



Pushing the envelope of minimally invasive esophagectomy

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Esophageal cancer surgery—which is traditionally performed through laparotomy and thoracotomy—carries significant risks in terms of morbidity and mortality (1). Over the last two decades, minimally invasive esophagectomy (MIE) has emerged as a valuable approach that may help reduce surgical trauma—ultimately minimizing complications rates. In 2012, the seminal European multicenter TIME trial demonstrated that total MIE—consisting of thoracoscopy and laparoscopy—was characterized by significantly lower rates of respiratory complications (9% *vs.* 29%, respectively) and a shorter length of stay (11 *vs.* 14 days, respectively) compared with the traditional open approach (i.e., thoracotomy and laparotomy) (2,3). In 2018, similar results were reported in the ROBOT (Robot-assisted Thoracoscopic Esophagectomy *vs.* Open Transthoracic Esophagectomy) trial (4). In this study, 55 patients were randomly assigned to an open three-field esophagectomy, whereas 54 patients were randomized to a robot-assisted three-field esophagectomy (with the thorax being approached robotically and the abdomen laparoscopically). The overall complication rate (59% *vs.* 80%, respectively), the median blood loss (400 *vs.* 568 mL, respectively), and the rate of pulmonary complications (60% *vs.* 80%, respectively) were all lower in the robot-assisted group. Although there were no significant intergroup differences in terms of overall and disease-free survival, pain was less severe and quality of life was higher in the robot-assisted group (4).

An important characteristic of thoracoscopic/robotic and laparoscopic surgery is the existence of a significant

learning curve—with the successful adoption of both approaches requiring a significant investment of time and resources (5-7). This limitation—coupled with the well-known technical complexity of the thoracoscopic/robotic and laparoscopic approaches—has limited the widespread adoption of MIE for patients with esophageal malignancies (7). In this context, a hybrid approach—consisting of either thoracoscopy/laparotomy or thoracotomy/laparoscopy—can represent a reasonable alternative with a less steep learning curve. Because of a lower burden in terms of pulmonary complications, avoidance of thoracotomy is generally considered a prerequisite to achieve better clinical outcomes. Therefore, hybrid MIE based on thoracoscopy and laparotomy has comparatively received more attention than the combination of thoracotomy and laparoscopy (8). Several retrospective studies have confirmed the benefits of hybrid thoracoscopic MIE over the open approach (9). However, the results of a recent randomized controlled trial conducted by the Federation de Recherche en Chirurgie (FRENCH) and French EsoGastric Tumors (FREGAT) Working Group challenged this traditional view (10). In this multicenter trial, the authors compared hybrid MIE (laparoscopic gastric mobilization and open thoracotomy) with open esophagectomy (open gastric mobilization and thoracotomy) in patients with thoracic esophageal cancer who were undergoing esophagectomy using an abdominal and right thoracic approach (Ivor Lewis procedure). The occurrence of intraoperative and postoperative complications (grade \geq II according to the Calvien-Dindo

classification) within 30 days was the primary outcome measure. Secondary endpoints included death within the first 30 post-operative days, tumor recurrence, and overall survival.

Although all patients had undergone open right thoracotomy for esophagectomy with an intrathoracic anastomosis, avoidance of laparotomy alone led to a significant reduction of major perioperative complications from 64% to 36%. The incidence of major pulmonary complications similarly decreased from 30% to 18%. The 30-day (1% and 2% in the hybrid MIE and open surgery groups, respectively) and 90-day (4% and 6% in the hybrid MIE and open surgery groups, respectively) mortality rates did not show significant intergroup differences. After a 3-year follow-up, overall and disease-free survival rates did not differ significantly in the two groups, although more favorable trends were observed in patients who received hybrid MIE.

Despite the promising results in patients treated with hybrid MIE, several comments on the study findings may be offered. First, the lower rate of pulmonary complications in the hybrid MIE group did not translate either into a shorter median length of stay or a lower surgical mortality. This phenomenon may be explained by the fact that the length of incisions has a lower impact on clinical outcomes than the time required for recovering from surgery-induced changes in gastrointestinal physiology and surgical dissections. An alternative explanation is that patients in this hybrid MIE trial might have been more promptly and effectively treated upon detection of a complication. Further cost-effectiveness analyses should help cast more light on this issue. Second, we should keep in mind that clinical trials do not invariably reflect real-world practice. This issue is even more pronounced in surgical trials, which can significantly be influenced by the learning curve effect. A nationwide study conducted in Japan on an unselected cohort of 5,534 patients who had undergone McKeown esophagectomy demonstrated that MIE did not significantly reduce the 30-day rates of death and postoperative pneumonia (11). In contrast, MIE was associated with higher 30-day reoperation rates compared with open surgery. Another study conducted in the UK on an administrative cohort of 18,673 patients (with the majority being treated with the Ivor Lewis procedure) similarly failed to show the superiority of MIE over open surgery (12). When interpreting findings from clinical trials, it is also paramount to take into account the quality metrics used in the selection of surgeons and recruiting centers (i.e., 25 previous laparoscopic procedures

in the hybrid MIE trial) (10).

Based on the currently available evidence from three European randomized trials, we therefore conclude that total and hybrid MIE are both significantly superior to open esophagectomy—with either technique leading to decreased complication rates when performed by experienced hands. Oncological outcomes of total and hybrid MIE are broadly similar and in line with the highest contemporary standards.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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