



Submitted:16/09/2024 Accepted:07/11/2024 Published:18/12/2024

Evaluating the Efficacy of Transoral Robotic Surgery (TORS) Versus Radiotherapy, Chemotherapy, and Open Surgery in Treating Oropharyngeal Squamous Cell Carcinoma (OPSCC): A Systematic Review of Reviews

> Abdulrahman Nasser Alsayeg AMC Hospital, Saudi Arabia Maha Naif Alshammari Ministry of Health, Saudi Arabia Abdulrahman Mesfer Alajmi Dar Aluloom University, Saudi Arabia Reem Faihan Alotaibi Alalami Dental Clinic, Saudi Arabia

Article Link: <u>https://www.jmlph.net/index.php/jmlph/article/view/154</u> DOI: https://doi.org/10.52609/jmlph.v5i2.154

Citation: Alsayeg, A. ., Alshammari, M. N., Alajmi, A. M., & Alotaibi, R. F. Evaluating the Efficacy of Transoral Robotic Surgery (TORS) Versus Radiotherapy, Chemotherapy, and Open Surgery in Treating Oropharyngeal Squamous Cell Carcinoma (OPSCC): A Systematic Review of Reviews. *The Journal of Medicine, Law & Public Health*, 5(1), 546–564. https://doi.org/10.52609/jmlph.v5i2.154
Conflict of Interest: Authors declared no Conflict of Interest.
Acknowledgement: Authors have no acknowledgements to declare.



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## Evaluating the Efficacy of Transoral Robotic Surgery (TORS) Versus Radiotherapy, Chemotherapy, and Open Surgery in Treating Oropharyngeal Squamous Cell Carcinoma (OPSCC): A Systematic Review of Reviews

Abdulrahman Nasser Alsayeg, Maha Naif Alshammari, Abdulrahman Mesfer Alajmi, Reem Faihan Alotaibi

Abstract—Introduction: Transoral robotic surgery (TORS) is a minimally invasive surgical approach for oropharyngeal squamous cell carcinoma (OPSCC) that aims to reduce morbidity and improve patients' quality of life without compromising oncological outcomes. In this study, we investigate the use of TORS in the management of OPSCC and compare it with intensity-modulated radiation therapy (IMRT), concurrent chemoradiation therapy (CCRT), and open surgery.

Method: We conducted a systematic review of systematic reviews using PubMed, Cochrane databases, and grey literature. We also searched the reference lists of these articles. The keywords used were "trans-oral robotic surgery" OR "TORS" AND "oropharynx" OR "oropharyngeal cancer". The inclusion criteria were systematic reviews of human studies that focused on patients diagnosed with OPSCC. We excluded non-English articles without translations and articles that did not meet the inclusion criteria.

*Result:* Our review included a total of 10 studies, comprising 16,917 patients. TORS was found to have better oncological outcomes than other modalities, and was associated with similar overall survival and disease-free survival rates as IMRT and CCRT. Additionally, TORS was associated with less postoperative bleeding than

Abdulrahman Nasser Alsayeg (a.n.alsayeg@gmail.com) is with the AMC Hospital, Saudi Arabia; Maha Naif Alshammari (mahashammari@outlook.com) is with the Ministry of Health, Saudi Arabia; Abdulrahman Mesfer Alajmi (aralajmi404@gmail.com) is with the Dar Aluloom University, Saudi Arabia; Reem Faihan Alotaibi (Reemfaihanotaibi@gmail.com) is with the Alalami Dental Clinic, Saudi Arabia. DOI: 10.52609/jmlph.v5i2.154 open surgery.

*Conclusion:* Our findings suggest that TORS is a safe and effective treatment option for OPSCC. It may be a good option for patients seeking a minimally invasive approach with less postoperative bleeding.

*Keywords*—Chemotherapy; Radiotherapy; Robotic Surgical Procedures; Squamous Cell Carcinoma of Head and Neck.

#### I. INTRODUCTION

Traditional open surgical approaches have long been considered the gold standard in the field of head and neck surgery. While these methods provide extensive visibility into the surgical field, enabling the removal of tumours with adequate margins, they often result in surgical morbidity [1]. In recent years, there has been a shift towards alternative treatment modalities, such as primary irradiation and concurrent chemoradiation therapy (CCRT), for head and neck cancer [2,3]. CCRT combines radiation therapy and chemotherapy, and has shown efficacy in tumour reduction and reducing risk of recurrence. Treatment decisions for head and neck cancer depend on various factors, including the location and stage of the tumour, patient health, and preferences.

Despite advancements in radiation therapy techniques, such as intensity-modulated radiotherapy (IMRT), CCRT still carries significant side effects. Patients undergoing CCRT often experience toxicities such as mucositis, xerostomia, and dysphagia, which adversely impact their quality of life [2,3]. To address these challenges, minimally invasive surgical approaches, such as transoral robotic surgery (TORS) and transoral laser microsurgery (TLM), have emerged as alternatives.

These approaches aim to reduce morbidity and improve patients' quality of life without compromising outcomes. While TLM is effective, it is associated with a restricted view of the surgical field and restricted tissue manipulation, both of which can affect surgical precision, particularly in areas outside the surgical field-of-view [3].

The development of robotic surgical systems, meanwhile, has revolutionised surgical approaches by overcoming certain limitations of traditional methods, such as limited visibility of the surgical site and the need for one-handed manipulation. The first TORS system was developed in 2005, and received approval in 2009 for the treatment of stage T1 and T2 oropharyngeal cancer. Since then, robotic-assisted maxillofacial surgery has gained popularity for its benefits, including a threedimensional magnified view, accurate movement, bimanual operation with articulated arms, and tremor suppression, all of which enhance surgeons' physical skills [4,5]. Various systems have been designed specifically for TORS, aiming to overcome anatomical constraints and improve surgical exposure in the head and neck region [6,7]. However, the evidence supporting the use of TORS in treating oropharyngeal squamous cell carcinoma (OPSCC) is still emerging and requires further investigation, especially given the increasing prevalence of the disease [3]. The aim of this study, therefore, is to investigate the uses of TORS in the management of OPSCC, exploring its potential, limitations, and function.

#### **II. METHODS**

This systematic review poses the research question: In patients with oropharyngeal squamous cell carcinoma, what is the impact of transoral robotic surgery (TORS) on overall survival and disease-free survival, compared with radiotherapy, chemotherapy and open surgery?

#### Search strategy:

The authors searched PubMed, Cochrane databases, and grey literature. Subject headings were also searched, as were the reference lists of the articles included in the study. The keywords used were "trans-oral robotic surgery" OR "TORS" AND "oropharynx" OR "oropharyngeal cancer". The search spanned articles from 2009 to January 2023. *Selection criteria:* 

Only systematic reviews were selected. The inclusion criteria were systematic reviews of human studies focusing on patients diagnosed with oropharyngeal squamous cell carcinoma. Studies were excluded if they were non-English articles that lacked translation, or did not meet the inclusion criteria.

# Data extraction, quality assessment, and qualitative synthesis:

The studies' eligibility for inclusion in this review was examined by the three authors independently. This review follows the Preferred Reporting Items for Review and Meta-analysis of Individual Participant Data [8].

#### Outcomes:

The primary outcome was to measure the overall survival and disease-free survival of patients undergoing TORS for OPSCC, compared with those receiving other treatment modalities. The secondary outcome was to explore the rate of complications.

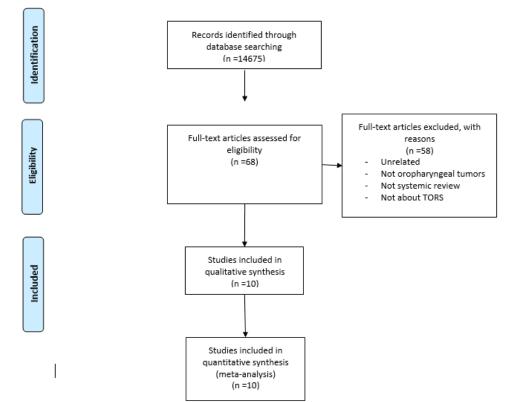
TORS is a surgical procedure designed to treat OPSCC, and its effectiveness is primarily influenced by tumour characteristics, patient anatomy, and surgical expertise. In this research, we aimed to evaluate the overall effectiveness of TORS for OPSCC, focusing on the procedure's general efficacy without distinguishing between male and female patients.

#### **III. RESULTS**

Out of 14,675 articles, 68 were identified as eligible, as illustrated in the PRISMA chart (Figure 1). After applying the inclusion and exclusion criteria, a total of 10 studies were included in our systematic review, with a total of 16,917 patients. Oropharyngeal SCC was seen in 13,791 of these patients. The characteristics of the included studies were summarised in Tables 1-3.

#### Overall survival and disease-free survival:

Six articles reported an overall survival rate ranging from 74—100% and disease-free survival for oropharyngeal cancer treated with TORS [3,9,11,12,13,17].



#### gure 1. PRISMA 2009 Flow Diagram

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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## **Table 1.** Transoral Robotic Surgery vs. Radiotherapy

Author, year	Aims	Study design	Number of papers included	I Sample size	Tumour staging	Follow up	Results
Yeh et al, 2015 [3]	Systematically review the current literature reporting oncological and functional outcomes of TORS and IMRT in the treatment of OPSCC. Additionally, explore the complication and toxicity rates.	Systematic review	Final analysis includes 44 papers published between 2001 and 2015.	Median sample size was 71 patients (range 14-2315; mean 198) for the IMRT studies and 30 patients (range 16-81; mean 38) for the TORS studies.	T1, T2, T3, T4	Median follow-up time was $36.2$ months (range 24-54 months) for the IMRT studies and 21.6 months (range $6-36$ months) for the TORS studies. The follow-up period was significantly longer in the IMRT cohort (p < 0.001).	No randomised trials were iden tified that compared TORS versus IMRT. Patients enrolled in the studie investigating IMRT had more advanced disease than those undergoing TORS.
De Virgilio et al, 2020 [9]	Perform a meta-analysis evaluating TORS and IMRT in the treatment of OPSCC.	Systematic review and meta-analysis	A total of 47 studies were included. The studies were prospective (n=17) or retrospective (n=27) non-randomised studies, and three RCTs. Only one RCT directly compared the two treatment strategies.	5624 patients (IMRT=4322; TORS=1302)	T1, T2, T3	No follow-up mentioned	IMRT cohort treated with concurren CT (n=3433, 81.3%). TORS cohort received adjuvan treatment (n=826, 67.8%). <b>OS:</b> IMRT subgroup showed a cumulative <i>survival rate</i> of 83.6% (99% CI 76.9-89.3%); TORS subgroup showed a cumulative <i>survival rate</i> of 91.3% (99% CI 81.2 97.8%) <b>DFS:</b> IMRT: 79.6% (99% CI 70.6 87.3%) TORS: 89.4% (99% CI 82.7-94.5%)

de Almeida et 2014 [10]	al, Compare effectiveness of TORS vs IMRT for early T-stage oropharyngeal cancer.	Systematic review	20 studies were included, of which 8 were IMRT studies, and 12 were TORS studies.	1,287 patients included in the IMRT studies; 772 patients included in the TORS studies.	T1, T2	No follow-up mentioned	Patients receiving definitive IMRT also received chemotherapy (43%) or neck dissections for persistent disease (30%), whereas patients receiving TORS required adjuvant radiotherapy (26%) or chemoradiotherapy (41%). Two-year overall survival estimates ranged from 84% to 96% for IMRT and 82% to 94% for TORS.
Egbunah et al, 20 [11]	221 Answer the question: "How effective are radiotherapy or chemotherapy as single or combined treatment modalities compared with any form of surgical intervention (with or without adjunct treatments) in the management of OPC in terms of treatment outcome: prognosis (overall survival), LRC, recurrence, complications, cost to patient, and/or post- treatment quality of life?"	Systematic review and meta-analysis	Five trials were included, which compared non- surgical with surgical interventions in the management of OPC. Of these 17-21, 1 compared radiotherapy with surgery,17 2 compared chemoradiotherapy with surgery 19,20, and 2 compared chemoradiotherapy with transoral robotic surgery (TORS).20,21 None of the included trials compared brachytherapy or immunotherapy/ target therapy with surgery. Four trials 22-26 were excluded because participants with OPC comprised less than 50% of the sample size.	80 patients (Definitive chemoradiothera py: N=38; TORS + ND + RT ± CT: N = 42)	T1, T2, T3, T4	Mean follow-up range: 33—50 months	In the trial by Smith et al, the CCRT group was reported to have a 57% 3- year OS compared with 83% for the TORS group ( $P = .06$ ). The study also reported 85% 3-year DFS and 92% 2- year LRC in the CCRT group, compared with 94% and 85% respectively for the TORS group ( $P = .08$ and .24). Recurrence was not reported.

Author, year	Aims	Study design	Number of papers included	s Sample size	Tumour staging	Follow-up	Results
Park et al, 2020 [12]	Investigate the clinical safety and effectiveness of robotic surgery compared with conventional open surgery in primary oropharyngeal cancer.	Systematic review and meta-analysis	9 papers met the inclusion criteria.	574 patients	T1, T2	Mean follow-up range: 20.3—34 months	TORS showed a lower mortality rate (n = 4 studies, RR: 0.81, 95% CI: 0.30, 2.20, I2=0%), recurrence rate (n = 8 studies, RR: 0.66, 95% CI: 0.36, 1.22, I2=0%), and positive margin rates (n = 4 studies, RR: 0.85, 95% CI: 0.47, 1.54, I2=0%) compared with open surgery, but there was no significant difference between the two groups. Disease-free survival rate was significantly higher in the TORS group than the open surgery group (n = 5 studies, RR: 1.13, 95% CI: 1.03, 1.24, I2=0%).
Roselló et al, 2020 [13]	Comduct a systematic review of the available literature in order to evaluate the safety and efficacy of transoral ro- botic surgery (TORS) against open surgery.	review	inclusion	A total of 371 patients were studied (305 men and 66 women). Of these, 186 were treated with TORS and 185 with conventional surgery.	Τ4	-	Overall, TORS, when compared with open surgery, appears to have better functional results (less hospital time, decannulation) and fewer intraoperative and post-operative complications. There is no significant difference between the two techniques when assessing oncological outcomes (positive margins, survival rate). With regards to the oncological results, 3 out of the 4 articles show no significant results in terms of disease-free and survival time, and the differences between the test and control groups were very similar. The study by White <i>et al.</i> shows significant results in both disease-free time (74% test group, 43% control group) and survival (74% test group, 43% control group).

## **Table 3.** Transoral Robotic Surgery and Complications

Author, year		Study design	Number of papers included	Sample size	Tumour staging	Follow up	Results
Daniel et al, 2021 [14]	Conduct a systematic review of the available literature on risk factors and rates of postoperative haemorrhage in patients undergoing TORS and transcervical arterial ligation.	review and meta-analysis	5 studies were included.	2008 patients	T1, T2, T3, T4	-	The overall and major/severe haemorrhage rates after oropharyngeal surgical resection were 6.7% (N = 135/2008) and 2.6% (N = 53/2008), respectively. Across all included studies, a significant proportion of patients with postoperative haemorrhage required return to the operating room (OR) or angioembolic therapy to control bleeding (66.7%, N = 90/135). Similarly in the TORS-only subgroup, 62.7% (N = 42/67) of patients with postoperative haemorrhage required return to the OR for control of haemorrhage.
Kelly et al,2014 [15]	-	Systematic review	11 studies were included.	190 patients	T1, T2	1—51 months	Seven studies with a total of 140 patients provided data on oncological outcomes including local, regional and distant disease recurrence rates, as well as disease-free and overall survival rates. For T1–2 OPSCC, the aggregate rates of local, regional, and distant disease control were 96.2% (I-squared = 0.0, p = 0.94), 91% (I-squared = 0.0, p = 0.54) and 100% respectively (no statistical analysis performed for uniform results). Disease-free survival was seen in 90% (I squared = 0.0, p = 0.65), with an overall survival rate of 95% (I-squared = 0.0, p = 0.68). Follow-up ranged from 1 to 51 months with a mean of 19.9 months.

Stokes et al,2020 [16]	factors for post-TORS	Systematic review and meta-analysis.	13 papers were in- cluded.	332 cases of post- TORS haemorrhage reported in the literature following a total of 5,748 TORS cases.	T1, T2, T3, T4	No follow- up mentioned	There have been 332 cases of post-TORS haemorrhage were reported in the literature, following a total of 5,748 TORS cases (5.78%). The post-TORS haemorrhage rate ranged from 3.1% to 19.7% among the studies. The pooled mean post-TORS bleeding rate was 5.78%, with a pooled median post- TORS bleeding rate of 6.47%. Overall, the median time to haemorrhage following TORS was on postoperative day 8.
Ramchandani et al, 2022 [17]	Assess the impact of the timing of ND in relation to oropharyngeal cancer TORS/TLM on intra- and postoperative complications. These complications include postoperative bleeding, intra- and postoperative fistula formation, disease- specific survival (DSS), overall survival (OS), and recurrence rates.	review	19 studies met the inclusion criteria in the qualitative analysis for the review. Of these, 5 were prospective studies, and 14 were retrospective studies.	546 patients who underwent neck dissection in conjunction with TORS/TLM	T1, T2, T3, T4	2—24.8 months	Ten studies described DSS and OS, with varying follow-up times. Five studies cited DSS and OS as 100% for 13 patients at follow-up times ranging from 2 months to 1 year. Three studies with a 2-year follow-up period found DSS to be 95%, 89%, and 78% while OS was 100%, 100%, and 94%. Dabas et al. cited a DSS of 88% and OS of 92% at a mean follow-up time of 29 months, and Jackel reported DSS and OS at 80% with a mean follow-up of 24.8 months. Ten studies (192 patients) recorded a recurrence rate, which was 5% on average. Five studies described no recurrence.
							In the cohort with neck dissection after TORS/TLM, 3% experienced minor

TORS/TLM, 3% experienced minor postoperative haemorrhage, and 8% had intraoperative fistulae. In the concurrent cohort, 1% had major postoperative bleeds and 0.3% had minor bleeds, while 4% developed intraoperative fistulae and 0.3% developed postoperative fistulae.

LRC: Locoregional Control, TORS: Transoral Robotic Surgery, IMRT: Intensity-Modulated Radiation Therapy, OPSCC: Oropharyngeal Squamous Cell Carcinoma, CCRT: Concurrent Chemoradiation Therapy, TAL: Transcervical Arterial Ligation, DSS: Disease-Specific Survival, OS: Overall Survival, DFS: Disease-Free Survival, TLM: Transoral Laser Microsurgery

Overall survival rates varied from 69—100% and disease free-survival from 64—96% for IMRT, compared with 74—100% and 85.7%—96%, respectively, for TORS [3]. Moreover, when the oncological outcome was compared in 5,624 patients (IMRT=4322; TORS=1302), the results showed that primary TORS obtained better oncological outcomes than primary IMRT, with overall survival of 91.3% (TORS) and 83.6% (IMRT) and disease-free survival of 89.4% (TORS) and 79.6% (IMRT) [9].

#### Comparison of CRT vs TORS:

The three-year overall survival in the TORS group (N=42) was 83%, compared with 57% for the CRT group (N=38), while the disease-specific survival was 94% compared with 85% [11].

#### Comparison of open surgery vs TORS:

The safety and efficacy of TORS was demonstrated in 186 patients, compared with open surgery (N=185), with tumour stages T1 (N=118), T2 (N=194), T3 (N=41) and 18 (N=18) [13].

The differences between the control group (open surgery) and the study group (TORS) in terms of overall survival and disease-free survival were not significant; overall survival in the control group was 78%—96.7%, and 85%—100% in the study group

(TORS), while disease-free time was 76%—91.6% in the control group and 81%—95.7% in the study group [13].

In addition, it should be mention that there was a subgroup in the systematic review of White et al. that presented statistically significant results in these two indices in both overall survival and disease-free time (74% TORS, 43% open surgery) [13].

Moreover, in a total of 574 patients, the TORS group (256 patients) showed lower mortality compared with the open surgery group (318 patients), as well as significantly higher disease-free survival rates than the open surgery group (95%) [12].

#### TORS complications:

One of the most common surgical complications in the TORS studies was postoperative haemorrhage [14]. The total number of patients who developed post-TORS haemorrhage is illustrated in Table 4. Two of the articles (11,18) referred to the amount of blood lost during surgery, finding a difference of over 200 ml between the control group (open surgery) and the study group (TORS) [13]. In terms of postoperative bleeding, the studies showed better results for TORS.

Other complications included temporary hypoglossal nerve injury (0.9%), lingual nerve injury (0.6%), and tooth injury (1.4%) [3].

Table 4. Total number of patients who developed haemorrhage post TORS

Included studies	Total patients	Haemorrhage post TORS
Yeh [3]	217	14
de Almeida [10]	247	6
Sharbel [14]	588	93
Stokes [16]	5,748	332
Ramchandani [17]	566	80
Park [18]	30	1
White [19]	64	7
Total Number	7400	533

#### **IV. DISCUSSION**

To our knowledge, this is the first systematic review of systematic reviews examining the effect of transoral robotic surgery on overall survival and disease-free survival compared with intensitymodulated radiation therapy. However, it may be limited by unfavourable patient anatomy and is most suitable for T1-T2 and select T3-T4 tumours. Comparing TORS with IMRT is challenging due to varying applications and limited availability of robotic systems.

### IMRT:

The results showed that primary TORS can obtain similar, but also better oncological outcomes when compared with primary IMRT. TORS is able to achieve oncological and functional outcomes that are at least comparable to primary radiotherapy. As we see in the results, the ratio is highly proportional between them, but the TORS results remain better in OS and DFS for T1, T2, and selected T3 tumours.

#### CRT:

Chemoradiotherapy can be a good option for patients whose disease is incurable or hard to access due to location, patients whose disease is severe and who cannot tolerate surgery, and those who refuse surgery [11].

The combination of chemotherapy and radiotherapy improved oncological outcomes but increased complications, toxicity was more common after chemoradiotherapy than after radiotherapy alone (56% vs. 30%), the adverse effects of chemoradiotherapy were more silent, and toxicities such as osteonecrosis, stenosis, and fibrosis appeared late and were difficult to treat [20].

## Open surgery:

Primary TORS has several notable advantages, including improved disease-free survival rates. It does come with limitations, however, such as high costs and bulky equipment [13]. Additionally, individual patient factors like obesity, a short neck, or a small

jaw can pose challenges during the procedure, potentially leading to discomfort or dental injuries. Nonetheless, TORS proves to be a cost-effective

## **V. CONCLUSION**

A systematic review of 10 studies found that transoral robotic surgery (TORS) is a safe and effective treatment for oropharyngeal squamous cell carcinoma (OPSCC). TORS was found to have similar overall survival and disease-free survival rates to intensity-modulated radiation therapy

option for early stage oropharyngeal cancer treatment [13].

## Haemorhage:

Haemorrhage is a common complication after TORS; it is also an effective and influential element in surgical and functional outcomes [10], with larger tumours and anticoagulant therapy increasing the risk. For example, larger tumours are more likely to require removal deeper into the parapharyngeal region or the base of the tongue. Anatomically, this places the incision nearer to the major branches of the lingual, upper pharyngeal, and facial arteries [21]. While intraoperative bleeding occurs less with TORS than with open surgery, postoperative bleeding poses a significant risk and may even lead to death [13]. While TORS offers enhanced visualisation and instrumentation, it can be less than ideal with regard to postoperative complications, and haemorrhage in particular.

#### Limitations:

The studies included in this review varied in terms of their designs and procedures, sample sizes, and follow-up durations (which ranged from 1—54 months), making them inadequate for sufficient oncological analysis and meta-analysis.

Due to potential selection bias (most patients were pre-screened for TORS suitability), 'surgeon bias' (surgeons conducting the studies may have an inherent bias toward demonstrating surgical success), and financial bias (all studies required large investments of time, money, and resources from the performing institutions, which may have influenced the desire for successful outcomes), all of the studies may be considered flawed.

This review may be further limited by factors such as not exploring the effect of gender difference on the results, and the fact that only articles in English were included. Publication bias may also present.

(IMRT) and concurrent chemoradiotherapy (CRT), and better overall survival and disease-free survival rates than open surgery. TORS was also associated with less postoperative bleeding than open surgery. Overall, based on the evidence presented in this systematic review, transoral robotic surgery (TORS) emerges as a promising treatment option for oropharyngeal squamous cell carcinoma (OPSCC). It offers comparable oncological outcomes to traditional methods such as radiotherapy and open surgery, while demonstrating advantages in terms of reduced postoperative bleeding and improved functional outcomes.

While TORS may not be suitable for all patients due to anatomical constraints or tumour stage, it represents a valuable minimally invasive approach that can enhance patient quality of life. Future research should focus on expanding the evidence base, particularly for advanced-stage tumours, and investigating the long-term outcomes of TORS compared with other treatment modalities.

#### **CONFLICT OF INTEREST**

None.

ACKNOWLEDGEMENTS

## None.

FUNDING

None.

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