

# Robotic versus open Ivor–Lewis esophagectomy: A more accurate lymph node dissection without burdening the leak rate

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## Abstract

**Background:** Robotic-assisted minimally invasive esophagectomy (RAMIE) combines the beneficial effects of minimally invasive surgery on postoperative complications, especially on pulmonary ones, with the safety of the anastomosis performed in open surgery. Moreover, RAMIE could allow a more accurate lymphadenectomy.

**Methods:** We reviewed our database to identify all patients with adenocarcinoma of the esophagus treated by Ivor–Lewis esophagectomy in the period January 2014 to June 2022. Patients were divided according to the thoracic approach into RAMIE and open esophagectomy (OE) groups. We compared the groups for early surgical outcomes, 90-day mortality as well as R0 rate, and the number of lymph nodes harvested.

**Results:** We identified 47 patients in RAMIE and 159 patients in the OE group. Baseline characteristics were comparable. Operative time was significantly longer for RAMIE procedures ( $p < 0.01$ ); however, we did not observe the difference in overall (RAMIE 55.5% vs. OE 61%,  $p = 0.76$ ) and severe complications rate (RAMIE 17% vs. OE 22.6%,  $p = 0.4$ ). The anastomotic leak rate was 2.1% after RAMIE and 6.9% after OE ( $p = 0.56$ ). We did not report the difference in 90-day mortality (RAMIE 2.1% vs. OE 1.9%,  $p = 0.65$ ). In the RAMIE group, we observed a significantly higher number of thoracic lymph nodes harvested, with a median of 10 lymph nodes in the RAMIE group versus 8 in the OE group ( $p < 0.01$ ).

**Conclusions:** In our experience, RAMIE has morbimortality rates comparable to OE. Moreover, it allows a more accurate thoracic lymphadenectomy which results in a higher thoracic lymph nodes retrieval rate.

## KEYWORDS

esophageal adenocarcinoma, esophagectomy, robotic surgery

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## 1 | INTRODUCTION

Ivor–Lewis esophagectomy is the preferred surgical procedure among surgeons in Western Countries for the treatment of distal esophageal and esophagogastric junctional adenocarcinoma.<sup>1</sup> Even if in various retrospective studies and two randomized controlled trials (RCTs), minimally invasive esophagectomy (MIE) was considered a feasible alternative to open surgery,<sup>2,3</sup> some concerns about the safety of thoracoscopic esophagogastric anastomosis have been raised.<sup>4,5</sup> Recently, a paper published by the International Esodata Study Group, evaluating data from high-volume surgical centers all over the world, reported a leak rate of 15.1% after MIE, significantly higher than with hybrid (10.7%) and open procedures (7.3%).<sup>6</sup> On the other hand, MIE is associated with fewer overall and pulmonary complications.<sup>2,7</sup>

Among the several factors which might explain the higher incidence of leaks associated with MIE, one of the most important is the technical complexity of thoracoscopic anastomosis.<sup>8</sup> This can also account for the growing interest in robotic-assisted minimally invasive esophagectomy (RAMIE). The advantages of robotic surgery, such as the high-definition three-dimensional (3D) vision and the presence of the endo wrist, facilitate the movements in hostile anatomical districts.<sup>9</sup> Early results from high-volume centers are encouraging, with an anastomotic leak rate for RAMIE Ivor–Lewis of 10.3% and 90-day mortality of 1.9%.<sup>10</sup> From this perspective, RAMIE might combine the benefits of MIE in terms of pulmonary complications and early recovery, with the advantage of a safer anastomosis. Moreover, recent studies suggested the possible advantage of RAMIE in the lymph node retrieval rate.<sup>8,11,12</sup> Waiting for the results of the ongoing ROBOT-2 trial,<sup>13</sup> results from thorough case series need to be taken into account to evaluate this relatively new procedure.

The Aim of this study is to investigate the possible advantages of the thoracic robotic approach over a thoracotomy approach for Ivor–Lewis esophagectomy for surgical and early oncological outcomes.

## 2 | METHODS

We reviewed our Institutional prospectively maintained database to identify all patients with esophageal or esophagogastric junctional adenocarcinoma submitted to Ivor–Lewis esophagectomy in the period January 2014 to June 2022.

No restrictions on the abdominal approach (open, laparoscopic, or robotic-assisted) were applied, while patients treated thoracoscopically without robotic assistance have been excluded (three patients).

Patients were divided into two groups based on the thoracic approach, irrespective of the abdominal technique: the open esophagectomy (OE) group and RAMIE group. Until January 2020, all Ivor–Lewis esophagectomies were conducted through a right thoracotomy. In January 2020, we started our robotic program

(beginning with a hybrid laparoscopic and thoracoscopic procedure) and RAMIE became the approach of choice. However, a thoracotomy was still used in selected cases or when the robotic platform was not available (being its availability once per week). We compared the groups in an intention-to-treat analysis.

Clinical and pathological staging was performed according to American Joint Committee on Cancer guidelines.<sup>14</sup> Lymph nodes were classified according to the Japanese Classification of Esophageal and Gastric Cancer.<sup>15</sup> Lymph node ratio was calculated as the ratio of metastatic to the number of harvested lymph nodes.

The study protocol was approved by our Ethical Committee; given the retrospective nature of the study, the need for patient-informed consent was waived. All authors have no disclosure nor affiliation with organizations that may have financial interests in the topic.

### 2.1 | Surgical technique details

Open esophagectomies were performed by three surgeons experienced in esophageal and gastric surgery (G. d. M.; S. G. and J. W.). RAMIE procedures were performed by two of the same surgeons (S. G. and J. W.) after adequate training in robotic surgery. For all RAMIEs, the da Vinci Xi System (Intuitive Surgical) robot was used.

### 2.2 | Open thoracic phase

The open thoracic phase was conducted through an anterolateral muscle-sparing right thoracotomy. After ligation of the arch of the azygous vein, full mobilization of the esophagus below this landmark was carried out, with preservation of the thoracic duct, along with a standard mediastinal lymphadenectomy. A lymphadenectomy extended to the right or left recurrent nerves was reserved for selected cases. In all cases, we performed an esophagogastric end-to-end 25 mm mechanical anastomosis, above the level of the azygous vein.<sup>16</sup>

### 2.3 | Robotic-assisted thoracic phase

RAMIE procedures were performed with the patient in a prone position through four robotic trocars and one 12 mm trocar for the assistant. Esophageal mobilization was conducted on the dissection plan of the mesoesophagus, including the thoracic duct in the en bloc resection. The thoracic duct was closed in the inferior mediastinum under the guidance of the robotic nearly infrared camera (Firefly; Intuitive Surgical) after injecting indocyanine green (ICG) in the inguinal lymph nodes.<sup>17</sup> A standard en bloc lymphadenectomy was carried out in all patients, reserving a more extended dissection to the left and/or right recurrent laryngeal nerve lymph nodes in selected cases. The assistant trocar was enlarged to a minithoracotomy of about 4 cm to allow the placement of the 25 mm anvil in the

esophagus, on a robotic hand-sewn purse string. The specimen was pulled out from the thorax through the same incision and the circular stapler was inserted through a pouch on the lesser curvature, to fashion the same end-to-end anastomosis as in the open procedure. The pouch was then resected using a linear stapler. Two hemi-circumferential running sutures, using barbed 3/0 monofilament absorbable stitches, were used to reinforce the anastomosis.<sup>18</sup>

## 2.4 | Outcomes

All patients were treated according to our enhanced recovery after surgery (ERAS) protocol.<sup>19,20</sup> Complications within 90 days after surgery were classified according to the Esophagectomy Complications Consensus Group<sup>21</sup> classification and graded according to the Clavien–Dindo Classification.<sup>22</sup> Anastomotic leak was therefore defined as a “Full thickness defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification” and classified into types I, II, and III according to the treatment.<sup>21</sup> We did not perform a routine assessment of the anastomosis, reserving any diagnostic evaluation to patients with clinical suspicion. We calculated the number of patients with textbook outcomes for each group, using the definition provided by the Dutch Upper Gastrointestinal Cancer Audit (DUCA) group. The textbook outcome was defined as: complete resection (R0), no intraoperative complications, a lymph node yield >15, no complications of Clavien–Dindo 3 or higher, no reinterventions, no readmission to the intensive care unit, no length of hospital stay >21 days, no hospital readmission <30 days, no mortality <30 days, and no in-hospital mortality.<sup>23</sup>

## 2.5 | Statistical analysis

Continuous data were summarized as the median and interquartile range. Categorical data were summarized as proportion. Data were analysed using Fisher exact test or  $\chi^2$  test as appropriate for nominal variables, and by Wilcoxon–Mann–Whitney test for continuous variables with skewed distribution.  $p < 0.05$  were accepted as significant. All  $p$  values reported were two-tailed. Analysis was performed using Stata statistical software, release 15 (StataCorp.).

## 3 | RESULTS

Some 206 patients have been included in the analysis: 159 of them had a right thoracotomy (OE group) while 47 were treated with robotic-assisted surgery (RAMIE group). Patients' characteristics according to the surgical procedure are listed in Table 1. The study groups were comparable for all the preoperative variables.

The robotic approach resulted in longer operative ( $p < 0.01$ ), while among these patients the need for blood transfusions decreased from 17.6% to 4.3% ( $p < 0.05$ ) (Table 2). Laparoscopy

**TABLE 1** Baseline characteristics.

	RAMIE group n = 47	OE group n = 159	p Value
Sex (M)	39 (82.9%)	131 (82.4%)	0.56
Age (median, IQR)	63 (57–71)	63 (55–71)	0.62
BMI (median, IQR)	27 (24–30)	25 (23–29)	0.08
ASA			
1–2	33 (70.2%)	105 (66%)	0.36
3–4	14 (29.8%)	54 (34%)	
Charlson Comorbidity Index			
0–1	25 (53.2%)	102 (64.1%)	0.36
2–3	16 (34%)	42 (26.4%)	
≥4	6 (12.7%)	15 (9.5%)	
cT			
1–2	6 (12.7%)	20 (12.6%)	0.74
3–4	41 (83.3%)	139 (87.4%)	
cN			
0	6 (12.7%)	18 (11.3%)	0.48
≥1	41 (83.3%)	141 (88.7%)	
cM			
1	1 (2.1%)	10 (6.3%)	0.23
Neoadjuvant therapy			
No	6 (12.7%)	23 (14.5%)	0.69
CT/CRT	41 (83.3%)	136 (85.5%)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CRT, chemoradiotherapy; CT, chemotherapy; IQR, interquartile range; M, male; OE, open esophagectomy; RAMIE, robotic-assisted minimally invasive esophagectomy.

was used in 13.8% of cases in the OE group, while about 95% of RAMIE patients were operated on through a totally minimally invasive approach ( $p < 0.01$ ). In the RAMIE group, the rate of conversion of the thoracic phase was 10.6%.

In both groups, for most of the patients, we performed a standard mediastinal lymphadenectomy (83% in RAMIE and 84.9% in the OE group,  $p = 0.74$ ). However, the robotic assistance guaranteed a significant improvement in thoracic lymph nodal harvesting (median of 10 lymph nodes in RAMIE group vs. 8 in OE group,  $p < 0.01$ ). Quality of surgery was adequate in both groups, with an R0 rate of about 90% ( $p = 0.92$ ).

Early postoperative outcomes are fully reported in Table 3. The overall complication rate was 55.3% in the RAMIE group and 61% in the OE group ( $p = 0.76$ ). No significant difference in severe ( $p = 0.4$ ), pulmonary ( $p = 0.9$ ), and cardiac ( $p = 1$ ) complications rate was found. We observed one grade III anastomotic leak among RAMIE patients (2.1%), successfully managed with a combined endoscopic/surgical

**TABLE 2** Surgical results.

		RAMIE group n = 47	OE group n = 159	p Value
Operative time, min (median, IQR)		667 (631–720)	480 (420–540)	<0.01*
Blood transfusions		2 (4.3%)	28 (17.6%)	<0.05*
Abdominal approach	Open	2 (4.3%)	136 (85.5%)	<0.01*
	Laparoscopy	41 (87.2%)	22 (13.8%)	
	Robotic	4 (8.5%)	1 (0.6%)	
Conversion rate		5 (10.6%)	–	
Thoracic phase				
Mediastinal lymphadenectomy	Standard	39 (83%)	135 (84.9%)	0.74
	Extended/complete	8 (17%)	24 (15.1%)	
Number of lymph nodes harvested (median, IQR)	Overall	28 (24–38)	30 (23–38)	0.95
	Thoracic	10 (7–16)	8 (5–11)	<0.01*
	Abdominal	18 (15–24)	22 (15–29)	0.07
Lymph node ratio (mean; ±SD)	Thoracic	2.5 (±6.9)	6.4 (±14.2)	0.23
Radicality	R0	43 (91.5%)	141 (88.7%)	0.78
	R1/2 proximal margin	1 (2.1%)	3 (1.9%)	0.92
	R1/2 circumferential margin	3 (6.4%)	15 (9.4%)	0.72
Textbook outcomes	Yes	27 (57.5%)	87 (54.7%)	0.74

Abbreviations: IQR, interquartile range; OE, open esophagectomy; RAMIE, robotic-assisted minimally invasive esophagectomy; SD, standard deviation.

treatment. In the OE group, anastomotic leak rate was 6.9% ( $p = 0.56$ ); in 7 out of 11 cases, the patients were treated conservatively or endoscopically, while 4 cases (2.5%) required a surgical revision. The length of hospital stay ( $p = 0.92$ ), readmission rate ( $p = 0.15$ ) as well as 90-day mortality ( $p = 0.65$ ) were comparable between the groups. Finally, the rate of textbook outcomes was 57.5% in the RAMIE group versus 54.7% in the OE group ( $p = 0.74$ ).

## 4 | DISCUSSION

In this retrospective study, we compared our initial experience with robotic esophageal surgery to a control group of patients treated with OE. Our main results can be summarized as follows: 1—RAMIE was associated with longer operative time and less blood transfusions; 2—morbidity, mortality, and length of hospital stay were comparable; and 3—the robotic-assisted thoracic approach allowed to increase in the number of thoracic lymph node retrieved.

As this series represents our first RAMIE experience, the outcomes are inevitably affected by the robotic learning curve, as it has been already described by several authors.<sup>24,25</sup> In our series, it is quite evident the elongation of the operative time: when this outcome is taken as an indicator of the surgeon's proficiency, the minimum number of esophagectomies needed to complete the learning curve is considered to be around 20,<sup>25,26</sup> even if according to

other authors this threshold should be set at 40 procedures.<sup>27</sup> However, there are other variables than the operative time that might be considered indicators of the surgeon's improvement. For instance, von Workum and colleagues analysed the learning curve for minimally invasive thoracoscopic Ivor–Lewis esophagectomy, choosing as an indicator of the completion of the learning process the achievement of a plateau in the anastomotic leak rate of 8%.<sup>28</sup> According to them, to reach this plateau, 119 procedures are needed. Considering these results, we can consider at least half of our series, if not more, as fully included in the learning process.

In our study, apart from the longer operative time, we did not observe other significantly worse surgical results with the robotic approach. Quite the opposite, we observed a nonsignificant trend toward a decrease in the anastomotic leak rate with the robotic approach, being 2.1% for RAMIE procedures and 6.9% in the OE group. It represents a quite good result also compared to the current literature: the international registry established by the UGIRA and including 622 robotic-assisted Ivor–Lewis esophagectomies reported a leakage rate of 17% when a circular stapled anastomosis, similar to ours, was performed.<sup>29</sup> We chose to replicate during RAMIE procedures the same end-to-end 25 mm circular stapled anastomosis we perform in open surgery, with the aim of reaching a comparable leak rate.<sup>30</sup> Interestingly, a similar anastomosis has been chosen also by the surgical team from Mainz, one of the European leading groups for robotic esophageal surgery. In a recent paper, these authors

**TABLE 3** Postoperative outcomes.

	RAMIE group n = 47	OE group n = 159	p Value
Overall complications rate	26 (55.3%)	97 (61%)	0.76
Overall severe complications rate ( $\geq$ 3A CD)	8 (17%)	36 (22.6%)	0.4
Pulmonary complications	13 (27.7%)	46 (28.9%)	0.9
Severe pulmonary complications ( $\geq$ 3A CD)	7 (14.9%)	23 (14.5%)	0.81
Cardiac complications	6 (12.8%)	24 (15.1%)	1
Infectious complications	2 (4.2%)	9 (5.7%)	1
Anastomotic leak rate			
Overall	1 (2.1%)	11 (6.9%)	0.56
Type I	0	5 (3.2%)	0.9
Type II		2 (1.7%)	
Type III	1 (2.1%)	4 (2.5%)	
Chyle leak rate			
Overall	2 (4.2%)	4 (2.5%)	0.54
Type I	1 (2.1%)	2 (1.3%)	0.41
Type II	0	0	
Type III	1 (2.1%)	2 (1.3%)	
Length of hospital stay, days (median, IQR)	8 (7–9)	7 (7–9)	0.92
Readmission rate	9 (19.1%)	19 (11.9%)	0.15
90-day mortality	1 (2.1%)	3 (1.9%)	0.65

Abbreviations: CD, Clavien–Dindo; IQR, interquartile range; OE, open esophagectomy; RAMIE, robotic-assisted minimally invasive esophagectomy.

reported for their 28 mm end-to-side circular stapled anastomosis a leak rate of around 10% in a series of more than 200 Ivor–Lewis esophagectomies.<sup>10</sup>

In our experience overall and specific morbidity, as well as the length of stay and mortality, are comparable between the groups.

We calculated for our RAMIE patients a textbook outcome rate of 57.4%, comparable with the results from the DUCA and the Oesophago-Gastric Anastomosis Audit database, reporting respectively a textbook outcome of 29.7%<sup>23</sup> and 39.7%.<sup>31</sup> Surprisingly, we did not report a reduction in the pulmonary complications rate, even it should be one of the most beneficial effects of MIE.<sup>6,11,12,32</sup> For instance, in the analysis by van der Sluis et al. on more than 400 patients treated by Ivor–Lewis esophagectomy with different approaches,<sup>12</sup> the rate of pulmonary complications decreased with the introduction of minimally invasive surgery, being 57% for open esophagectomies, 28% for conventional MIE and 21% for RAMIE. In our study, we observed a pulmonary complications rate of about 28% for both groups, a finding quite close to the results reported for MIE/RAMIE by van der Sluis, and perfectly in line with the 26.9% reported

by the International Esodata Study Group.<sup>33</sup> Probably, we did not observe a significant reduction in the pulmonary complication rate because, in our center, open esophagectomies were burdened by a relatively low rate of these complications. At least in part, this is due, in our opinion, to the extensive and systematic application of a well-coordinated ERAS protocol.<sup>19,20</sup> However, this lack of improvement might be once again an effect of our learning curve: in the RAMIE group, the longer operative time and the resulting prolonged intubation and single-lung ventilation probably impaired the beneficial effects of minimally invasive surgery. In addition, we observed a 10% of conversion rate in the RAMIE group: this relatively high rate of conversion, all occurring within the first 6 months of our robotic experience, may have biased the results of the robotic group. Even so, the most recent meta-analysis reported an overall pulmonary complication rate of 14.29% for RAMIE,<sup>32</sup> showing us that there is still room for improvement.

As for the chyle leak, we did not report a decrease in its rates with the use of robotic ICG identification. However, it should be noted that in OE, we performed a more limited mediastinal dissection, preserving the thoracic duct and therefore reducing the risk of damaging this structure.

In Table 4, we summarized the postoperative outcomes of the main studies published over the last years on robotic/hybrid Ivor–Lewis esophagectomy.

Being the worldwide experience of RAMIEs, as well as ours, is still at its very beginning, there are no data on long-term outcomes and survival. However, there are at least two surrogates of oncological outcomes that can be evaluated: the R0 resection rate and quality of lymphadenectomy. RAMIE and MIE showed, in almost all the published studies as well as in the present paper, to be at least equivalent to open surgery in terms of radicality of resection. The robot assistance might instead give an advantage over open surgery in performing a more accurate thoracic lymphadenectomy. Even without differences in the type of mediastinal lymphadenectomy carried out, we found that with the robot we increased the number of lymph nodes retrieved. Unfortunately, we failed to demonstrate an increase in the lymph nodal ratio. This finding has already been reported in some retrospective studies,<sup>34,35</sup> although recent meta-analysis did not describe any differences between open surgery and RAMIE.<sup>32,36</sup> Still, some evidence in this direction may be found in the recent RAMIE trial,<sup>11</sup> which compared robotic-assisted to laparoscopic-thoracoscopic three-field esophagectomy. In this trial, RAMIE was associated with a significantly higher number of thoracic lymph nodes retrieved, especially after neoadjuvant therapy. Even considering there is no strong evidence favoring the robot, it is reasonable to think that the endo wrist and the stable, 3D high-definition vision may facilitate the lymphadenectomy in difficult anatomical districts.

It should be noted, moreover, that during MIE (either robotic or conventional), it is usually performed a more extensive dissection with resection of the thoracic duct. In our series, this has certainly contributed to the significant increase in lymph node retrieval rate observed in the RAMIE group. However, in one of the few papers

**TABLE 4** Postoperative outcomes of some of the main studies on hybrid/robotic Ivor–Lewis esophagectomy.

	Type of esophagectomy	Approach	No. of patients	Overall morbidity	Pulmonary morbidity	AL	LoS
Our study	Ivor–Lewis	RAMIE/hybrid	47	55%	28%	2%	8
ECCG <sup>33</sup>	Ivor–Lewis/McKeown	all	6022	60.5%	27%	12.5%	17
Schmidt <sup>31</sup>	Ivor–Lewis	RAMIE/tMIE	188	53%	25.5%	15%	13
UGIRA <sup>29</sup>	Ivor–Lewis	RAMIE	331	53%	23%	20%	12
	Ivor–Lewis	Hybrid	207	67%	32%	26%	15
van der Sluis <sup>12</sup>	Ivor–Lewis	RAMIE/tMIE	214	42%	24%	12%	12

Abbreviations: AL, anastomotic leak; LoS, length of hospital stay; RAMIE, robotic-assisted minimally invasive esophagectomy; tMIE, totally minimally invasive esophagectomy.

conducted on western patients treated with esophagectomy and focused on the relevance of the thoracic duct resection, the authors reported that only in about 50% of cases, there were lymph nodes around the duct, with a rate of neoplastic invasion of 15%. It is reasonable to think that their removal at least allowed a more accurate pathological staging, even if the impact on the actual prognosis of these patients is hard to know.<sup>37</sup> Indeed, the clinical relevance of the removal of a slightly higher number of lymph nodes is still debated. Large series from Eastern Countries indicated that thoracic duct resection is associated with a higher lymph nodal harvesting rate and may give an advantage in the locoregional control of the disease, although this does not translate into a better long-term prognosis.<sup>38,39</sup> It should be mentioned that these studies included mainly squamous cell carcinomas and were performed in a population with different features than ours, and the results might not be appropriate for western patients.

Some answers to our questions might come from the results of the ROBOT-2 trial, which will compare minimally invasive and robotic-assisted Ivor–Lewis procedures.<sup>13</sup> Given the pivotal role played by the lymphadenectomy in cancer surgery, the authors choose as the primary outcome for this RCT the number of dissected lymph nodes. However, the trial is still recruiting, and the results are not expected soon.

The present paper has some limitations: it is retrospective in its nature, and it compares a series of consecutive RAMIE patients to a cohort mostly composed of historical patients, introducing therefore a time bias. As discussed, the results of the RAMIE group are necessarily burdened by the effect of the learning curve. Finally, even if the main components of our postoperative ERAS protocols have remained the same, they have been updated over the period analysed.

## 5 | CONCLUSIONS

In our first series of robotic-assisted Ivor–Lewis esophagectomies, we observed a morbimortality rate compared to open surgery, at the price of significantly longer operative times. We also reported a trend toward a more extensive mediastinal lymphadenectomy in RAMIE

procedures. Larger series, with longer follow-up periods, are needed to establish if the robotic approach can give long-term advantages over open surgery in the treatment of esophageal malignancies.

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## DATA AVAILABILITY STATEMENT

Research data are not shared.

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