



Hybrid approaches to minimally invasive esophagectomy

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Abstract: Esophageal cancer resection usually requires a two-field or three-field surgical approach to perform the resection and the reconstruction. With the progress of anaesthesiology and surgical skills, the possibility to reduce the surgical trauma has grown up and minimally invasive esophagectomy (MIE) has widespread worldwide. The hybrid approaches to MIE are the combination of minimally invasive approaches mixed to open approaches by applying the minimally invasive techniques at one level of the two stages (abdomen or thorax) of the procedure. The hybrid techniques can be decided prior to surgery in the surgical decision-making strategy to focus and to keep open approach for one the two stages, either because of expected surgical issues or to obtain a better exposure for confection of the intrathoracic anastomosis. Sometimes, the decision to opt for hybrid techniques can also results from the necessity to convert intraoperatively at both stages during total MIE. The most described hybrid techniques are represented by the laparoscopic hybrid Ivor Lewis esophagectomy where the gastric mobilization is performed laparoscopically whereas the confection of the intrathoracic anastomosis is performed with an open approach. This technique appears safe, reproducible, and easy to teach. The recent MIRO trial has provided evidences that the unique use of laparoscopy for the abdominal part of the esophagectomy resulted in a strong benefit on postoperative respiratory outcomes, with the same magnitude to those observed with total MIE. The MIRO trial suggests that the maximum benefits of minimally invasive techniques are more provided by laparoscopy rather than thoracoscopy. Moreover the laparoscopic approach results in better short, mid and long-term outcomes compared to open approach, without any compromise regarding oncological outcomes. At last, laparoscopy seems to improve health-related quality of life. The laparoscopic approach has to be seen as a new standard approach and should be incorporated to all esophageal cancer resections whenever possible.

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Introduction

The specificity of esophagectomy techniques stands in the necessity to have two-field or three-field surgical approaches to perform the oncological resection and the reconstruction. At the current time, esophagectomy is performed mostly in tertiary centers because of its complexity. With the progress

of anaesthesiology, instrumentations and surgical skills, the possibility to reduce the surgical trauma has grown up since the 90's. Since the last two decades, the global preference for smaller incisions and minimally invasive approaches in the field of esophageal surgery has become a reality worldwide (1-3). Moreover, this trend is progressively

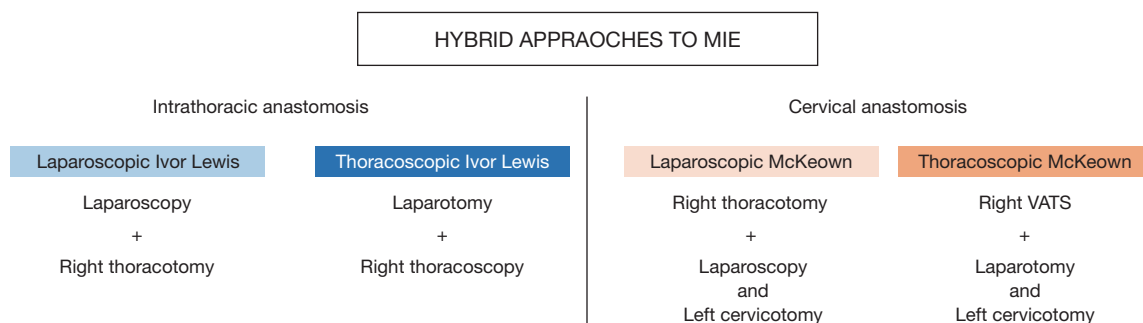


Figure 1 The several hybrid approaches to minimally invasive esophagectomy (MIE) according to the level of the reconstruction.

supported by level-one evidences in the literature review, with to date, three prospective and randomized clinical trials demonstrating the benefits of such approaches, even after neoadjuvant treatment (4-6). However, the major issue with minimally invasive esophagectomy (MIE) lays in the gastric reconstruction and the confection of the anastomosis. For these reasons, many surgeons remain unsatisfactory with the anastomosis confection using minimally invasive techniques. As a result, many of them have opted for a combination of mixed conventional and minimally invasive approaches to overcome this issue and to conserve the benefits of minimally invasive surgery (7,8).

The hybrid approaches to MIE are the combination of minimally invasive approaches mixed to open approaches by applying the minimally invasive techniques at one level of the two stages (abdomen or thorax) of the procedure. This can be at the level of the abdominal phase using a laparoscopy or at the thoracic phase by using a video-assisted thoracoscopic surgery (VATS). The hybrid techniques can be clearly decided prior to surgery in the surgical decision-making strategy to focus and to keep conventional surgery for one the two stages because of expected issues. Furthermore, decision to opt for hybrid techniques can also result from the necessity to convert intraoperatively at both stages of the technique during total MIE and to conserve the benefits of MIE for the remaining procedure.

The most described and studied of these hybrid techniques are is represented by the laparoscopic hybrid Ivor Lewis esophagectomy where the gastric mobilization is performed laparoscopically whereas the confection of the intrathoracic anastomosis is performed with a standard fashion. This technique is specifically indicated for adenocarcinoma of the gastro-esophageal junction (GEJ) or for tumor of the lower third esophagus. In addition, the

hybrid VATS esophagectomy combined with laparotomy has been described but data on this technique are scarce.

The goal of this review is to depict the several techniques of hybrid esophagectomy and to discuss the results of such techniques.

Surgical techniques

The several hybrid approaches to MIE avec summarized in *Figure 1* with the different levels of anastomosis.

Laparoscopic hybrid Ivor Lewis esophagectomy

The hybrid laparoscopic Ivor Lewis esophagectomy combines an abdominal laparoscopic approach for gastric mobilization and keeps a right thoracotomy for oncological transthoracic *en-bloc* esophagectomy with intrathoracic anastomosis. The laparoscopy is performed with CO₂ pneumoperitoneum insufflation with a patient in reverse Trendelenburg with a supine split-leg position (French position). The technique required mostly 5 ports (usually 2 ports of 5 mm, 2 of 11 mm and one of 12). Gastric mobilization is performed as an open procedure consisting in division of the gastro-hepatic ligament and the greater omentum until the short gastric vessels are reached. The greater omentum is completely divided keeping intact the right gastroepiploic vessels. The dissection is easily performed using ultrasonic energy (Harmonic scalpel®). The left gastric vessels are dissected and divided at the superior part of the pancreatic gland. Division is performed using clips or vascular automatic stapler. A radical abdominal lymph node dissection is performed according to the definition of standard D2-lymphadenectomy (celiac axis, splenic, left common hepatic and left gastric lymph node stations). An incomplete wide 4-cm gastric tubulization is

obtained by stapling the lesser curvature of the stomach parallel to the right gastro-epiploic artery (SC45 A Echelon Flex Endopath Stapler[®], reload 45 mm Gold). The tubulization is initiated at the abdominal phase and will be ended in the thorax. The integrity of the vascularization and the viability assessment of the gastric tube can be checked using the indocyanine green (ICG) fluorescence imaging. A laparoscopic feeding-jejunostomy is usually added at the end of the procedure. No abdominal drainage is required. The patient is then turned to the left lateral decubitus position. A right posterolateral thoracotomy is then performed requiring contralateral single-lung ventilation using a left double-lumen tube (or an endobronchial blocker in case of failure). *En-bloc* esophagectomy is performed through a standard fashion after division of the azygos arch. A radical and standardized mediastinal lymphadenectomy is performed including several lymph nodes stations whatever the histological subtype: subcarinal, right and left laterotracheal, paraesophageal and thoracic duct. The end to side intrathoracic anastomosis can be performed through different techniques depending of the surgeons convictions: hand-sewn, mechanical (25 mm echelon automatic circular powered) or semi-automatic. The anastomotic integrity is checked using a methylene blue test in the nasogastric tube. Two perianastomotic chest-tubes are let in place.

Thoracoscopic Ivor Lewis esophagectomy

The hybrid thoracoscopic Ivor Lewis esophagectomy combines an abdominal laparotomy approach for gastric mobilization and keeps a right VATS for oncological transthoracic *en-bloc* esophagectomy. The intrathoracic anastomosis is performed under thoracoscopy. At the current time, this technique has been abandoned because the difficult part lies in the confection of the anastomosis. This technique is now replaced by total MIE Ivor Lewis (VATS or robotic).

Hybrid McKeown esophagectomy

McKeown esophagectomy consists in a 3-field procedure with a cervical gastric reconstruction. In this setting the minimally approaches can be mixed to open approaches by applying the minimally invasive techniques either for the abdominal stage (laparoscopy) or for the thoracic stage by VATS. Hybrid McKeown can result also from a total MIE requiring conversion at both stages of the procedure.

Laparoscopic McKeown esophagectomy

The indications of such technique are when a troublesome dissection is expected into the chest, leading to consider a first-line thoracotomy. A minimally invasive approach is kept for the abdominal stage. This can be the case after high dose of radiation in the chest, after previous chest surgery, in case of a bulky tumor or in case of an associated pulmonary or mediastinal resection. The technique begins with a right posterolateral thoracotomy for esophageal mobilization and lymphadenectomy in a standard fashion. After completion of the thoracic stage, the patient is turned and positioned in a supine split-leg position (French position) with a left arm along the body to allow a left cervical incision. The laparoscopic abdominal stage is strictly identical as described above. The gastric mobilization and lymphadenectomy is performed in an usual way using CO₂ insufflation. The gastric tubulization is initiated 2-cm before the pylorus in order to obtain a long 4-cm wide gastric tube to reach the neck. The tubulization is performed intra-corporeally and completed under laparoscopy using almost 8 or 9 reloads of automatic stapler (45 Gold Echelon[®]). Then the gastric tube is attached to the resected specimen at the level of the GEJ in the hiatus with two stitches. Under laparoscopic vision, the resected specimen and the gastric tube are gently pulled-up to the left cervical incision though the posteris or mediastinum. The resected specimen is then removed through the cervicotomy. The anastomosis is then performed end-to-side or side-to-side by hand-sewn fashion or by semi-mechanical techniques. An alternative possibility is to fashion the gastric conduit extra-corporeally through a 5 cm midline laparotomy incision secured with an Alexis wound retractor. This option required to have previously positioned a tutor in the posterior mediastinum (nasogastric tube or a chest-tube) to pull the gastric tube to the neck. The resected specimen is then removed through the minilaparotomy. The gastric tube is then stitched to the tutor and gently pulled-up to the neck incision through the posterior mediastinum under laparoscopic vision.

VATS McKeown esophagectomy

The indications of such technique are when a difficult dissection is expected into the abdomen leading to consider a laparotomy. A VATS esophageal mobilization is normally performed before the laparotomy. This can be the case after high dose of radiation in the abdomen, after previous

abdominal surgery, in case of a bulky tumor invading the diaphragm or the pancreatic gland, in case of associated abdominal resection or when a different route is considered for the gastric tube reconstruction (pre or retrosternal). For note, the hybrid VATS esophagectomy can also be indicated when another substitute than the stomach is considered requiring laparotomy (colonic interposition). The technique begins with the thoracoscopic esophageal mobilization (9,10). The patient can be positioned in prone position but also in left-lateral decubitus. Each position has some advantages and disadvantages. Prone position does not require double-lumen. The patient is positioned in prone position with a single-lumen tube and the right lung is collapsed by CO₂ insufflation (8 mmHg). The disadvantages of prone position are the difficulty to turn the patient and a poor exposure in case of intraoperative conversion. Three or 4 ports are required generally (4th, 6th and 8th intercostal space). Esophageal mobilization is performed through a standardized technique consisting in pleural opening, division of azygos vein, *en-bloc* esophageal dissection and mediastinal lymphadenectomy. The dissection is made easier using the “suspension” technique using a Penrose drain around the esophagus. Thoracic duct is ligated at the base of the thorax. The esophagus is not transected to allow the digestive continuity and the gastric pull-up to the neck at the second step of the procedure. A perianastomotic chest-tube is let in place. Then the patient is turned supine. A median laparotomy and left cervical incision are performed through a standard fashion. The gastric tubulization is performed and the gastric tube is pulled-up to the neck through the posterior mediastinum. It is also possible in this technique to use the retrosternal route if needed.

Results of hybrid esophagectomy

Hybrid esophagectomy including laparoscopy

Even if several techniques of hybrid esophagectomy procedures have been described (2), the best knowledge to date come from the hybrid Ivor Lewis operation (5,7,11-15). The concept of a laparoscopic approach for gastric mobilization comes from the hypothesis that the laparoscopy would have the potential to significantly decrease the respiratory consequences when compared to a conventional laparotomy. This assumption was argued by the results of laparoscopic approach in others indications such as cholecystectomy for example (16-19). The post-

laparotomy diaphragmatic dysfunction, the immunological stress and the impairment of the respiratory function have been suggested as consequences of conventional laparotomy. In this setting, the laparoscopic approach has indubitably several advantages over the conventional laparotomy. Advantages can be summarized as follow: exploration of peritoneal cavity to rule out carcinomatosis and unnecessary laparotomy, standardization of the gastric mobilization, reduction of blood loss, possibility to ligate easily both left and short gastric vessels, good exposure whatever the patient's weigh and especially in overweighted patients, excellent visibility with magnification to perform radical lymphadenectomy, possibility to add a feeding jejunostomy if needed and at last allow the inclusion in an enhanced recovery after surgery (ERAS) program. In addition, all the abdominal part of the laparoscopic procedure seems easier to teach than a VATS approach. At last, this approach seems more attractive because the confection of the intrathoracic anastomosis is performed with an open approach making it easier compared to all the MIE techniques of anastomosis (20). This represents a strong argument for surgeons who have already faced problems in the confection of the anastomosis with VATS.

Majority of available literature of hybrid laparoscopic Ivor Lewis procedure come from non-controlled studies comparing such techniques with open conventional procedure. Very recently, the results of the French randomized MIRO trial have brought good informations regarding short, mid and long-term outcomes of laparoscopic hybrid Ivor Lewis procedure (5). The first and easiest point to be demonstrated was the beneficial effect of laparoscopy on 30-day major pulmonary complications (15% for laparoscopy *vs.* 42% for laparotomy) (7). This decrease was also confirmed by further studies (12-14). The second point demonstrated with laparoscopy was the substantial effect on postoperative mortality. Based on propensity-score matching study, a retrospective large nationwide study, including more than three thousand patients over two years, found a significant reduction in 30- and 90-day mortality rates favoring laparoscopy (30-day rate: 3.3% *vs.* 5.9%, P=0.029; 90-day rate: 6.9% *vs.* 10.1%, P=0.018) (11). The other supposed advantages of laparoscopy were reduction of blood loss, shortened operative time, and reduction of length of hospital stays. At last, the quality of surgery was equal with similar conversion rates, similar number of resected lymph nodes, similar rates of R0 resection and equivalent long-term outcome compared to laparotomy (15).

Table 1 Confrontation between TIME trial (total minimally invasive esophagectomy) (4) and MIRO trial (hybrid Ivor Lewis esophagectomy) (5)

Clinical variables	TIME trial (total MIE)		MIRO trial (hybrid Ivor Lewis)	
	Open (N=56)	Total MIE (N=59)	Open (N=104)	Hybrid (N=103)
Operative time [min]	299	329	330	327
Conversion [%]	–	8 (14)	–	3 (3)
Pulmonary complications [%]	19 [34]	7 [12]*	31 [30]	18 [17]*
Leakage [%]	4 [7]	7 [12]	5 [5]	8 [8]
Reoperation [%]	6 [11]	8 [14]	3 [3]	2 [2]
30-day mortality [%]	0	1 [2]	2 [2]	1 [1]
Length of hospital stay (days)	14 [1–120]	11 [7–80]	14 [7–95]	14 [3–218]
Number of resected LN [range]	21 [7–47]	20 [3–44]	22 [9–64]	21 [7–76]
R0 resection [%]	47 [84]	54 [92]	101 [98.1]	97 [95.1]
3-year survival (%; 95% CI)	40.4 [32–48]	50.5 [42–58]	55 [44–63]	67 [57–75]

*, P<0.05. LN, lymph node.

Recently, the MIRO trial was published and provides a level-1 evidence on the benefits of hybrid laparoscopic Ivor Lewis over laparotomy (5). In this prospective and randomized trial, 104 patients were assigned to laparotomy and 103 to laparoscopy. The primary outcome was achieved with a significant reduction of the major postoperative morbidity in the 37 patients of the laparoscopy group (35.9%) compared to the 67 patients (64.4%) of the open group (OR 0.3; 95% CI: 0.1–0.5; P<0.001). One of the secondary outcomes achieved was the reduction of the pulmonary complications in the laparoscopy group: 18 patients (17%) compared to 31 patients (30%) in the open group (P=0.037). With a similar 30-day mortality (1.9% vs. 1.0%), the MIRO trial demonstrated similar oncological outcomes in term of number of resected LN and completeness of resection. Moreover, the long-term outcomes were similar between both approaches. Laparoscopy even demonstrated an unexpected better 5-year overall and disease-free survival rates compared to laparotomy. In an ancillary study, the MIRO trial further demonstrated that laparoscopy has a beneficial effect of health-related quality of life compared to laparotomy. This prevailed mostly for pain, social and role functioning with persistent differences up to 24 months after surgery. These benefits can be attributable to the reduction of postoperative complications in the laparoscopy group (21).

Main results of MIRO trial are provided in *Table 1*. The short-term outcomes were given in confrontation with the results of the randomized TIME trial displaying the

comparison of total MIE with open approaches (4,5). Even if the two trials are not comparable in term of methodology and primary end-points, the question that remains is if the maximal benefit of a total MIE is in the abdominal or thoracic stage? The two trials resulted, with an equivalent magnitude, in a beneficial reduction on respiratory complications in the experimental group compared to conventional open techniques. The reduction seems to be however superior in TIME trial (RR: 0.35; 0.16–0.78) compared to MIRO trial (RR: 0.5; 0.26–0.96) but the numbers of patients included in the trial are different. As no surprise, MIRO trial demonstrated lower conversion rate compared to TIME trial because in MIRO trial one the two approaches was an open procedure. However, MIRO trial indicated a lower rate for reoperation requirement, suggesting less technical difficulties, which may likely revolve around the confection of the anastomosis. The oncological outcomes between the two trials seem equivalent. However, the control group of TIME trial demonstrated an unexpected high rate of incomplete resection compared to experimental group suggesting some bias in the inclusion protocol. At last, the long-term outcomes of both techniques have been reported and indicated a better survival in both experimental groups. In TIME trial, the 3-year overall survival rates were 40% in open group compared to 50% in MIE group. In MIRO trial, the 3- and 5-year overall survival rates were respectively 55% and 39% in open group and 67% and 60% in hybrid group. Out of TIME trial, two others retrospective studies

have compared hybrid Ivor Lewis esophagectomy to total MIE (22,23). The conclusions of both studies did not find any evident superiority for one of the two techniques.

On these bases and up till now, the conclusions that can be formulated are: whatever the techniques of MIE (hybrid or total), the use of a laparoscopy for the abdominal part of the esophagectomy demonstrates a strong benefit on postoperative respiratory outcomes without any compromise on oncological long-term outcomes. The laparoscopic approach should be seen as a new standard approach whatever the techniques used for the chest approach.

Hybrid esophagectomy including VATS

Data on results of hybrid esophagectomy including VATS associated to open laparotomy are scarce (1,9,10,24,25). The VATS techniques are heterogeneous including VATS Ivor Lewis with laparotomy and hybrid VATS McKeown esophagectomy. The VATS hybrid Ivor Lewis approach with performance of the anastomosis under thoracoscopy is not well reported due to the complexity of such procedures and the steep learning curve requiring at last 40 patients to be efficient. More details on the techniques of anastomosis are required for these procedures to be widespread worldwide with standardized and well-accepted methods. To date, there is at least 5 to 6 techniques described with in all huge results and outcomes (total mechanical, semi-automatic, circular, hand-sewn, transoral OrVil EEA, robotic) (26).

Conclusions

Hybrid esophagectomy is mostly represented by the laparoscopic hybrid Ivor Lewis esophagectomy. This technique appears safe, reproducible, and easy to teach without any modification of the technique of the intrathoracic anastomosis whereas total MIE requires to perform the anastomosis under thoracoscopy with disappointing results to date. This last point will be probably overcome in the near future by the standardization of the techniques of thoracoscopic anastomosis and the development of the robotic surgery.

The MIRO trial has provided good evidences that the unique use of laparoscopy for the abdominal stage of the esophagectomy resulted in a strong benefit on postoperative respiratory outcomes with the same magnitude to those

observed with total MIE. This suggests that the maximum benefits of minimally invasive techniques are more provided by laparoscopy rather than thoracoscopy. Moreover the laparoscopy provides an excellent quality of dissection without any compromise on oncological long-term outcomes. Whatever the technique of MIE, the laparoscopic approach has to be seen as a new standard approach and should be incorporated to all esophageal cancer resections whenever possible. The results of the ROMIO study will clarify the benefit of addition of the thoracoscopy and to consider total MIE as a new standard (27).

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