Review Article

Hybrid esophagectomy

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Abstract: Esophagectomy is a complex surgical procedure associated with high rates of mortality and morbidity, mainly dominated by pulmonary complications. Minimally invasive approaches have been developed in order to decrease postoperative morbidity, including totally minimally invasive esophagectomy (MIE) and hybrid esophagectomy in which one surgical step is achieved either by laparoscopy or thoracoscopy and the other step by open approach. In this review, we will discuss the main results of this hybrid approach in esophagectomy for cancer. Hybrid esophagectomy is associated with better postoperative outcomes compared to open approach, and similar outcomes compared to totally MIE, especially concerning pulmonary complications. For long-terms outcomes, hybrid approach showed similar, or even better, overall survival than open approach. With a short learning curve, hybrid esophagectomy with laparoscopic gastric mobilization will be the future gold standard for esophagectomy and should be further compared with totally MIE.

Keywords: Esophagus; cancer surgery; laparoscopy; thoracoscopy; minimally invasive; hybrid; review

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Introduction

Esophageal cancer is the seventh leading cause of cancer worldwide. In Western countries, the incidence of esophageal cancer, particularly adenocarcinoma histotype, is increasing, mainly caused by increased obesity and gastro-esophageal reflux disease (1). Surgical resection with radical lymphadenectomy, generally after radio ± chemotherapy, remains one of the main components to treat esophageal carcinoma. Esophagectomy is a complex procedure associated with a high rate of mortality and morbidity. However, in high volume centres with appropriate multidisciplinary teams, those rates could be reduced significantly (2,3).

The reasons for this improvement are multifactorial including better patient selection, preoperative nutritional support, prehabilitation, improvements in perioperative care and advances in surgical techniques (1). However, esophagectomy remains associated with high postoperative morbidity (30–50%), mainly dominated by pulmonary complications, which occurs in 10% to 40% of patients and accounts for 50% of postoperative deaths (4). Hence, minimally invasive approaches have been developed in numerous gastrointestinal procedures in order to decrease postoperative complications. Similarly, minimally invasive esophagectomy (MIE) could reduce postoperative morbidity and mortality. In the 90s, some surgical teams have introduced thoracoscopic approach, firstly restricted to early esophageal cancer (T1 or T2 stage) without preoperative treatment (2,3). Thereafter indications of minimally invasive approach were extended to advanced disease, including patients having received neoadjuvant treatments.

The techniques of MIE vary widely and thoracoscopy

was initially favoured over laparoscopy. Several authors described totally minimally invasive esophagectomy (TMIE), combining both laparoscopic and thoracoscopic approaches, whilst others describe hybrid esophagectomy (HO) where only one stage of the operation is performed by minimally invasive approach. Due to the small number of studies assessing HO including laparotomy and thoracoscopy, we will focus exclusively in this review on hybrid esophagectomy with laparoscopic gastric mobilization and thoracotomy (HELGM).

Hybrid esophagectomy—proof of concept and first description

HELGM, which has been developed in parallel with TMIE, is based on the hypothesis that surgical incisions on both sides of the diaphragm during esophagectomy is the main cause of postoperative complications, especially pulmonary complications, due to deterioration of respiratory mechanisms. It has been shown that an upper-midline laparotomy can significantly affect respiratory function to the same degree as a thoracotomy (5,6). Laparoscopic approach could lead to better respiratory function than after open approach as demonstrated in other and more common surgery such as cholecystectomy (7,8).

First studies assessing HELGM for cancer showed that hybrid approach was feasible in most cases, with an estimated conversion rate of 0% to 7.4%, and an operating time similar to the open approach (9-11). No gastric necrosis was observed and the gastric transplant fashioned laparoscopically was long enough to reach the upper thoracic inlet or the cervical esophagus.

When compared to TMIE, HELGM may offer several advantages, including (I) reproducibility of the technique after a short learning curve, (II) no need to dissect the tumor laparoscopically and therefore applicability of this approach to more patients regardless of tumor stage or preoperative treatments and (III) lower risk to deteriorate oncological and long-term outcomes. In addition, the laparoscopic approach during gastric mobilization seems more reproducible and easier than thoracoscopic approach. An optimal volume threshold of 25 laparoscopic gastric mobilizations was chosen for entry into the prospective randomized MIRO trial, assessing the potential benefit of HELGM versus open esophagectomy for cancer (12). This volume threshold for entry into the trial was selected through a Delphi consensus process with the participating centers. This threshold has been also validated as being suitable for MIE in a nationwide study (13). Finally, this approach is attractive because it doesn't change the construction of esophagogastric anastomosis performed, which is a pivotal moment during the surgical procedure conditioning post-operative outcomes

Hybrid esophagectomy—postoperative outcomes

The first purpose of MIE is to reduce the rate of surgical complication associated with open esophagectomy. Most data available for hybrid procedure come from retrospective or prospective non-randomized series (10,14-18). These studies propound that complication rate decrease after HELGM compared with open esophagectomy. Thus, Briez *et al.* in a prospective non-randomized study showed that HELGM reduced major postoperative pulmonary complications at 30 days by 63% compared to open esophagectomy, associated with a decrease in overall morbidity rate (18). This decrease in postoperative pulmonary complications was also observed in three retrospectives studies comparing open and HELGM (14,16,19).

HELGM may also be associated with a decrease in postoperative mortality rates when compared to open esophagectomy, although most studies were not designed and powered to identify a potential impact of HELGM on postoperative mortality. Recently, a French Nationwide study has been published, including 3,009 patients who underwent esophagectomy for cancer, with gastric pull-up reconstruction between January 2010 and September 2012 (17). Among those patients, 663 had HELGM. After a propensity score matching to compensate for the differences in baseline characteristics between open and hybrid group, the authors showed that 30-day postoperative mortality was significantly lower after laparoscopic gastric mobilization (3.3% *vs.* 5.9%, P=0.029), as were in-hospital (5.6% *vs.* 8.4%, P=0.026) and 90-day (6.9% *vs.* 10.1%, P=0.018) postoperative mortality. Independent predictive factors of postoperative mortality at 30 days were age ≥60 years, malnutrition, cardiovascular comorbidity and gastric mobilization by open approach in the non-matched population studied. The other benefits of hybrid procedure were decrease in operative bleeding, reduction in operative time, shortening of ICU and hospital stays without negative impact on oncological resection i.e., the number of retrieved lymph nodes and complete resection rate (19,20).

Up till now, only one randomized controlled phase III trial has been reported confronting HELGM versus open

procedure: the MIRO trial (21). This trial hypothesized that HELGM is associated with a decrease in major postoperative morbidity (main objective) with similar oncological outcomes than open approach, through an easily reproducible surgical procedure. One hundred and four patients were randomly assigned to open procedure and 103 to hybrid approach. Major postoperative morbidity was observed in 67 patients (64.4%) in the open group and in 37 patients (35.9%) in the hybrid group (OR 0.31; 95% CI, 0.18–0.55; P=0.0001). After hybrid procedure, 18 patients (17.7%) had major pulmonary complications compared to 31 patients (30.1%) after open approach (P=0.037). Globally, HELGM was associated with less medical related postoperative complications than open esophagectomy (19.6% *vs.* 39.8%), whereas surgical complications were comparable between the groups and even in favor of HELGM. Mortality rates after 30 days were also comparable between open and hybrid approach (1.9% *vs.* 1.0%). In addition, this study confirmed the absence of negative impact on oncological resection i.e., the number of retrieved lymph nodes and complete resection rate (12,22).

Hybrid esophagectomy—long-term outcomes

Although HO reduces the rate of postoperative complications, it is necessary that hybrid approach does not impair oncological outcomes. Increased visibility due to magnification provided by laparoscopy can promote accurate dissection and optimal lymph node dissection. However, no large prospective randomized studies with long-term follow-up have been published yet to demonstrate the true oncological value of hybrid approach. Thus, only few retrospective studies with small effective compared long-term outcomes between HELGM and open esophagectomy without showing any difference on overall and disease-free survival (14,23).

In the French multicenter phase III MIRO trial, the 3-year overall survival rate in the HELGM (67.0%; 95% CI, 57–75.2%) was improved compared to open surgery group (54.8%; 95% CI, 44.8–63.8%; P=0.054). Thus, MIRO study brings further evidence for minimally-invasive approach to decrease postoperative morbidity without impairing long-term oncological outcomes.

Totally versus hybrid esophagectomy

Due to the good results of HELGM on the decrease of major postoperative pulmonary complications rate, it is necessary to consider whether a TMIE could further improves these outcomes.

Very few studies compared postoperative outcomes after HE versus TMIE. Bonavina *et al.* published a retrospective study with propensity-matched comparative analysis of 80 HELGM versus 80 TMIE (24). In this study, there was no difference found between the 2 groups in the incidence of complication and in the overall survival rates. Of note, in the TMIE group, the esophago-gastric anastomosis was performed in the left neck incision whereas it was performed in the upper thoracic inlet in HELGM group. A recent study published by Berlth *et al.* showed that TMIE had similar postoperative outcomes compared to HELGM with significantly shorter ICU stay (1 *vs.* 2 nights) and less postoperative pain. However, the rate of anastomotic leak observed was 15% in TMIE group versus 5% in HELGM group (P=0.186) (25).

According to the two prospective randomized trials published, the TIME trial confronting TIMO versus open procedure (26) and the MIRO trial confronting HELGM versus open procedure (21), similar conclusions can be drawn. The decreases observed on postoperative complications, according to odd ratios reported, were comparable: 0.30 (0.12–0.76) in the TIME trial and 0.31 (0.18–0.55) in the MIRO trial. Regarding oncological results, TIME trial reports similar 3-year overall and disease-survival rates between TMIE (27) and open approach whereas the MIRO trial reported long-term outcomes also comparable between groups, slightly favoring hybrid MIE (see above).

Conclusions

HELGM appears ease to perform, reproducible, and does not require modification of the surgical technique (i.e., site of anastomosis). It seems feasible regardless of tumor and patients' characteristics and does not compromise carcinologic resection, at least for middle third and lower third esophageal tumors including Siewert I Tumor.

TMIE with intra-thoracic anastomosis (i.e., Ivor Lewis) is a technically demanding approach with a significant learning curve up to 119 cases with an increased risk of anastomotic leakage at least at the beginning of experience. This may consequently require initially modifications of the surgical technique with performance of a cervical anastomosis instead of intra-thoracic anastomosis as observed in the TIME or the ROBOT trial (26-32).

TMIE is a technically demanding approach leading to

a higher risk of error, which requires modifications of the surgical technique with cervical anastomosis instead of intra-thoracic anastomosis, and associated with its proper morbidity . Thus, TMIE seems less easily reproducible and more time-demanding approach than HELGM, even in experienced hands.

Future studies comparing TMIE and HELGM are expected to demonstrate the interest of each surgical approaches. Comparison between TMIE and HELGM is theoretically of scientific interest. However, based on the results of randomized trials published to date, offering similar odd ratios, we can expect small differences between the two approaches while requiring a very large number of patients to be enrolled. The results of the prospective randomized ROMIO study that compares these 2 surgical are awaited (33,34)

Rather than oppose TMIE and HELGM, it would be more interesting to choose one of these approaches depending on the patient's characteristics, the tumor extension and the expertise of the center. Moreover, the advent of robotic surgery will surely overcome technical difficulties related to perform minimally invasive intrathoracic esophago-gastric anastomosis and further improve postoperative outcomes of TMIE

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Footnote

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

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