Thoracoscopy in prone position with two-lung ventilation compared to conventional thoracotomy during Ivor Lewis procedure: a multicenter case–control study

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Abstract

Background Intraoperative management based on thoracoscopy, prone position and two-lung ventilation could decrease the rate of postoperative pulmonary complications after esophagectomy. The aim of this study was to compare this multifaceted approach (MIE-PP) and conventional thoracotomy for Ivor Lewis procedure after a systematic laparoscopic dissection.

Methods Data from 137 consecutive patients undergoing Ivor Lewis procedures between 2010 and 2017 at two tertiary centers was analyzed retrospectively. The outcomes of patients who underwent MIE-PP ($n=58$; surgeons group 1) were compared with those of patients undergoing conventional approach ($n=79$; surgeons group 2). Our primary outcome was major postoperative pulmonary complications. Our main secondary outcomes were anastomotic leak, quality of resection and mortality.

Results Female patients were more prevalent in the MIE-PP group ($p=0.002$). Other patient characteristics, cTNM staging and neoadjuvant treatment rate were not different between groups. Major postoperative pulmonary complications were significantly lower in the MIE-PP group compared to Conventional group (24 vs. 44%; $p=0.014$). Anastomotic leak occurred in 31 versus 18% in MIE-PP group and Conventional groups, respectively ($p=0.103$). Complete resection rate (98 vs. 95%; $p=0.303$) and mean number of harvested lymph nodes (16 (4–40) vs. 18 (3–37); $p=0.072$) were similar between the two groups. Postoperative mortality rates were 0 versus 2% at day 30 ($p=0.508$) and 0 versus 7.6% at day 90 ($p=0.038$).

Conclusion Short-term outcomes of minimally invasive Ivor Lewis using thoracoscopy, prone position and two-lung ventilation are at least equivalent to the hybrid approach. Anastomotic leak after MIE-PP remains a major concern.

Keywords Esophageal cancer · Prone position · Minimally invasive · Ivor Lewis · Pulmonary complications

Ivor Lewis procedure is a major part of the multimodal treatment in patients with resectable lower- or middle-third esophageal cancer [1]. Despite progress in minimally invasive surgery and perioperative management, the postoperative morbidity rate of this procedure remains high, between 17 and 74%, with a significant mortality rate of 0.9–10%,

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due to major postoperative pulmonary complications [2–6]. Major postoperative pulmonary complications (MPPCs) occur in 10–40% of patients and remain responsible for 50% of the postoperative deaths [7–9]. An improvement in morbi-mortality rates by using a laparoscopic approach for the abdominal part was suggested first by retrospective studies. Preliminary results of randomized MIRO study showed that the laparoscopic approach decreased the postoperative morbidity rate by reducing the pulmonary complications [9–11]. A thoracoscopic approach seems to reduce postoperative pulmonary complications, blood loss, length of hospital stay and quality of life without impairing the quality of resection compared to open approach [6, 8, 12–14]. MIE with prone position technique allows the cardiopulmonary bloc to fall anteriorly, giving optimal exposure of the esophagus. One-lung ventilation is not required, simplifying the anesthetic procedure and allowing a better oxygenation than lateral decubitus [13, 15]. However, the encouraging results of MIE in prone position were obtained by combining several procedures (intrathoracic or cervical anastomosis) and one- or two-lung ventilation [16–20]. Moreover, the absence of standardized intrathoracic anastomosis, the potential increased risk of anastomotic leak and the risk of thoracotomy conversion in prone position remain great concerns for surgeons [21–23].

There is a lack of studies focused on postoperative pulmonary complications comparing a standardized approach based on thoracoscopy, prone position and two-lung ventilation versus a conventional thoracotomy in a homogeneous cohort of patients requiring an Ivor Lewis procedure [24].

The present study aimed to compare this multifaceted approach and conventional thoracotomy for Ivor Lewis procedure after a systematic laparoscopic dissection.

Patients and methods

Study design and population

Data from consecutive patients requiring an Ivor Lewis procedure in curative intent for esogastric junction (Siewert I/II), lower-third or middle-third esophageal cancers in two French tertiary centers was collected from January 2010 to June 2017. Data was entered in a prospectively maintained database and retrospectively analyzed. The local institutional review board in each center approved the study.

Abdominal approach was systematically performed by laparoscopy. Patients underwent a thoracoscopic approach using prone position with two-lung ventilation (MIE-PP group) or a hybrid procedure with conventional thoracotomy in left lateral position (Conventional group) (Fig. 1).

All procedures were performed by at least one experienced esogastric surgeon (> 40 procedures). Four surgeons performed MIE-PP approach systematically (surgeons group 1: J.M.F.; F.B.; R.C. and E.H.). The outcomes of patients who underwent MIE-PP were compared with those of patients undergoing systematic conventional approach by the surgeons group 2 (R.S.; I.D.; M.P. and J.J.T.) at the same centers during the same period.

The volume, type of esophagectomy and the distribution of MIE-PP approach and conventional approach were

Fig. 1 Study design

studied and grouped according to different time: Period 1 (January 2010–December 2013) and Period 2 (January 2014–June 2017).

Patients presenting histology other than squamous cell carcinoma/adenocarcinoma, or synchronous/metachronous neoplasms were excluded. Patients with cTNM stage > T2 or N+ status received neo-adjuvant chemoradiation, combining 5-fluorouracil/cisplatin or folinic acid, fluorouracil and oxaliplatin (4 cures) with concomitant radiotherapy. Esophageal cancer patients were considered to be operable based on physical examination, standard laboratory tests, upper gastrointestinal endoscopy, bronchoscopy, computed tomography (CT scan) of the thorax, mediastinum and abdomen, endoscopic ultrasonography and, more recently, positron emission tomography (PET). The decision of when to perform an Ivor Lewis procedure was taken by expert senior surgeons and was approved by a multidisciplinary institutional staff.

Procedures

Perioperative procedures were standardized independently of the MIE-PP or conventional approaches. Perioperative thoracic epidural analgesia was routine and was active at least 4 days after surgery unless the patient refused or in case of contraindication. A lung-protective ventilation strategy with low tidal volumes and positive end-expiratory pressure was used in all patients [25].

In both groups, Ivor Lewis procedure started with a laparoscopic approach with section of gastro-colic ligament, gastric mobilization and “en bloc” lymphadenectomy (lymph node stations 1–4, 7–9, 11 and 12) according to the 10th edition of the JSED classification [26].

For the transthoracic step, patients in the MIE-PP group were in prone position. A thoracoscopy using three 12 mm trocars in 5, 7 and 9th intercostal spaces was performed. A two-lung ventilation using a single lumen armed tube was used, and a pneumothorax of 8 mmHg (CO₂) was maintained during the procedure.

In conventional group, the patient was installed in left lateral decubitus position, the right lung was excluded and only the left lung was ventilated. A right postero-lateral thoracotomy in the 6th intercostal space was performed.

In both groups, the lower- and middle-third of the esophagus was mobilized using an ultrasonic device. An en bloc lymphadenectomy was performed of peri-esophageal, bronchial and subcarinal lymph nodes according to the 10th edition of the JSED classification [26]. The esophagus was divided above the arcus of the azygos vein. An anastomosis between the proximal esophagus and the gastric tube was performed.

The anastomosis was performed using different methods according to the surgeon’s habits in the different

participating centers. Some centers perform an end-to-side anastomosis using a circular stapler with the 25-mm Orvil device. Others perform a side-to-side anastomosis with a linear endostapler and closure of the defect with a V-Loc® suture. Others perform an end-to-side hand-sewn anastomosis.

At the end of the MIE-PP approach, extraction of a sample was performed via an Endobag® through a small thoracotomy in the 7th intercostal space, using an Alexis® retractor. Chest tubes were placed, and the thoracotomy was closed.

During the postoperative period, all patients received pulmonary physiotherapy twice daily. Noninvasive ventilation was based on arterial partial pressure of oxygen (PaO₂) levels. Nasogastric aspiration for 2–5 days, thromboprophylaxis, proton pump inhibitors and prokinetics were all used routinely. Monitoring for complications was similar in all included centers. Patients were clinically examined daily, and additional examinations were performed on indication. Examination of anastomosis consisted of systematic CT scan with oral contrast on postoperative day 5 [27, 28].

Study outcomes

We aimed to test the hypothesis that the MIE-PP approach decreases pulmonary complications rate compared to conventional thoracotomy in a homogeneous cohort of patients requiring Ivor Lewis procedure.

The primary outcome was the rate of major postoperative pulmonary complications (MPPCs) after 30 day. MPPCs is a composite criteria, including severe atelectasis without fever or hyperleucocytosis requiring bronchoscopy; pneumonia defined as radiological alveolointerstitial infiltration and the presence of at least two of the following: purulent sputum, temperature above 38.5 °C or < 35 °C, or leucocyte count > 10,000/mm³ or fewer than 1500/mm³; respiratory insufficiency, defined as the inability of a patient to maintain PaO₂ above 60 mmHg or arterial partial pressure of carbon dioxide (PaCO₂) below 55 mmHg, requiring an orotracheal tube and assisted ventilation; and ARDS, defined as severe hypoxia (PaO₂/fraction of inspired oxygen (FiO₂) ratio below 200), diffuse bilateral pulmonary infiltration and pulmonary wedge pressure of less than 18 mmHg. Acute lung injury, defined as a PaCO₂/FiO₂ ratio between 200 and 300, was included in ARDS.

MPPCs were verified by an independent specialist observer (reanimation unit). Due to a common continuum in MPPCs, the most severe event was retained for analysis in line with the previous Mariette et al. studies [9, 11].

Secondary outcomes were the postoperative ventilation data, rate of anastomotic leak, mortality rate, reoperation rate, and length of hospital stay, pathological parameters of the resected specimen and feasibility of adjuvant treatment

when indicated. All postoperative 90-day complications were recorded and graded according to the Clavien–Dindo classification (the most severe grade for each patient was retained for analysis) [29].

Anastomotic leak was defined as either clinical (sepsis and gastrointestinal contents in a drain) or radiological disruption based on a routine CT scan with contrast swallow performed on postoperative day 5. The CT scan findings for anastomotic leak included mediastinal fluid collection, air, abscess and induration. Other CT scan findings included a visible discontinuity of the esophagogastric wall $\pm$ extradiaphragmatic contrast swallow and fistula (fluid- or air-filled tract between the esophagogastric anastomosis and another anatomic cavity [skin, trachea, pleural cavity or mediastinum]). Severity of anastomotic leak was graded according to the Low et al. classification [3].

Statistical analysis

The median and range are reported for continuous variables, and absolute and relative frequencies are reported for categorical variables. Continuous variables were compared by nonparametric test (Mann–Whitney U). Categorical data were compared by Chi square test or Fisher's exact test depending on size. MPPCs occurrence was compared between groups using Kaplan–Meier method and the log-rank test. To determine independent predictors of MPPCs, a stepwise logistic regression model was used in which all co-variables with $p < 0.100$ were adjusted simultaneously. All statistical tests were two-sided; a p value < 0.05 was considered as statistically significant. Statistical analyses were performed using SPSS Statistics, version 20.0, for Macintosh (IBM Corp, Armonk, NY).

Results

Patient and surgical data

An Ivor Lewis esophagectomy with laparoscopic dissection was performed in 137 consecutive patients at our two institutions. In summary, 58 patients (42%) underwent a MIE-PP approach and 79 patients (58%) a conventional thoracotomy.

The total esophagectomy volume and the number of Ivor Lewis procedures were higher during Period 2 as shown in Fig. 2A (36.5% vs. 89%; $p < 0.0001$). The use of the MIE-PP approach for Ivor Lewis procedure was more common during period 2 compared to period 1 (20% vs. 48.5%; $p = 0.006$) (Fig. 2B) and became distributed with conventional approach equally.

Female patients were more prevalent in the MIE-PP group. MIE-PP and conventional groups were comparable for other demographic data: median BMI, ASA score,

rates of comorbidities, tumor location, histological subtype, cTNM stages and neoadjuvant treatment. Table 1 summarizes the demographic and preoperative data of the two groups.

Surgical data are resumed in Table 2. Active epidural anesthesia was performed in most patients with no differences between the two groups (71% vs. 81%, $p = 0.158$). The median length of surgery was longer in the MIE-PP group than the conventional group due to prone position installation, without significant differences in duration of thoracic surgery. Conversion to laparotomy during the abdominal surgery was required in $< 2.5\%$ of cases due to strong upper abdominal adhesences.

An end-to-side mechanic circular anastomosis was performed with a 25-mm stapler in 71 patients (45%); 3 in MIE-PP group and 68 in conventional group. A side-to-side semi-mechanic anastomosis was performed in 45 patients (27%) exclusively in MIE-PP group. An end-to-side hand-sewn anastomosis was performed in 21 patients (8%); 10 in MIE-PP group versus 11 in Conventional group.

No conversion to posterior thoracotomy was required in the MIE-PP group. The intraoperative complication rate was 12 of 157 (7.5%), with no statistically significant differences between the groups (3 of 58 for MIE-PP vs. 9 of 79 for conventional group; $p = 0.237$), despite the fact that the thoracoscopic learning curve effect was included. Intraoperative difficulties were difficulties for exclusion (2 of 79 in conventional group); intraoperative hemorrhage (0 of 58 vs. 2 of 79) and clinically significant hypercapnia (3 of 58 vs. 5 of 79). No significant differences were found for intraoperative estimated blood loss and transfusion rate.

Outcomes and complications

As shown in Table 3 describing postoperative results in both groups, the MPPCs rate was significantly lower in the MIE-PP group compared to the conventional group (24 vs. 44%; $p = 0.014$). Comparison of MPPCs occurrence according to time after surgery was also in favor of the MIE-PP approach ($p = 0.022$) (Fig. 3).

Reintubation rate, overall length of mechanical ventilation and rate of mechanical ventilation > 48 h were not different between the two groups. Univariate analysis showed that the MIE-PP approach, high ASA grade, cardiopathy and neoadjuvant chemotherapy were significantly associated with MPPCs. Potential confounding factors as gender, absence of active epidural anesthesia or anastomotic leak were not associated with MPPCs. Multivariable analysis showed that the MIE-PP approach was a protective factor, whereas an ASA score ≥ 3 was predictive of MPPCs (Table 4).

No significant differences were found concerning the Dindo–Clavien grades for postoperative morbidity.

Fig. 2 Volume, the type of esophagectomy (**A**) and the distribution of MIE-PP approach and conventional approach over the time (**B**) according to period 1 (January 2010–December 2013) and period 2 (January 2014–June 2017)

	Ivor Lewis procedure	Other procedure	Total
Period 1	30	52	82
Period 2	107	13	120
Total	137	65	202

	MIE-PP group	Conventional group	Total
Period 1	6	24	30
Period 2	52	55	107
Total	58	79	137

Table 1 Preoperative variables

Variables	MIE-PP group (n = 58)	Conventional group (n = 79)	p
Sex			
Male	38 (66)	69 (87)	0.002 [‡]
Female	20 (34)	10 (13)	
Age, years	62 (± 10)	64 (± 10)	0.178 [¶]
< 60	21 (36)	19 (24)	–
> 60	37 (64)	60 (76)	0.122 [‡]
Body mass index, kg/m ²	25.5 (± 7)	25.5 (± 6)	0.940 [¶]
ASA score			
1	4 (7)	12 (15)	–
2	44 (76)	44 (56)	0.100 [§]
3	10 (17)	23 (29)	0.065 [‡]
Performance status OMS			
0	26 (45)	30 (38)	–
1	26 (45)	41 (52)	0.726 [‡]
2	6 (10)	8 (10)	0.777 [§]
History of tobacco use	35 (60)	48 (61)	0.960 [‡]
COPD	14 (24)	19 (24)	0.992 [‡]
Cardiopathy	6 (10)	14 (18)	0.351 [‡]
Diabetes mellitus	10 (17)	13 (16)	0.903 [‡]
History of abdominal surgery	18 (31)	24 (30)	0.593 [‡]
Malnutrition	25 (44)	40 (51)	0.383 [‡]
Histological subtype			
Adenocarcinoma	45 (78)	68 (86)	–
Squamous cell carcinoma	13 (22)	11 (14)	0.196 [‡]
Tumor location			
Middle third	8 (14)	7 (9)	–
Lower third	20 (34)	39 (49)	0.165 [‡]
Esogastric junction	30 (52)	33 (42)	0.123 [‡]
cT stage ^a			
T1	4 (7)	13 (16)	–
T2	7 (12)	10 (13)	0.464 [§]
T3	27 (46)	46 (58)	0.785 [‡]
T4	1 (2)	1 (1)	1.000 [§]
cN stage ^b			
N0	22 (38)	27 (34)	–
N+	30 (52)	49 (62)	0.438 [‡]
Neoadjuvant treatment			
No	7 (12)	16 (20)	–
Chemotherapy alone	26 (45)	35 (44)	0.307 [‡]
Chemoradiation	25 (43)	28 (36)	0.626 [‡]

Values in parentheses are percentages unless indicated otherwise; continuous values are expressed with median (± SD)

ASA American Society of Anesthesiologists, COPD chronic obstructive pulmonary disease

[‡]χ² test

[§]Fisher's exact test

[¶]Mann–Whitney U test

^aValues on 109 with known cT stage

^bValues on 128 patients with known cN stage

An anastomotic leak, based on clinical results and CT scan findings, was diagnosed in 31 versus 18% of patients in MIE-PP and conventional groups, respectively ($p = 0.103$). The rates of anastomotic leak were 22% after mechanical circular anastomosis (16 of 71 patients), 24% after linear side-to-side anastomosis (11 of 45 patients, $p = 0.651$) and 28% after hand-sewn anastomosis (6 of 21 patients, $p = 0.384$). Using the Low et al. classification, anastomotic leak was in majority grade I in the MIE-PP group compared to the conventional group. The rate of patients with anastomotic leak and MPPCs was significantly lower in MIE-PP group (50 vs. 86.6%; $p = 0.034$). Anastomotic leak was complicated by chronic bronchoesophageal fistula in three patients (1 vs. 2 patients) treated with endoscopic esogastric/bronchial stents in one patient and a reoperation in two patients. No differences were observed in leak rates between the participating centers ($p = 0.417$).

Postoperative 30-day mortality was not significantly different between the two groups. 90-day mortality rates were nil in the MIE-PP group and significantly higher in the Conventional group (0 vs. 6 patients; $p = 0.038$), due to MPPC in majority (Table S1, Supplementary Data). No differences between the two groups were found concerning other standardized post-Ivor Lewis adverse events. Wound infection rate was lower in the MIE-PP group ($p = 0.044$). A reoperation was required in six patients in both groups. In addition to reoperation for anastomotic leak, a reoperation for symptomatic paraesophageal herniation was required in two patients in the MIE-PP group and in one patient in the conventional group.

Overall, median length of hospital stay was similar between the two approaches. Median length of hospital stay for uncomplicated patients was 12 (11–19) days in the MIE-PP group and 14 (11–16) days in the conventional group ($p = 0.089$). In case of anastomotic leak, length of hospital stay was 31 (15–116) days versus 42 (18–74) days in the MIE-PP and conventional groups, respectively ($p = 0.093$).

A microscopic radical R0 resection was obtained in more than 95% of patients without differences between the groups. Median number of resected lymph nodes was similar between the groups. Histopathology examination data is detailed in Table 2.

After postoperative multidisciplinary staff discussion with final pathologic results of the resected specimen, an adjuvant treatment was indicated in 39 patients (67%) in the MIE-PP group and in 44 patients (56%) in the conventional group ($p = 0.215$). A significantly higher proportion of patients in the MIE-PP group were able to receive indicated adjuvant chemotherapy (8% (n = 3/39) vs. 25% (n = 11/44); $p = 0.043$).

Table 2 Intraoperative and histologic variables

Variables	MIE-PP group (n = 58)	Conventional group (n = 79)	p
Active epidural anesthesia	41 (71)	64 (81)	0.158 [‡]
Duration of operation (min)	380 (180–514)	307 (210–483)	<0.0001 [¶]
Duration of thoracic surgery	143 (80–287)	140 (90–310)	0.224 [¶]
Duration of right pulmonary exclusion (min)	0 (0)	89 (65–157)	0.007 [§]
Conversion to laparotomy	1 (1.7)	2 (2.5)	1.000 [§]
Conversion to thoracotomy	0 (0)	–	
Esogastric anastomosis			
Hand sewn	10 (17)	11 (14)	–
25-mm Orvil device®	3 (5)	68 (86)	<0.0001 [§]
Semi mechanical S/S + V-Loc® closure	45 (78)	0 (0)	<0.0001 [§]
Estimated blood loss (ml)	121 (10–290)	160 (50–390)	0.261 [¶]
Intraoperative transfusion	2 (3.5)	6 (7.6)	0.306 [§]
Tumor size (mm)	33 (0–65)	30 (0–90)	0.362 [¶]
No. of resected lymph nodes	16 (4–40)	18 (3–37)	0.072 [¶]
Radicality of resection			
R0	57 (98.3)	75 (95)	–
R1	1 (1.7)	4 (5)	0.303 [§]

Values in parentheses are percentages unless indicated otherwise; continuous values are expressed with median (range)

[‡] χ^2 test

[§]Fisher's exact test

[¶]Mann–Whitney U test

Discussion

To our knowledge, this is the first multi-institutional study focused on pulmonary outcomes comparing a standardized multifaceted approach based on thoracoscopy, prone position and two-lung ventilation to the conventional thoracotomy in a homogeneous cohort of 137 consecutive Ivor Lewis procedures. The MIE-PP approach resulted in a lower incidence of MPPCs, a lower rate of wound infections, a lower 90-day mortality rate and a better access to adjuvant therapy when indicated. The present study provides additional evidence in favor of MIE-PP with two-lung ventilation over conventional thoracotomy for Ivor Lewis procedure. In line with previous reports, we found benefits in postoperative outcomes without compromising the oncological quality of resection [19, 20, 24, 30].

In the present study, the MIE-PP approach was an independent protective factor against MPPCs, whereas high ASA grade was a risk factor in multivariate analysis. Despite similar respiratory insufficiency and ARDS rates (<8%) in line with recent reports [9, 21, 23], the positive impact of the MIE-PP approach on severe atelectasis, or pneumonia, resulted in the reduction in MPPCs and 90-day mortality rate. The reduction in MPPCs rate is probably multifactorial resulting from the absence of one-lung mechanical ventilation and lateral decubitus position inducing a combination

of mechanical, hydrostatic and inflammatory lesions known as ventilator-induced lung injury [7]. During the right lung re-expansion, activated mediators of inflammation may be transferred to the other lung, causing ischemia–reperfusion injury. In addition to a laparoscopic approach, thoracoscopy in prone position with two-lung ventilation may have a protective effect on these mechanical and immunological events by decreasing musculoskeletal trauma, pain, and related cough limitation and ventilatory mechanical dysfunction, and by limiting the metabolic and inflammatory responses to surgical trauma [9].

Similar to recent reports, our main conclusion is that this MIE-PP approach can be considered safe with a low risk of thoracotomy conversion but the intrathoracic esogastric anastomosis remains a challenging step [21, 23]. Several observations should be addressed since reported anastomotic complication occurred more often in the MIE-PP group compared to the conventional group. Differences in the use of anastomotic technique in the MIE-PP group reflect the search for optimal technique. The rates of anastomotic leak in the present study should be interpreted by considering our postoperative protocol with systematic CT scan with oral contrast and our anastomotic leak definition [31]. Our results are close to that reported in recent studies on full MIE [21, 22, 32]. Anastomotic leak in the MIE-PP group was mostly grade I leak compared to the conventional group. However,

Table 3 Postoperative outcomes

Variables	MIE-PP group (<i>n</i> = 58)	Conventional group (<i>n</i> = 79)	<i>p</i>
Primary outcomes			
MPPC	14 (24.1)	35 (44.3)	0.014 [‡]
Atelectasis	0 (0)	6 (7.6)	–
Pneumonia	6 (10.3)	19 (22.8)	–
Respiratory insufficiency	3 (5.2)	3 (3.8)	–
ARDS	5 (8.6)	7 (8.9)	–
Secondary outcomes			
Mortality			
30-day	0 (0)	2 (2.5)	0.508 [§]
90-day	0 (0)	6 (7.6)	0.038 [§]
Dindo–Clavien grade for morbidity			
II	10 (17.2)	21 (26.5)	–
III	8 (13.8)	9 (11.3)	0.311 [‡]
IV	12 (20.7)	13 (16.4)	0.231 [‡]
Ventilation data			
Reintubation	8 (13.8)	14 (17.7)	0.536 [‡]
Overall length of mechanical ventilation (days)	1 (0–19)	1 (0–67)	0.305 [¶]
Length of mechanical ventilation > 48 h	8 (13.8)	16 (20.3)	0.325 [‡]
Anastomotic leak	18 (31)	15 (18.5)	0.103 [‡]
Grade I ^a	7 (12)	2 (2.5)	–
Grade II	7 (12)	8 (10)	0.209 [§]
Grade III	4 (7)	5 (6)	0.334 [§]
Anastomotic leak and MPPC	9/18 (50)	13/15 (86.6)	0.034 [§]
Others complications			
Gastric pull-up necrosis	0 (0)	3 (3.8)	0.068 [§]
Bleeding	1 (1.7)	4 (5.1)	0.395 [§]
Atrial fibrillation	10 (17.2)	14 (17.7)	0.941 [‡]
Wound infection	1 (1.7)	9 (11.4)	0.044 [§]
Left recurrent laryngeal nerve injury	0 (0)	4 (5.1)	0.137 [§]
Bronchoesophageal fistula	1 (1.7)	2 (2.5)	1.000 [§]
Paraesophageal herniation	2 (3.4)	2 (2.5)	1.000 [§]
Reoperation	6 (10.3)	6 (7.6)	0.761 [‡]
Length of hospital stay (days) ^a	19 (10–116)	20 (11–102)	0.272 [¶]

Values in parentheses are percentages unless indicated otherwise; continuous values are expressed with median (range)

MPPC major postoperative pulmonary complications, ARDS acute respiratory distress syndrome

[‡] χ^2 test

[§]Fisher's exact test

[¶]Mann–Whitney U test

^aAccording to the Low et al. classification

the incidence of grade III anastomotic leak was in line with reported rates in the literature [9, 23]. These results highlight the trends toward a higher risk of intrathoracic anastomotic leak when anastomosis is performed by thoracoscopy, and this remains a major concern for esogastric surgeons [21, 33]. The ideal technique for intrathoracic anastomosis during this full minimally invasive approach remains non-standardized. MPPCs were not closely related to anastomotic

complications and subsequent pleural/mediastinal contamination. The rate of patients with anastomotic leak and MPPCs was significantly lower in the MIE-PP group suggesting that (i) the continuum between anastomotic leak and MPPCs could become less evident when thoracoscopy in prone position was performed, (ii) the benefits of MIE-PP approach on pulmonary complications could persist in case of anastomotic leak.

Fig. 3 Comparison of MPPCs occurrence in MIE-PP and Conventional groups using Kaplan–Meier method

Table 4 Multivariate analysis of factors linked to major postoperative pulmonary complications

	χ^2	Odds ratio	<i>p</i>
MIE-PP approach	7.4	0.377 (0.185–0.767)	0.037
High ASA grade	8.6	3.33 (1.460–7.610)	0.029
Cardiopathy	4.1	2.67 (0.992–7.184)	0.449
Neoadjuvant CT	2.7	1.84 (0.893–3.790)	0.112

ASA American Society of Anesthesiologists, CT chemotherapy

The present study did not demonstrate any differences between the two groups with regard to intraoperative blood loss, blood transfusion, length of hospital stay, 30-day overall postoperative morbidity; only wound infection rate was significantly lower in the MIE-PP group in line with literature data [33]. No differences were found according to Clavien–Dindo classification. Several studies on MIE did not consider Clavien–Dindo classification [14, 22, 23]; others reported benefits of MIE on pulmonary complications with no substantial effect on Clavien–Dindo ≥ 3 -complication rate [9, 21, 24]. It suggests that this classification of surgical complications is probably not adapted for esophageal surgery and its specific medical complications. Postoperative courses after Ivor Lewis procedure are often complex and a novel metric of postoperative morbidity, as the recent comprehensive complication index (CCI®) integrating each single complication, independently of their inter-connection, should be included in further prospective studies [34].

Although a thorough evaluation of oncological outcomes was not conducted by considering only short-term results, quality of resection and lymphadenectomy were not different between the MIE-PP and Conventional groups. Other teams reported that lymph nodes clearance was similar between these two approaches [19–21, 24]. Moreover, there was a

significantly higher proportion of patients in the conventional group who did not receive adjuvant chemotherapy, when indicated, compared with that in the MIE-PP group. Thus suggests that a full minimally approach promotes better application of adjuvant multimodal treatments.

Although observed outcomes are promising, this study has several limitations. Its design was retrospective and possible surgeon bias cannot be dismissed. A major obstacle in the field of this study remains the lack of standardized definitions of pulmonary complications after esophagectomy [7]. The definition of the composite criteria MPPCs (majority but not strictly Clavien–Dindo grade ≥ 3 pulmonary complications) was arbitrary but is supported in the literature [9, 11, 14, 21]. The limited sample size expose to the inherent risk of type II error and did not permit us to perform a matched study using propensity score and comprehensive analysis of mortality risk factors. However, our findings were obtained from a homogeneous cohort of consecutive patients and reflect real life. Missing data in our database were inferior to 5%.

To conclude, full minimally invasive Ivor Lewis procedure using the thoracoscopy, prone position and two-lung ventilation seems to be at least equivalent to the hybrid approach with encouraging effects on the rate of MPPCs. The anastomotic leak rate after MIE-PP remains a major concern. Further randomized controlled trials are required to compare this multifaceted approach with the conventional hybrid procedure, to standardize the esogastric anastomosis by thoracoscopy in prone position and to assess long-term results.

Acknowledgements We thank the University of Montpellier and the University of Rouen for their support. We thank the surgeons Paul Martre, Lilian Schwarz, Thibaut Coste, Eric Bouley, Françoise Guillon, John Chauvat and Yvan Pouzeratte, Marie Genies, Bruno Souche, Audrey De Jong (reanimators) for their advice regarding the pulmonary

complication analysis. We are grateful to Sarah Kabani for editorial assistance and Dr Jacqueline Butterworth for proofreading of the manuscript. We thank the residents, fellows, and nurses of our division for the care they provided to these patients. The authors have no source of funding to disclose for this study.

Compliance with ethical standards

Disclosures R. Souche, M. Nayeri, R. Chati, E. Huet, I. Donici, J. J. Tuech, F. Borie, M. Prudhomme, S. Jaber and J. M. Fabre have no conflicts of interest or financial ties to disclose.

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