Learning Curve for Minimally Invasive Oesophagectomy of Esophageal Cancer and contrast with Open Oesophagectomy

Yunpeng Zhao
The Second Hospital of Shandong University
Fanshuo Zeng
The Second Hospital of Shandong University
Zongbao Mou
Zhucheng People's Hospital
Xuefeng Liang
Shandong Blood Centre
Bo Cong
The Second Hospital of Shandong University
Chuanliang Peng
The Second Hospital of Shandong University
Xiaogang Zhao (zhaoxiaogang@sdu.edu.cn)
The Second Hospital of Shandong University

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Abstract

Purpose: Minimally invasive oesophagectomy is a technically demanding procedure; thus, the learning curve of this procedure should be explored. Then the relatively mature minimally invasive oesophagectomy procedure should be contrasted with the open procedure. Methods: 214 consecutive patients underwent minimally invasive oesophagectomy were retrospectively reviewed. To evaluate the development of thoracoscopic-laparoscopic oesophagectomy and compare the mature minimally invasive oesophagectomy and open oesophagectomy (OE), we comprehensively studied the clinical and surgical parameters. The cumulative sum (CUSUM) plot was used to study the learning curve for systemic lymphadenectomy. Cox proportional hazards regression analysis was performed to evaluate the clinical factors affecting survival. Results: The bleeding volume, operation time, and postoperative mortality within 3 months significantly decreased after 20 patients. The rise point for the lymph nodes dissection number was visually determined to be at patient 57 in the CUSUM plots. Patients who underwent relatively mature thoracoscopic-laparoscopic oesophagectomy had better surgical data and short-term benefits than patients who underwent an open procedure. Cox proportional hazards regression analysis showed that the maximum diameter of the tumour cross-sectional area and the number of positive nodes had a significant influence on survival. Conclusions: The short-term benefits of thoracoscopic-laparoscopic oesophagectomy were suggested. There was no evidence that it is associated with a significantly better prognosis for patients with oesophageal cancer.

Introduction

The incidence of oesophageal carcinoma has increased significantly over the past twenty years, and it is currently the sixth leading cause of cancer death[1−2]. Radical surgical resection remains the main treatment of early and locally advanced lesions [3] but has a high rate of morbidity and mortality[4], which may be attributed to the level of lymph node dissection[5]. During the 1990s, several doctors explored the safety and effectiveness of minimally invasive oesophagectomy (MIE) [6−10] due to the high rate of cardiopulmonary complications with transthoracic oesophagectomy[11]. MIE was reported to result in low morbidity and mortality rates with equal mid- and long-term oncological outcomes [12−16].

The minimally invasive approach is performed via a distinct view of the surgical anatomy, and specialized surgical schemes and skills are required. Although learning curves and other parameters for lymph node dissection have been reported over the past few years [17−20], systematic analyses of these learning curves, as well as the clinical indexes and survival outcomes, with more than 200 cases or long monitoring times, are still limited. From July 2010 to August 2016, 214 patients underwent MIE for oesophageal cancer and were followed up. The clinical parameters were analyzed to present the learning curve and characteristics of MIE, a clinical comparative study of mature MIE versus open oesophagectomy (OE) for oesophageal carcinoma was performed, and a Cox proportional hazards regression analysis was implemented to determine clinical risk factors on overall survival.

Patients And Methods

Patients

Between July 2010 and August 2016, 214 patients underwent MIE (thoracoscopic-laparoscopic oesophagectomy) for oesophageal squamous cell carcinoma in the Thoracic Department, The Second Hospital of Shandong University in our cohort study. Eight of these 214 patients were converted to thoracotomy or laparotomy, one patient was unable to tolerate single-lung ventilation due to a history of left upper lobectomy, and the other seven patients were due to bleeding controlling. Among the 214 patients enrolled, there were 182 males and 32 females in the MIE group. A total of 170 patients underwent oesophagectomy by open thoracotomy from August 2014 to August 2016, and these patients were defined as the open group. The data from the patients in the open group were compared with those of the patients who underwent thoracoscopic-laparoscopic oesophagectomy during the same clinical period. All patients were preoperatively diagnosed with oesophageal cancer by endoscopy and biopsy, with routine thoracic and abdominal enhanced computed tomography (CT) scans and endoscopic ultrasonography to evaluate the clinical TNM stage. The operations were performed by a single surgical team. This study was approved by the ethics committee and Medical Administration Division of the Second Hospital of Shandong University. Written informed consent was obtained from each of the enrolled patients. All methods performed in our study were conducted in accordance with the relevant guidelines and regulations.

Surgical techniques

All patients underwent curative thoracic oesophagectomy and lymphadenectomy. The MIE group underwent surgery with thoracoscopic and laparoscopic approaches. We performed both cervical anastomosis (McKeown oesophagectomy) and thoracic anastomosis (Ivor-Lewis oesophagectomy). The incised margin was at least 5 cm from the superior border of the tumour. The MIE procedures were performed by the same surgical team.

The extent of lymphadenectomy included the following regions: periesophageal lymph nodes; subcarinal lymph nodes; left and right recurrent laryngeal nerve lymph nodes; hilar lymph nodes; the lesser omentum, especially the left gastric vessel region; and the suspicious lymph nodes near the common hepatic artery. The cervical lymph nodes were selectively dissected according to the location of the tumour and the ultrasound examination.

The development process for the MIE group could be divided into four stages: the first stage was from July 2010 to April 2011 and included 20 patients with relatively high mortality. The second stage was from June 2011 to July 2014 and included 37 patients. A hybrid procedure, which was not included in the analysis, was performed to determine the maturation process. The third stage was from August 2014 to May 2015 and included 50 patients who underwent the mature procedure, not the hybrid procedure. The fourth stage was from June 2015 to August 2016 and included 117 patients. The work has been reported in line with the STROCSS criteria [21].

Statistical analysis

The bleeding volume, operation time, and number of lymph nodes dissected were analysed within the MIE group; these values are presented as the means ± SD. The P values were calculated using one-way analysis of variance (ANOVA) with tests for equal variances. If heterogeneity of variance existed, one-way ANOVA was used after the data were ranked with a nonparametric test. The CUSUM plot was used to study the learning curve for systemic lymphadenectomy. The lymphadenectomy completion and complication rates were compared using the chi-square test. The survival rate was calculated, with the survival curves drawn according to the Kaplan-Meier method.

T-tests were used to compare the bleeding volume, operation time, number of lymph nodes dissected and number of lymph node dissection sites between the MIE group and the open group. The Pearson chi-square test was used for all the theoretical frequencies $T \geq 5$; the chi-square test or Fisher's exact test was used to calibrate the four-grid data when $1 \leq T < 5$, and Fisher's exact test was used when $T < 1$. The Kaplan-Meier method was used to draw the survival curve. The clinical factors were evaluated for their impact on survival through Cox proportional hazards regression analysis.

$P < 0.05$ indicated statistical significance. All analyses were performed using Stata 12.0 (StataCorp LP, College Station, TX, USA).

Results

1. Clinical data of the MIE group

The clinical and pathological features of these 214 patients are shown in Table 1. A minority of the patients received neoadjuvant chemoradiation or neoadjuvant chemotherapy, which was based on the patients' informed consent status or economic conditions. Most patients were male with a history of smoking, and four patients died within 3 months due to severe complications. Postoperative adjuvant therapy was performed according to the T stage and N stage.

Table 1

The clinical and pathological features of patients in MIE team

1st stage 2nd stage 3rd stage 4th stage P value
Cases 20 37 50 107 Proportion of males (%) 95 89 88 81 0.340 Age mean(SD) 58.210.6 63.110.8 60.98.9 64.710.4 0.351 Proportion of smoking (%) 83 87 80 80 0.637 Neoadjuvant therapy (%) 15 16.2 22 13 0.479
Histology type Squamous Cell Carcinoma 20 37 49 106 Adenocarcinoma 0 0 1 0 Small Cell Carcinoma 0 0 0 1 0.543
Differentiation grade Middle or high differentiated 16 16 17 42 Poorly differentiated 4 21 33 65 0.004
Pathological stage 0 0 0 6 13 23 28 52 7 14 22 49 0.103
Negative margin 100% 100% 100% 98.13%

2. Surgical characteristics of the MIE group

The data are shown in Table 2. There was a significant difference in the bleeding volume between the four stages (P = 0.0092) (Fig. 1a). There was a statistically significant difference between the 1st and the 2nd stages (P = 0.0263), and no significant difference was found among the latter three stages (P = 0.4625). These findings were similar for the operation time (Fig. 1b), with a P value of 0.0000. The P value between the 1st stage and the 2nd stage was 0.0000, and the P value among the latter three stages was 0.1107. In the subgroup analysis, there were no significant differences in the complication rates among the four stages (P = 0.105) (Fig. 1c) or in the incidence of cervical anastomotic fistula, chest anastomotic fistula, and recurrent laryngeal nerve injury (P values of 0.759, 0.632, and 0.813 respectively). The postoperative mortality within 3 months differed significantly among the four stages (P = 0.0092) (Fig. 1d); the postoperative mortality was not significantly different between the 1st and 2nd stages (P = 0.607); however, this parameter was different among the 1st, 2nd and 3rd stages (P = 0.005).

Table 2

Surgical characteristics of MIE team

	1st stage	2nd stage	3rd stage	4th stage	P value
Cases	20	37	50	107	
Bleeding volume(ml)	265.5 ± 107.2	199.4 ± 102.8	189.1 ± 90.7	185.9 ± 86.1	0.0092
Operation time(mins)	420.2 ± 64.3	263.5 ± 47.6	244.9 ± 60.2	248.1 ± 51.2	0.0000
Complication rate(%)	50.0	29.7	26.1	23.5	0.105
Cervical anastomotic fistula(%)	16.7(3/18)	14.8(4/27)	8.7(3/34)	9.8(6/61)	0.759
Chest anastomotic fistula(%)	0	0	0	4.3(2/46)	0.632
laryngeal nerve injury(%)	5	5.4	4	3.7	0.813
Mortality within 3 months(%)	10.0	5.4	0	0	0.0024
Lymph node dissection	12.65 ± 4.13	15.91 ± 3.36	20.16 ± 7.71	22.67 ± 7.39	0.0000
Node dissection ≥ 12	14	36	50	101	0.0000
Node dissection ≥ 18	1	12	29	71	0.0000
Location					
Upper or mid to upper	1	8	9	15	
Mid or lower to mid	18	23	30	65	
Lower	1	6	11	27	0.367
Procedure					
Ivor-Lewis	2	10	16	46	
McKeown	18	27	34	61	0.021

The lymphadenectomy parameters were significantly different among the 4 stages (P = 0.0000) (Fig. 2a). The rise point for the number of lymph nodes dissected was visually assessed to be at the 57th operation (Fig. 2b), which means that the number of lymph nodes dissected increased from the 3rd stage. A comparison of stage 1 and stage 2 yielded a P value of 0.677, and a comparison of stage 3 and stage 4 yielded a P value of 0.0523; for stages 1 combining stage 2, stages 3 combining stage 4, the numbers of lymph nodes dissected were 13.51 ± 3.25 and 21.26 ± 7.72 (P = 0.0000), respectively.

There were no significant differences in the tumour location among the four stages (P = 0.367); nonetheless, a statistically significant difference was found in the proportion of Ivor-Lewis procedures performed (P = 0.021). Specifically, the proportion of Ivor-Lewis procedures in the 3rd stage did not differ significantly from that in the former two stages (P = 0.271); however, the proportion of Ivor-Lewis procedures in the 4th stage was significantly greater (P = 0.010).

3. Survival analysis of the MIE group

The 2-year overall survival curve and disease-free survival curve of the first three stages are shown in Fig. 3a and Fig. 3b. There were no significant differences in the 2-year overall survival or disease-free survival among the three stages (72.2%, 67.7%, 68.01%, P = 0.9284) (66.7%, 58.06%, 59.6%, P = 0.7912).

4. Comparison between the MIE group and the open group

As seen in the analysis above, the number of lymph nodes dissected increased from the 3rd stage, which indicated that the oncological effect of MIE reached a relatively high level in the 3rd stage with low complication rate and mortality rate. The 3rd stage and 4th stage was regarded as mature MIE procedures. the A total of 157 patients of the 3rd stage and 4th stage who underwent the MIE procedure and 170 patients who underwent the open procedure were enrolled. The patient characteristics are shown in Table 3, and the pathological characteristics are shown in Table 4.

Table 3
Patient characteristics of MIE team and open team

	MIE team	Open team	P value
Cases	157	170	
Proportion of males (%)	83	82	0.794
Age mean(SD)	63□4□9□2□	62□0□7□6□	0.933
Proportion of smoking (%)	79	76	0.503
Neoadjuvant therapy (%)	16	10	0.110

Table 4
Pathological characteristics of MIE team and open team

	MIE team	Open team	P value
Cases	157	170	
Histology type			
Squamous Cell Carcinoma	155	163	
Adenocarcinoma	1	5	
Small Cell Carcinoma	1	2	0.638
Differentiation grade			
Middle or high differentiated	59	63	
Poorly differentiated	98	107	0.922
Pathological stage			
□	6	18	
□	80	82	
□	71	70	0.063
Negative margin	98.73%	100%	0.230

The surgical characteristics of the MIE group and open group are shown in Table 5. There was a significant difference in the bleeding volume between the MIE group and the open group (187.2 ± 88.6 ml vs. 241.8 ± 127.4 ml, P = 0.0000). There was a statistically significant difference in the operation time between the MIE group and the open group (246.1 ± 53.9 min vs. 262.7 ± 65.4 min, P = 0.0132). The difference in the incidence of postoperative pulmonary inflammation between the MIE group and the open group yielded a P value of 0.0000 (24.2% vs. 40%). There were statistically significant differences in the lymph node dissection parameters between the MIE group and the open group (number of lymph nodes dissected: 21.26 ± 7.72 vs. 23.99 ± 10.15, P = 0.0069 and number of dissection sites: 4.87 ± 1.43 vs. 4.16 ± 1.26, P = 0.0000). For dissecting the No.106rec and No.106tbL lymph nodes, the MIE group had a statistical advantage; however, the open group had a statistical advantage for dissecting the left gastric artery lymph nodes.

Table 5

Surgical characteristics of MIE team and open team

	MIE team	Open team	P value
Cases	157	170	
Bleeding volume(ml)	187.2 ± 88.6	241.8 ± 127.4	0.0000
Operation time(mins)	246.1 ± 53.9	262.7 ± 65.4	0.0132
Complication rate(%)	24.2	40	0.359
Cervical anastomotic fistula(%)	9.5(9/95)	5.5(2/36)	0.726
Chest anastomotic fistula(%)	3.2(2/62)	0.75(1/134)	0.236
laryngeal nerve injury(%)	3.8	2.4	0.527
pulmonary inflammation	12.1(19/157)	29.4(50/170)	0.0000
Mortality within 3 months(%)	0	0	
Lymph nodes dissection	21.26 ± 7.72	23.99 ± 10.15	0.0069
Node station	4.87 ± 1.43	4.16 ± 1.26	0.0000
No.106rec (right or left)(%)	78.4 (123/157)	23.5 (40/170)	0.0000
No.106rec (right and left)(%)	64.7 (102/157)	7.1(12/170)	0.0000
No.106tbL nodes dissection(%)	31.8(50/157)	16.5(28/170)	0.001
Left gastric artery lymph nodes(%)	12.1 (19/157)	47.1 (80/170)	0.0000
No.107 nodes dissection(%)	80.4 (126/157)	80.0 (136/170)	0.937
Paraesophageal lymph nodes (including No.105, No.108, No.110) dissection(%)	90.4 (142/157)	92.9 (158/170)	0.413
Paracardia lymph nodes dissection(%)	41.4 (65/157)	42.4 (72/170)	0.862
Paragastric lymph nodes dissection(%)	47.1 (74/157)	47.1 (80/170)	0.278

5. Survival analysis and Cox proportional hazards regression analysis

Patients with a follow-up time reaching 2 years were selected for the survival analysis. In total, 120 patients were eligible, with a mean age of 63.0 ± 7.4 years, and 82% of these patients were male. 50 patients were from the MIE group, and 70 patients were from the open group. There were 13 patients in stage I, 61 patients in stage II, and 46 patients in stage III. The overall survival curves are shown in Fig. 4, and there was a statistically significant difference in 2-year overall survival (MIE group 68% vs. open group 43%, P = 0.0321). However, there was a significant difference in the proportion of stage III patients between the MIE group and the open group (14/50 vs. 23/70,P = 0.049). Consequently, a Cox proportion hazards regression was used to evaluate the impact of the clinical factors on overall survival. The following six parameters were screened: age, surgical procedure (MIE or open), differentiation degree (poor or middle- high), tumour excision area (≥ 5 cm or < 5 cm), infiltration depth (T1, T2, T3), and the number of positive lymph nodes; the results are shown in Table 6. The tumour excision area and the number of positive lymph nodes had significant impacts on overall survival. The Cox proportion hazards model was used; the hazard ratios (HRs) were calculated, and these values are presented in Table 7.

Table 6
The screening of the six clinical parameters

	Statistic	P value
Age	chi2(23) = 23.61	0.4258
Surgical procedure	chi2(1) = 2.93	0.0869
Differentiation degree	chi2(1) = 1.93	0.1645
Tumor cutting area	chi2(1) = 4.54	0.0332
Infiltration depth	chi2(2) = 1.26	0.5332
Positive lymph nodes	chi2(8) = 22.75	0.0037

Table 7
HR value

	Haz.Ratio	Std.Err	Z	P>|z|	[95Conf. Interval]
Size	2.632207	1.038634	2.45	0.014	1.21464–5.704174
node	1.286079	0.0842952	3.84	0.000	1.131035–1.462376

Discussion

Minimally invasive oesophagectomy (MIE) is defined as a thoracoscopic-laparoscopic procedure for oesophageal cancer. MIE is considered to reduce postoperative pain, drainage volume and inflammation reactions, while shortening the hospital stay. However, MIE requires surgeons to have a deeper understanding of the endoscopic anatomy, surgical procedure, accidental bleeding, and lymph node dissection process, all of which may contribute to the operation quality. MIE has been performed since July 2010 in our department, and the improvements are clear based on bleeding volume, operation time, mortality within 3 months, and lymphadenectomy parameters. Our dataset showed that surgical process proficiency could be achieved through at least 57 surgeries with adequate lymph node dissection and favourable safety outcomes.

Ankit Dhamija[17] reported the learning curve for lymph node resection in MIE for oesophageal cancer and suggested that the ability to dissect lymph nodes completely during MIE was affected by the surgeons' experience, which might accumulate over time; a significant increase in experience could be achieved after the first 25 cases. The number of dissections was regarded as an important measurement of lymphadenectomy, and different lymphadenectomy thresholds were proposed based on various scholars' findings. Dutkowski[22] found that the diagnostic sensitivity of lymph node metastasis increased with an increasing number of dissections. When the dissection number reached 12, the sensitivity could reach at least 90%; at this point, more lymph node dissections only increased the complication rate since the diagnostic sensitivity reached a plateau. Rize[23] believed that the ideal number of lymph node dissections should be no less than 18. There was no significant difference in the pathological characteristics between the 4 stages except for differentiation. Nonetheless, the numbers of lymph nodes dissected in each stage were 12.65 ± 4.13, 15.91 ± 3.36, 20.16 ± 7.71, and 22.67 ± 7.39, respectively, with a significant difference among the stages. To intuitively observe the upward trend, scatter plots were drawn, and the cumulative sum was calculated. In the present series, the inflection point was observed at the 57th case, which suggests that proficiency in lymphadenectomy during MIE was gained after 57 patients underwent the procedure. Significant increases were also discerned at both dissection numbers 12 and 18 during the 4 stages. Oncologic benefits were implied with this progress. These benefits were due to the actions implemented during the 2nd stage, including performing hybrid operations and attending academic communications.

MIE could be divided into a thoracoscopic-laparoscopic McKeown technique (cervical anastomosis) and a thoracoscopic-laparoscopic Ivor-Lewis technique (chest anastomosis). The former is preferred by surgeons because of the maturity of the surgical procedure[24], and the latter is not widely performed due to its difficulty and the risk of the occurence of a thoracic fistula; the surgical position and anastomosis type were also different in each clinical unit[25]. However, the thoracoscopic-laparoscopic Ivor-Lewis method was suggested to be less invasive, with a shorter operation time, lower anastomotic leakage rate and lower recurrent laryngeal nerve injury rate than the thoracoscopic-laparoscopic McKeown method[26]. In our series, an increase in the proportion of Ivor-Lewis procedures appeared during the 4th stage, which is after when the lymphadenectomy proficiency reached a relatively high level.

The importance of the surgical procedure were for accurate staging of the disease and an improvement in survival outcomes. The differences in 2-year overall survival and disease-free survival between the first three stages were not significant (72.2%, 67.7%, 68.01%, P = 0.9284) (66.7%, 58.06%, 59.6%, P = 0.7912), which may be due to the inadequate follow-up time and sufficient lymph node dissection, even when performed in the 1st stage (12.65 ± 4.13).

We retrospectively analysed 327 patients who underwent oesophagectomy for oesophageal cancer at our institution. A total of 157 patients underwent MIE (from the 3rd stage), and 170 patients underwent open oesophagectomy (OE). In our study, the MIE group had a smaller bleeding volume (P = 0.0000) and shorter operation time (P = 0.0132) than the OE group. There was no significant difference in the complication rates between the two groups; nonetheless, the MIE group had a lower incidence of postoperative pulmonary inflammation (12.1% vs. 29.4%, P = 0.0000), which is very similar to the results of the randomized controlled trial reported by Biere SS[27] (12% vs. 34%, P = 0.005). Additionally, according to Parameswaran R[28] and Verhage RJ[29], the postoperative respiratory complication rate of OE was higher than that of MIE. This result might be due to the large incision, rib fractures, respiratory muscle detachment, injury and repair of the diaphragm, and retention of sputum; thus, MIE was superior to OE in terms of protecting respiratory function.

The open group had more lymph nodes dissected than the MIE group (23.99 ± 10.15 vs. 21.26 ± 7.72, P = 0.0069); however, the number of lymph nodes dissected in the MIE group was similar to the results reported by another study[30]. Lymph nodes were dissected from more sites in the MIE group than in the

OE group (4.87 ± 1.43 vs. 4.16 ± 1.26, P = 0.0000), which might be due to the comprehensive view available with the thoracoscope. In the subgroup analysis, the dissection rate of the No.106rec (right or left) lymph nodes in the MIE group reached 78.4%, while that of the open group was 23.5% (P = 0.0000). The No.106rec (both right and left) lymph node dissection rate in the MIE group was 64.7%, which was significantly different from that of 7.1% in the open group (P = 0.0000). No.106tbL lymph node dissection followed a similar trend, and the MIE group had a statistically significant advantage over the OE group (31.8% vs. 16.5%, P = 0.001). Nonetheless, the open group had a statistical advantage (47.1% vs. 12.1%, P = 0.0000) in left gastric artery lymph node dissection, which reflects the capability limitations of the thoracic surgeon during laparoscopic abdominal lymphadenectomy.

Survival outcomes are crucial for the treatment of carcinoma. MIE is still not widely performed in medical institutions, and reports on long-term survival are rare. The 1-year survival rates between MIE and OE were demonstrated to have no significant differences[31]. Jingpei Li[32] reported that the 1-year, 2-year, and 3-year survival rates of patients who underwent MIE were not significantly different from those of patients who underwent the open procedure; however, the proportion of early-stage disease in the MIE group was higher than that in the open procedure group. A systematic review[33] also provided information that the proportion of early-stage disease in the MIE group exceeded that in the open procedure group, which might be inevitable while the surgeons are still learning. Mitzman B[34] performed a propensity analysis using data from the National Cancer Database of the United States, and equivalent oncological outcomes and survival outcomes were found for the MIE and open procedure groups. No significant differences in long-term survival were found in patients who underwent robotic-assisted minimally invasive oesophagectomy (RAMIE), MIE or OE; thus, surgeon expertise and experience might be considered the most important aspects[35]. In our series, although the overall 2-year survival rate differed significantly between the groups (MIE group: 68%, open group: 43%, P = 0.0321), the proportion of stage III patients who underwent OE was statistically greater than that of patients who underwent MIE. This study did not provide evidence of improvements in the survival outcomes of patients who underwent MIE. As a result, a Cox proportional hazards regression was used to evaluate the effects of clinical factors on survival for patients who underwent radical surgery with curative intent. The clinical parameters included age, surgical procedure (MIE or open), differentiation degree (poor or middle-high), tumour excision area (≥ 5 cm or < 5 cm), infiltration depth (T1, T2, T3), and the number of positive lymph nodes. The maximum diameter of the tumour excision area and the number of positive lymph nodes had a significant influence on postoperative survival. There was no evidence that the surgical procedure (MIE or open) had a significant influence on the prognosis of patients with oesophageal cancer.

There are also some limitations to this study; the management of chest drainage and nasogastric drainage and inflammatory factors were not taken into account, but there are also important indicators for presenting a learning curve. Additionally, the number of lymph node was used as a reflection of lymphadenectomy completeness, and this number might be influenced by fracturing of the nodes or pathological diligence. Moreover, our study was a retrospective analysis, and challenging cases were avoided in the early stage of the learning process; thus, selection bias was inevitable. Finally, only a few patients received neoadjuvant therapy, which was recommended by the medical guidelines.

In conclusion, our findings provide evidence of the learning curve for MIE and its short-term benefits. However, there is still no evidence that MIE and OE contribute differently to postoperative survival outcomes.

Declarations

Conflict of Interest Statement: All the authors had no conflict of interest.

Ethics approval and consent to participate: This study was approved by the ethics committee and Medical Administration Division of the Second Hospital of Shandong University.

Consent for publication: Written informed consent was obtained from each of the enrolled patients.

Availability of data and material: They are all on request.

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Authors' contributions: Yunpeng Zhao and Fanshuo Zeng: Formal analysis; Methodology; Roles/Writing - original draft; Writing - review & editing. Zongbao Mou: Data curation. Xuefeng Liang: Data curation. Bo Cong: Conceptualization. Chuanliang Peng: Resources. Xiaogang Zhao: Supervision; Funding acquisition.

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Figures

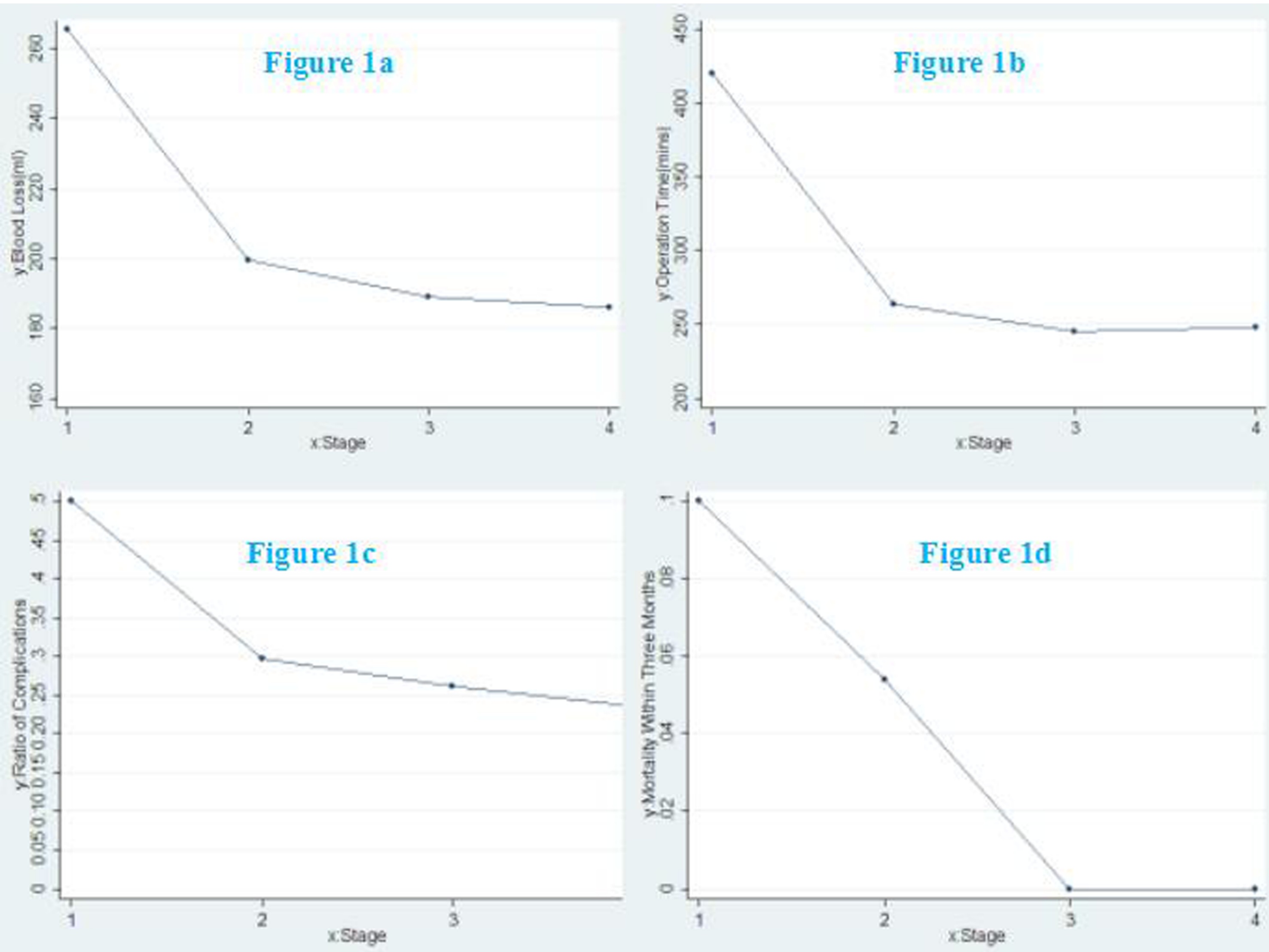

Figure 1

Comparisons of the basic clinical characteristics among the four stages. Figure 1a: bleeding volume. Figure 1b: operation time. Figure 1c: complication rate. Figure 1d: postoperative mortality.

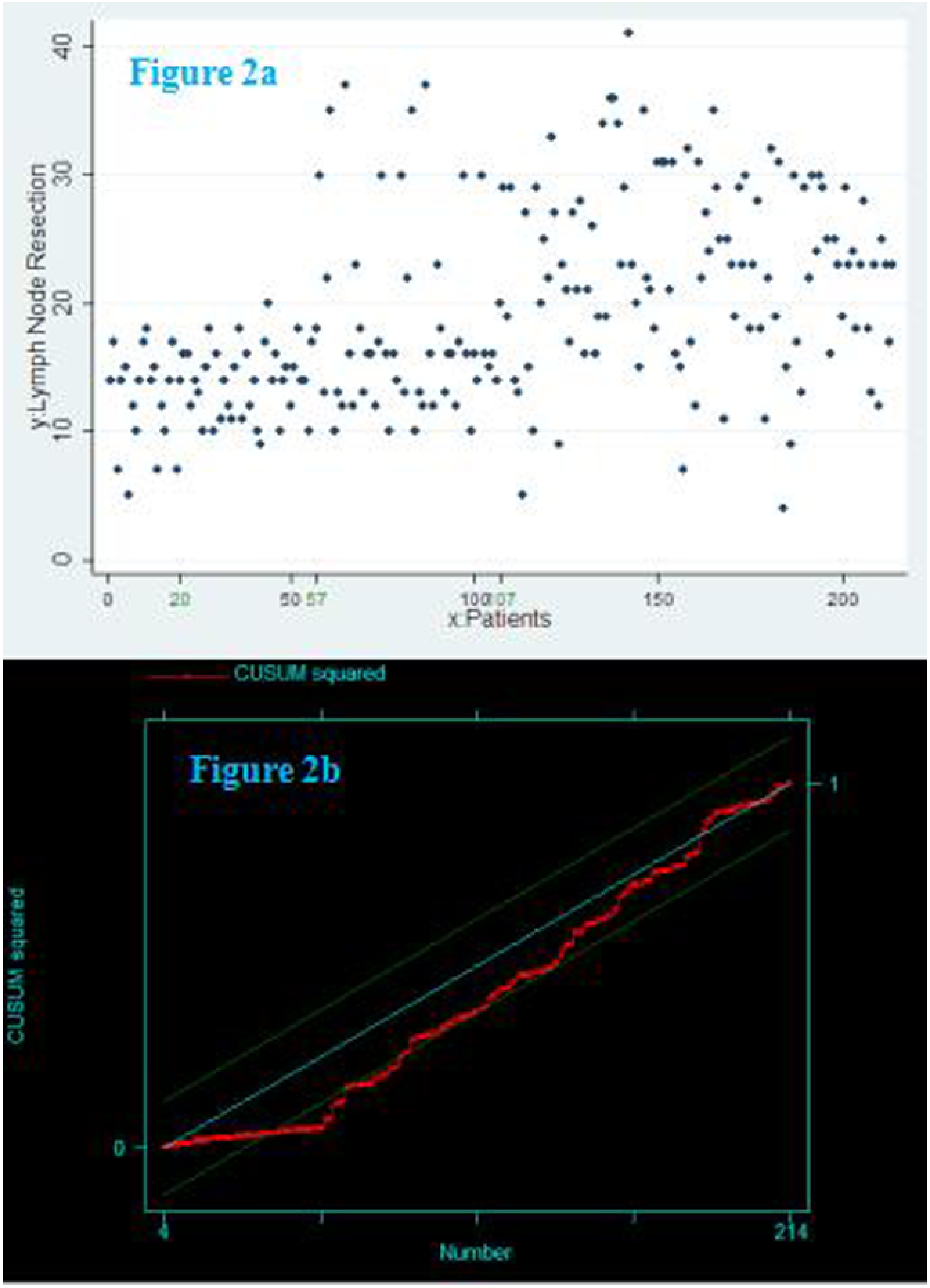

Figure 2

Lymph node dissection. Figure 2a: scatter diagram of the lymphadenectomy procedure. Figure 2b: CUSUM plots of the lymphadenectomy procedure.

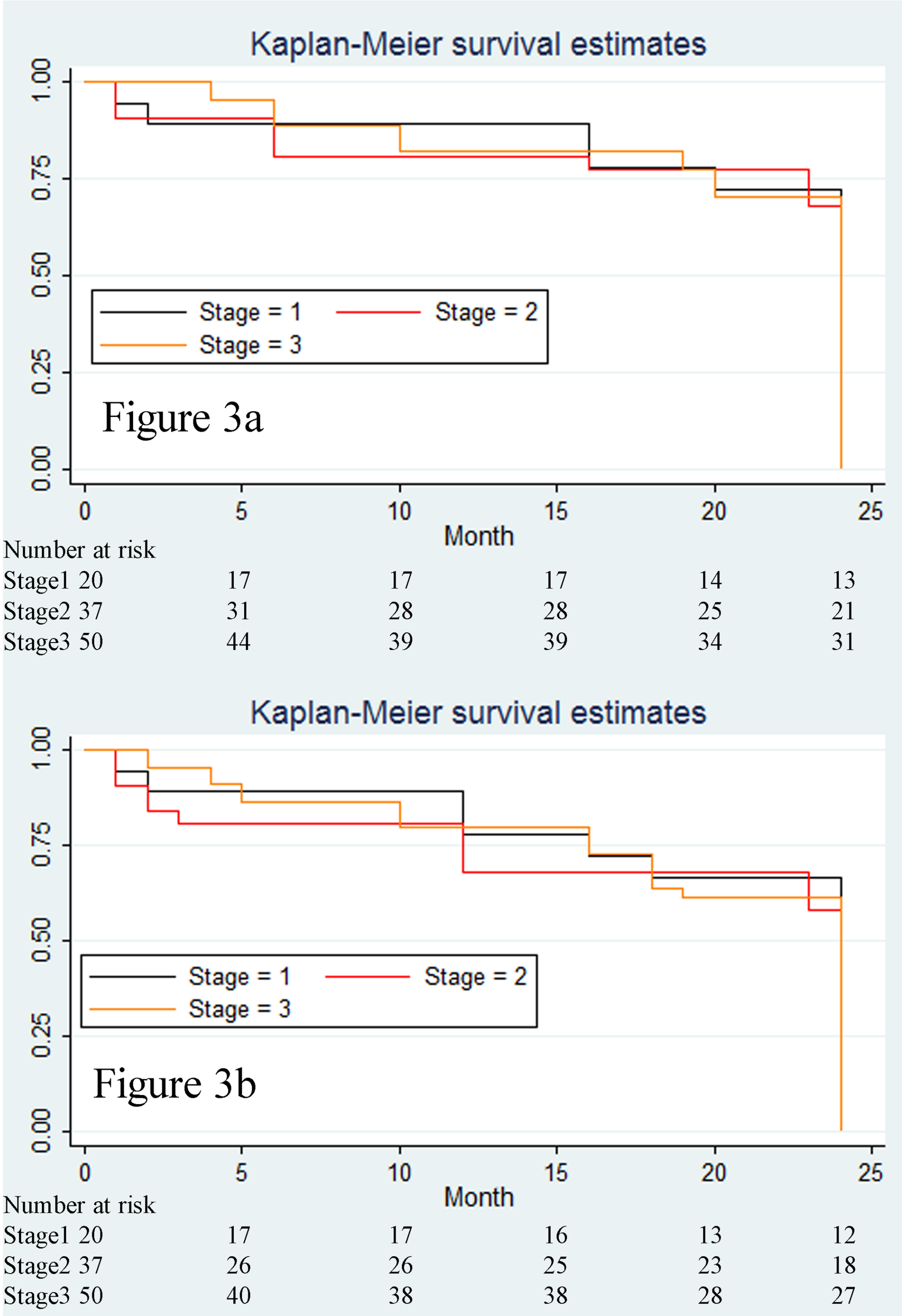

Figure 3

2-year overall survival curve and disease-free survival curve of the 1st, 2nd, and 3rd stages. Figure 3a: 2-year overall survival curve of the former three stages. Figure 3b: 2-year disease-free survival curve of the former three stages.

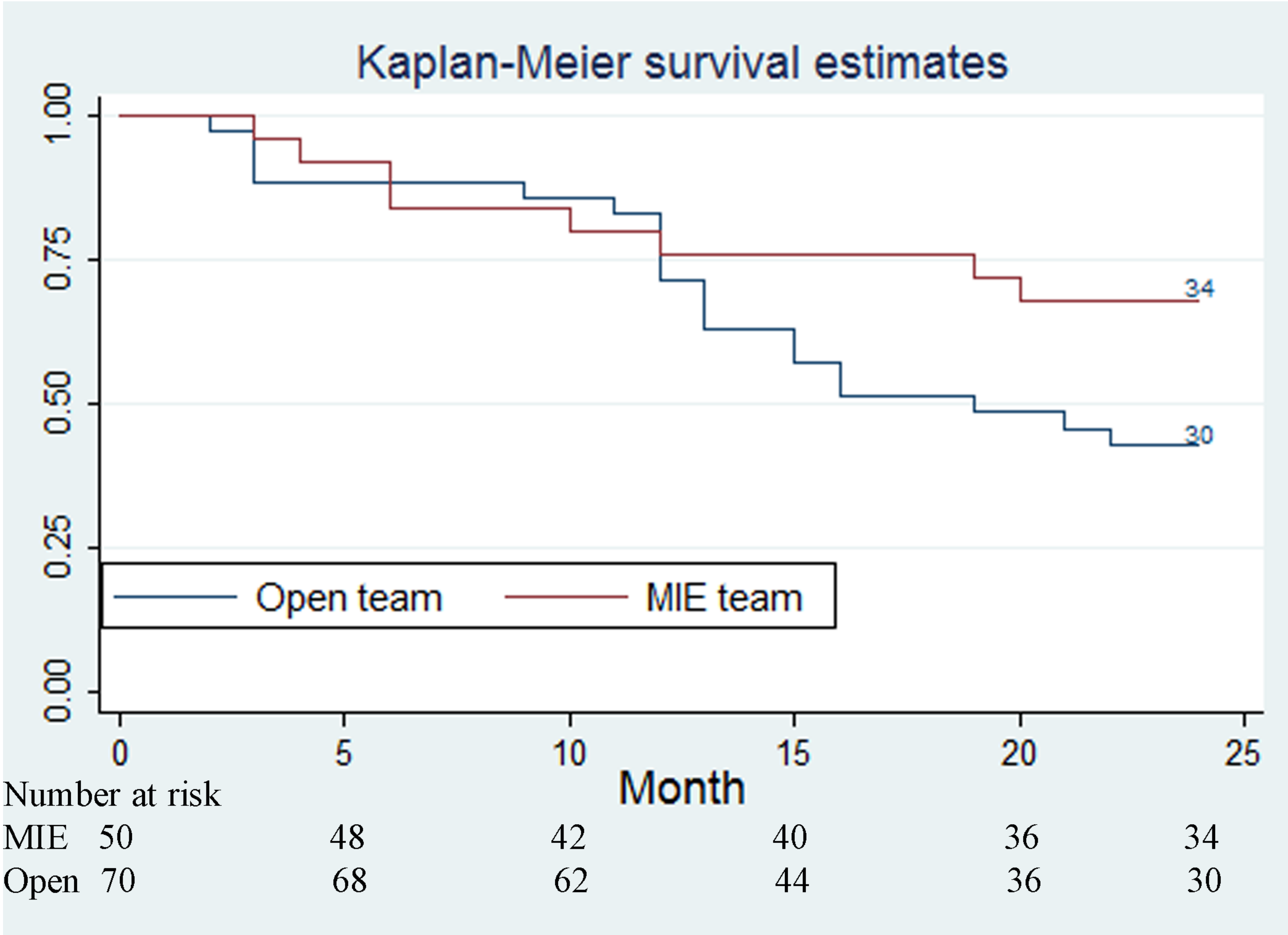

Figure 4

2-year overall survival curve of the MIE group and the open group.