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COMMENTARY

Surgical robotics for esophageal cancer

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We present an update on robotic techniques and their advantages and use in esophageal cancer surgery. Recent work has shown tremendous progress in robotic-assisted minimally invasive esophagectomy (RAMIE) and lymphadenectomy for esophageal cancer, as well as benefits of robotic surgery in high upper esophageal tumors and T4b disease. We discuss the different RAMIE techniques, especially for intrathoracic anastomosis. The ongoing ROBOT trial had demonstrated superiority of robotic esophageal cancer surgery over open esophagectomy. There are various putative technical advantages of RAMIE over minimally invasive esophagectomy, which need to be proven in future trials.

Keywords: RAMIE; robotic; esophagectomy; OESO; minimally invasive

Introduction

Esophageal cancer is one of the most severe and deadly human diseases.[1] Despite many achievements in diagnostics, multimodal treatment plans, surgical techniques, and advanced intensive care, short- and long-term survival for esophageal cancer patients remains unsatisfying.[2] Improvements in minimally invasive surgical techniques in recent years have led to reduced morbidity and mortality.[3,4] However, the thoracoscopic part of esophageal resection is a demanding procedure that requires a surgeon highly experienced in minimally invasive surgery. Owing to the implementation of robotic systems, the thoracoscopic aspect has transitioned in experienced centers toward robotic-assisted minimally invasive esophagectomy (RAMIE). Because of several technical advantages of the robotic system over the conventional thoracoscopic approach, the reintroduction of robotic hand-sewn intrathoracic anastomosis has become possible, with promising results, as well as conventional stapling techniques.[5–7] The 30-day and in-hospital mortality in high-volume centers performing minimally invasive esophagectomy (MIE) or RAMIE could be reduced to below 5%[4] and is not comparable to the morbidity and mortality rates of the past century. Additionally, long-term outcomes seem to be superior in RAMIE and MIE over open approaches, possibly due to advanced lymph node harvest in the video-supported and optically magnified resections; however, prospective trials have not been reported.[8,9] Owing to the rapid development of robotic systems, data reported from previous robotic systems used for esophageal resections have to be re-evaluated, since newer and more delicate systems (e.g., da Vinci Xi) are now available.[7] Minimally invasive robotic surgery for esophageal cancer has been proven to be feasible, safe, ontologically at least comparable or even superior to the open approach, and associated with less morbidity. In recent years, the use of RAMIE for cancers has increased rapidly and seems to exhibit at least of the same quality as minimally invasive laparoscopic/thoracoscopic esophageal surgery. Today, in light of multimodal treatment strategies with rapidly changing treatment protocols and additionally changing surgical strategies and techniques,

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a variety of questions remain unanswered, which we assess in this article.

Robotic surgery in high upper esophageal tumors and T4b disease

Patients with esophageal carcinoma with ingrowth in nonresectable adjacent structures like the trachea or aorta are precluded from surgery and are usually treated with definitive chemoradiation. Results of definitive chemoradiation are poor, with poor functional outcomes and a median overall survival of 14–21 months, due to high locoregional failure rates.[10–15] However, neoadjuvant chemoradiation might result in downstaging of the tumor, enabling a radical, curative resection of an initially irresectable esophageal carcinoma.[16,17] RAMIE provides an enlarged, three-dimensional (3D) field of view and facilitates dissection through articulating instruments allowing seven degrees of freedom and tremor filtering. Precise dissection is facilitated by articulating surgical instruments. These advantages enabled a meticulous esophageal and mediastinal lymph node dissection.[18] To improve oncologic results, we performed RAMIE in patients with cT4b esophageal cancer after downstaging with chemoradiation (50.4 Gy/28 fractions, combined with weekly paclitaxel and carboplatin).[19,20] The enlarged 3D image allows for very precise dissection of the irradiated tumor tissue from the trachea, bronchi, and aorta. The level of precision makes dissection in downstaged T4b tumors feasible.[20,21] So far, we have treated 10 patients using this strategy (unpublished data). We are awaiting the long-term oncologic and functional results with this approach before it can be recommended for all patients. Moreover, the upper mediastinum and thoracic aperture can be reached with an excellent 3D view and magnified observation of the operative field.

Intrathoracic anastomosis in RAMIE

Totally minimally invasive esophagectomies performed laparoscopically or thoracoscopically and RAMIE have been shown to be superior compared with open surgery.[3,22] Surgeons with experience in both MIE and RAMIE consider the latter approach to be superior.[23] To date, there has been no randomized comparison of RAMIE versus MIE. Such a trial would require many patients and an association coordinating a multicenter approach among robotic and minimally invasive high-volume centers. These centers should have passed the learning curve for MIE as well as RAMIE. Recently, the Upper GI International Robotic Association was established, with the aim of conducting such a trial in the near future.

One major issue during the minimally invasive approach is intrathoracic anastomosis. Many surgeons do not want to move toward adopting MIE or RAMIE, owing to the apprehension of causing more leaks by compromising their safe intrathoracic anastomotic stapling techniques. Therefore, it is essential to determine the best intrathoracic anastomotic technique and the possibilities of robotic-assisted anastomotic techniques, including possible combination with circular stapling techniques. The *best anastomosis* for the intrathoracic esophagogastrostomy after a gastric pull up in robotic surgery is not easy to define and is discussed in comparison with cervical anastomosis at this point. Several issues have to be considered, such as safety and costs to perform the intrathoracic anastomosis. Even advanced locking sutures, such as V-Loc^{TM} (Medtronic), which are often used in minimally invasive and robotic surgery for the anastomosis, are cheaper than circular or longitudinal stapler devices. Additionally, the time to perform an esophagogastrostomy in RAMIE has to be considered; however, different techniques can probably be performed with comparable durations.

RAMIE has the advantage of facilitating an intrathoracic hand-sewn technique, which is very complicated with the rigid instruments used in MIE (Fig. 1). Important aspects to be considered are leak rate, reoperation rate, and accessibility for treatment options. The three most commonly used techniques for intrathoracic anastomosis during RAMIE are

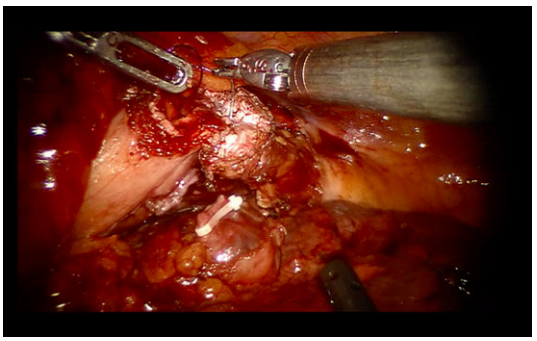

Figure 1. **A robotic-assisted intrathoracic hand-sewn anastomosis.**

hand-sewing (robotic assisted), linear stapling, and circular stapling. Each of these techniques has its own advantages and disadvantages, and outcome is also dependent on the surgeon's expertise. However, the circular stapling technique has been proven in both hybrid esophagectomy and MIE to be safe and standardized. Key advantages of intrathoracic circular stapler for MIE[24] or RAMIE[7,25] procedures are as follows: (1) the circular stapling procedure is standardized and reproducible, and different circular stapling sizes can be adapted to the individual diameter (our standard is to use a 28-mm stapler); (2) stapled anastomosis in the chest seems to lead to a lower leakage rate than anastomosis in the neck, although quality of life, stricture rate, and reintervention rate are under current investigation;[26–29] (3) in the case of leakage of an intrathoracic anastomosis, the circular stapled esophagogastrostomy can be treated endoscopically owing to the defined diameter of the anastomosis (intraluminal endosponge/Endo-VAC treatment is possible or esophageal stents, which do not dislocate owing to the defined anastomotic diameter); (4) circular stapling can be performed very high intrathoracically, even at the thoracocervical transition (Fig. 2) (however, in upper esophageal cancer, cervical anastomosis may be necessary to achieve an R0 resection); (5) circular stapler anastomosis provides a circular resection margin (the esophageal donut), which is a very clear and defined resection margin for the pathologist and is useful to prevent tumor infiltration of the resection margin; and (6) the circular stapling technique has been proven feasible in RAMIE".[7]

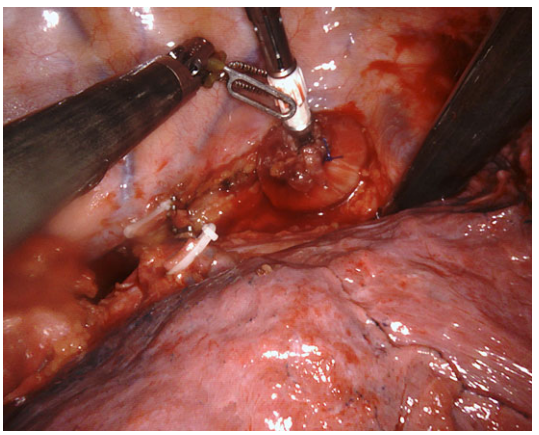

Figure 2. **The circular stapler head is placed in the esophageal stump high intrathoracic at the transition of the thorax to the neck. The clipped azygos vein is shown on the left and the collapsed right lung on the lower right.**

The robotic anastomosis techniques in RAMIE have been described but not assessed. Therefore, the "best" intrathoracic anastomosis is unknown. In the literature, there are several meta-analyses showing that the use of a circular stapler contributed to reducing the length of the operation but was associated with an increased risk of anastomotic strictures.[30] Both the circular stapler and the hand-sewn methods are viable alternatives for reconstruction after esophagectomy.[7,31] However, the hand-sewn method performed thoracoscopically cannot be compared to the robotic-assisted hand-sewn method. In a review by Deng *et al.*, the stapled methods were shown to lead to a reduced leak rate;[32] however, this does not prove the superiority of this method.

There are no data available on the comparison of robotic-assisted anastomotic hand-sewn and stapling techniques. Further prospective trials are needed to determine which is the superior anastomosis technique in terms of handling, safety, perioperative and long-term complications (e.g., strictures), and patients' quality of life. At present, we recommend using the technique that works best for the robotic surgeon as long as the results are comparable to the results for open, MIE, and hybrid procedures.

The up-to-date advantages of RAMIE over MIE in esophageal surgery

In recent years, the interest in robot-assisted surgery among general and thoracic surgeons has increased dramatically. This interest came together with, and appears to be caused by, the introduction of new robotic systems that are easier to operate in multiple quadrants without the need to redock the system multiple times during a procedure. RAMIE is increasingly used. The standard MIE is a long and complex procedure, and it is believed that a robot-assisted approach could be advantageous for both patient and surgeon.

We performed a brief review of the literature in order to search for any scientific evidence of the assumed advantages of RAMIE over MIE. A PubMed search was performed with the terms "Robot" AND "Esoph*," producing 178 hits. There were no randomized clinical trials, and only 16 publications described a RAMIE cohort, predominantly

the initial experiences in small series. In three publications, comparisons were made between RAMIE cohorts and historical MIE cohorts.[33–35] Only one of the studies found a statistically significant larger lymph node yield for RAMIE. On all the other parameters, RAMIE proved to be "safe and noninferior to MIE."

Without the support of scientific publications, we debated the differences between RAMIE and MIE and where we might search for advantages. For the patient, both RAMIE and MIE are minimally invasive approaches for an esophagectomy that apply the same steps and approaches. A real difference is the instrument with which the surgeon performs the procedure. Therefore, one advantage could be found in the field of ergonomics. Many surgeons experience ergonomic concerns when performing conventional minimally invasive surgery.[36] These concerns are solved by various interventions in robotic surgery. First and most important, the surgeon is moved away from the patient into an ergonomically designed working console that restores the natural eye–hand axis of the operator and provides stable and 10× enlarged 3D vision. Second, the robotic instruments have articulating wrists, providing seven degrees of freedom; the robotic system corrects for the pivoting and scaling movements of the instruments on the bowel/thoracic wall, known as the Fulcrum effect.[37] Natural tremors are filtered out of the movements, and, with the touch of a button, the scaling of the instrument movements can be adjusted to the preferences of the surgeon for the task to be performed.

All of these ergonomic advantages should provide a better ergonomic balance, leading to a procedure that is performed with greater detail and accuracy in which the surgeon experiences less musculoskeletal and physical stress while performing the task. Translating this to esophagectomy, we could expect that an oncologic resection would be performed with more accuracy and may lead to a higher lymph node yield[38,39] and a higher radical (R0) resection rate. Asian studies have shown superior upper mediastinal lymphadenectomy with the robot.[34] A recent propensity score–matched study showed higher lymph node yield in robotic versus thoracoscopic eosophagectomy.[33] However, more studies need to be performed to attain solid evidence for a higher lymph node yield after RAMIE. In addition, complications resulting from the esophagectomy, such as recurrent laryngeal nerve palsy, chylothorax, and anastomotic leakage, might be reduced.

An additional advantage of a high-tech electronic and computer-powered platform is the possibility to incorporate other upcoming techniques that can further improve the ergonomic balance and quality of the surgery.[38] Augmented reality is a technology that incorporates computer-generated data into the visible working field inside the patient, providing the surgeon with information that cannot be seen otherwise. A technique that is already incorporated into the latest robotic system is near-infrared fluorescence (NIRF). In NIRF, a contrast agent is illuminated with a laser, causing it to emit light in the near-infrared spectrum that is captured with a special filter on the robotic camera system. With this technique, anatomical structures, such as blood vessels, ducts, and lymph nodes, can be visualized, and tissue perfusion can be monitored. Another technological possibility is the real-time overlay of preoperative imaging studies, allowing the surgeon to work more precisely and helping her to find specific structures that have to be removed or avoided.[40]

Concluding comments

An important advantage of RAMIE over conventional MIE is the greater ergonomics of the robotic system, which significantly improves the ergonomic balance of the working process in many areas. It can be expected that this improved working process will lead to better, more precise surgery for the patient, resulting in a reduction of complications and expansion of the indications for curative surgery. Additionally, current and future developments, such as augmented reality, can be incorporated into the computer-based robotic platform and provide the surgeon with extra information to further enhance surgical resection quality and decision making.

Competing interests

M.v.D., R.v.H., and J.R. are proctors for Intuitive Surgical. The other authors declare no competing interests.

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