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EDITORIAL – GASTROINTESTINAL ONCOLOGY

Comment on: "Early Outcomes of Robot-Assisted Versus Thoracoscopic-Assisted Ivor Lewis Esophagectomy for Esophageal Cancer: A Propensity Score-Matched Study"

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Zhang and colleagues are to be complimented for recently conducting an interesting study that compared the perioperative outcomes of two-stage robot-assisted minimally invasive esophagectomy (RAMIE) versus two-stage conventional minimally invasive esophagectomy (MIE).[1] In that study, it was concluded that RAMIE and MIE are similar regarding intraoperative blood loss, postoperative complications, length of hospital stay, and lymph node yield; however, the operating time was significantly longer in the RAMIE group. These findings are a valuable addition to the existing evidence for RAMIE and we would like to place this into a broader perspective.

Although open esophagectomy is still the worldwide standard, MIE is increasingly applied, aiming to decrease surgical trauma and ultimately improve postoperative outcomes in terms of postoperative complications. This paradigm shift is largely based on evidence from case series and a randomized controlled trial, which indicated that MIE may be superior to open esophagectomy in terms of intraoperative blood loss, postoperative pulmonary complications, length of hospital stay, and quality of life.[2] However, several recent population-based studies have reported a higher re-intervention rate in patients who underwent MIE, while no evident reduction in postoperative pulmonary complications or overall morbidity was observed.[3–6] It was postulated that these findings might be explained by the learning curve of MIE as the early adaptation phase was within the inclusion years for most countries. In this context and in addition to the authors' statement that the learning curve of MIE takes 35–45 cases to complete, it should be noted that a recent multicenter study concluded that approximately 119 cases are required to acquire proficiency in two-stage MIE (i.e. MIE with an intrathoracic anastomosis).[7] This extensive learning curve is illustrative for the technical complexity of the procedure, which is most pronounced in the thoracic phase.

Although a hybrid procedure that combines a laparoscopic abdominal phase with an open thoracic phase has been proposed as an alternative,[8] robotic assistance can aid to overcome many limitations of conventional minimally invasive techniques. The main advantages of robotic assistance include an improved three-dimensional view of the surgical field, deterrence of the fulcrum effect, a greater range of movement of the instrument tips, and tremor filtration. After its introduction in 2003, RAMIE was shown to be feasible and safe, with good oncological results in several case series. The recent randomized controlled ROBOT trial demonstrated superiority of three-stage RAMIE over three-stage open esophagectomy in terms of intraoperative blood loss, postoperative pain, morbidity, length of hospital stay, and quality of life.[9–13] Based on these results, three-stage RAMIE can be regarded as a good alternative to both open esophagectomy and MIE.

Although considerable evidence exists on three-stage RAMIE, two-stage esophagectomy is increasingly preferred to resect tumors of the mid to distal thoracic esophagus, as intrathoracic anastomoses seem to be associated with less anastomotic leakage when compared with cervical anastomoses.[14] Several case series have already shown promising results for two-stage RAMIE, and have suggested that this technique is safe and feasible.[15–17] Nonetheless, the currently available evidence from the

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literature is too limited for any definite conclusions regarding the outcomes of two-stage RAMIE in relation to traditional techniques.

The comparison with conventional MIE is of particular interest and randomized controlled trials would ideally be conducted to provide insight in this regard. The lack of such studies can, in part, be explained by the fact that only a few surgeons are capable of performing both RAMIE and MIE at a high-performance level, which is a prerequisite to guarantee a non-biased analysis of randomized data. Moreover, the potential clinical differences of RAMIE over MIE are expected to be relatively small, which means that a large sample size would be needed to detect these potential clinical differences with sufficient power. For instance, one could hypothesize that conversion to an open procedure is less frequently required when using robotic assistance as the robotic arms allow for a substantially greater range of motion than the conventional minimally invasive instruments.

The ROLARR trial recently investigated this hypothesis in 471 patients who underwent surgery for rectal cancer (i.e. high anterior resection, low anterior resection, or abdominoperineal resection).[18] The primary outcome measure was conversion to an open procedure and the sample size calculation was based on an anticipated relative reduction of 50% in the robot-assisted group. Although a lower conversion rate was indeed seen in the robot-assisted arm, the actual difference was considerably smaller (8.1% vs. 12.2%). Although this difference in conversion rates may truly be present, it was not statistically significant with the chosen sample size. An enormous number of patients would have to be randomized in order to detect such a small difference with adequate power. The results of this trial are therefore demonstrative of the challenges that are faced when performing a randomized trial that aims to compare robot-assisted versus conventional minimally invasive surgery in terms of clinical outcomes.

In this context, the current study by Zhang et al. addresses an important hiatus in esophageal cancer literature by comparing the outcomes of RAMIE versus MIE after propensity score matching. Based on their analyses, the authors concluded that the perioperative outcomes of RAMIE and MIE are similar, except for a significantly longer duration of surgery that was observed in the RAMIE group; however, these findings should be considered in the context of the cohort that was investigated. The center of inclusion had performed a total of 76 RAMIE procedures at the time of performing the study, of which 66 procedures were propensity score matched. This means that a substantial part of the included patients in the RAMIE group underwent surgery during the learning phase, as a previous study indicates that the learning curve for RAMIE takes up to 70 cases to complete.[19] Intraoperative blood loss and operating time are known to decrease with increasing experience, which might imply that the reported longer duration of surgery in the RAMIE group might not be present anymore and that even less intraoperative blood loss might be observed after completion of the learning curve. However, to adequately investigate such outcomes, studies on larger case series of patients who undergo RAMIE after completion of the surgeon's learning curve are warranted.

The learning curve of RAMIE is important to keep in mind when implementing the technique, and strenuous efforts should be made to minimize its duration. To this end, thorough (pre-)clinical training is fundamental prior to adopting the technique. A recent study reported that the learning curve of RAMIE can be decreased from 70 to 24 cases when adhering to a structured training pathway, which successively involves a robotic cadaver course, case observations, and proctoring by an experienced peer.[19] By shortening the learning curve of RAMIE, structured training pathways likely increase the safety and efficacy of the implementation phase. The facilitation and promotion of such structured training pathways in one of the key aims of the 'Upper GI International Robotic Association (UGIRA)', which was established in 2017 and serves as an important platform to connect surgeons who are willing to implement RAMIE (and other robot-assisted esophagogastric techniques) to proctors worldwide. The efficacy of the structured training programs is monitored by the prospective collection of data regarding the perioperative outcomes of all procedures in the UGIRA Registry. These collected data will also allow analyses to further develop the structured training pathways and to establish individualized approaches to surgeons of varying baseline experience levels.

The current technical advantages of robotic assistance mainly reside in the ability to gain more control over the procedure, which is especially desirable when operating in anatomically challenging areas. For example, it was reported that RAMIE is safe and feasible to resect tumors located near the upper thoracic inlet, which would have been extremely difficult to reach by conventional minimally invasive or open techniques.[20] In addition, a previous study from Taiwan concluded that RAMIE is associated with a higher lymph node yield along the left recurrent nerve when compared with conventional MIE, which may provide survival benefits.[21,22] This topic will be further addressed in a randomized controlled trial by the same group.[23]

In addition to the current advantages that are experienced in robot-assisted surgery, robotic systems have a tremendous potential to be developed further. Substantial improvements have already been seen with the latest Da Vinci Xi model, which is more easy to dock and has a

fourth robotic arm that can be used to take control over tasks that would otherwise be performed by the table assistant. Future developments might be sought in the direction of artificial intelligence. The high quality of the recordings by stable robotic cameras could allow for surgical videos to be meticulously analyzed.

Augmented reality might have a particular potential to lift the current surgical practice to a higher technological level as it can add a real-time computer-generated layer to what is seen by the naked eye. For instance, this could be used to indicate structures that should be targeted or avoided during surgery or to enhance surgical training. In the even further future, computer recognition of certain anatomical structures or surgical situations could be translated to actions of the robotic arms. The overall technological developments are moving forward at an incredible pace and robotic systems may offer a platform for the surgical profession to keep up.

In summary, the study by Zhang et al. presented important data regarding the outcomes of two-stage RAMIE in relation to MIE; however, more research is warranted to gain insight into these outcomes after completion of the RAMIE learning curve and in larger cohorts. Furthermore, the use of a structured training pathway is recommended to safely and effectively implement RAMIE as it has been shown to substantially reduce the length of the learning curve. In addition to the current technical advantages of RAMIE, robotic systems are expected to be developed further and offer advanced technological applications in the future.

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