Efficacy of robotic transoral surgery (TORS) in the setting of oropharyngeal squamous cell carcinomas (OPSCC). An integrative literature review

Review Article

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Abstract

Introduction: Transoral robotic surgery (TORS) demonstrates surprising oncological results from remarkable precision, maneuverability and expanded vision, but there is a gap in surgeons' knowledge regarding its effectiveness compared to other therapeutic methods. Objective: To review the indications, advantages, disadvantages and complications of transoral robotic surgery for oropharyngeal tumors (TORS) compared to other therapeutic methods. Methods: Integrative literature review conducted through PubMed/MEDLINE, Google Scholar and Cochrane Library databases from 2011 to 2022. 25 articles were included in the study Discussion/Results: There was a significant reduction in the risk of margin invasion compared to the traditional open technique (9.5% vs. 19.1%), as well as a reduction in the recurrence of primary tumors (8.3% vs. 17.8%). TORS together with transoral laser microsurgery (TLM) are associated with a higher primary screening rate than open lingual tonsillectomy (80% vs. 72%). Conclusion: TORS is a safe and concise surgical technique that allows resection with millimeter margins and superhuman precision. Furthermore, there is a need for more studies with more robust databases in order to analyze the gaps that are still present regarding the results of TORS outcomes in the long term.

Keywords: Transoral Robotic Surgery (TORS); Head and Neck Squamous Cell Carcinoma (HNSCC), Oropharyngeal Cancer (OPSCC)

Introduction

Emergence of transoral robotic surgery (TORS)

Robot-assisted surgery was introduced in the 1980s, although the concept of creating a system that supported remote control surgery originated during World War II[1,2]. Robotic surgery opened a new era of minimally invasive procedures, which have become the gold standard in certain specialties. Thus, robotic surgery allows surgeons to perform operations

that were previously deemed impossible due to its remarkable precision, tremor cancellation, degrees of freedom (DOF), improved ergonomics, and magnified three dimensional view of the surgical field[2].

TORS has gained popularity since the paper published by Weinstein et al. (2007) on radical tonsillectomy using TORS for the treatment of tumors of the oropharyngeal region, which is challenging to access surgically, especially when the tumors are complex[3,15]. The robotic technique was developed with the aim of replacing open surgery, which was until then the treatment of choice for oropharyngeal tumors. In addition, the principle of TORS is based on surgical resection in the operating room, a technique described by Huet et al. (1951) for tonsillar tumors that involves transoral resection of the tonsil and superior constrictor muscle deep into the parapharyngeal space, producing significantly superior surgical results due to the ergonomics and magnified views provided by the robot[3].

The robot consists of the surgeon's console, the patient's cart with articulated or rotating arms, and the imaging tower. The most widely used robotic system is the Da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, US) that currently uses a 3D high-definition (HD) view with seven DOFs. The system is controlled by articulated pulses that allow stereoscopic vision, which results in greater dexterity and improved visual magnitude[2].

Main advantages of the technique

The surgical precision of TORS facilitates a less invasive approach, which implies significantly less complications, such as bleeding and fistulas, better aesthetic results, improved quality of life of the patient, and lower rates of infection and hospitalization compared to the open technique. TORS has also been shown to reduce the postoperative pain and patient recovery time [1,6,16,17,18]. Thus, TORS can be used in conditions that require high surgical precision due to the difficult access to the oropharyngeal region, which can be aggravated by the proximity of the tumor to critical structures. TORS allows greater maneuverability of the instruments and better visualization of the lesion, thus allowing microsurgical reconstructions of anastomoses in extremely confined spaces, which provides a wider range of vascularized grafts for closing the surgical site[2,9,10,12,16,17,18].

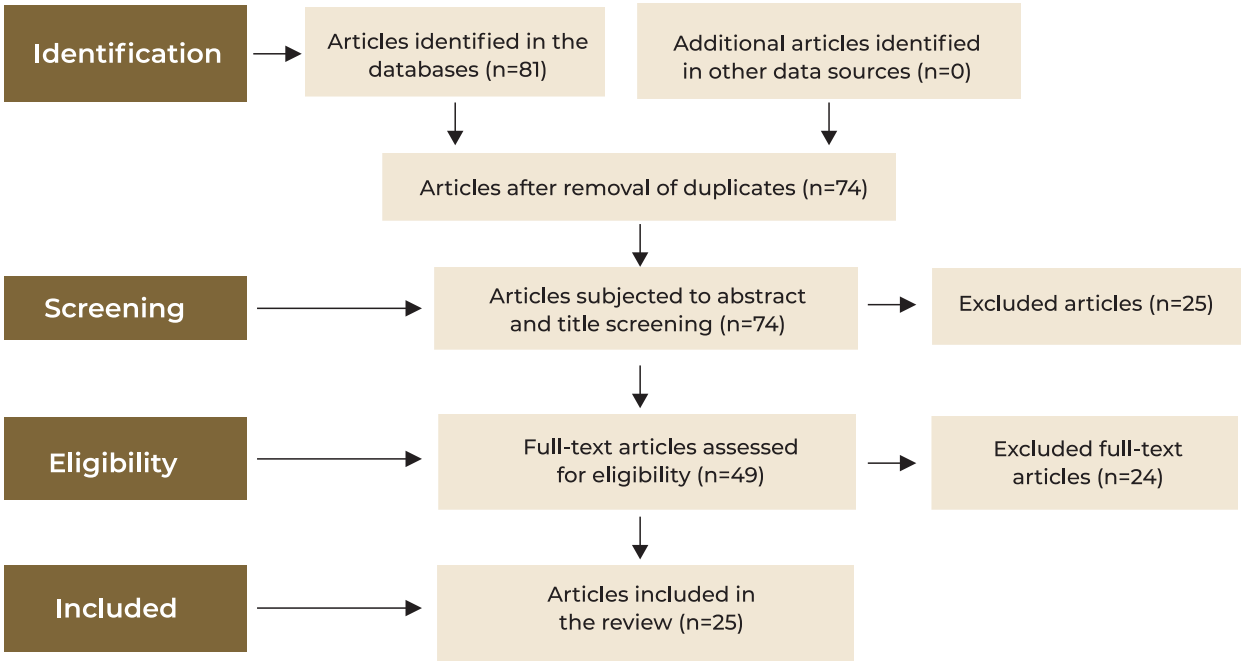
Use of TORS with other technologies

In addition to the use of robotic technology in the intraoperative period, it is also possible to improve the surgical planning experience by using methods such as virtual surgical planning (VSP) and 3D printing of anatomical models [1,2,4,5]. VSP has been shown to be a major advance, especially in cases in which mandibular reconstruction is necessary. It can also be used to plan a modified face-lift incision, a smaller incision that is used for cervical dissection in cases of oral cavity cancers. Although the use of smaller incisions is linked to better aesthetic outcomes and faster patient recovery, it is also associated with greater technical difficulty during surgery due to the smaller operative window; limitations such as this can be overcome through the use of VSP with TORS[2,5].

Methods

This is an integrative literature review of studies published in the PubMed/MEDLINE, Google Scholar, and Cochrane Library databases between 2011 and 2022. The search terms "Transoral Robotic Surgery" (TORS), "Head and Neck Squamous Cell Carcinoma" (HNSCC), and "Oropharyngeal Cancer" (OPSCC) were used. Independent reviewers performed the electronic search separately. All articles were initially screened for relevance by the title and abstract, and the full text of the article was subsequently obtained. A total of 81 articles were initially retrieved and the selection process yielded 25 articles that were included in this review, as described in Table 01. The inclusion criteria were as follows: articles available in full, written in English and/or Portuguese, published between 2011 and 2022, and on the subject matter. The exclusion criteria were as follows: full text of the articles not available, written in languages other than English or Portuguese, published before 2011, and not relevant to the subject.

Table 1
Prisma data flow diagram protocol. Source: Page *et al*., 2020



Results

Table 2
Results and conclusions of the retrospective studies, meta-analyses, and systematic and integrative reviews on the efficacy of TORS

Title of the article	Author/ year	Design of the study	Results	Conclusion
Robotics in oral surgical procedures: Integrative review	Queiroga *et al.* 2021	Integrative review of the literature	The use of robots as a tool has been shown to be successful in several areas such as minimally invasive surgery, treatment of head and neck cancer, craniomaxillofacial surgery, and pre-programmed robotic osteotomy.	In view of the above, we can state that there is a consensus in the literature on the potential of using robotics in dental surgical procedures, namely regarding safety, precision, post-operative functional recovery, and aesthetic results.
Is There Room for Microsurgery in Robotic Surgery?	Silva *et al.* 2022	Systematic review of the literature	The evaluated parameters were the surgeon's level of fatigue, degree of tremor, and ease of performing the procedure. The authors approved the system in the three evaluations and stated that it is a precise and high-quality technique for micro-neurosurgery.	There is plenty of room for robotics in microsurgery. The selected studies indicate a growth in techniques that use robotics in a variety of fields. Transoral surgery is a safe and effective option for identifying and treating various head and neck tumors. The superior dexterity, visual acuity, and surgical precision make it a safe and promising technique, applicable to different areas of microsurgery.
Transoral Robotic Surgery for Oropharyngeal Cancer	Paleri *et al.* 2018	Systematic review of the literature	Transoral robotic surgery has shown significant promise in the management of oropharyngeal cancer since its description in 2007. The oncological efficacy of this procedure has been proven in several single-center studies, multicenter collaborative publications, and systematic reviews.	The increase in disease incidence, new surgical and non-surgical treatment techniques, and a younger patient population have created the need to generate robust evidence. It is very likely that the treatment methods for this disease will change over the next decade.

Title of the article	Author/ year	Design of the study	Results	Conclusion
Transoral robotic surgery and intensity-modulated radiotherapy in the treatment of the oropharyngeal carcinoma: a systematic review and meta-analysis	De Virgilio *et al.* 2021	Meta-analysis	The cumulative survival rate was 83.6% (99% CI 76.9%–89.3%) in the IMRT subgroup and 91.3% (99% CI 81.2–97.8%) in the TORS subgroup. Disease-free survival was significantly different between IMRT (79.6%, 99% CI 70.6–87.3%) and TORS (89.4%, 99% CI 82.7–94.5%).	TORS appears to be a consolidated effective surgical approach in the treatment of OPSCC, according to the oncological and functional results. Further randomized controlled trials comparing TORS and IMRT with homogeneous cohorts in terms of tumor staging and HPV status are required.
Oncological and functional outcomes of trans-oral robotic surgery for pyriform sinus carcinoma: A French GETTEC group study	Mazerolle *et al.*, 2018	Retrospective multicentric study	The median hospital stay was 10 days; preventive tracheostomy was performed in seven cases (12%) and these patients were successfully decannulated; oral refeeding was possible in 93% of patients after a median of 5 days; adjuvant therapy was proposed in 31 cases (54%); the median follow-up was 23 months; the overall survival and disease-free survival were 84% and 74% at 24 months, and 66% and 50% at 48 months, respectively; at the end of the follow-up, the organ preservation rate was 96%. None of the surviving patients required tracheostomy and oral diet was possible for 96% of patients.	TORS is considered a conservative and safe procedure for small lesions in the pyriform sinus, as an initial or salvage therapy. It has acceptable oncological results and excellent functional outcomes. However, it is one of the most complex types of robot-assisted surgery, requiring rigorous case selection, especially in cases of lesions involving the anterior angle, for which exposure is difficult and safe margin excision is difficult to achieve.
Robotic compared with open operations for cancers of the head and neck: a systematic review and meta-analysis	Liu *et al.*, 2019	Systematic review	The meta-analysis showed that robotic surgery can significantly reduce the risk of invaded surgical margins compared to open surgery, particularly in the resection of oropharyngeal cancer (9.5% vs 19.1%; RR 0.54; [95% CI 0.34 to 0.86]; p = 0.01; I 2 = 0%). There was no difference between robotic surgery and open surgery regarding death and disease-free survival, but robotic surgery significantly reduced the recurrence rate of primary tumor resection (8.3% vs 17.8%; RR 0.48 [95% CI 0.25 to 0.91]; p = 0.02; I 2 = 0%).	According to the studies included in the review and our results, we concluded that the robotic surgical system has notable benefits in reducing the rate of invaded margins, decreasing complications, and improving the patients' quality of life compared to conventional open surgery for head and neck cancer. However, the lack of tactile feedback and its high cost are the main limitations so far. Only a few authors have investigated the oncological outcomes and long-term functional recovery and quality of life, so there is still a long way for the development of robotic surgery before it becomes a universal treatment.
The role of transoral robotic surgery, transoral laser microsurgery, and lingual tonsillectomy in the identification of head and neck squamous cell carcinoma of unknown primary origin: a systematic review	Fu *et al.*, 2016	Systematic review	TORS/TLM detected the primary tumor in 111/139 patients overall (80%) and in 36/54 patients (67%) without notable findings in the physical examination, radiological imaging, and panendoscopy with targeted biopsy. Lingual tonsillectomy detected the primary tumor in 18/25 patients (72%) with no findings. Bleeding was the most common perioperative observation (5%).	This systematic review supports the use of TORS and TLM to aid in the identification of primary head and neck squamous cell carcinoma of unknown origin as the detection rates are superior to those of traditional diagnostic investigation. It was also demonstrated that the addition of formal lingual tonsillectomy using TORS/TLM is a safe and effective option that increases the detection rate of occult primary tumors.

Title of the article	Author/ year	Design of the study	Results	Conclusion
Transoral robotic surgery in head neck cancer management	Kwong *et al.*, 2015	Systematic review	TORS allows the surgeon to control the instruments and camera. Endoscopic resection of the skull base tumors requires two surgeons, as an assistant is needed to control the endoscope. In addition, the da Vinci system has a unique feature of eliminating tremors during instrumentation. Robotic surgery can help overcome this problem because 3D vision allows the surgeon to place and secure sutures in the confined spaces of the skull base.	Despite a short gestation period, TORS has been shown to be of significant value in head and neck cancer surgery. Further refinements in the technology and new models are inevitable and we foresee a growing role for this modality in the future.
Decision management in transoral robotic surgery (TORS): indications, individual patient selection, and role in the multidisciplinary treatment of head and neck cancer from a european perspective	Lörincz *et al.*, 2016	Retrospective study	Transoral robotic resection of primary tumors and appropriate neck dissection, as indicated, allowed sparing of adjuvant treatment in 20 patients (40%). Another five patients refused the recommended adjuvant therapy (two of them subsequently developed recurrent nodal disease and both were successfully salvaged with chemoradiotherapy). Seventeen patients received adjuvant radiotherapy of 60 Gy and eight patients underwent adjuvant chemoradiotherapy of 66 Gy. In 37 patients (74%), adjuvant treatment was completely spared or the chemotherapy component was omitted and radiotherapy reduced by at least 10 Gy, compared to the standard protocol of primary chemoradiotherapy with 70 Gy. Adding the three patients who refused adjuvant treatment and have not relapsed to date, this percentage rises to 80%.	As with any new therapy, it is essential that prospective randomized multicenter studies confirm the safety and efficacy of TORS as the first-line treatment of HNSCC. These studies should be designed based on the unique advantages and limitations of the DaVinci Surgical System in TORS; rigorous patient selection is essential for these studies. We believe that the advantages offered by TORS over conventional treatment modalities applied on a large scale will result in a paradigm shift in the quality of life outcomes for patients with head and neck cancer.
Systematic Review of Validated Quality of Life and Swallow Outcomes after Transoral Robotic Surgery	Castellano *et al.*, 2019	Systematic review	When patients who underwent TORS and those who underwent open surgery or CRT were compared, the TORS group had higher quality of life scores in several domains at various times. Moreover, several authors reported better swallowing results in the TORS group.	The available evidence suggests that patients who undergo TORS and adjuvant therapy for head and neck cancer have a good quality of life and swallowing outcomes after treatment, but the results depend on the baseline function, T stage, and adjuvant treatment status. When compared with patients who underwent open surgery or CRT, patients who underwent TORS had better results in terms of the quality of life and swallowing function. More high-quality studies on this topic will be beneficial to determine which patients will benefit the most and achieve the best outcomes after TORS.
Robot-Assisted Reconstruction in Head and Neck Surgical Oncology: The Evolving Role of the Reconstructive Microsurgeon	Chalmers *et al.*, 2018	Systematic review	As experience increases, more extensive and complex resections, including salvage surgery, are becoming possible with TORS. The natural evolution of this process has led reconstructive surgeons to investigate the role of robot-assisted reconstruction (RAR) and transoral robotic reconstructive surgery (TORRS). In the short term, a reduction in surgical time and length of hospital stay has been observed, as well as a faster recovery of swallowing. In the long term, a reduction in primary CRT and de-escalation of post-operative CRT via TORS will reduce the incidence of osteoradionecrosis, which carries a large economic burden and has a significant impact on the quality of life.	With the advance of robot-assisted surgery, RAR is evolving. This article discussed the evolving role of reconstruction for post-TORS defects, as well as the role of RAR in current practice.

Title of the article	Author/ year	Design of the study	Results	Conclusion
Clinical Value of Transoral Robotic Surgery: Nationwide Results From the First 5 Years of Adoption	Li *et al.*, 2018	A retrospective analysis	TORS was more frequently associated with a lower probability of positive margins than non-robotic surgery, but not more than TLM (non-robotic surgery: hazard ratio [HR] 1.51, P < 0.001, TLM: HR 1.13, P = 0.582). TORS was associated with a lower likelihood of post-surgical chemoradiotherapy (TLM: HR 2.07, P < 0.001, non-robotic surgery: 1.65, P < 0.001), but not with adjuvant radiotherapy alone (TLM: HR 1.06, P = 0.569, non-robotic surgery: 0.96, P = 0.655). In multivariate Cox regression analysis for overall survival, the use of TORS was not associated with increased survival (TLM: HR 1.31, P = 0.233, non-robotic surgery: HR 1.12, P < 0.303).	The advantages of TORS for early-stage OPSCC may be a lower likelihood of positive post-surgical margins and of the subsequent need for adjuvant chemoradiotherapy.

Abbreviations: TORS, transoral robotic surgery; CI, confidence interval; HR, hazard ratio; OPSCC, oropharyngeal squamous cell carcinoma ; TLM, transoral laser microsurgery ; IMRT, intensity-modulated radiation therapy; RR, relative risk; CRT, chemoradiotherapy; HNSCC, head and neck squamous cell carcinoma.

Discussion

Indications for TORS

TORS has several advantages, particularly in terms of increasing the surgical precision, and is an excellent option when correctly indicated[16,20,21,22]. Li et al. conducted a study in 2019 based on the National Cancer Database in the United States for evaluating the potential for reducing the risk of positive margins and need for adjuvant chemotherapy in patients undergoing TORS, transoral laser microsurgery (TLM), and non-robotic surgery. They concluded that the survival rate was the same for all patients but those who underwent TORS had lower rates of histologically positive margins as well as lower rates of adjuvant chemoradiotherapy (CRT)[2,13].

In a study conducted by Hanna et al. in 2020 on the use of TORS in early-stage laryngeal tumors, a comparison was made between TORS, TLM, and partial open surgery based on the survival rates, and it was concluded that there were no significant differences in the rates of negative margins between TORS and TLM (68.7% and 64.8%, respectively), but both methods were superior to open surgery (59.1%)[14].

TORS is used more frequently in patients with stages T1 and T2 tumors; however, a minority of patients with stages T3 and T4 can also benefit from this approach[3,16,20,21,22]. In addition, it is mandatory to implement a treatment plan using RT and/or CRT, especially in cases of HPV-positive tumors, as there is still much debate about the oncological efficacy of surgery for these tumors[3].

Disadvantages of TORS

Despite the many benefits of TORS, it has some disadvantages too. The following are some limitations of TORS: a high level of surgical expertise and the surgeon needs to be familiarized with the robotic system; lack of tactile feedback, which may appear strange to the surgeon; and longer operative time, which only decreases over time with the learning curve[1,2]. In addition, there is a distortion of the location of deep tumors because when the surgical retractors are positioned, they create a discrepancy between the location of the tumor in magnetic resonance imaging (MRI) and the actual location in the surgical field; however, it can be remedied by using an intraoral ultrasound during the procedure, which improves the delimitation of the tumor's margins even in case of deep tumors[3]. Although the Da Vinci Surgical System allows TORS, it was not designed to carry out this procedure. It was initially conceived for intra-abdominal surgery, and there is a large space in the abdominal cavity, unlike in the oral cavity and oropharynx. Thus, the difference

between the intra-abdominal and intra-oral spaces can be a considerable disadvantage in cases with complex anatomy due to the size of the articulated arms and position of the robot's camera[16]. TORS requires an exclusive space for the robot (its own operating room) and time for installation, and is expensive to buy and maintain, which warrants a thorough selection of patients. However, studies such as that by Borumandi et al. (2018) have reinforced the cost-benefit advantage of using the robot because of the direct effect of reducing the hospitalization time and complications, thereby generating savings for the healthcare system. Like any other robotic surgery, TORS shares the complications of traditional surgery along with an additional risk, which is the possibility of mechanical failure of the equipment and the inconvenience of converting to traditional surgery or suspending the procedure[1,7].

Different operation times

There is currently much debate about the operation time of TORS. The discussion revolves around whether the oral cavity and neck should be approached together in the same operation or in separate stages/operations, so that the neck is operated in the first stage using the traditional approach and the robotic surgery is performed in the second stage after some days, focusing exclusively on the oral cavity. The division of the operation into two stages has been suggested for reducing the number of complications related to the formation of fistulas between the cervical spaces and oral cavity[3]. Among the factors that influence fistula formation, the level of neck dissection is the most important. Therefore, some surgical teams choose to dissect levels II to IV of the neck in patients classified as N1 and N2a, while others dissect levels I to IV. Performing the procedure at different times reduces the risk of complications, namely intra- and/or postoperative bleeding because of the more precise identification of the branches of the external carotid artery, such as the lingual, facial, and ascending pharyngeal arteries[3].

Oncological efficacy of TORS

Currently, there is a controversy about the real potential of TORS, which has resulted in many studies comparing the various surgical and non-surgical treatment methods. According to Fu et al. (2016), who compared the surgical techniques of TORS, TML, and open lingual tonsillectomy in patients with the primary diagnosis of OPSCC, the tumor detection rates of TORS and TLM were higher than those of open surgery (80% vs 72%). Moreover, it was possible to reach a consensus on the safety and efficacy of tonsillectomy using TORS and TLM for the surgical screening of occult primary tumors, with TORS/TLM locating the primary tumor in 111 out of 139 cases (80%)[2,8].

In addition to the advantage of better tumor detection rates, TORS is superior for preserving the quality of life and swallowing function of patients. Castellano and Sharma et al. (2019) compared patients undergoing TORS and open surgery, and reported superior results for patients in the TORS group both in the quality of life and swallowing questionnaires. However, there are some other factors that can influence the quality of life and swallowing, such as the patient's performance status, T stage, and adjuvant treatment status. Considering that the vast majority of advanced tumors require a more aggressive open approach, there is a considerable difficulty in comparing the two groups[2,11]. Moreover, some studies have shown the efficacy of TORS by comparing it to primary RT. Thus, early TORS may reduce the need for RT, which is of great importance because high doses of RT increase patient morbidity in the short and long term [3]. Despite the favorable results regarding the efficacy of TORS, there is a lack of robust evidence, which makes it impossible to establish its superiority[16].

TORS vs intensity-modulated radiotherapy (IMRT)

TORS and IMRT are the two therapies of choice for patients with early-stage OPSCC, and there has been much debate about the oncological efficacy of both treatments. Some studies such as that by Yeh et al. (2015) showed favorable

survival rates for patients undergoing TORS but the rates were very similar and the differences were not clinically significant (74–100% and 69–100% for TORS and IMRT, respectively)[16,23]. In the ORATOR trial by Nichols et al. (2019), a comparison was made between TORS and IMRT in terms of the quality of life and toxicity of the two modalities. The results showed the superiority of IMRT with regard to the swallowing function one year postoperatively, but no significant differences were observed between the two methods, with comparable disease-free progression rates (88.2% vs. 82.4% for IMRT and TORS, respectively)[16, 24].

Although the difference between the disease-free survival rates was not statistically significant, there were some differences between the two treatment methods. For TORS, a radiological study is needed to locate the tumor to analyze the feasibility of the surgical procedure as well as suitability of the patient for the surgical procedure. In addition, due to the high cost of TORS and precise criteria for selection, it ends up being more demanding for the healthcare team in terms of planning and patient selection, which can result in the early detection of comorbidities and more targeted and personalized patient care. However, due to the limitations associated with randomized clinical trials, it is difficult to draw a definite conclusion regarding the superiority of any of the treatments[16].

Complications of TORS

Because TORS is a relatively new method of treatment and diagnosis, many surgeons are still wary of using it due to the need for specific training courses to work with the robot and uncertainty about the surgical complications associated with the method. In a systematic review with an overall sample size of 772 patients, the rates of hemorrhage and fistulas were 2.4% and 2.5%, respectively[3]. In a study conducted by Su et al. (2016), who analyzed a total of 305 patients, the complication and mortality rates were 7.9% and 0.7%, respectively, over a 30-day period, with hospital stay being the main factor contributing to increased comorbidity. In addition, TORS is associated with a low rate of swallowing disorders, which in the vast majority of patients disappear within six weeks of surgery; however, according to Fu et al. (2016), normal function does not return in around 1% of patients and a nasogastric tube is required during adjuvant treatment[3,25].

Conclusion

TORS is a safe and precise surgical technique that enables resection with millimetric margins and superhuman precision; however, despite the advantages of the robotic technique, currently there are several obstacles, such as the high cost of the robot and institutional requirements regarding infrastructure and specific care flow diagrams. A minimum difference in the oncological outcome (without statistical significance) was reported between TORS and IMRT; however, due to the technical hindrances in conducting randomized clinical trials, it is difficult to determine the superiority of one technique. Thus, further meta-analyses with more robust data are necessary to analyze the long term results of TORS. Overall, TORS is a very promising technique because it overcomes the barriers imposed by human limitations, and when associated with other technologies such as augmented reality (AR) and VSP, it has the potential for enormous developments in the future.

Conflict of interest

The authors declare no conflict of interest regarding this article.

Data confidentiality

The authors declare that they followed the protocols in use at their working center regarding the publication of patients' data.

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Availability of scientific data

There are no publicly available datasets related to this study.

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