**Novel strategies for managing retropharyngeal lymph node metastases in head and neck and thyroid cancer with TransOral Robotic Surgery (TORS)**

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**Abstract**

Retropharyngeal metastases is encountered in a variety of head and neck malignancies, imposing significant surgical challenges due to their distinct location and proximity to neurovascular structures. Radiotherapy is the recommended treatment in most cases due to its oncological efficacy. However, retropharyngeal irradiation affects the superior pharyngeal constrictor muscles and parotid glands, with the potential for long term dysphagia and xerostomia.

A younger oropharyngeal and thyroid cancer patient demographic is trending, fueling interest in treatment de-escalation strategies. Consequently, reducing radiotoxicity and its long-term effects is of special relevance in modern head and neck oncology practice.

Through its unique ability to safely extirpate these traditionally difficult-to-access retropharyngeal lymph nodes via a natural orifice, TransOral Robotic Surgery (TORS) can considerably lower the surgical morbidity of retropharyngeal lymph node dissection (RPLND), compared to current existing approaches.

This review summarizes the latest developments in the field, exposing current research gaps and discusses specific clinical settings where TORS could enable treatment de-escalation. In early-stage node-negative oropharyngeal cancer, single modality surgical treatment with TORS RPLND may improve risk stratification of metastasis and recurrence in this region. TORS RPLND is also a potentially viable treatment option in salvage of an isolated retropharyngeal node recurrence or in the primary setting of a thyroid malignancy with a single positive retropharyngeal node.

In time, TORS RPLND may provide an alternative de-escalation strategy in these three scenarios. However, with the reported morbidities, further prospective trials with long-term follow up data are required to prove oncological safety and functional benefits over existing strategies.

Abstract word count: 250

Keywords: Transoral robotic surgery, Retropharyngeal lymph node metastases, Head and neck cancer, Thyroid cancer, Salvage treatment

**Main Manuscript**

**Introduction**

Retropharyngeal lymph nodes (RPLN) are recognised as first echelon nodes for tumors originating in the nasopharynx and posterior pharyngeal wall [1,2] and are also among the first echelon nodes of the oropharynx [3]. Hypopharyngeal and cervical oesophageal squamous cell carcinoma (SCC) are other primary site candidates and are linked with regional involvement of this distinct nodal basin [4]. Differentiated thyroid cancer (DTC) is a less commonly recognised origin of retropharyngeal metastasis. A background of extensive N1b disease in the context of residual and/or recurrent DTC has been documented as a more anticipated scenario for retropharyngeal metastasis within this disease category [2,5].

The challenges of surgical access to the retropharyngeal area purports that only limited pathological data is available on the incidence of RPLN metastases. With respect to oropharyngeal squamous cell cancer (OPSCC), surgical series are small and highly selective [2,6]. Although, relatively larger radiology series have reported an approximately 10% rate of RPLN involvement in patients with oropharynx cancer at staging [7–9] independent of human papilloma virus (HPV) status [8,10].

The consensus within the literature is that positive RPLN infers an adverse prognosis in both head and neck and thyroid cancer [5,11], including HPV-related OPSCC [7]. Despite early studies advocating retropharyngeal lymph node dissection (RPLND) [4,12], the historically linked unacceptable morbidity of this procedure stunted its implementation into routine surgical practice [6]. Instead, elective irradiation of ipsilateral and sometimes bilateral RPLN has been incorporated into international radiotherapy target volume guidelines [13]. However, irradiation of the RPLN region inevitably increases radiation dose to adjacent organs at risk, including the parotid glands and superior pharyngeal constrictors, with an increase in treatment impact upon late xerostomia and dysphagia [8].

Current treatment approaches with curative intent for patients with head and neck and thyroid cancer represent an often narrow therapeutic window between maintaining cure rates whilst minimising toxicity. This delicate balance is most obvious in the treatment of HPV-related oropharyngeal malignancy with a younger patient demographic. In these cohort, high cure rates are paramount and standard of care chemoradiotherapy is associated with significant acute side effects [14]. Multiple potential long term side effects may consequently impact their quality of life [15], including xerostomia, degrees of dysphagia extending up to gastrostomy dependence[16].

There are similar considerations in the treatment of DTC which is on the rise, especially in adolescents and young women. This necessitates different management strategies, focused on reducing adjuvant treatment doses of radioactive iodine ablation (RAI), that may impact fertility [17]. Isolated recurrent head and neck cancer in the RPLN is rare, and is considered an indication for reirradiation; however this is associated with significant morbidity with potential for skull base osteoradionecrosis, cranial nerve palsies, radiation myelitis, temporal lobe necrosis and major carotid artery events [18,19].

There has been considerable interest in exploring ‘de-escalation’ strategies in view of the substantial toxicity of chemo-radiotherapy [20], and this remains a research priority as seen in Post-operative Adjuvant Treatment for HPV-positive Tumours (PATHOS), E3311 and NRG HN005 (NCT03952585) [21–24]. The integration of trans-oral surgical resection with stratified adjuvant treatment represents a potential avenue to minimise overall treatment toxicity [25]. However, the presence of retropharyngeal lymphadenopathy significantly complicates the potential surgical plan for head and neck cancer patients, with it being a common exclusion criterion in such studies.

This review aims to identify the available, relevant literature related to addressing RPLND with TransOral Robotic Surgery (TORS). Its scope is to assess whether this is an alternative, feasible and safe technique that should be considered in the management plan for patients with RPLN involvement; with particular focus on patients with OPSCC, DTC and as a potential salvage treatment in the setting of recurrent disease.

**Material & Methods**

A literature search was conducted using PubMed, Scopus, Ovid, Embase and Cochrane databases. The search was current as of 20th November 2021.   
The following terms were used: ("transoral"[All Fields] OR "transorally"[All Fields]) AND ("robot"[All Fields] OR "robots"[All Fields] OR "robotically"[All Fields] OR "robotics"[MeSH Terms] OR "robotics"[All Fields] OR "robotic"[All Fields] OR "robotization"[All Fields] OR "robotized"[All Fields] OR "robots"[All Fields]) AND "retropharyngeal"[All Fields]. The reference lists of the relevant papers were also reviewed.

Inclusion criteria involved studies composed of patients with head and neck (including thyroid) cancer and suspicion of RPLN metastasis based on pre-operative imaging that underwent TORS RPLD as part of their treatment. Both primary and salvage TORS RPLND cases were included.

Exclusion criteria included: studies evaluating pediatric patients, known benign retropharyngeal pathology, approaches to the retropharyngeal space other than TORS (whether open or endoscopic but not robotic assisted) and studies with unspecified heterogeneous cohorts (not permitting segregation of data by primary tumor site). Review articles and articles not published in the English language were excluded.

**Results**

23 articles were found using the reported search. Two authors (G.G. and J.C.F.) independently assessed the titles and abstracts of the identified articles to determine potential relevance. Any disagreement was resolved by consensus. After reviewing the abstracts, 21 papers were selected to be fully appraised in view of their relevance.

10 papers were excluded as follows:

* Five were case reports describing TORS for the excision of benign retropharyngeal masses/pathology (two parathyroid adenomas, one lipoma, one schwannoma, and one vascular malformation)
* Two involved RPLN performed through a non-robotic approach (one endoscopic-assisted and one transcervical after the completion of the lateral neck dissection),
* Two reconsidered contraindications to TORS (retropharyngeal internal carotid arteries)
* One was not in English (Chinese)

Based on design, number of patients and origin (high volume/specialized centres); 11 papers were chosen as representing the best evidence to answer the clinical question and summarized in **Table 1**. A more in-depth review for each study has been outlined in **Table 2** (appendix I).

Further to this, a descriptive analysis of the literature for TORS RPLND in OPSCC, thyroid cancer and head and neck recurrence has been detailed below.

**TORS RPLND in OPSCC**

Byeon et al. (2013) were the first to describe transoral RPLND for metastatic SCC using the da Vinci surgical robot (Intuitive Surgical®, Inc., Sunnyvale, CA) in the clinical setting [11]. Whilst the study’s originality in using TORS for RPLND served as initial supporting evidence for the technique, its preliminary nature meant that it was naturally characterised by numerous limitations [26]. These included a small sample size (n=5), short follow-up period (confined to the inpatient stay) and absence of a control group. Moreover, there was significant heterogeneity in terms of both the primary tumor site (oropharynx and hypopharynx) and more so crucially the extent of additional procedures performed in the same setting (e.g. lateral oropharyngectomy, lateral neck dissection). Thus, this study can be best viewed as proof-of-concept supporting the feasibility of TORS RPLND [27].

Givi et al. (2016) also took on TORS RPLND to manage 12 patients for a mixture of pathologies that included OPSCC (n=9) and papillary thyroid carcinoma (n=3) [28]. The latter group is discussed in the next section. OPSCC patients were compared to matched controls (2:1), where TORS was only used to perform the oropharyngectomy (without proceeding to RPLND). The presence of a control group and mean follow-up exceeding 12 months constituted the key strengths of the study. However, the lack of comparison in follow-up/survival outcomes in the analysis, together with small patient cohort and sample heterogeneity (different primary tumors with mixture of primary and salvage surgery) does raise concerns. The authors concluded that the addition of RPLND to TORS oropharyngectomy carries a significantly higher risk of complications, with an emphasis on dysphagia and aspiration pneumonia. Nonetheless, this needs to be carefully balanced against the 56% pick up rate of occult metastatic disease that they found in the RPLN that was not apparent on pre-operative imaging (all patients underwent pre-operative CT, PET-CT, or both).

The same clinical group published a further study one year later [1]. Comparisons were made between TORS outcomes (and selective neck dissection levels II-IV) with and without RPLND (30 vs. 37 age- and stage-matched controls, respectively) for the treatment of early-stage tonsillar SCC.

This was the largest study reviewed on the subject to date with other strengths relating to the presence of a matched control group and the reporting of a multitude of clinical outcomes. Limitations related primarily to the study’s methodology, in view of the lack of standardization regarding prophylactic vessel ligation and indications for RPLND. The timeline of this cohort between 2010 and 2013 overlaps with their previously published series [28]. Considering the different indications for RPLND between the two publications, a discussion of the differences between the two cohorts would have been a welcome addition.   
Reviewing their more recent study, the authors reported TORS RPLND not being associated with higher complication rates; heavily contrasting with their earlier published findings [28]. This was, in part, explained by the fact that the authors progressed further ahead in their robotic RPLND learning curve at the time of their second study [29,30]. Swallowing outcomes and length of stay (LOS) were reported not be compromised by the addition of RPLND to conventional TORS oropharyngectomy; albeit surrogate measures were used as opposed to validated tools for the assessment of swallowing.   
One further conclusion proposed by the study was the additional value of robotic RPLND as a (pathological) staging tool in patients with N0 lateral neck disease. This was deduced through reports of their RPLN metastatic rate; found to be 20% (6/30). This enabled the possibility of achieving single (surgical) modality treatment in scenarios where this is already accepted practice (11/30 TORS RPLND patients did not receive adjuvant treatment, 9 of which were N0).   
Conversely, only 3.3% (one patient) were upstaged from N1 to N2b following TORS RPLND, triggering an alteration of treatment recommendations (addition of post-operative radiotherapy). With such a low treatment escalation rate, and additional risks of dysphagia and aspiration, the clinical utility of TORS RPLND as a staging procedure in the N+ lateral neck is called into question.

The literature search concluded with a number of case reports or small series, demonstrating the feasibility of TORS RPLND in different specialist centers and treatment settings. These included one case report where the single port da Vinci SP surgical robot (Intuitive Surgical®, Inc., Sunnyvale, CA) was used (n=1) [31] and a small case series (n=3) where TORS RPLND was used to evaluate (radiologically) suspicious RPLNs [3]. In the latter, only one patient was shown not to have metastatic foci on histopathological examination of the excised RPLN. Even in this single case, new findings did not influence the recommendation for adjuvant therapy, as the patient also had lateral neck metastatic disease. This reinforces the point that the role of TORS RPLND in the N+ lateral neck is questionable as it is unlikely to alter adjuvant treatment recommendations [1].

**TORS RPLND in Thyroid Cancer**

The first two cases of TORS RPLND for the management of RPLN metastases from DTC were reported by Moore et al. (2011) [2]. The patients, aged 66 and 73, both presented with recurrent retropharyngeal metastases several years after having undergone total thyroidectomy, neck dissection and RAI for papillary thyroid carcinoma. The first patient had two nodes excised, whilst a solitary node was excised from the second with the operative time being two hours two minutes and two hours 30 minutes, respectively. Complications were only encountered in the first case in the form of odynophagia lasting four days (not requiring a PEG) and a self-limiting secondary hemorrhage that was successfully managed with conservative measures. The patient was well and disease-free at 1-year follow-up. This is the first-in-human study on TORS RPLND, not just for metastatic DTC, but also for any primary site. Whilst this is a significant strength of the paper, it may also address the high complication rates and extended operative times, emphasizing the importance of TORS’ learning curve. Limitations relate to the fact that this was a case report with no long-term follow-up reported for the second patient.

Goepfert (2015) described a further case report on the subject [32]. The report detailed the combination of surgeon-performed intraoperative transoral ultrasound (US) with TORS RPLND for the excision of a metastatic 2.6-centimeter RPLN in a 64-year-old woman that two years prior had undergone total thyroidectomy, neck dissection and RAI for pT3 N1b papillary thyroid carcinoma. The operation was uneventful and total operative time was 35 minutes.

The following year, Givi et al. [28] evaluated 12 patients that underwent TORS RPLND for a mixture of pathologies that included OPSCC (n=9) and papillary thyroid carcinoma (n=3), previously discussed above. All three patients in the DTC group had been previously treated with total thyroidectomy and neck dissection. During the study period, they underwent TORS RPLND procedures and uneventfully resumed oral diet within the first two post-operative days. No complications were noted and they were all confirmed to have metastatic disease on histopathology. Importantly, none of these patients required further treatment with none reported to have evidence of recurrence on latest follow-up (6, 8, and 12 months, respectively).

The most recent, largest, and only comparative study on the subject to date is that by Harries et al. [5], which included 65 patients with RPLN metastases from DTC, of which 38% (25/65) were managed conservatively (observation), 20% (13/65) with non-surgical treatment (eg. RAI, external beam radiotherapy, and/or systemic therapy), and 42% (27/65) underwent surgery (RPLND). From the surgical group, 70% (19/27) had a transcervical approach and 30% (8/27) a transoral approach; of which 22% (6/27) underwent TORS RPLND.

This study carries a number of strengths as it is not only the largest on the subject but it also aimed to directly compare the different management strategies for RPLN metastases from DTC. However, as the authors themselves acknowledge, its limitations make such ‘head-to-head’ comparisons impossible in view of the inherent selection bias present. In the study, there was a tendency for small volume, non-progressive RPLN metastases to be managed conservatively whilst large, progressive ones tended to undergo surgery [33]. Other limitations include its retrospective design, significant heterogeneity and that for the majority of outcomes including within the surgical arm, these were cumulatively reported.

Despite these drawbacks, key conclusions can be derived from this study. Transoral RPLND route appears to be safer and with lower cranial nerve morbidity compared to the transcervical approach, although they are both characterised by equal and high (25%) dysphagia rates. Furthermore, the authors make important recommendations regarding patient selection for the transoral route for RPLND which include the presence of isolated DTC retropharyngeal metastasis located supero-medially (conversely, they advocate the transcervical route for infero-lateral metastatic RPLN and in patients requiring a concurrent lateral neck dissection).

**TORS RPLND in the Salvage Setting**

Two studies have specifically evaluated the role of TORS RPLND in the salvage setting, both published in 2021. Prior to these, there were only a handful of cases reported in the literature, either within larger preliminary studies [28], or published as individual case reports [34]; all of which have already been discussed above.

Ding et al. [18] evaluated TORS RPLND as a salvage option for recurrent nasopharyngeal carcinoma manifesting with RPLN metastases. In all TORS RPLND patients (n=10), oncologic resection was complete with negative margins achieved. However, in two patients, open conversion was necessitated due to failure of identifying the recurrent RPLN(s) transorally.

As expected, most complications were encountered in the open conversion group (one pharyngocervical fistula requiring repair and a hypoglossal nerve palsy, both in the same patient) [35]. In the non-converted TORS RPLND cohort, one patient with grade three dysphagia required nasogastric feeding tube placement. The morbidity reported with TORS RPLND was much lower in comparison to both alternative surgical routes, namely maxillary swing and endoscopic-assisted transcervical approach based on the authors’ previous published experience.

The main strength of this study relates to the novel application of TORS RPLND as a salvage treatment option in recurrent NPC that had not been reported before. The limitations relates to pre-operative selective employment of interventions, in particular pre-operative internal carotid artery (ICA) embolization (preceded by balloon occlusion testing) and induction chemotherapy, without clear pre-defined criteria. The impact of such interventions on the reported safety and oncological outcomes witnessed in this series is uncertain and undetermined, with long-term neurological outcomes for those patients that underwent pre-operative ICA embolization requiring further scrutiny. Finally, the introduction of intraoperative US in the latter half of the cohort appears to represent an important adjunct in terms of reducing the risk of open conversion (and thus complications) as well as operative time and blood loss (although the latter two did not reach statistical significance).

The second and latest study on the subject by Dabas et al. [19] also included 10 patients. However, in this study TORS RPLND was employed as a standalone salvage treatment for recurrent disease originating from a multitude of different primary tumor sites in the head and neck.

In nine cases, one RPLN was excised, whilst in the last case, two were removed, with all 11 confirmed to be metastatic on histopathological examination (extranodal extension confirmed in three specimens). One case necessitated open conversion (via a transcervical approach) due to ICA encasement. No major complications were reported or tracheostomies performed, although all patients were fed via a nasogastric feeding tube for five days following surgery. The mean console time was 28.5 minutes (with an additional mean docking time of five minutes).

These early findings support TORS RPLND as a safe, feasible and promising oncological treatment and reiterate the importance of careful patient selection for TORS (one of the exclusion criteria was an inter-incisor distance less than three centimeters) [36]. The key strength of this study is that oncological outcomes were evaluated in addition to functional ones though its small sample size and significant heterogeneity made it unfeasible to comment on its potential impact on survival. This mandates larger prospective studies with inclusion of a control group, another important study limitation.

**Discussion**

RPLN metastases are encountered in a variety of head and neck malignancies and pose significant surgical challenges in view of their distinct location and proximity to critical neurovascular structures (**Figure 1**). Of note, multiple radiology series have demonstrated that RPLN involvement is limited in head and squamous cell carcinomas to the lateral rather than medial retropharyngeal compartment [8–10,37,38]. This is reflected in updated international radiotherapy contouring atlases [39] and lymph node level selection guidelines [13], which can logically also be reflected in surgical approaches.

Recommended treatment of RPLN involves (chemo)radiotherapy in many squamous cell carcinoma cases [40]. Of particular concern is the proximity of this region to the superior pharyngeal constrictor muscles, identified as a key organ at risk related to long term swallow dysfunction [41], fueling a renewed interest in de-escalation strategies [21]. Recognition of the potential toxicity impact of irradiation of the RPLN region has been an important factor behind a number of international radiation oncologists arguing in favour of sparing the contralateral retropharyngeal nodal basins in the clinically uninvolved side of the neck [42–44].

In addition to concern regarding the potential toxicity of irradiation of the RPLN, consideration of a surgical approach to the retropharyngeal region has been driven by:

1. Advancement of TORS technology
2. Widespread uptake as a treatment modality in relation to other upper aerodigestive tract tumours
3. High morbidity from traditional open surgical approaches to the retropharynx.

Proxy evidence from the published literature offers the potential that morbidity resulting from TORS RPLND in early series can be ameliorated once the learning curve has been surpassed. The ability to surgically resect this region without an open operation certainly offers another potential treatment modality for this relatively inaccessible area. However, the role for this surgery is far from clear, and the evidence from early proponents of this technique still offers significant concerns from both an oncological and patient safety aspect.

Higher quality evidence is needed and the studies reported all offer level IIIb/IV evidence at best with heterogenous patients groups, short follow-up, no quality of life data and a lack of standardized reporting tools for dysphagia and other complications. Furthermore, the morbidity data is far from insignificant. Although attempts are made in the literature for case-control comparisons with patients not undergoing RPLND, the retrospective nature makes this difficult to interpret with a high risk of bias.

However, complication rates of significant dysphagia (with prolonged nasogastric feeding), pneumonia, bleeding and velopharyngeal insufficiency are all described and common. Whilst we appreciate that any treatment modality addressing this difficult anatomical region will have a morbidity profile; the lack of evidence in favor of RPLND demonstrating a change in oncological management plan for OPSCC in Troob et al.’s case-control study [1] is concerning. Nevertheless, the poor prognosis that RPLN involvement imparts does help alleviate and justify this concern. The potential for an isolated positive RPLN in the absence of other nodal disease in such OPSCC cases is highly unlikely [45]. Subsequently, given the poor prognosis on disease behaviour that even a single node in this region would predict, avoidance of adjuvant treatment is unlikely [9].  
The involvement of retropharyngeal nodal basin in positive lateral neck disease is negatively associated with locoregional control, recurrence-free, disease-free, and overall survival [9]. In OPSCC, this cohort are therefore inappropriate to target in de-intensification strategies and RPLND would be likely to add significant complications to the overall treatment package, without eliminating the need for adjuvant therapy.

However, on this point one area of potential interest for a RPLND is in the management of some early stage oropharyngeal, node-negative cancer patients, for whom single modality treatment with radiotherapy or surgery is intended. International guidelines for the selection of uninvolved lymph node levels for elective irradiation include the ipsilateral RPLN region for even radiologically node negative oropharyngeal cancer patients [13]. By contrast, with standard transoral surgical approaches combined with a neck dissection the RPLN is untreated. Detailed recurrence pattern analyses from single modality surgical treatment of this type will help stratify which of these patients are at risk of RPLN metastasis and require elective treatment of this region. However, currently, in the absence of a RPLND, this represents an inherent limitation of a surgical approach, for patients with a pattern of disease suggestive of a RPLN risk, for example patients with soft palate involvement which carries an increased risk of RPLN metastases [8]. Development of a safe approach to a RPLND would increase the group of patients for whom a trans-oral surgical approach may offer an alternative to radiotherapy. This is not a cohort of patients addressed with the current evidence base for RPLND.

The published series addressing TORS RPLND certainly demonstrate that this is a feasible approach to the RPLN, and a potential desirable alternative to traditional open approaches. The low level oncological data of TORS RPLND support further research into two further clinical scenarios: the first relates to the management of an isolated RPLN recurrence in the salvage setting of head and neck malignancy; the second, for therapeutic management of confirmed DTC metastasis. Both scenarios would require detailed consent of the potential complications as well as comprehensive multidisciplinary support, with pre- and post-op speech and language therapy involvement of key importance. Indeed, thyroid indications are perhaps even more nuanced given that most retropharyngeal involvement is in a recurrent disease setting and even then, small, non-progressive nodes appear safe to be observed [5].

In summary, specialist centres report a feasible minimally invasive TORS approach to the retropharynx, providing an alternative surgical approach compared to open techniques. The procedure still demonstrates a significant morbidity burden, even after robotic learning curve progression, and therefore patients and multidisciplinary teams must be fully engaged with a prolonged post-operative recovery.

The potential role for TORS RPLND in de-intensification strategies has not been adequately demonstrated and this rare presentation makes a multi-centre randomized control trial unlikely and indeed undesirable given the poor prognostic group involved. However the role of RPLND in node-negative OPSCC deserves further investigation, allowing the potential of single modality (surgery) to address a typically at risk site. Isolated disease recurrence in a salvage setting would appear to represent an appropriate indication, in a carefully selected patient and confined to high volume centres, with experienced head and neck surgeons trained in both open and transoral robotic surgery. Thyroid cancer patients should be considered separately and an update on the long-term natural history of recurrent RPLND in this setting would be welcome. In line with modern oncological practice, multidisciplinary input remains paramount for patient optimization and recovery.

**References**

[1] Troob S, Givi B, Hodgson M, Mowery A, Gross ND, Andersen PE, et al. Transoral robotic retropharyngeal node dissection in oropharyngeal squamous cell carcinoma: Patterns of metastasis and functional outcomes. Head Neck 2017;39:1969–75. https://doi.org/10.1002/hed.24786.

[2] Moore MW, Jantharapattana K, Williams MD, Grant DG, Selber JC, Holsinger FC. Retropharyngeal lymphadenectomy with transoral robotic surgery for papillary thyroid cancer. J Robot Surg 2011;5:221–6. https://doi.org/10.1007/s11701-011-0269-4.

[3] Park YM, Cha D, Koh YW, Choi EC, Kim SH. Transoral robotic surgery with transoral retropharyngeal lymph node dissection in patients with tonsillar cancer: Anatomical points, surgical techniques, and clinical usefulness. J Craniofac Surg 2019;30:145–8. https://doi.org/10.1097/SCS.0000000000004994.

[4] Amatsu M, Mohri M, Kinishi M. Significance of Retropharyngeal Node Dissection at Radical Surgery for Carcinoma of the Hypopharynx and Cervical Esophagus. Laryngoscope 2001;111(6):1099-103.

[5] Harries V, McGill M, Tuttle RM, Shaha AR, Wong RJ, Shah JP, et al. Management of Retropharyngeal Lymph Node Metastases in Differentiated Thyroid Carcinoma. Thyroid 2020;30:688–95. <https://doi.org/10.1089/thy.2019.0359>.

[6] Chung EJ, Kim GW, Cho BK, Cho SJ, Yoon DY, Rho YS. Retropharyngeal Lymph Node Metastasis in 54 Patients with Oropharyngeal Squamous Cell Carcinoma Who Underwent Surgery-Based Treatment. Ann Surg Oncol 2015;22:3049–54. https://doi.org/10.1245/s10434-014-4364-4.

[7] Lin TA, Garden AS, Elhalawani H, Elgohari B, Jethanandani A, Ng SP, et al. Radiographic retropharyngeal lymph node involvement in HPV-associated oropharyngeal carcinoma: Patterns of involvement and impact on patient outcomes. Cancer 2019;125:1536–46. https://doi.org/10.1002/cncr.31944.

[8]Iyizoba-Ebozue Z, Murray LJ, Arunsingh M, Vaidyanathan S, Scarsbrook AF, Prestwich RJD. Incidence and patterns of retropharyngeal lymph node involvement in oropharyngeal carcinoma. Radiother Oncol. 2020;142:92–9. https://doi.org/10.1016/j.radonc.2019.07.021.

[9] Gunn GB, Debnam JM, Fuller CD, Morrison WH, Frank SJ, Beadle BM, et al. The impact of radiographic retropharyngeal adenopathy in oropharyngeal cancer. Cancer 2013;119:3162–9. https://doi.org/10.1002/cncr.28195.

**[10]** Tang C, Komakula S, Chan C, Murphy JD, Jiang W, Kong C, et al. Radiologic assessment of retropharyngeal node involvement in oropharyngeal carcinomas stratified by HPV status. Radiother Oncol 2013;109:293–6. https://doi.org/10.1016/j.radonc.2013.09.001.

[11] Byeon HK, Duvvuri U, Kim WS, Park YM, Hong HJ, Koh YW, et al. Transoral robotic retropharyngeal lymph node dissection with or without lateral oropharyngectomy. J Craniofac Surg 2013;24:1156–61. https://doi.org/10.1097/SCS.0b013e318293f860.

[12] Kamiyama R, Saikawa M, Kishimoto S. Significance of retropharyngeal lymph node dissection in hypopharyngeal cancer. Jpn J Clin Oncol 2009;39:632–7. https://doi.org/10.1093/jjco/hyp080.

[13] Biau J, Lapeyre M, Troussier I, Budach W, Giralt J, Grau C, et al. Selection of lymph node target volumes for definitive head and neck radiation therapy: a 2019 Update. Radiother Oncol 2019;134:1–9. https://doi.org/10.1016/j.radonc.2019.01.018.

[14] Nutting CM, Morden JP, Harrington KJ, Sydenham MA, Emson M, Hall E, et al. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Onco 2011;12:127–63. https://doi.org/10.1016/S1470.

[15] Langendijk JA, Doornaert P, Verdonck-de Leeuw IM, Leemans CR, Aaronson NK, Slotman BJ. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. Journal of Clinical Oncology 2008;26:3770–6. https://doi.org/10.1200/JCO.2007.14.6647.

[16] Dixon L, Ramasamy S, Cardale K, Dyker K, Garcez K, Lee LW, et al. Long term patient reported swallowing function following chemoradiotherapy for oropharyngeal carcinoma. Radiother Oncol 2018;128:452–8. <https://doi.org/10.1016/j.radonc.2018.06.014>.

[17] Scott AR, Stoltzfus KC, Tchelebi LT, Trifiletti DM, Lehrer EJ, Rao P, et al. Trends in Cancer Incidence in US Adolescents and Young Adults, 1973-2015. JAMA Netw Open 2020;3:e2027738. https://doi.org/10.1001/jamanetworkopen.2020.27738.

[18] Ding X, Lin QG, Zou X, Liu YP, Hua YJ, Xie YL, et al. Transoral Robotic Retropharyngeal Lymph Node Dissection in Nasopharyngeal Carcinoma With Retropharyngeal Lymph Node Recurrence. Laryngoscope 2021;131:E1895–902. https://doi.org/10.1002/lary.29319.

[19] Dabas SK, Chaddha Y, Sharma A, Shukla H, Ranjan R, Gurung B, et al. Robotic transoral approach for salvage retropharyngeal node dissection: an analysis of functional and oncological outcomes. J Robot Surg 2021. https://doi.org/10.1007/s11701-021-01241-4.

[20] Anderson CM, Kimple RJ, Lin A, Karam SD, Margalit DN, Chua MLK. De-Escalation Strategies in HPV-Associated Oropharynx Cancer—Are we Putting the Cart Before the Horse? Int J Radiat Oncol Biol Phys Biology Physics 2019;104:705–9. https://doi.org/10.1016/j.ijrobp.2019.02.054.

[21] Iorio GC, Arcadipane F, Martini S, Ricardi U, Franco P. Decreasing treatment burden in HPV-related OPSCC: A systematic review of clinical trials. Crit Rev Oncol Hematol 2021;160. https://doi.org/10.1016/j.critrevonc.2021.103243.

[22] Kovatch KJ, Hoban CW, Shuman AG. Thyroid cancer surgery guidelines in an era of de-escalation. Eur J Surg Oncol 2018;44:297–306. https://doi.org/10.1016/j.ejso.2017.03.005.

[23] Ferris RL, Flamand Y, Weinstein GS, Li S, Quon H, Mehra R, et al. Phase II Randomized Trial of Transoral Surgery and Low-Dose Intensity Modulated Radiation Therapy in Resectable p16+ Locally Advanced Oropharynx Cancer: An ECOG-ACRIN Cancer Research Group Trial (E3311). J Clin Oncol. 2021:JCO2101752. https://doi.org/10.1200/JCO.21.01752.

[24] 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. https://doi.org/10.1186/s12885-015-1598-x.

[25] Carnevale C, Ortiz-González I, Ortiz-González A, Bodi-Blanes L, Til-Pérez G. Early T1-T2 stage p16+ oropharyngeal tumours. Role of upfront transoral robotic surgery in de-escalation treatment strategies. A review of the current literature. Oral Oncol2021;113. https://doi.org/10.1016/j.oraloncology.2020.105111.

[26] Garas G, Cingolani I, Panzarasa P, Darzi A, Athanasiou T. Network analysis of surgical innovation: Measuring value and the virality of diffusion in robotic surgery. PLoS ONE 2017;12. https://doi.org/10.1371/journal.pone.0183332.

[27] Garas G, Cingolani I, Patel V, Panzarasa P, Alderson D, Darzi A, et al. Surgical Innovation in the Era of Global Surgery: A Network Analysis. Ann Surg 2020;271:868–74. https://doi.org/10.1097/SLA.0000000000003164.

[28] Givi B, Troob SH, Stott W, Cordeiro T, Andersen PE, Gross ND. Transoral robotic retropharyngeal node dissection. Head Neck 2016;38:E981–6. https://doi.org/10.1002/hed.24140.

[29] Tolley N, Arora A, Palazzo F, Garas G, Dhawan R, Cox J, et al. Robotic-assisted parathyroidectomy: A feasibility study. Otolaryngol Head Neck Surg 2011;144:859–66. https://doi.org/10.1177/0194599811402152.

[30] Tolley N, Garas G, Palazzo F, Prichard A, Chaidas K, Cox J, et al. Long-term prospective evaluation comparing robotic parathyroidectomy with minimally invasive open parathyroidectomy for primary hyperparathyroidism. Head Neck. 2016;38 Suppl 1:E300-6. https://doi.org/10.1002/hed.23990

[31] Tsang RK, Wong EWY, Chan JYK. Transoral radical tonsillectomy and retropharyngeal lymph node dissection with a flexible next generation robotic surgical system. Head Neck. 2018;40(6):1296-1298. https://doi.org/10.1002/hed.25118.

[32] Goepfert RP, Liu C, Ryan WR. Trans-oral robotic surgery and surgeon-performed trans-oral ultrasound for intraoperative location and excision of an isolated retropharyngeal lymph node metastasis of papillary thyroid carcinoma. Am J Otolaryngol 2015;36:710–4. https://doi.org/10.1016/j.amjoto.2015.04.011.

[33] Garas G, Ibrahim A, Ashrafian H, Ahmed K, Patel V, Okabayashi K, et al. Evidence-based surgery: Barriers, solutions, and the role of evidence synthesis. World J Surg 2012;36:1723–31. https://doi.org/10.1007/s00268-012-1597-x.

[34] Petruzzi G, Zocchi J, Moretto S, Pichi B, Cristalli G, Mercante G, Spriano G, De Virgilio A, Pellini R. Transoral robotic retropharyngeal lymph node dissection in a recurrent head and neck carcinoma. Head Neck. 2019;41(11):4051-4053. https://doi.org/10.1002/hed.25874.

[35] Garas G, Markar SR, Malietzis G, Ashrafian H, Hanna GB, Zacharakis E, et al. Induced Bias Due to Crossover Within Randomized Controlled Trials in Surgical Oncology: A Meta-regression Analysis of Minimally Invasive versus Open Surgery for the Treatment of Gastrointestinal Cancer. Ann Surg Oncol 2018;25:221–30. https://doi.org/10.1245/s10434-017-6210-y.

[36] Arora A, Kotecha J, Acharya A, Garas G, Darzi A, Davies DC, et al. Determination of biometric measures to evaluate patient suitability for transoral robotic surgery. Head Neck 2015;37:1254–60. <https://doi.org/10.1002/hed.23739>.

[37] Bussels B, Hermans R, Reijnders A, Dirix P, Nuyts S, van den Bogaert W. Retropharyngeal nodes in squamous cell carcinoma of oropharynx: Incidence, localization, and implications for target volume. Int J Radiat Oncol Biol Phys 2006;65:733–8. <https://doi.org/10.1016/j.ijrobp.2006.02.034>.

[38] Samuels SE, Vainshtein J, Spector ME, Ibrahim M, McHugh JB, Tao Y, et al. Impact of retropharyngeal adenopathy on distant control and survival in HPV-related oropharyngeal cancer treated with chemoradiotherapy. Radiotherapy and Oncology 2015;116:75–81. <https://doi.org/10.1016/j.radonc.2015.06.006>.

[39] Grégoire V, Ang K, Budach W, Grau C, Hamoir M, Langendijk JA, et al. Delineation of the neck node levels for head and neck tumors: A 2013 update. DAHANCA, EORTC, HKNPCSG, NCIC CTG, NCRI, RTOG, TROG consensus guidelines. Radiotherapy and Oncology 2014;110:172–81. https://doi.org/10.1016/j.radonc.2013.10.010.

[40] Gross ND, Ellingson TW, Wax MK, Cohen JI, Andersen PE. Impact of retropharyngeal lymph node metastasis in head and neck squamous cell carcinoma. Arch Otolaryngol Head Neck Surg. 2004;130(2):169-73. https://doi.org/10.1001/archotol.130.2.169

[41] Strojan P, Hutcheson KA, Eisbruch A, Beitler JJ, Langendijk JA, Lee AWM, et al. Treatment of late sequelae after radiotherapy for head and neck cancer. Cancer Treat Rev2017;59:79–92. https://doi.org/10.1016/j.ctrv.2017.07.003.

[42] Spencer CR, Gay HA, Haughey BH, Nussenbaum B, Adkins DR, Wildes TM, et al. Eliminating radiotherapy to the contralateral retropharyngeal and high level ii lymph nodes in head and neck squamous cell carcinoma is safe and improves quality of life. Cancer 2014;120:3994–4002. https://doi.org/10.1002/cncr.28938.

[43] Kjems J, Gothelf AB, Håkansson K, Specht L, Kristensen CA, Friborg J. Elective nodal irradiation and patterns of failure in head and neck cancer after primary radiation therapy. Int J Radiat Oncol Biol Phys 2016;94:775–82. https://doi.org/10.1016/j.ijrobp.2015.12.380.

[44] Leeman JE, Gutiontov S, Romesser P, McBride S, Riaz N, Lee N, et al. Sparing of high retropharyngeal nodal basins in patients with unilateral oropharyngeal carcinoma treated with intensity modulated radiation therapy. Pract Radiat Oncol 2017;7:254–9. https://doi.org/10.1016/j.prro.2016.11.002.

[45] Vartanian JG, Pontes E, Agra IM, Campos OD, Gonçalves-Filho J, Carvalho AL, et al. Distribution of metastatic lymph nodes in oropharyngeal carcinoma and its implications for the elective treatment of the neck. Arch Otolaryngol Head Neck Surg 2003;129(7):729-32. https://doi.org/10.1001/archotol.129.7.729

**Figure Caption**

**Figure 1.** Transoral anatomical illustration of the retropharyngeal lymph node group. The classic division into 2 anatomically distinct subgroups, namely the medial (yellow) and lateral (purple) chains is depicted. The latter are also known as the nodes of Rouviere. Note their close proximity to critical neurovascular structures including the internal carotid artery, cervical sympathetic chain (superior cervical ganglia), and medial pterygoid, superior pharyngeal constrictor, and longus colli muscles.

**Table 1**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Study  (year) | Study Type  (EL) | Primary Ca Site (no. of patients) | Measured Outcomes | Strengths | Limitations | | Conclusions |
| Byeon et al  (2013) [11] | CS (IV) | OPSCC (4; 3 T2, 1T3)  HPSCC (1) | Complications/ BL Lymph node yield  Operative time  NGT feed duration | First study evaluating TORS; RPLND as primary treatment | Small study;  No follow-up;  Heterogenous sample | Feasible & Safe;  No increased risk of fistula formation | |
| Givi et al (2016) [28] | CCS (IIIb) | OPSCC w RPLND  (9; 2 recurrence) OPSCC without RPLND (24) PTC(3) | Complications Follow up NGT Feed duration  LOS | Control group presence;  Mean follow-up exceeds 12 months | Small cohort;  Follow-up not stated for control group;  Heterogeneous sample;  Selective comparison with OPSCC only | Significantly higher complications rates;  None of PTC group required further treatment | |
| Troob et al  (2017) [1] | CCS (IIIb) | Tonsil OPSCC w RPLND (30)  Tonsil OPSCC without RPLND (37) | Surgical Complications weight/ BMI change  NGT feed duration LOS | Largest study to date;  Control group present;  Several reported outcomes | Short follow-up period;  Significant overlap with previous study (Givi 2016);  No standardization of measured outcomes | Does not increase risk of complications, LOS or NGT dependence;  Valuable staging information in N0/N1 | |
| Tsang et al  (2018) [31] | CR  (V) | Tonsil OPSCC T1N2b HPV +ve (1) | Surgical margins  Complications  Operative time  NGT feed & LOS | First to assess safety of da Vinci SP robot in RPLND | Single patient;  Short follow up period | Feasible to perform RPLND as single surgery with primary tumor excision | |
| Petruzzi et al (2019) [34] | CR  (V) | Isolated RPLN metastasis (1) | Surgical Margins  Complications  Operative Time  NGT feed duration  LOS | First study to asses feasibility of TORS RPLND in recurrent cancer treatment | Single patient  Not possible to comment on need for tracheostomy (previous laryngectomy) | TORS RPLND is safe and feasible for recurrent cancer in retropharynx, even if previous radiotherapy | |
| Park et al  (2019) [3] | CS  (IV) | Tonsillar OPSCC (3) | Operative Findings  Complications  Lymph Node yield | TORS potential for diagnostic importance in RPLN | Smll study & no control group; No follow-up | Morbidity of TORS RPLND is minimal;  Oropharyngeal defects heal by 2nd intention;  Imaging accuracy of RPLN is limited | |
| Moore et al  (2011) [2] | CR (V) | DTC (2; previous total thyroidectomy & RAI) | Complications  Operative Time | First study to evaluate TORS RPLND in DTC | Small cohort & no control group; no follow-up | Morbidity compared to conventional approaches is minimal | |
| Goepfert et al (2015)  [32] | CR (V) | T3N1b DTC (1) | Complications  Operative Time  LOS  Follow-up | Use of transoral US;  Low operative time, no complications; Complete RAI uptake on follow-up | Single patient and short follow-up;  No validated tool for dysphagia | Transoral US can further add to safety and oncological value;  Low morbidity provided careful patient selection and expertise | |
| Harries et al  (2020) [5] | CS (IV) | DTC (25 conservative,  13 non-surgical;  27 surgery – 6 TORS) | Disease Specific Survival & metastasis Free Probability  Complications | Evaluated different management for RPLN in DTC | Retrospective study  Selection bias;  Cannot differentiate TORS RPLND from non-robotic approaches | TORS RPLND less complications than transcervical approach; High dysphagia rate;  Recommend TORS in supero-medial RPLN | |
| Ding et al.  (2020) [18] | CS  (IV) | Recurrent NPC (10) | Surgical Margins  Complications  Relapse free survival  Intra-operative US Follow-up | First to study TORS RPLND as salvage in recurrent NPC;  Relatively Long follow-up | Sample Size & retrospective design;  Pre-op embolization and induction chemotherapy may impact safety/ oncological outcomes | TORS RPLND feasible in recurrent NPC; Associated with lower morbidity compared to other approaches | |
| Dabas et al (2021) [19] | CS  (IV) | OPSCC (6), Nasopharynx (1), DTC (1), Ethmoid sinus (1), Unknown primary (1). 9 previously treated with RT | Lymph Node Yield  Complications  Operative Time  NGT dependence/ Tracheostomy  LOS | Only Study to assess TORS RPLND for salvage treatment;  Relatively Long Follow-up period | Sample size & retrospective design;  Heterogenous sample;  No control group | TORS RPLND is feasible in the salvage setting  Patient selection is important - consider ICA encasement and inter-incisor distance | |

**Table 1. Summary of literature reporting the role of TORS for retropharyngeal metastases in head and neck and thyroid cancer.**

Abbreviations: EL – Evidence Level; CS – Case Series; CCS - Case Control Study; CR – Case report; TORS – transoral robotic surgery; RPLND – retropharyngeal lymph node dissection; OPSCC – oropharyngeal squamous cell carcinoma; HPSCC – hypopharyngeal squamous cell carcinoma; NPC – nasopharyngeal carcinoma; PTC – papillary thyroid cancer; RAI – radioactive iodine ablation; LOS – length of stay; HPV – Human Papilloma Virus; BMI – body mass index; PEG – percutaneous endoscopic gastrostomy; US – ultrasound; ENE – extranodal extension.

**Table 2 (Appendix I)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Byeon et al. 2013 (South Korea)** [11] | | | *Case Series (Retrospective): Level IV Evidence* |
| Patient Group | 5 patients; mean age 56 years (range: 38-69) | | |
| Aetiology of Disease Studied | OPSCC (total n=4: tonsillar T2 n=3, tonsillar T3 n=1), HPSCC (total n=1: posterior pharyngeal wall T2) | | |
| Operative Interventions | All OPSCC patients had N2b disease, underwent Selective neck dissections (levels II-IV) before TORS (single-stage procedure). 2 patients had bilateral neck dissections.  HPSCC patient had N1 disease (retropharyngeal); neck not treated for disease | | |
| Measured Outcomes | Safety and feasibility of TORS RPLND with da Vinci surgical robot (Intuitive Surgical®, Inc., Sunnyvale, CA) | | |
| * Complications & Blood Loss | No complications (0 fistulae), Intraoperative blood loss: 11.2+1.5ml | | |
| * Lymph yield & ratio (RPLND) | Mean lymph node yield: 1 (range: 1-2); involved retropharyngeal lymph node excised in 4/5 cases | | |
| * Operative & Console Time | Mean total TORS operative time: 84+18.5min; mean console time for RPLND: 29.2+9.4min | | |
| * Duration of NGT feed | Mean duration of nasogastric feeding tube dependence: 5 days (range: 1-13 days) | | |
| * Need for Covering Tracheostomy | 1 patient required a covering tracheostomy with 14-day decannulation time; in patient necessitating reconstruction with a free flap (returned to oral diet after 13 days and hospitalised for 24 days) | | |
| * LOS | 11 days (range: 7-24) | | |
| Study Strengths | First clinical study to evaluate the safety and feasibility of TORS for performing RPLND as primary treatment for metastatic squamous cell carcinoma of the head and neck | | |
| Study Limitations | * Small study (n=5), with a retrospective design and no control group * No follow-up beyond immediate post-operative period * Heterogeneous sample, despite small population, both in terms of primary tumor site (oropharynx and hypopharynx) and crucially type/extent of additional surgery performed as single stage | | |
| Conclusions | * TORS is a feasible & safe minimally invasive approach for RPLND +/- lateral oropharyngectomy * TORS RPLND does not appear to increase the risk of fistula formation (even when lateral neck dissection is performed as single-stage procedure) * The role of TORS RPLND when free flap reconstruction is required appears questionable | | |
| **Givi et al. 2016 (USA)** [28] | | *Single centre case series & case control study (for OPSCC group) series (Retrospective): Level IIIb Evidence* | |
| Patient Group | 12 patients; Median age 63 years (range: 43-73) | | |
| Aetiology of Disease Studied | OPSCC (total n=9: 2 patients treated for recurrence), OPSCC matched controls (TORS without RPLND, n=24) PTC (n=3, all previously treated with thyroidectomy and neck dissection) | | |
| Operative Interventions | TORS for RPLND | | |
| Measured Outcomes | Assess risk-benefit ratio of elective RPLND, OPSCC group compared with matched controls | | |
| * Complications | Complication rates were higher in OPSCC TORS RPLND vs. OPSCC control (78% vs. 33%, *p*=0.02) 66% overall complication rate for TORS RPLND group (n=8): aspiration pneumonitis (n=5),Horner’s syndrome (n=1), Velopalatine insufficiency with Horner’s syndrome (n=1) & Haemorrhage requiring return to theatre (n=1) | | |
| * Follow-up | Median 10 months (mean: 14, range: 2.4-24.3) | | |
| * Duration of NGT feed & LOS | OPSCC control vs. OPSCC TORS RPLND groups: no difference in duration of NGT tube dependence or LOS | | |
| Study Strengths | Control group present and mean follow-up period exceeding 12 months | | |
| Study Limitations | * Small patient cohort (n=11) * Follow up status reported for TORS RPLND group but not control group * Heterogeneous sample, with different pathologies (OPSCC/PTC) & primary/recurrent disease * Selective comparison for OPSCC group only * No validated tools used for dysphagia evaluation | | |
| Conclusions | * TORS RPLND is feasible & safe (PTC & OPSCC), although exhibited significantly higher complication rates * 56% of OPSCC patients treated with TORS RPLND had occult metastatic disease * None of the 3 PTC patients required further treatment, with no evidence of recurrence reported on their follow-up (6, 8, and 12 months, respectively) | | |
| **Troob et al. 2017 (USA)** [1] | | | *Case Control Study: Level IIIb Evidence* |
| Patient Group | 30 patients TORS RPLND (median age 61 years, range: 44-75 years)  37 matched controls (median age 60 years, range: 40-88 years) undergoing TORS without RPLND | | |
| Aetiology of Disease Studied | Both groups had early (T1 or T2) primary OPSCC tonsillar tumours, only 1 patient in each group having a T3 tumour with the vast majority (in both groups) being HPV-positive | | |
| Measured Outcomes | Safety and feasibility of TORS RPLND with da Vinci surgical robot (Intuitive Surgical®, Inc., Sunnyvale, CA) | | |
| * Incidence and grade of surgical complications * Complications &  post-operative haemorrhage * Net changes in weight and BMI * Duration of NGT feed * LOS | Metastatic OPSCC in the retropharyngeal lymph nodes was detected in 6 patients (20% of TORS RPLND cases). The results of TORS RPLND altered the recommendations for adjuvant therapy in 1 patient (3.3%). There was no statistically significant difference in *complications* between the TORS RPLND and control groups (10/30 vs. 9/37), *post-operative haemorrhage* (6/30 vs. 7/37, *p*=0.98), pre- and post-operative *net changes in weight* (5.5kg (SD=3.5kg) vs. 3.2kg (SD=3.2kg), respectively, *p*=0.18) & *BMI* (0.7kgm-2 vs. 1.4kgm-2, respectively, *p*=0.27), *length of NGT dependence* (median: 12 vs. 9 days group, p=0.89) or *LOS* (median: 4 days for both groups, range: 2-11 days vs. 3-17 days, *p*=0.58) | | |
| Study Strengths | Largest study to date, control group present, numerous clinical outcomes reported | | |
| Study Weaknesses | * Short follow-up period * Potential significant overlap of cohorts with previously reported series [28] * Vessel ligation for postoperative haemorrhage prevention was performed at the surgeon’s discretion; this lack of standardization makes postoperative haemorrhage rates challenging to compare * Lack of standardization regarding duration of NGT dependence; patients who received a PEG at the time of surgery were excluded from the duration of feeding tube use * Indications for RPLND were not standardised but based on surgeon preference * No validated tools to assess swallowing outcomes were used | | |
| Conclusions | * TORS RPLND is feasible & safe. It does not substantially increase the risk of complications, LOS, or duration of NGT dependence compared to TORS alone for early tonsillar tumours (T1-T2) * TORS RPLND may provide valuable staging information in N0-N1 disease; although the number of patients that have altered management based on RPLND pathology report is very small. | | |
| **Tsang et al. 2018 (Hong Kong)** [31] | | | *Case Report: Level V Evidence* |
| Patient Group | 63-year-old male | | |
| Aetiology of Disease Studied | T1 N2b M0 HPV-positive SCC of left tonsil | | |
| Operative Interventions | RPLND immediately after TORS oropharyngectomy with no intra- and post-operative complications | | |
| Measured Outcomes | Evaluation of safety & feasibility of TORS RPLND with single port robotic system da Vinci SP surgical robot (Intuitive Surgical®, Inc., Sunnyvale, CA) | | |
| * Pathology Report | Surgical margins were clear on final histopathological specimen | | |
| * Complications | Minor capsule rupture of RPLND occurred; attributed to the lack of haptic feedback with the da Vinci robot | | |
| * Operative & Console Time | Exposure time (Boyle-Davis gag): 5min, docking: 4min and console time: 85min | | |
| * Need for NGT/ Tracheostomy | No tracheostomy or NGT insertion was required with the patient returning to oral diet on day 1 | | |
| * LOS | 5 days | | |
| Study Strengths | First clinical study to evaluate safety and feasibility of da Vinci SP surgical robot | | |
| Study Weaknesses | * Single patient (case report) * Short follow-up period (30 days) | | |
| Conclusions | * It is both feasible and safe to perform RPLND at the same as TORS for early tonsillar tumors with the single port robot | | |
| **Petruzzi et al. 2019 (Italy)** [34] | | | *Case Report: Level V Evidence* |
| Patient Group | 68-year-old male | | |
| Aetiology of Disease Studied | Isolated retropharyngeal metastasis (2 previous head and neck primaries) | | |
| Operative Interventions | TORS RPLND | | |
| Measured Outcomes | Evaluation of safety and feasibility of TORS RPLND in recurrent head and neck cancer (including previous radiotherapy to the area) | | |
| * Pathology Report | Surgical margins were clear on final histopathological specimen | | |
| * Complications | None (despite previous radiotherapy) | | |
| * Operative & Console Time | Exposure (FK retractor) and docking time: 14min and console time: 42min | | |
| * Duration of NGT feed | NGT removed after 3 days, soft diet for 20 days prior to restarting normal diet | | |
| * LOS | 4 days | | |
| Study Strengths | First clinical study to evaluate the safety and feasibility of TORS RPLND for the treatment of recurrent  head and neck cancer | | |
| Study Weaknesses | * Single patient (case report) * Not possible to comment on need for covering tracheostomy (previous total laryngectomy) | | |
| Conclusions | * TORS RPLND appears to represent a safe and feasible salvage option for recurrent head and neck cancer in the retropharynx, even in the presence of previous radiotherapy to the area | | |
| **Park et al. 2019 (South Korea)** [3] | | | *Case Series (Retrospective): Level IV evidence* |
| Patient Group | 3 patients; Mean age 42 years (range: 31-50 years) | | |
| Aetiology of Disease Studied | Primary tonsillar SCC and suspicion of RPLN metastases (pre-operative imaging), 2 P16 positive | | |
| Operative Interventions | TORS lateral oropharyngectomy & TORS RPLND with lateral neck dissection (single stage) | | |
| Measured Outcomes | Evaluation of the clinical usefulness of TORS RPLND | | |
| * Intra-operative Findings | Metastatic foci following TORS RPLND confirmed in 2/3 patients | | |
| * Complications | There were no intraoperative neurovascular injuries (despite initial internal exposure of a short segment of the ICA in all 3 cases) All oropharyngeal defects were allowed to heal by secondary intention.  One patient developed mild velopalatine insufficiency that eventually resolved with conservative measures | | |
| * Lymph node yield | The lymph node yield for RPLND was 1 in all 3 cases | | |
| Study Strengths | This study illustrates the important role that TORS RPLND may have from a diagnostic viewpoint by directly comparing pre-operative imaging characteristics with post-operative histopathological examination of the resected retropharyngeal lymph nodes | | |
| Study Weaknesses | * Small retrospective study (n=3) * No control group * No follow-up beyond immediate post-operative period | | |
| Conclusions | * TORS provides a safe and ‘natural’ approach for performing RPLND * Current imaging modalities (CT, MRI and PET-CT) have limited accuracy when it comes to assessing retropharyngeal lymph nodes for the presence of metastases. Thus, TORS RPLND may have an important diagnostic role to play in the accurate (pathological) staging of OPSCC (which in turn can have important clinical implications) * The morbidity of TORS RPLND is minimal (in direct contrast to all open approaches to the retropharyngeal space which are inherently challenging, associated with poor access and a high morbidity) * Oropharyngeal defects following TORS lateral oropharyngectomy and RPLND can be generally left to heal by secondary intention | | |
| **Moore et al. 2011 (USA)** [2] | | | *Case Report: Level V Evidence* |
| Patient Group | 2 patients, aged 66 and 73 | | |
| Aetiology of Disease Studied | Recurrent metastatic PTC to the RPLN  (both originally treated with total thyroidectomy, neck dissection and RAI) | | |
| Operative Interventions | Nasotracheal intubation & TORS RPLND (first case wound healed by secondary intention, local pharyngeal flap used for second case) | | |
| Measured Outcomes | Evaluation of safety and feasibility of TORS RPLND in recurrent metastatic PTC to the retropharyngeal lymph nodes | | |
| * Complications | Odynophagia and secondary haemorrhage managed conservatively (25ml estimated blood loss) (patient 1) | | |
| * Operative Time | Total operative time: 2h 2min and 2h 30min, respectively | | |
| Study Strengths | First clinical study to evaluate the safety and feasibility of TORS RPLND for the treatment of metastatic PTC involving the retropharyngeal lymph nodes | | |
| Study Weaknesses | * Two patients (case report) * No follow-up data beyond immediate post-operative period for second patient * No control group | | |
| Conclusions | * TORS is both feasible and safe for RPLND * TORS RPLND is oncologically sound for the management of metastatic PTC involving the retropharyngeal lymph nodes * The morbidity of TORS RPLND is minimal (in comparison to conventional approaches) | | |
| **Goepfert et al. 2015 (USA)** [32] | | | *Case Report: Level V Evidence* |
| Patient Group | 63-year-old male | | |
| Aetiology of Disease Studied | Recurrent metastatic 2.6cm left retropharyngeal lymph node from pT3 N1b PTC originally treated with total thyroidectomy, neck dissection and RAI 2 years prior. | | |
| Operative Interventions | TORS RPLND - intraoperative transoral US facilitated incision placement and operative localisation of RPLN | | |
| Measured Outcomes | Evaluation of safety and feasibility of surgeon-performed intraoperative transoral US combined with TORS RPLND in recurrent metastatic PTC | | |
| * Complications | Minimal bleeding (not quantified) | | |
| * Operative Time | 35 minutes | | |
| * LOS | 1 days | | |
| * Follow-up | At 4-month follow-up no issues and complete resolution of RAI uptake in retropharyngeal area | | |
| Study Strengths | * Use of surgeon performed transoral US facilitated incision placement and lymph node localisation * Low operative time (35 minutes), minimal bleeding, no complications, 1 night LOS * Complete resolution of RAI uptake in retropharyngeal area at 4 months | | |
| Study Weaknesses | * Single patient (case report) and short follow-up (4 months) * No validated tools used to assess swallowing outcomes for initial reported dysphagia | | |
| Conclusions | * Surgeon-performed intraoperative transoral US can further add to the safety and oncological value of TORS RPLND; through improved localisation of the retropharyngeal lymph node(s) itself and its relationship to major neurovascular structures at risk due to their very close proximity * Low morbidity provided careful patient selection, surgical expertise and equipment availability | | |
| **Harries et al. 2020 (USA)** [5] | | | *Single Centre Case Series: Level IV Evidence* |
| Patient Group | 65 patients (all RPLN from PTC), Median age: 42 (16-82) years for whole cohort, 38/27 F:M ratio   * 25 (38%) managed conservatively (observation) * 13 (20%) managed with non-surgical treatment (RAI, EBRT, and/or systemic therapy) * 27 (42%) underwent surgery (RPLND), 19 (70%) through a transcervical approach & 8 (30%) through a transoral approach, of which 6 (22%) underwent TORS RPLND | | |
| Operative Interventions | Trans-oral and trans-cervical RPLND | | |
| Measured Outcomes | Determining indications for RPLND and for optimal surgical route (transcervical vs. transoral) | | |
| * Disease Specific Survival & Metastasis-Free Probability | In the (combined) RPLND group (n=27) the estimated 5-year rate of local retropharyngeal metastasis control was 92%. In the transoral RPLND group (n=8) there were no locoregional recurrences by final follow-up, although one patient developed pulmonary metastases at 49 months | | |
| * Complications | The rate of dysphagia was 25% in both the transcervical and the transoral RPLND routes. In the transcervical route subgroup, one patient developed a hypoglossal nerve palsy. | | |
| Study Strengths | * Largest study on the subject * Evaluated different management strategies for RPLN metastases in PTC | | |
| Study Weaknesses | * Retrospective study * Cannot differentiate TORS RPLND from non-robotic transoral approaches for most outcomes * Selection bias (related to both physicians and patients) and more quiescent disease in conservative arm compared to treatment arms as well as small numbers in each make it difficult to compare ‘head-to-head’ the different approaches (e.g. small volume, non-progressive RPLN metastases tended to be managed conservatively whilst large, progressive ones tended to undergo surgery) | | |
| Conclusions | * TORS RPLND is safe and associated with less complications than the transcervical approach * High dysphagia rate (25%), same for transcervical and transoral approaches * TORS RPLND is recommended for isolated PTC metastasis in supero-medially located retropharyngeal lymph nodes | | |
| **Ding et al. 2020 (China)** [18] | | | *Case Series (retrospective): Level IV Evidence* |
| Patient Group | 10 patients; Median age: 38 (32-47) years, 3/7 F:M ratio | | |
| Aetiology of Disease Studied | Recurrent NPC manifesting with retropharyngeal lymph node metastases | | |
| Operative Interventions | TORS RPLND; 2 patients underwent open conversion due to failure to identify the recurrent RPLN | | |
| Measured Outcomes | Evaluation of safety and feasibility of TORS RPLND using the da Vinci Si/Xi surgical robot (Intuitive Surgical®, Inc., Sunnyvale, CA) for recurrent NPC manifesting with RLPN | | |
| * Intra-Operative findings | Clear margins | | |
| * Complications | Grade 3 dysphagia in 1 TORS RPLND patient (requiring NGT), 1 pharyngocervical fistula (requiring repair) and a hypoglossal nerve palsy in 1 of the open conversion patients | | |
| * Relapse free survival | 86% at 3 years | | |
| * Intra-Operative Ultrasound | The introduction of intraoperative US (last 5 cases) was associated with no further need for open conversion as well as a reduction (not statistically significant) in both operative time (229+30min vs. 363+141min, *p*=0.117) and blood loss (21+17ml vs. 58+54ml, *p*=0.136) | | |
| * Follow-up | Median follow-up of 19 (3-40) months, with 1patient developing cervical recurrence | | |
| Study Strengths | * This is the first study to examine the safety and feasibility of TORS RPLND as a salvage option in recurrent NPC manifesting with retropharyngeal lymph node metastases * Relatively long follow-up (still short of 5 years post-treatment completion). | | |
| Study Weaknesses | * Small sample size (n=10) and retrospective design * Pre-operative ICA embolization and induction chemotherapy indications need clarification; their selective makes it difficult to understand their impact on the reported safety and oncological outcomes witnessed in this series | | |
| Conclusions | * TORS RPLND is safe, feasible and appears to be an oncologically sound salvage treatment option for managing RPLN metastases in recurrent NPC * TORS RPLND was associated with a lower morbidity than both the maxillary swing and endoscopic-assisted transcervical approaches for RPLND from the authors’ previous published experience | | |
| **Dabas et al. 2021 (India)** [19] | | | *Single Centre Case Series Level IV Evidence* |
| Patient Group | 10 patients; Mean age 59 years (range: 51-71 years) | | |
| Aetiology of Disease Studied | Site of primary tumor: oropharynx (n=6), nasopharynx (n=1), thyroid (n=1), ethmoid sinus (n=1), unknown primary (n=1).  9/10 patients had been previously treated with radiotherapy (adjuvant/ primary) and all had evidence of retropharyngeal lymph node metastases on post-treatment PET-CT. | | |
| Operative Interventions | TORS RPLND - intraoperative transoral US facilitated incision placement and operative localisation of RPLN   * 9 patients had one RPLN excised, whilst 1 patient had 2 * All 11 excised lymph nodes contained metastatic tumour deposits, with 3 specimens exhibiting ENE * 1 patient required an open approach (partial encasement of the ICA) | | |
| Measured Outcomes | Evaluation of safety and feasibility of surgeon-performed intraoperative transoral US combined with TORS RPLND in recurrent metastatic PTC | | |
| * Lymph Node Yield for RPLND | Minimal bleeding (not quantified) | | |
| * Complications | 2 patients developed post-operative wound dehiscence that required secondary suturing. 4 patients developed velopalatine insufficiency that conservatively resolved after 3 weeks, and another 4 patients reported hypernasality | | |
| * Operative Time | Exposure (FK retractor) and mean docking time: 5min and console time: 28.5min | | |
| * NGT dependence/ Tracheostomy | All patients were fed via a NGT for 5 days post-operatively, no tracheostomy performed | | |
| * LOS | 1.8 days | | |
| * Follow-up | At median follow-up of 20 months: 4 patients developed distant recurrence, 3 dying from their disease | | |
| Study Strengths | * First and only study assessing role of TORS RPLND as a standalone treatment in the salvage setting * In addition to safety, feasibility, and functional (swallowing) outcomes, authors also reported on oncological outcomes * Relatively long follow-up (still short of 5 years post-treatment completion) | | |
| Study Weaknesses | * Small sample size (n=10), retrospective design * Also, heterogeneous sample in view of multiple different primary tumour sites * No control group | | |
| Conclusions | * TORS is both feasibility and safe for RPLND in the salvage setting * TORS RPLND appears to also be oncologically sound in the salvage setting, though based on this study no conclusions can be derived about its impact on survival * Importance of patient selection evident in view of need for open conversion in one patient due to partial encasement of ICA and exclusion of all patients with inter-incisor distance <3cm | | |

**Table 2. Comprehensive Summary of Studies evaluating the role of TORS for retropharyngeal metastases in head and neck and thyroid cancer.**

Abbreviations: TORS – transoral robotic surgery; RPLND – retropharyngeal lymph node dissection; SCC – squamous cell carcinoma; OPSCC – oropharyngeal squamous cell carcinoma; HPSCC – hypopharyngeal squamous cell carcinoma; NPC – nasopharyngeal carcinoma; PTC – papillary thyroid cancer; RAI – radioactive iodine ablation; LOS – length of stay; SD – standard deviation; HPV – Human Papilloma Virus; ICA – internal carotid artery; ECA – external carotid artery; IJV – internal jugular vein; BMI – body mass index; PEG – percutaneous endoscopic gastrostomy; SP – single port; US – ultrasound; CT – computed tomography; MRI – magnetic resonance imaging; PET-CT – positron emission tomography computed tomography, ENE – extranodal extension.