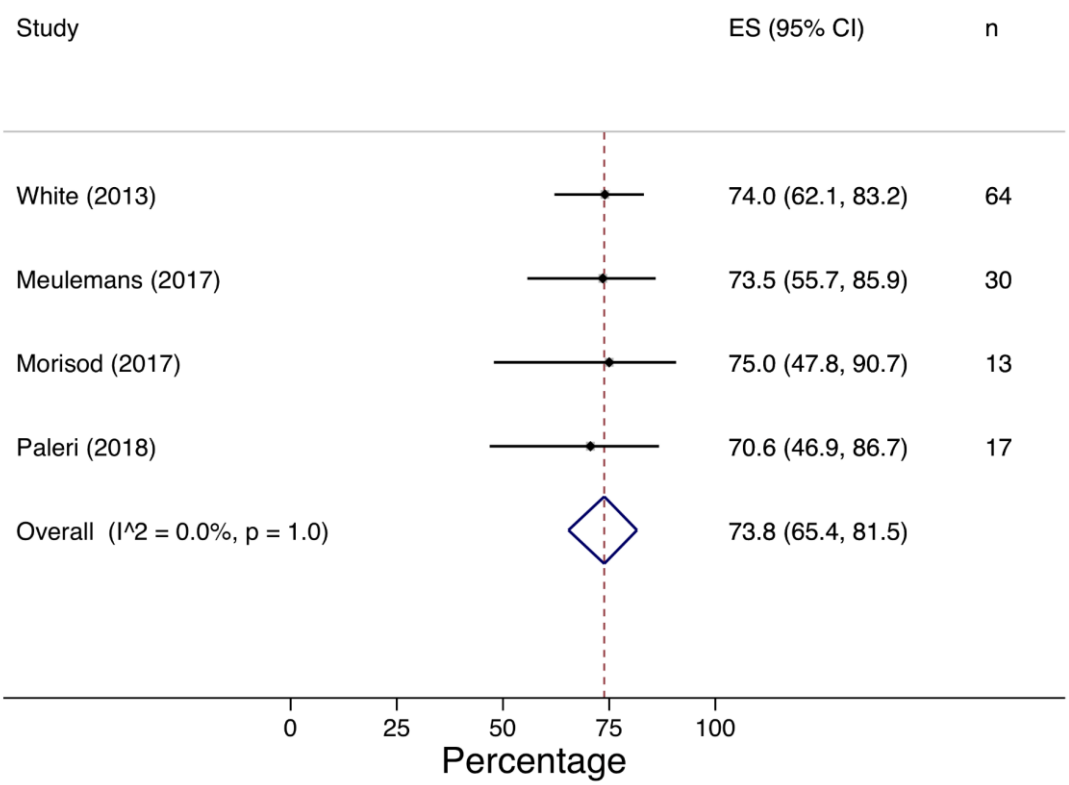

Figure 2: Pooled 2-year overall survival rate. ES = effect size.

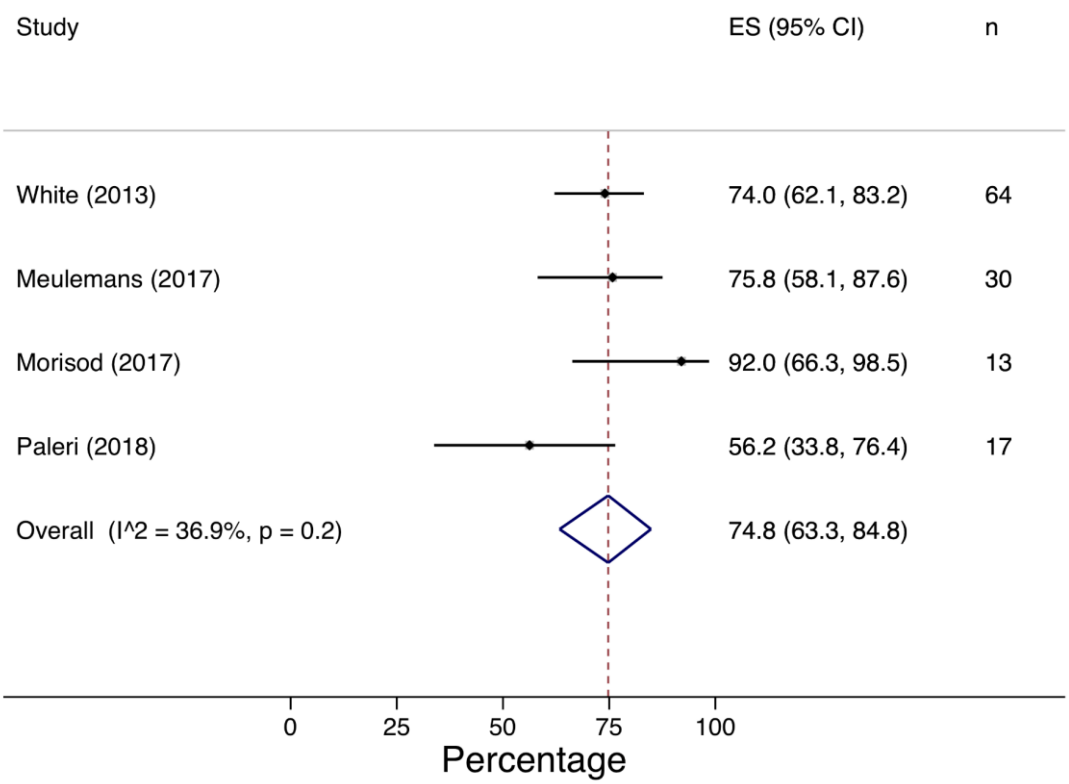

Figure 3: Pooled 2-year disease-free survival. ES = effect size.

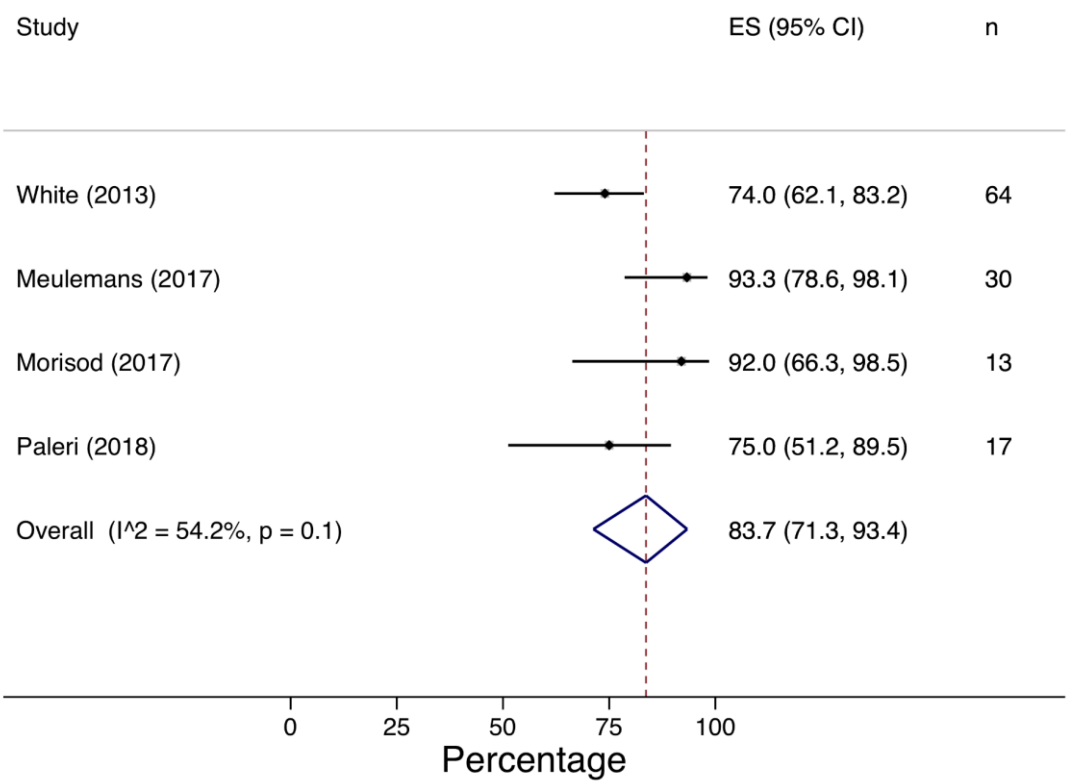

Figure 4: Pooled 2-year disease-specific survival. ES = effect size.

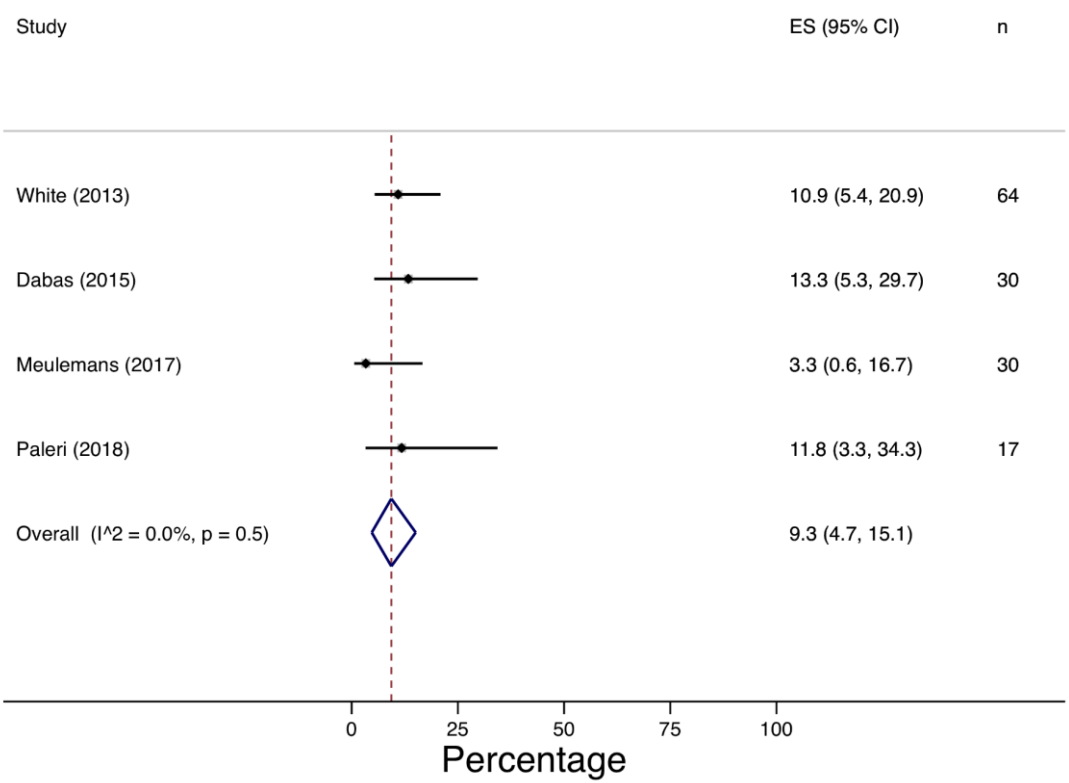

Figure 5: Pooled post-operative haemorrhage rate. ES = effect size.

Study	Country	Centre(s)	Summary	n	Previous radiotherapy?	Mean age /yrs [range]	Sex proportion [M:F]	Interval between initial treatment and surgery	Sub-sites	T stage after surgery	N stage after surgery	Histology	HPV +ve rate	MINORS score
Blanco 2013[21]	USA	Johns Hopkins, Baltimore, Maryland	Early experience of TORS	4	Not reported	Not reported	Not reported	Not reported	Oropharynx and/or larynx	Not reported	Not reported	SCC	Not reported	8
Hans 2013[22]	France	Hôpital Européen Georges-Pompidou, Paris	TORS with free flap for recurrent hypopharyngeal SCC	2	100% (1 RT 1 CRT)	66.6 [59-74]	1:1	5 and 13 years	Hypopharynx (n=2)	T3 (n=2)	N0 (n=2)	SCC	Not reported	11
White 2013[23]	USA	University of Alabama, Birmingham; M.D. Anderson Cancer Center, Houston, Texas; Mayo Clinic, Rochester, Minnesota; Henry Ford Hospital, Detroit, Michigan	TORS for recurrent oropharyngeal SCC, comparing to open surgery	64	100% (25 RT 37 CRT)	61 [not reported]	48:16	Not reported	Oropharynx (n=64)	T1 (n=25) T2 (n=34) T3 (n=2) T4 (n=3)	N0 (n=37) N1 (n=7) N2b (n=17) N2c (n=2) N3 (n=1)	SCC	Not reported	10
Dabas 2015[15]	India	Rajiv Gandhi Cancer Institute & Research Centre, Delhi	TORS for recurrent or residual H&N SCC	30	100% (8 RT 22 CRT)	56.8 [31-86]	29:1	Not reported	Oropharynx (n=26) Larynx (n=3) Hypopharynx (n=1)	T0 (n=2)[d] T1 (n=10) T2 (n=14) T4 (n=4)	NX (n=20) N0 (n=3) N1 (n=1) N2b (n=5) N2c (n=1)	SCC	Not reported	13
Krishnan 2017[24]	Australia	Royal Adelaide Hospital, Adelaide	TORS total laryngectomies, 5 cases with single incidence of recurrent cancer	1	100% (1 RT)	80	1:0	Not reported	Glottis (n=1)	T2 (n=1)	N0 (n=1)	SCC	Not reported	14
Meulemans 2017[16]	Belgium	University Hospitals of Leuven; General Hospital AZ Sint-Lucas, Ghent; General Hospital AZ Sint-Jan, Bruges	TORS for primary and salvage oropharyngeal, supraglottic and hypopharyngeal cancers	30	Not reported	[c]	[c]	Not specified “10 local recurrence 20 second primaries”	Oropharynx (n=17) Hypopharynx (n=6) Supraglottis (n=6) Glottis (n=1)	T1 (n=18) T2 (n=12)	N0 (n=25) N1 (n=3) N2 (n=2)	SCC (n=29) mucinous cystadenocarcinoma (n=1) [b]	0.0% (0/9)	13
Morisod 2017[25]	Switzer-land	Lausanne University Hospital	TORS for oropharyngeal SCC, looking to minimise adjuvant therapy. 13/29 were 'second primaries'	13	46.2% (6 RT)	[a]	[a]	Not specified “13 second primaries”	[a]	[a]	[a]	SCC	[a]	13
Paleri 2018[9]	UK	Freeman Hospital, Newcastle upon Tyne	TORS for recurrent oropharyngeal SCC	17 [e]	100% (2 RT 15 CRT)	59.7 [51-85]	16:1	Median 24.5 months [3-96]	Oropharynx (n=17)	T1 (n=3) T2 (n=13) T3 (n=1)	N0 (n=13) N1 (n=2) N2b (n=2)	SCC	60.0% (11/17)	13

Table 1: Study Characteristics. [a] no separate data for second primary cohort; [b] author contacted for clarification; [c] no separate data for salvage cohort, [d] authors report “biopsy proven residual/recurrent disease had no evidence of malignancy on final histopathology report”, [e] author provided updated data for the 17 of the 26 patients who underwent TORS for confirmed SCC of the oropharynx.

Study	n	Follow-up [Mean and range] /months	2-yr survival data	Other reported survival data	Positive margins % (n)	Close margins % (n)	Margin cut-offs -Close -Positive
Blanco 2013[21]	4	Not reported	OS 100% DFS 25% DSS 100%	-	Not reported	Not reported	- -
Hans 2013[22]	2	27 [24-30]	OS 100% DFS 100% DSS 100%	-	0% (0/2)	0% (0/2)	- -
White 2013[23]	64	Not reported	OS 74% DFS 74% DSS 74%	-	15.6% (10/64) [d]	Not reported	- -
Dabas 2015[15]	30	Median 19 [range 7 -122][b]	Not reported	OS 86% DFS 56.7% (at median of 19 [7-122] months)	6.7% (2/30)	6.7% (2/30)	2mm -
Krishnan 2017[24]	1	54 [-]	OS 100% DFS 100% DSS 100%	DFS 100% at 54 months	0% (0/1)	Not reported	- -
Meulemans 2017[16]	30	16.9 [0-38][a]	OS 73.5% DFS 75.8% DSS 93.3%	-	33% (10/30)	26.7% (8/30)	5mm -
Morisod 2017[25]	13	20.8 [8-35][a]	OS 75% DFS 92% DSS 92%	-	[e]	[e]	3mm 1mm
Paleri 2018[9]	17[c]	28 [3-68]	OS 70.6% DFS 56.3% DSS 75.0% [c]	-	23.5% (4/17)	52.9% (9/17)	3mm -

Table 2: Survival data and surgical margins. [a] derived from Kaplan Meier, [b] as reported, [c] author provided updated data for the 17 of the 26 patients who underwent TORS for confirmed SCC of the oropharynx, [d] 4 returned to theatre for re-resection and subsequently achieved negative margins, [e] no separate data for second primary cohort. OS overall survival, DFS disease-free survival, DSS disease-specific survival.

Study	n	Concurrent neck surgery	Peri-operative gastrostomies % (n)	Peri-operative tracheostomies % (n)	Long-term gastrostomies % (n)	Long-term tracheostomies % (n)	Free flap rate	Fistula rate	Return to theatre with haemorrhage rate	Additional long-term functional results
Blanco 2013[21]	4	-	Not reported	Not reported	25.0% (1/4) [f]	0.0% (0/4) [g]	0.0% (0/4)	0.0% (0/4)	0.0% (0/4)	-
Hans 2013[22]	2	100% (2/2)	50% (1/2)	50% (1/2)	0.0% (0/2) [g]	0.0% (0/2) [g]	100% (2/2)	0.0% (0/2)	0.0% (0/2)	-
White 2013[23]	64	-	35.9% (23/64)	21.9% (14/64)	3.1% (2/64) [h]	Not reported	0.0% (0/64)	0.0% (0/64)	10.9% (7/64)[e]	-
Dabas 2015[15]	30	33.3% (10/30)	16.7% (5/30)[b]	Not reported	3.3% (1/30) [f]	10.0% (3/30) [f]	0.0% (0/30)	3.3% (1/30)	13.3% (4/30)	-
Krishnan 2017[24]	1	100% (1/1)	100.0% (1/1)	NA[c]	100.0% (1/1) [f]	NA[c]	0.0% (0/1)	100% (1/1)	0.0% (0/1)	'Soft diet with enteral supplementation'; 'Failed electrolarynx, poor voice outcomes following secondary TEP'
Meulemans 2017[16]	30	-	20.0% (6/30)	23.3% (7/30)	20.0% (6/30) [f]	0.0% (0/30) [g]	0.0% (0/30)	3.3% (1/30)	3.3% (1/30)	-
Morisod 2017[25]	13	100% (13/13)	Not reported	Not reported	Not reported	Not reported	[d]	[d]	[d]	[d]
Paleri 2018[9]	17	100% (17/17)[a]	Not reported	58.8% (10/17) [i]	0.0% (0/17) [i]	0.0% (0/17) [g i]	23.5% (4/17) [i]	0.0% (0/17) [i]	11.8% (2/17) [i]	Normalcy of diet scores recorded pre-op and at 3 and 6 months.

Table 3: Functional outcomes and complications. [a] minimum of neck surgery for vessel ligation in all cases, [b] all inserted for the procedure, [c] laryngectomy, [d] no separate data for second primary cohort, [e] unclear if any returned to theatre, [f] no time point given for assessment, [g] no usage beyond peri-operative period, [h] assessed at 1 year, [i] author provided updated data for the 17 of the 26 patients who underwent TORS for confirmed SCC of the oropharynx

Study selection

A total of 878 potentially relevant records were identified, reducing to 588 once duplicates had been removed. Figure 1 displays the results of the review process in a PRISMA flowchart. On detailed review of full text articles, many records were ineligible as they were review articles, [11,26–33] did not report any TORS salvage cases,[34–57] the salvage cases were indistinguishable from the primary cases/combined cohort,[58–63] there were insufficient survival data,[64–76] reports were only conference abstracts,[27,77–102] related to nasopharyngeal carcinoma only,[26,29–31,65,73,103,104] or the reports were superseded by more contemporary publications from the relevant institutions.[105,106] A total of eight studies met the eligibility criteria and have been presented in the results.[9,15,16,21–25]

Study characteristics

Table 1 summarises the characteristics of the studies included in this systematic review. The studies were published between 2013 and 2018 and originate from centres in the USA,[21,23] Europe,[9,16,22,25] India[15] and Australia.[24] Two of the studies were multi-institutional.[16,23] All of the studies identified their patients based on the intervention and reported on the subsequent outcomes and, as such, were considered observational cohort studies. A single study compared outcomes to matched open surgery patients[23] and another study compared 'salvage' patients to primary surgery patients.[16] The remaining studies made no comparisons. The eight reports were published in seven different journals from publishing houses across the world.

The eight studies included 161 cases in total, ranging from a single eligible case to a cohort of 64 patients. In three studies, the final number of cases eligible for inclusion in this review was small (1[24], 2[22] and 4[21] cases). All these studies satisfied the predetermined eligibility criteria, presenting valid outcome data which were discernible for the included cases. In one study, the author provided updated data for the oropharyngeal SCC cohort covering 17 of the 21 TORS patients that were included in the original publication.[9]

In six of the eight studies, the previous treatment was clearly reported, with the majority of patients having previously undergone radiotherapy or chemoradiotherapy to the head and neck. No studies reported the use of bioradiotherapy. The most common subsite for the TORS intervention was the oropharynx, with surgeries also covering the hypopharynx, supraglottis, glottis and nasopharynx. There was a male preponderance and the mean ages were around 60 years. Nearly all cases were SCC, but HPV rates were inconsistently reported. Most cases were early stage disease, rT0-T2 and rN0-N2b (Table 1).

The timing of treatment for the cancers in the included studies was not consistently reported. Studies often contained cases presenting at a variety of timepoints, including residual disease (within 12 months of prior treatment)[9,16], recurrent disease (within 5 years of prior treatment)[9,16] and some including cases of new primaries either at a new subsite (any time after initial treatment)[9,16,22,25] or at a new subsite (within 5 years of initial treatment)[9,16,25].

Risk of bias within studies

MINORS scores are presented alongside study characteristics in table 1, with full scores displayed in supplementary table 2. The mean MINORS score was 12 (range 8-14) out of a maximum score of 16. In general, studies were good at prospectively identifying their aims and the data to be collected, at specifying and assessing the study end points, and following up consecutively identified patients. However, no prior consideration was

given to the cohort size and minimum follow-up was inconsistently reported, or not adequate, impacting on the reliability of the survival data presented.

Risk of bias across studies

Publication bias may be suggested in the studies identified by this review by the higher survival rates seen in studies reporting on fewer patients. The survival data reported therein did not include any statistical analysis and so publication of only statistically relevant studies could not be assessed. In the majority of cases, it was not possible to identify any selective reporting within the studies, and the majority of studies implied that consecutive cases were included (see MINORS scores, supplementary table 2).

Survival

Survival data at 2-years were available in seven of the eight studies (table 2), having contacted two authors to obtain further data.[9] Survival estimations were presented in Kaplan Meier charts in two studies.[16,25]

The pooled survival rates were as follows: 2-year overall survival 73.8% (4 studies, range 70.6 to 75.0, 95% CI 65.4 to 81.5, [I^2 0.0%, p=1.0]) (figure 2); 2-year disease-free survival 74.8% (4 studies, range 56.2 to 92.0, 95% CI 63.3 to 84.8, [I^2 36.9%, p=0.2]) (figure 3); 2-year disease-specific survival 83.7% (4 studies, range 74.0 to 92.0, 95% CI 71.3 to 93.4, [I^2 54.2%, p=0.1]) (figure 4).

Margins

All but one study reported on rates of positive resection margins, with five studies also reporting rates of close resection margins (table 2). In a single study, the margin data could not be distinguished between primary and secondary cancers, and so they were not included.[25]

The pooled positive margin rate was 18.2% (4 studies, range 6.7 to 33.3, 95% CI 8.4 to 30.4, [I^2 60.1%, p=0.1]).

The pooled close margin rate was 25.7% (3 studies, range 6.7 to 52.9, 95% CI 4.9 to 54.2, [I^2 84.3%, p=<0.01]).

The criteria used for a 'close' margin cut off was reported by 4 studies, ranging between 2 and 5 mm. A single study reported criteria for considering a margin as 'positive' (table 2).

Functional outcomes

Functional outcomes are summarised in table 3.

The pooled peri-operative gastrostomy rate was 25.0% (3 studies, range 16.7 to 35.9, 95% CI 13.7 to 38.2, [I^2 56.9%, p=0.1]).

The pooled peri-operative tracheostomy rate was 22.3% (3 studies, range 21.9 to 23.5, 95% CI 14.7 to 30.8, [I^2 0.0%, p=1.0]).

Definitions of what constituted 'long-term' outcomes are reported in table 3. Only a single study declared the time point at which this assessment was made in the published report,[23] with another study providing clarification via communication.[9]

The pooled long-term gastrostomy rate was 5.0% (4 studies, range 0.0 to 20.0, 95% CI 0.1 to 13.9, [I^2 63.7%, p=0.04]).

The pooled long-term tracheostomy rate was 1.9% (3 studies, range 0.0 to 10.0, 95% CI 0.0 to 10.6, [I^2 54.3%, p=0.1]).

Complications

Data on complications are reported in table 3.

The pooled post-operative haemorrhage rate was 9.3% (4 studies, range 3.3 to 13.3, 95% CI 4.7 to 15.1, [I^2 0.0%, p=0.5]) (figure 5).

Not all studies reported rates of concurrent neck dissection, but rates are reported in table 3 as they are relevant to pharyngocutaneous fistula formation. Similarly, free flap reconstruction may be utilised prophylactically to address potential fistula formation and so these data are reported in table 3.

The pooled post-operative fistula rate was 0.6% (4 studies, range 0.0 to 3.3, 95% CI 0.0 to 3.3, [I^2 3.1%, p=0.4]).

The pooled free flap rate was 1.6% (4 studies, range 0.0 to 23.5, 95% CI 0.0 to 10.4, [I^2 75.8%, p=0.01]).

Discussion

Despite the broad search strategy, a relatively limited number of studies were identified which reported on TORS to treat H&N tumours in previously treated patients. TORS in this context remains a relatively infrequent procedure conducted in a limited number of centres across the world. There are no randomised trials to inform us of comparative outcome data with open surgery and there is significant heterogeneity within the cohorts identified in this review. As such, the data presented here must be interpreted with great caution.

Survival

The principal objective of this review was to report on survival amongst patients undergoing TORS who had had a previously treated H&N cancer. In the present review, 2-year survival was the longest standardised follow-up in the identified studies. TORS is a relatively recently developed technique and so longer-term outcome data have not yet permeated the literature.[107]

This review has identified overall survival and disease-free survival rates of 73.8% and 74.8%, respectively. The similarity between these two rates suggest a low incidence of death from other causes during the follow-up period, implying appropriate case selection. This may be anticipated where tumour boards may have a higher threshold for listing new cases for an emerging surgical technique. Unfortunately, rates of adjuvant therapy for the previous cancers were inconsistently reported in the identified studies. This information is essential for interpreting the impact of TORS for recurrence in patients who may not be able to undergo re-irradiation, chemotherapy or 'salvage' Inotuzumab ozogamicin (IO). Future reports on TORS for recurrence should clearly report the rates of adjuvant therapies to better understand the complex management of this patient group.

The 2-year survival rates are reassuring when compared to equivalent rates for open surgery.[108] White et al. compared their TORS salvage results to matched open surgery cases, reporting disease-free survival of 74% vs 43%, respectively (p=0.01).[23] It is acknowledged that significantly fewer patients in the open surgery group had had their primary tumours treated with radiation and chemotherapy, and so the recurrent tumour biology may have differed. The positive margin rate was also seen to be higher in the matched open surgery group (29% vs 9%) which is likely to account for some of this difference. Criticism of TORS, when compared to open surgery, has included a lack of tactile feedback, theoretically making resection more problematic if the tumour cannot be handled to aid the surgeon's decision-making in attempting to achieve appropriate clearance. Reassuringly, this does not appear to be the case for the White et al. cohort but more data will be needed on margins to give confidence to this assessment.

Margins

Across the four applicable studies, the positive margin rate for included patients was 18.2% (table 2). A further 25.7% of cases were reported to have close margins. Whilst these rates may seem high, the role of close margins in recurrent H&N cancers has not been definitively established, and certainly not in the heterogeneous group included in this review.

There was also notable variation between the studies in what was considered a 'close' margin with four studies reporting three different distances, ranging between 2mm and 5mm. Additionally, the locations of these margins were not consistently reported; specifically, whether the margin was mucosal or deep, which may be considered differently. For example, for tonsillar tumours, a deep margin of more than 2-3mm may be unachievable, as this is the depth of the superior constrictor muscle in this location.[109] It is proposed that this anatomical barrier

should be taken into consideration when interpreting the histopathology results of these resections. If it is not breached, then it could be argued that there is limited justification for further resections, or adjuvant therapy, if available. Morisod et al 2017[25] undertook further resections of the deep margin in two cases, including of the parapharyngeal fat. In a further two cases, further resections were indicated, according to their management protocol, but surgery did not take place, as in one case the patient refused and in the other case surgery was precluded due to co-morbidities. Unfortunately, we do not have specific outcome data for this subgroup, but we do know that the two patients undergoing further surgery had their major vessels exposed and so required free flap reconstruction. As such, further resections in these patients are not without morbidity, with the inevitable donor site trauma and the impact the free flap will have on functional outcomes. To be able to adequately address this question of margins in the patients, a larger cohort is needed with more information about previous treatments and adjuvant therapy.

Complications

Post-operative haemorrhage remains a concern in TORS in general, particularly when wounds are left to heal by secondary intention, potentially leaving vulnerable vessels exposed to the effects of saliva.[110] The 9.3% pooled rate seen in this review is in keeping with rates seen for primary oropharyngeal resections and may have been reduced by the small number of patients also undergoing concurrent free flap reconstruction. The low rate is perhaps surprising, however, considering the majority of patients identified had previously undergone radiotherapy or chemoradiotherapy to the region, theoretically worsening the healing potential of the exposed tissues. Delayed healing contributed to a late fatalities in Meuleman's cohort, where necrosis at the resection site reportedly led to a carotid blowout. However, most bleeds identified here were not life-limiting and were managed with or without a return to theatre for local haemorrhage control.

TORS offers notable advantages to this group of patients. Open surgery to this area may necessitate mandibulotomy for adequate exposure of the tumour, inviting a range of complications not seen in TORS alone, namely osteoradionecrosis, oro/pharyngocutaneous fistulae, bone exposure, malunion and the potential need for hardware removal.[111] The fistula rate was only 0.6% in this review. This may be attributed to the reduced tissue disruption seen in TORS when compared to open surgery.[9] It may also be due to low rates of concurrent neck surgery for vessel identification if free flap reconstruction can be avoided. It seems, therefore, that the side effect profile of TORS, in this context, is acceptable, and even preferable to open surgical options.

Functional outcomes

In primary H&N cancer patients, the long-term swallowing results may be worse in radiotherapy patients than those undergoing surgical resection.[112,113] Additionally, swallowing outcomes following radiation frequently continue to worsen over time.[114,115] Newer techniques like intensity-modulated radiation therapy (IMRT) attempt to spare sensitive structures important for swallowing, such as the superior constrictors, to mitigate the impact of irradiation.[116]

The majority of cases identified in this review had their TORS for tumours present in previously irradiated volumes (table 1) and, so, their swallowing potential may have been inherently limited. Despite this, perioperative and long-term gastrostomy rates were relatively low at 25.0% and 5.0%, respectively. Tracheostomy rates were also low (22.3% perioperatively, 1.9% long-term).

The peri-operative use of gastrostomies and tracheostomies may be particularly influenced by local departmental policies and practices. The principal indication for peri-operative tracheostomy usage in these patients is for

airway control in the event of haemorrhage. At around 1 in 10 patients having a bleed, it is unlikely that this tracheostomy rate will change considerably in the future. Conversely, rates of prophylactic peri-operative gastrostomies may fall as better understanding is gained of the predictors of post-operative swallowing function in this cohort.

The presence of a gastrostomy tube has often been used as a surrogate measure of swallowing in the literature.[117] This may underestimate the extent of oropharyngeal dysphagia in the head and neck cancer population as many will continue eating and drinking in the absence of a feeding tube, despite patient-reported and instrumentally-defined swallowing safety and efficiency issues. However, more granular and validated measures of swallowing function are utilised widely, both in clinical practice and in the literature. For example: Morisod et al. used the Functional Outcome Swallowing Scale (FOSS) to report outcomes but did not differentiate results for the second primary tumour cohort[25,118] and Paleri et al. used the Performance Status Scale for Head and Neck Cancer Patients (PSS-HN), reporting 11 patients with valid data at 6 months with variable outcomes.[9,119] The MD Anderson Dysphagia Inventory has also been widely utilised to record the impact of dysphagia on head and neck cancer patients.[120] Consistent reporting of any change in swallow function would be welcomed in future reports of TORS in previously treated H&N cancer patients, as would the adoption of a consistent timeframe for what is considered 'long-term' for these functional outcomes. Increasing numbers of head and neck cancer clinical trials are adopting a more uniform and targeted approach to multidimensional swallowing evaluation.[121,122] Careful consideration should be given to which swallowing measures are selected. A recent study evaluated commonly used dysphagia outcome measures and mapped them to the International Classification of Functioning, Disability and Health (ICF).[123] Measures primarily addressed body functions with few concepts linking to activity, participation and environmental factors. This impacts on a more holistic and representative understanding of the impact of dysphagia following head and neck cancer treatment. The authors propose the use of PSS-HN pre-operatively and at 12 months as a minimum dataset for future reports.

Voice outcomes have not been well reported in the studies in this review. A significant proportion of the patients identified had had oropharyngeal resections, which would have inevitably affected the soft palate, and so the naso-oropharyngeal junction, integral to normal voice production and avoidance of hypernasality. Velopharyngeal insufficiency is further impaired by low rates of free flap reconstruction in these TORS oropharyngeal resections, giving less tissue bulk at the junction, and reduced tissue pliability, as a result of previous irradiation.[114,115] Two of the included studies made comment on voice outcomes: Dabas et al.[15] reported altered resonance in 10% of patients in the immediate post-operative period that persisted into the long-term and Krishnan and Krishnan[24] reported 'poor voice outcomes' following secondary tracheoesophageal puncture in their single case of TORS total laryngectomy performed for recurrent glottic SCC. Full functional outcome data, including any impact on speech production, should be presented to patients considering TORS for recurrence, to enable informed decision-making. Mandatory prospective, systematic data collection of both survival and functional outcomes should be considered to ensure high quality reliable data are available to facilitate decision making by patients and clinicians alike.

Limitations

Due to the relative scarcity of these surgeries, the search strategy for this review was intentionally broad and the inclusion/exclusion criteria were not too strict. As a result, the case mix included is fairly heterogeneous. The cases identified covered surgery for residual disease, for recurrence and for new primaries, both at the same subsite and elsewhere in the head and neck. The tumour biology for all these cases may be very different and ideally

these groups would be considered separately. Similarly, a variety of H&N subsites are reported here, although the majority are acknowledged to be oropharyngeal SCCs.

Conclusions

TORS in patients with previously treated head and neck cancers is an emerging but relatively infrequent procedure. The functional and oncological outcomes are favourable, though the follow-up is limited in the contemporary literature and multidimensional swallowing and communication evaluation should be mandated. The minimum surgical margin, to achieve local control, is yet to be established in this complex anatomical site. Larger cohorts with longer follow-up are needed to enable reliable conclusions to be drawn. This team has commenced an individual patient data (IPD) meta-analysis from international centres performing TORS for previously treated head and neck cancers to help address this issue.

References

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011;61(2):69–90.

2. Shield KD, Ferlay J, Jemal A, Sankaranarayanan R, Chaturvedi AK, Bray F, et al. The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. CA Cancer J Clin 2017;67(1):51–64.

3. De Felice F, Tombolini V, Valentini V, de Vincentiis M, Mezi S, Brugnoletti O, et al. Advances in the Management of HPV-Related Oropharyngeal Cancer. J Oncol 2019;2019:9173729.

4. Shi W, Kato H, Perez-Ordonez B, Pintilie M, Huang S, Hui A, et al. Comparative prognostic value of HPV16 E6 mRNA compared with in situ hybridization for human oropharyngeal squamous carcinoma. J Clin Oncol 2009;27(36):6213–21.

5. Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI, Nguyen-Tân PF, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med 2010;363(1):24–35.

6. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol 2006;24(14):2137–50.

7. Chuang S-C, Scelo G, Tonita JM, Tamaro S, Jonasson JG, Kliewer EV, et al. Risk of second primary cancer among patients with head and neck cancers: A pooled analysis of 13 cancer registries. Int J Cancer 2008;123(10):2390–6.

8. INTEGRATE (The National ENT Trainee Research Network). British Association of Head and Neck Oncologists Surveillance audit 2018. Unpublished;

9. Paleri V, Fox H, Coward S, Ragbir M, McQueen A, Ahmed O, et al. Transoral robotic surgery for residual and recurrent oropharyngeal cancers: Exploratory study of surgical innovation using the IDEAL framework for early-phase surgical studies. Head Neck 2018;40(3):512–25.

10. Gross ND, Hanna EY. The Role of Surgery in the Management of Recurrent Oropharyngeal Cancer. Recent Results Cancer Res 2017;206:197–205.

11. Hamilton D, Paleri V. Role of transoral robotic surgery in current head & neck practice. Surgeon 2017;15(3):147–54.

12. Weinstein GS, O'Malley BW, Cohen MA, Quon H. Transoral robotic surgery for advanced oropharyngeal carcinoma. Arch Otolaryngol Head Neck Surg 2010;136(11):1079–85.

13. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. International Journal of Surgery 2010;8(5):336–41.

14. Microsoft. Excel for Mac [Internet]. Redmond, Washington, USA: Microsoft Corporation; 2018. Available from: https://products.office.com/

15. Dabas S, Dewan A, Ranjan R, Dewan AK, Shukla H, Sinha R. Salvage Transoral Robotic Surgery for Recurrent or Residual Head and Neck Squamous Cell Carcinoma: A Single Institution Experience. Asian Pac J Cancer Prev 2015;16(17):7627–32.

16. Meulemans J, Vanclooster C, Vauterin T, D'heygere E, Nuyts S, Clement PM, et al. Up-front and Salvage Transoral Robotic Surgery for Head and Neck Cancer: A Belgian Multicenter Retrospective Case Series. Frontiers in Oncology [Internet] 2017 [cited 2019 Feb 4];7. Available from: http://journal.frontiersin.org/article/10.3389/fonc.2017.00015/full

17. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Archives of Public Health 2014;72(1):39.

18. Freeman MF, Tukey JW. Transformations Related to the Angular and the Square Root. Ann Math Statist 1950;21(4):607–11.

19. Wilson EB. Probable Inference, the Law of Succession, and Statistical Inference. Journal of the American Statistical Association 1927;22(158):209–12.

20. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. ANZ Journal of Surgery 2003;73(9):712–6.

21. Blanco RGF, Fakhry C, Ha PK, Ryniak K, Messing B, Califano JA, et al. Transoral robotic surgery experience in 44 cases. J Laparoendosc Adv Surg Tech A 2013;23(11):900–7.

22. Hans S, Jouffroy T, Veivers D, Hoffman C, Girod A, Badoual C, et al. Transoral robotic-assisted free flap reconstruction after radiation therapy in hypopharyngeal carcinoma: report of two cases. Eur Arch Otorhinolaryngol 2013;270(8):2359–64.

23. White H, Ford S, Bush B, Holsinger FC, Moore E, Ghanem T, et al. Salvage surgery for recurrent cancers of the oropharynx: comparing TORS with standard open surgical approaches. JAMA Otolaryngol Head Neck Surg 2013;139(8):773–8.

24. Krishnan G, Krishnan S. Transoral Robotic Surgery Total Laryngectomy: Evaluation of Functional and Survival Outcomes in a Retrospective Case Series at a Single Institution. ORL J Otorhinolaryngol Relat Spec 2017;79(4):191–201.

25. Morisod B, Venara-Vulpe II, Alzuphar S, Monnier Y, Bongiovanni M, Hagmann P, et al. Minimizing adjuvant treatment after transoral robotic surgery through surgical margin revision and exclusion of radiographic extracapsular extension: A Prospective observational cohort study. Head Neck 2017;39(5):965–73.

26. Xu T, Tang J, Gu M, Liu L, Wei W, Yang H. Recurrent nasopharyngeal carcinoma: A clinical dilemma and challenge. Current Oncology 2013;20(5):e406–19.

27. Chan JYW. Advances in the management of recurrent nasopharyngeal carcinoma. Head and Neck 2015;37(SUPPL. 1):E123.

28. Dolivet G, Cortese S, Mastronicola R, Phulpin B, Kaminski MC, Mecellem H, et al. Salvage surgery for upper aerodigestive tract tumours. Bulletin du Cancer 2011;98(1):59–71.

29. Wei WI, Kwong DLW. Recurrent nasopharyngeal carcinoma: surgical salvage vs. additional chemoradiation. Curr Opin Otolaryngol Head Neck Surg 2011;19(2):82–6.

30. Chan JYW. Surgical management of recurrent nasopharyngeal carcinoma. Oral Oncol 2014;50(10):913–7.

31. Tsang RK, Wei WI. Salvage surgery for nasopharyngeal cancer. World Journal of Otorhinolaryngology - Head and Neck Surgery 2015;1(1):34–43.

32. Sload R, Silver N, Jawad BA, Gross ND. The Role of Transoral Robotic Surgery in the Management of HPV Negative Oropharyngeal Squamous Cell Carcinoma. Curr Oncol Rep 2016;18(9):53.

33. Qureshi HA, Abouyared M, Barber B, Houlton JJ. Surgical Options for Locally Advanced Oropharyngeal Cancer. Current treatment options in oncology 2019;20(5):36–36.

34. Cohen MA, Weinstein GS, O'Malley BW, Feldman M, Quon H. Transoral robotic surgery and human papillomavirus status: Oncologic results. Head Neck 2011;33(4):573–80.

35. Iyer NG, Nixon IJ, Palmer F, Kim L, Whitcher M, Katabi N, et al. Surgical management of squamous cell carcinoma of the soft palate: factors predictive of outcome. Head Neck 2012;34(8):1071–80.

36. Ford SE, Brandwein-Gensler M, Carroll WR, Rosenthal EL, Magnuson JS. Transoral robotic versus open surgical approaches to oropharyngeal squamous cell carcinoma by human papillomavirus status. Otolaryngology - Head and Neck Surgery (United States) 2013;149(2 SUPPL. 1):P80–1.

37. Mendelsohn AH, Remacle M, Van Der Vorst S, Bachy V, Lawson G. Outcomes following transoral robotic surgery: supraglottic laryngectomy. Laryngoscope 2013;123(1):208–14.

38. de Almeida JR, Li R, Magnuson JS, Smith RV, Moore E, Lawson G, et al. Oncologic Outcomes After Transoral Robotic Surgery: A Multi-institutional Study. JAMA Otolaryngol Head Neck Surg 2015;141(12):1043–51.

39. Lorincz BB, Knecht R. TORS for head and neck squamous cell carcinoma (HNSCC): the Hamburg experience. B-ENT 2015;33–6.

40. Lorincz BB, Mockelmann N, Busch CJ, Knecht R. Functional outcomes, feasibility, and safety of resection of transoral robotic surgery: Single-institution series of 35 consecutive cases of transoral robotic surgery for oropharyngeal squamous cell carcinoma. Head and Neck 2015;37(11):1618–24.

41. Lorincz BB, Busch CJ, Mockelmann N, Knecht R. Two-Year survival analysis of fifty consecutive Head and Neck sqamous Cell Carcinoma Patients treated primarily with transoral robotic Surgery (TORS) in a single European Academic Centre. Oncology Research and Treatment 2016;39(SUPPL. 1):107.

42. Jackson RS, Sinha P, Zenga J, Kallogjeri D, Suko J, Martin E, et al. Transoral Resection of Human Papillomavirus (HPV)-Positive Squamous Cell Carcinoma of the Oropharynx: Outcomes with and Without Adjuvant Therapy. Ann Surg Oncol 2017;24(12):3494–501.

43. Park YM, Kim HR, Cho BC, Keum KC, Cho NH, Kim S-H. Transoral robotic surgery-based therapy in patients with stage III-IV oropharyngeal squamous cell carcinoma. Oral Oncol 2017;75:16–21.

44. Cannon RB, Houlton JJ, Patel S, Raju S, Noble A, Futran ND, et al. Patterns of cervical node positivity, regional failure rates, and fistula rates for HPV+ oropharyngeal squamous cell carcinoma treated with transoral robotic surgery (TORS). Oral Oncology 2018;86:296–300.

45. Duek I, Sviri GE, Billan S, Gil Z. Minimally Invasive Surgery for Resection of Parapharyngeal Space Tumors. Journal of Neurological Surgery, Part B: Skull Base 2018;79(3):250–6.

46. Moore EJ, Van Abel KM, Price DL, Lohse CM, Olsen KD, Jackson RS, et al. Transoral robotic surgery for oropharyngeal carcinoma: Surgical margins and oncologic outcomes. Head and Neck 2018;40(4):747–55.

47. Moore EJ, Olsen SM, Laborde RR, García JJ, Walsh FJ, Price DL, et al. Long-term functional and oncologic results of transoral robotic surgery for oropharyngeal squamous cell carcinoma. Mayo Clin Proc 2012;87(3):219–25.

48. Chan JYK, Tsang RK, Eisele DW, Richmon JD. Transoral robotic surgery of the parapharyngeal space: a case series and systematic review. Head Neck 2015;37(2):293–8.

49. Mattheis S, Hasskamp P, Holtmann L, Lang S. The flex robotic system for hypopharyngeal and laryngeal tumors. Otolaryngology - Head and Neck Surgery (United States) 2017;157(1 Supplement 1):P72.

50. Stenberg B, Cooke V, Paleri V, McQueen A. Intra-operative ultrasound guided trans-oral robotic surgery (TORS) for recurrent oropharyngeal cancers. Ultrasound in Medicine and Biology 2017;43(Supplement 1):S181–2.

51. Lawson G, Bachy V, Mendelsohn A, Remacle M, Rijckaert M, Degrelle I, et al. Transoral robotic surgery: Total laryngectomy new technique to restore swallowing function in case of laryngeal incompetency. Dysphagia 2013;28(2):329–30.

52. Chen W, Xu FL, Chen Y, Zhang Y, Wu KM, Cheng Y, et al. Application of transoral robotic surgery in pharyngolaryngeal tumour resection. Zhonghua er bi yan hou tou jing wai ke za zhi = Chinese journal of otorhinolaryngology head and neck surgery 2016;51(9):695–8.

53. Fang JG, Meng LZ, Wang JH, Yuan XD, Rao YS, Yang F, et al. [Exploration of feasibility and safety of transoral robotic surgery in pharyngolaryngeal tumors]. Zhonghua er bi yan hou tou jing wai ke za zhi = Chinese journal of otorhinolaryngology head and neck surgery 2018;53(7):512–8.

54. Meng LZ, Fang JG, Wang JH, Yuan XD, Yang F, Rao YS, et al. [Preliminary experience of transoral robotic surgery in laryngeal and hypopharyngeal tumors with da Vinci surgical system]. Lin chuang er bi yan hou tou jing wai ke za zhi = Journal of clinical otorhinolaryngology, head, and neck surgery 2018;32(14):1065–70.

55. Sims JR, Van Abel K, Martin EJ, Lohse CM, Price DL, Olsen KD, et al. Management of Recurrent and Metastatic HPV-Positive Oropharyngeal Squamous Cell Carcinoma after Transoral Robotic Surgery. Otolaryngol Head Neck Surg 2017;157(1):69–76.

56. Sethi N, Gouzos M, Padhye V, Ooi EH, Foreman A, Krishnan S, et al. Transoral robotic surgery using the Medrobotic Flex system: the Adelaide experience. Journal of robotic surgery 2019;

57. Meccariello G, Montevecchi F, D'Agostino G, Iannella G, Calpona S, Parisi E, et al. Trans-oral robotic surgery for the management of oropharyngeal carcinomas: a 9-year institutional experience. Acta otorhinolaryngologica Italica : organo ufficiale della Societa italiana di otorinolaringologia e chirurgia cervico-facciale 2019;39(2):75–83.

58. Iseli TA, Kulbersh BD, Iseli CE, Carroll WR, Rosenthal EL, Magnuson JS. Functional outcomes after transoral robotic surgery for head and neck cancer. Otolaryngol Head Neck Surg 2009;141(2):166–71.

59. Mazerolle P, Philouze P, Garrel R, Aubry K, Moriniere S, El Bedoui S, et al. Oncological and functional outcomes of trans-oral robotic surgery for pyriform sinus carcinoma: A French GETTEC group study. Oral Oncology 2018;86:165–70.

60. Panda S, Sikka K, Thakar A, Sharma SC, Krishnamurthy P. Transoral robotic surgery for the parapharyngeal space: expanding the transoral corridor. Journal of robotic surgery 2019;

61. White HN, Moore EJ, Rosenthal EL, Carroll WR, Olsen KD, Desmond RA, et al. Transoral robotic-assisted surgery for head and neck squamous cell carcinoma: one- and 2-year survival analysis. Arch Otolaryngol Head Neck Surg 2010;136(12):1248–52.

62. Genden EM, Park R, Smith C, Kotz T. The role of reconstruction for transoral robotic pharyngectomy and concomitant neck dissection. Arch Otolaryngol Head Neck Surg 2011;137(2):151–6.

63. Lallemant B, Moriniere S, Ceruse P, Lebalch M, Aubry K, Hans S, et al. Transoral robotic surgery for squamous cell carcinomas of the posterior pharyngeal wall. Eur Arch Otorhinolaryngol 2017;274(12):4211–6.

64. Vural E, Tulunay-Ugur OE, Suen JY. Transoral robotic supracricoid partial laryngectomy with cartilaginous framework preservation. Journal of robotic surgery 2012;6(4):363–6.

65. Wei WI, Ho W-K. Transoral robotic resection of recurrent nasopharyngeal carcinoma. Laryngoscope 2010;120(10):2011–4.

66. Gorphe P, Temam S, Kolb F, Qassemyar Q. Cervical-transoral robotic oropharyngectomy and thin anterolateral thigh free flap. Eur Ann Otorhinolaryngol Head Neck Dis 2018;135(1):71–4.

67. Dean NR, Rosenthal EL, Carroll WR, Kostrzewa JP, Jones VL, Desmond RA, et al. Robotic-assisted surgery for primary or recurrent oropharyngeal carcinoma. Arch Otolaryngol Head Neck Surg 2010;136(4):380–4.

68. Al-Khudari S, Bendix S, Lindholm J, Simmerman E, Hall F, Ghanem T. Gastrostomy tube use after transoral robotic surgery for oropharyngeal cancer. ISRN otolaryngology 2013;2013:190364.

69. Gorphe P, Von Tan J, El Bedoui S, Hartl DM, Auperin A, Qassemyar Q, et al. Early assessment of feasibility and technical specificities of transoral robotic surgery using the da Vinci Xi. J Robot Surg 2017;11(4):455–61.

70. Lawson G, Mendelsohn A, Fakhoury R, Van Der Vorst S, Remacle M, Bachy V, et al. Transoral Robotic Surgery Total Laryngectomy. ORL 2018;80(3–4):171–7.

71. Olarte L, Dhir K, Genden E. Excision of a recurrent oropharyngeal malignant lesion utilizing a minimally invasive transoral robotic surgical (TORS) technique. Laryngoscope 2010;120(SUPPL. 3):S44.

72. Asher SA, White HN, Kejner AE, Rosenthal EL, Carroll WR, Magnuson JS. Hemorrhage after transoral robotic assisted surgery. Otolaryngology - Head and Neck Surgery (United States) 2012;147(SUPPL. 2):P59.

73. Yin Tsang RK, Ho WK, Wei WI. Combined transnasal endoscopic and transoral robotic resection of recurrent nasopharyngeal carcinoma. Head Neck 2012;34(8):1190–3.

74. Smith RV, Schiff BA, Sarta C, Hans S, Brasnu D. Transoral robotic total laryngectomy. Laryngoscope 2013;123(3):678–82.

75. Barton B, Riley CA, Hasney C, Moore BA, Flowers T. The submental flap for reconstruction following transoral robotic surgery. Otolaryngology - Head and Neck Surgery (United States) 2017;157(1 Supplement 1):P186–7.

76. Petruzzi G, Zocchi J, Moretto S, Pichi B, Cristalli G, Mercante G, et al. Transoral robotic retropharyngeal lymph node dissection in a recurrent head and neck carcinoma. Head & neck [Internet] 2019;Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medp&NEWS=N&AN=31293005

77. Lawson G, Mendelsohn A, Bachy V, Van Der Vorst S, Remacle M. Transoral robotic surgery total laryngectomy (TORS-TL). European Archives of Oto-Rhino-Laryngology 2012;269(4):1338.

78. Kakarala K, Durmus K, Agrawal A, Carrau RL, Old MO, Teknos TN, et al. Survival following tors for oropharyngeal SCC. Otolaryngology - Head and Neck Surgery (United States) 2012;147(SUPPL. 2):P68.

79. Lubek JE, Shum J, Qaisi M. Transoral robotic surgery in a North American oral & maxillofacial surgery unit: Early data outcomes assessment. British Journal of Oral and Maxillofacial Surgery 2013;51(6):e93–4.

80. Melder K, Walvekar R. Transoral robotic surgery in oropharyngeal cancer: A retrospective study. Journal of Investigative Medicine 2015;63(2):469.

81. Shukla H, Dabas S, Dinesh A, Ranjan R. Transoral robotic surgery for recurrent or residual head and neck cancers: A prospective study of feasibility and functional outcomes. Journal of the American College of Surgeons 2015;221(4 SUPPL. 2):e135.

82. Meulemans J, Delaere P, Vander Poorten V. Early experience in transoral robotic surgery (TORS) for non-oropharyngeal head and neck malignancies: a review of functional and oncologic outcomes. B-ENT 2015;Suppl 24:21–31.

83. Funk R, Stoddard DG, Vencio EF, Garcia JJ, Moore EJ, Foote RL, et al. Risk factors for locoregional recurrence after transoral robotic surgery for HPV+ oropharyngeal squamous cell carcinoma. International Journal of Radiation Oncology Biology Physics 2014;90(1 SUPPL. 1):S122–3.

84. Lawson G, Van Der Vorst S, Mendelsohn A, Bachy V, Desgain O, Sohinto J, et al. Transoral robotic surgery supraglottic laryngectomy (TORS-SL) earlier experience from single institution. European Archives of Oto-Rhino-Laryngology 2012;269(4):1338.

85. Min M, Gowda R, Micklem J, Roos D, Penniment M, Rees G, et al. Patterns of care and outcome in HPV p16+ oropharyngeal squamous cell carcinoma treated at a tertiary hospital. Radiotherapy and Oncology 2014;111(SUPPL. 1):S27.

86. Giurintano JP, Tompkins JJ, Samant S. Learning curve of tors/lp with respect to functional outcome. Otolaryngology - Head and Neck Surgery (United States) 2015;153(1 SUPPL. 1):65.

87. Ghanem T, Olden H, Abrol A, Chang S, Hall F, Williams AM. TORS treated oropharyngeal Cancers: Is p16 status significant? Otolaryngology - Head and Neck Surgery (United States) 2016;155(Supplement 1):P86.

88. Kahn L, Jackson D, Wang Y, Dyer BA, Farwell DG, Bewley A, et al. Outcomes and prognostic grouping of human papillomavirusepositive oropharyngeal squamous cell carcinoma undergoing TORS/TLM and adjuvant radiation therapy. International Journal of Radiation Oncology 2016;96(2 Supplement 1):E390–1.

89. Meulemans J, Vanclooster C, Delaere P, Vander Poorten V. Transoral robotic surgery (TORS) for malignant head and neck cancer: A multicenter retrospective case series. B-ENT 2016;12(Supplement 25):50.

90. Chouake RJ, Ting PG, Chai R, Teng MS, Genden EM, Miles BA. Transoral robotic surgery in human papillomavirus-positive oropharyngeal squamous cell carcinoma. Otolaryngology - Head and Neck Surgery (United States) 2017;157(1 Supplement 1):P97.

91. Gan R, Nistor M, Wijayasingam G, Mortimore S, De M. Transoral partial oropharyngectomy for oropharyngeal cancer. Journal of Laryngology and Otology 2017;131(6):E3.

92. Gupta K, Dabas S. Oncological outcome following intensification of treatment by transoral robotic surgery (TORS) for HPV negative stage IV oropharyngeal cancer: A prospective trial. Annals of Oncology 2017;28(Supplement 10):x101.

93. Hassid S, Van Der Vorst S, Delahaut G, Bachy V, Desgain O, Lawson G. Transoral robotic surgery (TORS) hypopharyngectomy: Feasibility and outcomes. B-ENT 2018;14(Supplement 28).

94. Melville P, Dowthwaite S, Bhuta S. Transoral Robotic Surgery (TORS); State of the Art Imaging and Preoperative Planning. Neuroradiology 2018;60(1 Supplement 1):197.

95. Hwang A, Galati L, Pinheiro-Neto CD. Use of transoral robotic surgery for resection of parapharyngeal space lesions: A case series. Journal of Neurological Surgery Part B: Skull Base 2017;78(Supplement 1).

96. Delahaut G, Gersdorff G, Van Der Vorst S, Bachy V, Desgain O, Lawson G. Transoral robotic total laryngectomy (TORS-TL): The experience of CHU UCL Namur. B-ENT 2018;14(Supplement 28).

97. Krishnan S, Goodyear PWA, Hodge JC, Boase S, Watson K. Robotic assisted minimal access narrow field total laryngectomy. European Archives of Oto-Rhino-Laryngology 2013;270(2 2013):785.

98. Moriniere S, Hammoudi K, Beutter P, Pinlong E. Transoral robotic surgery versus external approach: Oncologic results and comparison of the cost of treatment. Otolaryngology - Head and Neck Surgery (United States) 2013;149(2 SUPPL. 1):P199–200.

99. Olsen SM, Moore EJ, Laborde RR, Garcia JJ, Janus JR, Price DL, et al. Transoral surgery alone for human-papillomavirus-associated oropharyngeal squamous cell carcinoma. Ear Nose Throat J 2013;92(2):76–83.

100. Gersdorff G, Lawson G, Delahaut G, Bachy V, Desgain O, Remacle M, et al. Transoral robotic supraglottic laryngectomy (TORS-SL): The experience of CHU UCL Namur. B-Ent 2019;15 (Supplement 29 Supplement 29):26–26.

101. Speaker RB, O'Dwyer T, Moran T. Robotic head and neck cancer surgery a single center experience of trans-oral robotic surgery. Irish Journal of Medical Science 2019;188 (Supplement 5):S23–4.

102. Hassid SA, Delcour L, Delahaut G, Van Der Vorst S, Lawson G. Transoral robotic surgery and geriatric population: Which beneft? B-Ent 2019;15 (Supplement 29 Supplement 29):63–63.

103. Tsang RK, To VS, Ho AC, Ho W-K, Chan JY, Wei WI. Early results of robotic assisted nasopharyngectomy for recurrent nasopharyngeal carcinoma. Head Neck 2015;37(6):788–93.

104. Han P, Liang FY, Chen RH, Cai Q, Yu ST, Luo MR, et al. [Robotic nasopharyngectomy via combined approach of nose and oral for local recurrent nasopharyngeal carcinoma]. Lin chuang er bi yan hou tou jing wai ke za zhi = Journal of clinical otorhinolaryngology, head, and neck surgery 2018;32(14):1048.

105. Dabas S, Dewan A, Ranjan R, Dewan AK, Puri A, Shah SH, et al. Transoral robotic surgery in management of oropharyngeal cancers: a preliminary experience at a tertiary cancer centre in India. Int J Clin Oncol 2015;20(4):693–700.

106. Poorten VV, Meulemans J, Nuyts S, Clement P, Hermans R, Hauben E, et al. Postoperative photodynamic therapy as a new adjuvant treatment after robot-assisted salvage surgery of recurrent squamous cell carcinoma of the base of tongue. World Journal of Surgical Oncology 2015;13(1):214.

107. Weinstein GS, O'Malley BW, Snyder W, Sherman E, Quon H. Transoral robotic surgery: radical tonsillectomy. Arch Otolaryngol Head Neck Surg 2007;133(12):1220–6.

108. Jayaram SC, Muzaffar SJ, Ahmed I, Dhanda J, Paleri V, Mehanna H. Efficacy, outcomes, and complication rates of different surgical and nonsurgical treatment modalities for recurrent/residual oropharyngeal carcinoma: A systematic review and meta-analysis. Head Neck 2016;38(12):1855–61.

109. Hinni ML, Zarka MA, Hoxworth JM. Margin mapping in transoral surgery for head and neck cancer. Laryngoscope 2013;123(5):1190–8.

110. Morton RP, Fielder CP, Dorman EB. Prediction and prevention of fistulae after major head and neck surgery: a preliminary report. Aust N Z J Surg 1988;58(12):951–3.

111. Dai T-S, Hao S-P, Chang K-P, Pan W-L, Yeh H-C, Tsang N-M. Complications of mandibulotomy: midline versus paramidline. Otolaryngol Head Neck Surg 2003;128(1):137–41.

112. Hutcheson KA, Barringer DA, Rosenthal DI, May AH, Roberts DB, Lewin JS. Swallowing outcomes after radiotherapy for laryngeal carcinoma. Arch Otolaryngol Head Neck Surg 2008;134(2):178–83.

113. Yang H, Han D, Ren X, Luo H, Li X. Investigation of swallowing function and swallowing-related quality of life after partial laryngectomy in Chinese patients with laryngeal carcinoma. Health Qual Life Outcomes 2019;17(1):132.

114. Patterson JM, McColl E, Carding PN, Wilson JA. Swallowing beyond six years post (chemo)radiotherapy for head and neck cancer; a cohort study. Oral Oncology 2018;83:53–8.

115. Hutcheson KA, Lewin JS, Barringer DA, Lisec A, Gunn GB, Moore MWS, et al. Late dysphagia after radiotherapy-based treatment of head and neck cancer. Cancer 2012;118(23):5793–9.

116. Eisbruch A, Kim HM, Feng FY, Lyden TH, Haxer MJ, Feng M, et al. Chemo-IMRT of oropharyngeal cancer aiming to reduce dysphagia: Swallowing organs late complication probabilities and dosimetric correlates. Int J Radiat Oncol Biol Phys 2011;81(3):e93–9.

117. Hutcheson KA, Lewin JS. Functional outcomes after chemoradiotherapy of laryngeal and pharyngeal cancers. Curr Oncol Rep 2012;14(2):158–65.

118. Salassa JR. A functional outcome swallowing scale for staging oropharyngeal dysphagia. Dig Dis 1999;17(4):230–4.

119. List MA, Ritter-Sterr C, Lansky SB. A performance status scale for head and neck cancer patients. Cancer 1990;66(3):564–9.

120. Chen AY, Frankowski R, Bishop-Leone J, Hebert T, Leyk S, Lewin J, et al. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the M. D. Anderson dysphagia inventory. Arch Otolaryngol Head Neck Surg 2001;127(7):870–6.

121. Petkar I, Rooney K, Roe JWG, Patterson JM, Bernstein D, Tyler JM, et al. DARS: a phase III randomised multicentre study of dysphagia- optimised intensity- modulated radiotherapy (Do-IMRT) versus standard intensity- modulated radiotherapy (S-IMRT) in head and neck cancer. BMC Cancer 2016;16(1):770.

122. Owadally W, Hurt C, Timmins H, Parsons E, Townsend S, Patterson J, et al. PATHOS: a phase II/III trial of risk-stratified, reduced intensity adjuvant treatment in patients undergoing transoral surgery for Human papillomavirus (HPV) positive oropharyngeal cancer. BMC Cancer 2015;15:602.

123. Nund RL, Brown B, Ward EC, Maclean J, Roe J, Patterson JM, et al. What Are We Really Measuring? A Content Comparison of Swallowing Outcome Measures for Head and Neck Cancer Based on the International Classification of Functioning, Disability and Health (ICF). Dysphagia 2019;34(4):575–91.

Supplementary tables

Search	Entry
1	Robotic Surgical Procedures/ (5244)
2	(TORS or robot*).ab,ti. (36657)
3	(transoral or "trans oral" or pharyn* or oropharyn* or hypopharyn* or nasopharyn* or glott* or subglott* or supraglott* or larynx* or laryng* or "upper aerodigestive tract" or "H&N" or head or "head and neck" or "head & neck").ab,ti. (458794)
4	exp "Head and Neck Neoplasms"/ (293542)
5	1 or 2 (37067)
6	3 or 4 (663940)
7	(recurren* or salvage).ab,ti. (532127)
8	5 and 6 and 7 (322)

Supplementary table 1: Example search strategy from Ovid MEDLINE(R). Including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to March 15, 2019>

Study	Clearly Stated Aim	Inclusion of Consecutive Patients	Prospective Data Collection	Appropriate Endpoints	Unbiased Assessment of Endpoint	Follow-up Appropriate Length	Loss to Follow-Up less than 5%	Prospective Calculation of Study Size	(Total max 16)
Blanco 2013	2	2	0	2	2	0	0	0	8
Hans 2013	2	0	2	1	2	2	2	0	11
White 2013	2	2	2	2	2	0	0	0	10
Dabas 2015	2	2	2	2	2	1	2	0	13
Krishnan 2017	2	2	2	2	2	2	2	0	14
Meulemans 2017	2	2	2	2	2	1	2	0	13
Morisod 2017	2	2	2	2	2	1	2	0	13
Paleri 2018	2	2	2	2	2	1	2	0	13

Supplementary table 2: MINORS scores for included studies. Items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score for non-comparative studies is 16.