Int J Clin Exp Med 2018;11(3):2350-2360
www.ijcem.com /ISSN:1940-5901/IJCEM0029274

*Original Article*

# Comparative outcomes of laparoscopy-assisted and open Ivor Lewis esophagectomy for esophageal squamous cell carcinoma: experience at a single, high-volume center

Wei-Ming Fang, Wei-Zhong Ruan, Shao-Feng Lin, Yuan-Mei Chen, Kun-Shou Zhu

*Department of Thoracic Surgery, Teaching Hospital of Fujian Medical University, Fujian Provincial Cancer Hospital, No. 420 Fuma Road, Fuzhou 350014, Fujian, People's Republic of China*

Received March 27, 2016; Accepted December 20, 2017; Epub March 15, 2018; Published March 30, 2018

**Abstract:** This study compared the oncologic outcomes of Ivor Lewis esophagectomy in laparoscopy-assisted surgery versus open surgery for resectable middle and lower thoracic esophageal squamous cell carcinoma. Short-term and long-term data for 685 consecutive patients who underwent Ivor Lewis esophagectomy for resectable middle and lower thoracic esophageal squamous cell carcinoma via laparoscopy-assisted surgery or open surgery between January 2010 and November 2015 were retrospectively reviewed. The primary study endpoints were overall survival and disease-free survival. A total of 685 Ivor Lewis esophagectomies for resectable middle and lower thoracic esophageal squamous cell carcinoma were performed, with 432 esophagectomies performed using laparoscopy-assisted surgery and 253 esophagectomies performed using open surgery. Patient demographic data, tumor pathological stage, and residual tumor remaining were similar in both groups. Blood loss, postoperative analgesia requirement, and length of hospital stay were all less with laparoscopy-assisted surgery than with open surgery. Overall morbidity was similar in the two groups. However, the rate of major complications was higher after open surgery than after laparoscopy-assisted surgery. There were no 30-day mortalities, and both overall and disease-free survival were comparable between the two surgical groups. From this study, laparoscopy-assisted Ivor Lewis esophagectomy performed by dedicated thoracic surgeons is safe and can achieve long-term survival similar to an open approach.

**Keywords:** Esophageal carcinoma, Ivor-Lewis esophagectomy, laparoscopy-assisted surgery, minimally invasive esophagectomy

## Introduction

Ivor Lewis esophagectomy, which consists of laparotomy and right thoracotomy for the resection of operable esophageal cancer, is a recognized primary procedure for the treatment of middle and lower thoracic esophageal cancer [1-6]. Although Ivor Lewis esophagectomy provides optimal locoregional control and long-term survival, it is also associated with a mortality rate of 2%-10% and a morbidity rate of 30%-50% [7-10]. Therefore, alternative procedures are required that diminish surgical trauma without compromising oncologic outcomes [11-13]. Laparoscopic surgical procedures, such as laparoscopic cholecystectomy, laparoscopic colectomy, and laparoscopic appendectomy, have achieved worldwide popularity because they produce less postoperative trauma and morbidity than open surgery [14-27]. Some thoracic surgeons have employed laparoscopic gastric mobilization and abdominal lymph node dissection for esophagectomy to decrease surgical trauma and postoperative morbidity [11-13].

Laparoscopy-assisted Ivor Lewis esophagectomy consists of laparoscopic gastric tube formation and abdominal lymph node dissection, followed by open thoracotomy and intrathoracic anastomosis [11-13]. This procedure represents a minimally invasive technique in the treatment of esophageal cancer that has become more widely adopted because it results in fewer complications and facilitates faster recovery than with open esophagectomy [11-

**Table 1.** Demographic data

| | Laparoscopy-assisted ($n$ = 432) | Open ($n$ = 253) | $P$ value |
|---|---|---|---|
| Age (y) (median and range) | 60.00 (43-72) | 65.00 (45-76) | 0.512 |
| Gender (Male:Female) | 301:131 | 175:78 | 0.136 |
| Comorbidity | | | 0.598 |
| COPD | 10 (2.3%) | 5 (2.0%) | |
| Hypertension | 48 (11.1%) | 20 (7.9%) | |
| Diabetes Mellitus | 29 (6.7%) | 6 (2.4%) | |
| Atrial fibrillation | 20 (4.6%) | 9 (3.6%) | |
| Stable angina | 6 (1.4%) | 3 (1.2%) | |
| Clinical T stage | | | 0.810 |
| $T_{1b}$ | 18 (4.2%) | 7 (2.8%) | |
| $T_2$ | 168 (39.8%) | 101 (39.9%) | |
| $T_3$ | 246 (56.9%) | 145 (57.3%) | |
| Clinical N stage | | | 0.607 |
| $N_0$ | 125 (28.9%) | 70 (27.7%) | |
| $N_1$ | 136 (31.5%) | 89 (35.2%) | |
| $N_2$ | 171 (39.6%) | 94 (37.2%) | |
| Clinical M stage | | | |
| $M_0$ | 482 (100%) | 253 (100%) | - |
| ASA score | | | 0.754 |
| I | 258 (59.7%) | 156 (61.7%) | |
| II | 158 (36.6%) | 86 (34.0%) | |
| III | 16 (3.7%) | 11 (4.3%) | |

COPD: chronic obstructive pulmonary disease

13]. However, the oncologic outcomes following laparoscopy-assisted Ivor Lewis esophagectomy as measured by long-term survival have not been established [28-30]. Indeed, there is a paucity of data from multi-center, randomized controlled trials comparing laparoscopic and open approaches and their long-term oncological outcomes. We introduced laparoscopy-assisted Ivor Lewis esophagectomy for esophageal cancer at our institution in January 2009. The surgeons in the department of thoracic surgery of our cancer center have acquired and mastered the basic skill of performing laparoscopy-assisted Ivor Lewis esophagectomy. The aim of this study was to retrospectively assess our 5-year experience with oncologic outcomes after laparoscopy-assisted Ivor Lewis esophagectomy.

## Patients and methods

### *Patient evaluation*

This study complied with the Declaration of Helsinki rules. This retrospective research was approved by the Ethics Committee of Fujian Provincial Cancer Hospital. The need for informed consent from all patients was waived because of retrospective study.

We retrospectively reviewed the records of 685 consecutive patients with resectable middle and lower thoracic esophageal squamous cell carcinoma who underwent Ivor Lewis esophagectomy at the Department of Thoracic Surgery, Fujian Provincial Cancer Hospital from January 2010 to November 2015. All patients underwent upper gastrointestinal endoscopy; endoscopic ultrasonography; computed tomographic scans of the brain, chest, and abdomen; and ultrasonography of the neck to determine the tumor clinical stage and to exclude clinical cervical metastasis. Positron emission tomography-computerized tomography was not routinely performed due to its cost. Preoperative chemotherapy or radiotherapy was not routinely performed [31-36].

The clinical stage of esophageal carcinoma was based on the 7th edition of the TNM classification of esophageal carcinoma [37-40], which was proposed by Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC). The lymph nodes map was based on the tenth edition of Japanese Classification of Esophageal Cancer as previously reported [37-40].

### *Surgical technique*

All surgical procedures were performed by two experienced surgeons with proven expertise in esophageal carcinoma. For all 685 patients, resection was performed with curative intention. After consultation, patients and their families chose between laparoscopy-assisted and open Ivor Lewis esophagectomy. For patients undergoing laparoscopy-assisted surgery, lapa-

**Table 2.** Surgical and pathological data

| | Laparoscopy-assisted (*n* = 432) | Open (*n* = 253) | *P* value |
|---|---|---|---|
| Operative time (min) (median and range) | 260.00 (180-330) | 230.00 (180-300) | 0.000 |
| Blood loss (ml) (median and range) | 330.00 (250-600) | 390.00 (300-650) | 0.000 |
| Pathological T stage | | | 0.452 |
| $T_{1b}$ | 12 (2.8%) | 5 (2.0%) | |
| $T_2$ | 143 (33.1%) | 98 (38.7%) | |
| $T_3$ | 258 (59.7%) | 138 (54.5%) | |
| $T_{4a}$ | 19 (4.3%) | 12 (4.7%) | |
| Pathological N stage | | | 0.971 |
| $N_0$ | 87 (20.1%) | 52 (20.6%) | |
| $N_1$ | 154 (35.6%) | 87 (34.4%) | |
| $N_2$ | 141 (32.6%) | 82 (32.4%) | |
| $N_3$ | 50 (11.6%) | 32 (12.6%) | |
| Residual tumor (R0/R1/R2) | 429 (99.3%)/3 (0.7%)/0 | 251 (99.2%)/2/(0.8%)/0 | 0.887 |
| Number of harvested lymph nodes (median and range) | 25.00 (16-42) | 26.00 (17-43) | 0.360 |
| Mediastinal lymph nodes dissected | 12.00 (6-20) | 12.00 (7-21) | 0.395 |
| Abdominal lymph nodes dissected | 13.00 (10-22) | 14.00 (10-22) | 0.403 |
| Post-operative analgesia (d) (median and range) | 3.0 (2-5) | 4 (2-6) | 0.000 |
| Hospital stay (d) (median and range) | 18.00 (10-30) | 19.00 (15-30) | 0.000 |

roscopic gastric mobilization was followed by gastric tube construction, abdominal lymphadenectomy, open right transthoracic en bloc mediastinal lymphadenectomy, and en bloc esophagectomy with anastomosis in the upper chest using stomach [11-13].

*Surgical outcome and post-operative complications*

Operative time, blood loss, pathological stage, overall number of lymph nodes involved, residual tumor present, postoperative morbidity occurring within 30 days after surgery, and length of hospital stay were assessed. Postoperative morbidity assessment included major and minor complications that were graded according to Clavien-Dindo classification, as previously reported: major complications were defined as grades 3b, 4a, 4b, and 5, whereas minor complications were classified as 1, 2, and 3a [41-51]. Operative death was defined as all-cause mortality within 30 days after esophagectomy.

*Follow up*

During the first year after treatment completion, patients were seen every 3 months at the outpatient department. During the second year post surgery, follow-up occurred every 6 months. Thereafter, follow-up occurred at the end of each year. Follow-up diagnostic investigations included CT scans of the chest and upper abdomen, and cervical ultrasonography was performed before discharge and before each follow-up visit. Upper gastrointestinal endoscopy was performed once per year. Any postoperative complications and medical conditions requiring hospitalization were reviewed. Disease recurrence and patient death were also documented. Cancer recurrence was defined as locoregional or distant metastasis verified by radiology or pathology [52-65]. The last follow-up appointment occurred in March 2016.

*Statistical analysis*

All statistical analyses were performed using SPSS 14.0 for windows (SPSS Inc., Chicago, IL, USA). Data are reported as means and standard deviations for variables that followed a normal distribution and were analyzed by *t* test. For variables that were not normally distributed, results were expressed as the median and range and were compared using a nonparametric statistical test. Group differences in semi-

Table 3. Post-operative complications

| | Laparoscopy-assisted ($n$ = 432) | Open (n = 253) | $P$ value |
|---|---|---|---|
| Post-operative complications ($n$, %) | 106 (24.5%) | 71 (28.1%) | 0.601 |
| Severity of complications | | | 0.021 |
| Major (3b, 4a, 4b and 5) | 16 (3.7%) | 21 (8.3%) | |
| Minor (1, 2 and 3a) | 90 (20.8%) | 50 (19.8%) | |
| Major complications | | | 0.944 |
| Pulmonary embolism | 2 (0.5%) | 3 (1.2%) | |
| Acute coronary syndrome | 3 (0.7%) | 2 (0.8%) | |
| Respiratory insufficiency | 5 (1.2%) | 8 (3.2%) | |
| DIC | 1 (0.2%) | 1 (0.4%) | |
| Heart failure | 5 (1.2%) | 7 (2.8%) | |
| Minor complications | | | 0.947 |
| Pneumonia | 24 (5.6%) | 13 (5.1%) | |
| Vocal code palsy | 6 (1.4%) | 4 (1.6%) | |
| Chylothorax | 6 (1.4%) | 2 (0.8%) | |
| Anastomotic leakage | 7 (1.6%) | 2 (0.8%) | |
| Wound infection | 16 (3.7%) | 12 (4.7%) | |
| Sepsis | 8 (1.9%) | 4 (1.6%) | |
| Acute renal failure | 12 (27.8%) | 8 (3.2%) | |
| Urinary tract infection | 11 (25.5%) | 5 (2.0%) | |
| Mortality within 30 days after surgery | 0 (0.0%) | 0 (0.0%) | - |

Respiratory insufficiency was defined as lung failure demanding prolonged ventilation more than 10 days. DIC: disseminated intravascular coagulation. The severity of complications was graded according to the Clavien-Dindo classification.

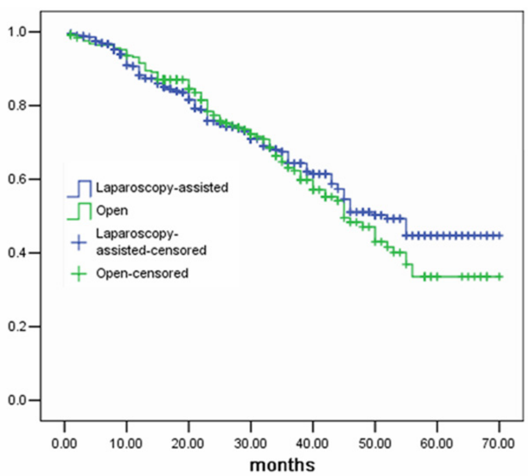


**Figure 1.** Overall survival in relation to approach of esophagectomy in 685 consecutive patients.

quantitative results were analyzed using the Mann-Whitney $U$-test. Differences in qualitative results were analyzed using the chi-square test or the Fisher exact test where appropriate. Survival rates were analyzed using the Kaplan-Meier method, with differences between the 2 groups analyzed using the log-rank test. Patient overall survival was assessed from the date of surgery until the last follow-up day or death from any cause. The disease-free survival was calculated from the date of surgery until the date of cancer recurrence or death of any cause. Univariate analyses were performed to identify prognostic variables related to overall survival and disease-free survival. Univariate variables with probability values less than 0.05 were selected for inclusion in a multivariate Cox proportional hazard regression model. Adjusted hazard ratios (HR) along with the corresponding 95% confidence intervals (CI) were calculated. $P$ < 0.05 was considered statistically significant.

## Results

### *Demographic data*

Patient demographic data are summarized in **Table 1**. This study evaluated 432 esophagectomies performed using a laparoscopy-assisted approach and 253 esophagectomies performed using an open Ivor Lewis approach. There were no significant surgical group differences in age, gender, comorbidity, clinical stage, or ASA score ($P$ > 0.05).

### *Surgical outcome and pathological data*

Patient surgical and pathological outcomes are summarized in **Tables 2** and **3**, respectfully. There were no laparoscopy-assisted case that required conversion to open laparotomy and no intraoperative or in-hospital mortality. Laparoscopy-assisted procedures took longer to complete than open surgery ($P$ < 0.05). There were no significant group differences in pathological stage or residual tumor ($P$ > 0.05). The number of harvested lymph nodes was similar between the 2 groups ($P$ > 0.05), with more than 15 in each case. Patients in the laparoscopy-assisted group enjoyed significantly faster recovery, in-

**Table 4.** Multivariate Cox regression analyses of overall survival

| Regression variables | Adjusted hazared ratio | 95% CI | Beta value | *P* value |
|---|---|---|---|---|
| Age | | | | |
| < 70 years | 1.00 | | | |
| ≥ 70 years | 1.35 | 0.69-1.58 | 0.69 | 0.102 |
| ASA score | | | | |
| I-II | 1.00 | | | |
| III | 1.26 | 0.70-1.38 | 0.60 | 0.206 |
| Comorbidity | | | | |
| No | 1.00 | | | |
| Yes | 1.39 | 0.51-1.59 | 0.49 | 0.108 |
| Major complications | | | | |
| No | 1.00 | | | |
| Yes | 1.50 | 0.85-1.98 | 0.85 | 0.109 |
| Adjuvant chemotherapy | | | | |
| Yes | 1.00 | | | |
| No | 1.69 | 0.74- | 0.60 | 0.100 |
| Pathological T stage | | | | |
| $T_{1b}$ | 1.00 | | | |
| $T_2$ | 1.23 | 0.26-1.63 | 0.58 | 0.802 |
| $T_3/T_{4a}$ | 3.36 | 1.23-4.69 | 1.36 | 0.002 |
| Pathological N stage | | | | |
| $N_0$ | 1.00 | | | |
| $N_1$ | 1.68 | 0.45-1.20 | 0.74 | 0.520 |
| $N_2/N_3$ | 3.69 | 2.12-5.23 | 1.68 | 0.001 |
| Differentiation grade | | | | |
| G1 (good) | 1.00 | | | |
| G2 (moderate) | 1.38 | 0.37-3.25 | 0.85 | 0.213 |
| G3 (poor) | 3.48 | 2.40-8.30 | 1.36 | 0.005 |

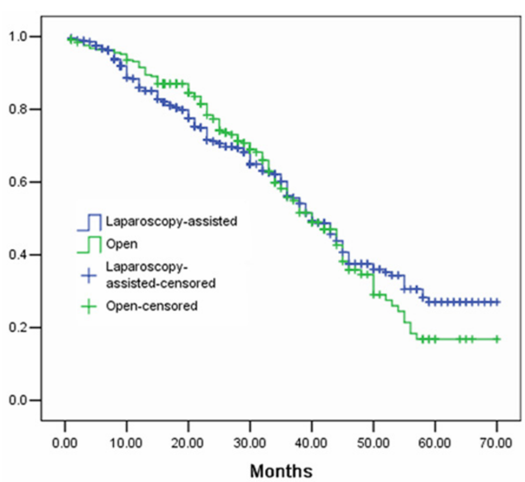


**Figure 2.** Disease-free survival in relation to approach of esophagectomy in 685 consecutive patients.

cluding less blood loss (*P* < 0.05), requiring less postoperative analgesia (*P* < 0.05), and earlier hospital discharge (*P* < 0.05).

*Post-operative complications*

All postoperative complications are summarized in **Table 3**. Overall morbidity within the first 30 days after surgery was similar in each group (*P* > 0.05). However, open Ivor Lewis esophagectomy resulted in more major complications than laparoscopy-assisted surgery (*P* < 0.05). There were no intraoperative deaths or mortality within the first 30 days after surgery in the overall cohort.

*Overall survival*

The median follow-up duration was 36 months and was similar in each group. There was no difference in overall survival between the laparoscopy-assisted group and the open surgery group (**Figure 1**, *P* = 0.472). Three- and five-year overall survival were 65.6% and 45.2%, respectively, in the laparoscopy-assisted group compared with 63.2% and 37.5%, respectively, in the open group. When multivariate Cox regression analysis of all patient overall survival was also performed, advanced pathologic T3 or T4a stage, pathologic N2 or N3 disease, and poorly differentiated tumors were significant predictors of worse survival (**Table 4**). However, surgical approach by laparoscopy-assisted surgery was not found a significant predictor of overall survival by univariate analysis.

*Disease-free survival*

When disease-free survival was evaluated, 3- and 5-year disease-free survival were 60.3% and 26.3%, respectively, in the laparoscopy-assisted group compared with 58.6% and 18.9%, respectively, in the open group (**Figure 2**, *P* = 0.840). Recurrence patterns and time to

**Table 5.** Comparison of recurrence pattern and site after esophagectomy

| | Laparoscopy-assisted (*n* = 432) | Open (n = 253) | *P* value |
|---|---|---|---|
| Overall recurrence *n* (%) | 159 (36.8) | 99 (39.1) | 0.771 |
| Locoregional *n* (%) | 95 (22.0) | 53 (20.9) | 0.863 |
| Cervical lymph node | 3 | 2 | 1.000 |
| Mediastinal lymph nodes | 38 | 21 | 0.823 |
| Abdominal lymph nodes | 19 | 14 | 0.503 |
| Anastomosis | 11 | 4 | 0.405 |
| Pleura | 12 | 8 | 0.773 |
| Stomach graft | 12 | 4 | 0.317 |
| Distant *n* (%) | 64 (14.8) | 45 (17.8) | 0.568 |
| Brain | 13 | 9 | 0.695 |
| Lung | 31 | 21 | 0.592 |
| Liver | 9 | 8 | 0.381 |
| Bone | 11 | 7 | 0.862 |
| Time to recurrence (median) | 15 months | 12 months | 0.580 |

recurrence were also examined to determine whether patients who underwent a laparoscopy-assisted surgery had a higher incidence of recurrent cancer compared with open surgery patients (**Table 5**). The location of the recurrence and the time to recurrence were not significantly different between the 2 groups. No port site recurrence occurred in the laparoscopy-assisted group. Multivariate Cox regression analysis of disease-free survival showed that significant predictors of worse disease-free survival were advanced pathologic T3 or T4 a stage, pathologic N2 or N3 disease and poor tumor differentiation (**Table 6**). The laparoscopy-assisted approach was not a significant predictor of decreased disease-free survival.

## Discussion

Minimally invasive esophagectomy has been performed over the last 10 years reduce postoperative complications without compromising long-term survival [66-68]. This technique corresponds to a collection of surgeries that combine thoracoscopic and/or laparoscopic approaches, including total minimally invasive esophagectomy (thoracoscopy and laparoscopy approaches) or hybrid minimally invasive esophagectomy (thoracoscopy with laparotomy or thoracotomy with laparoscopy) [69]. The laparoscopy-thoracotomy approach has the advantages of causing fewer complications (due to less trauma and reduced deterioration of the ventilatory mechanisms), ease of performance, avoidance of tumor dissemination, and applicability to patients irrespective of cancer stage [11-13, 69]. However, the most important measurement of any radical surgery is the long-term outcome. In the absence of survival data from phase 3 trials comparing Ivor Lewis esophagectomy done by laparoscopy-thoracotomy and open surgery, a high volume, center-based analysis was performed to compare 2 groups of patients and investigate their perioperative as well as long-term outcomes. Our results showed that laparoscopy-assisted esophagectomy achieves similar overall survival and disease-free survival compared with open surgery. These oncological outcomes were comparable with those from other reports [11-13]. To our knowledge, our study of 432 patients underwent laparoscopy-assisted surgery, is the largest series of comparing laparoscopy-assisted Ivor Lewis esophagectomy and open surgery.

Some reports have shown that laparoscopy-assisted Ivor Lewis esophagectomy slightly improves long-term survival and disease-free survival after Laparoscopy [11-13]. The potential survival advantage of minimally invasive surgery can be seen in other radical cancer resections [70-72], such as video-assisted thoracoscopic surgery (VATS) for lobectomy of lung cancer [73-75], laparoscopic colectomy for colon cancer [76], and laparoscopic gastrectomy for gastric cancer [77]. In our series, the patients who underwent laparoscopy-assisted surgery had slightly improved survival and slower recurrence. This phenomenon may be hard to explain. Some surgeons hypothesized that this phenomenon may be due to fewer traumas and quicker recovery with minimally invasive surgery, during which earlier adjuvant therapy is administered which aids compliance with additional cycles of adjuvant therapy [73-75]. The other reason may be reduced immunologic suppression with minimally invasive surgery increases a patient's ability to scavenge residual tumor cells shed into the blood or lymphatics

**Table 6.** Multivariate Cox regression analyses of disease-free survival

| Regression variables | Adjusted hazard ratio | 95% CI | Beta value | *P* value |
|---|---|---|---|---|
| Age | | | | |
| < 70 years | 1.00 | | | |
| ≥ 70 years | 1.35 | 0.69-1.58 | 0.69 | 0.102 |
| ASA score | | | | |
| I-II | 1.00 | | | |
| III | 1.26 | 0.70-1.38 | 0.60 | 0.206 |
| Comorbidity | | | | |
| No | 1.00 | | | |
| Yes | 1.39 | 0.51-1.59 | 0.49 | 0.108 |
| Major complications | | | | |
| No | 1.00 | | | |
| Yes | 1.50 | 0.85-1.98 | 0.85 | 0.109 |
| Adjuvant chemotherapy | | | | |
| Yes | 1.00 | | | |
| No | 1.69 | 0.74- | 0.60 | 0.100 |
| Pathological T stage | | | | |
| $T_{1b}$ | 1.00 | | | |
| $T_2$ | 1.89 | 0.88-2.36 | 0.68 | 0.126 |
| $T_3/T_{4a}$ | 2.59 | 1.25-5.63 | 1.29 | 0.003 |
| Pathological N stage | | | | |
| $N_0$ | 1.00 | | | |
| $N_1$ | 1.50 | 0.36-2.34 | 0.89 | 0.523 |
| $N_2/N_3$ | 3.12 | 2.39-6.53 | 1.59 | 0.012 |
| Differentiation grade | | | | |
| G1 (good) | 1.00 | | | |
| G2 (moderate) | 1.58 | 0.54-4.01 | 0.28 | 0.201 |
| G3 (poor) | 3.52 | 1.38-5.68 | 2.98 | 0.009 |

at esophagectomy [73-75]. However, the detailed mechanism underlying any minimally invasive esophagectomy-associated survival advantage remains to be investigated.

We employed laparoscopy, but not thoracoscopy, as minimally invasive Ivor Lewis esophagectomy. Many reports have assessed the advantages of thoracoscopy, such as less blood loss, less pain, earlier recovery, and earlier hospital discharge [66-69]. However, thoracoscopy approaches are time-consuming and are not easy to perform. The learning curve was steeper in the thoracoscopy approaches.

In a study performed by Makoto Yamasaki and his colleagues [12], cervical lymph node dissection was performed in about 55% patients underwent laparoscopy-assisted Ivor Lewis esophagectomy. Cervical lymph node dissection accompanied by abdominal and mediastinal lymph nodes dissection was named 3-field lymphadenectomy. Whether 3-field lymphadenectomy had the survival advantage over 2-field lymphadenectomy has been controversial due to the paucity of high quality research. A latest meta-analysis demonstrated that given the lack of large-sample randomized controlled studies, further evaluations comparing 3-field lymphadenectomy and 2-field lymphadenectomy are necessary [78]. In our study, clinical cervical metastasis was excluded by preoperative work-ups and the recurrence of cervical lymph node was very low. Therefore, we did not perform cervical lymph nodes dissection.

In the previous studies concerning laparoscopy-assisted Ivor Lewis esophagectomy, most patients underwent neoadjuvant chemo-radiotherapy [11-13]. Theoretically, neoadjuvant chemo-radiotherapy has the advantage of longer overall and disease-free survival than esophagectomy alone. In our series, we did not perform neoadjuvant chemo-radiotherapy. However, the overall and disease-free survival reported in these studies was similar to our series. P. van Hagen has reported a multi-center, randomized controlled clinical trial concerning esophagectomy alone versus neoadjuvant chemo-radiotherapy with surgery [31]. This trial showed that neoadjuvant chemoradiotherapy had the survival advantage over esophagectomy alone. However, the role of neoadjuvant chemo-radiotherapy for squamous cell esophageal cancer is in doubt because of the small sample size in the squamous cell carcinoma subgroup (only 84 patients), though neo-adjuvant chemoradiotherapy has the survival advantage over esophagectomy alone in the trail. Whether neoadjuvant therapy has the survival advantage over surgery alone need to be confirmed by large sample, randomized controlled clinical trial.

Some limitations of this study have to be acknowledged. This study is based on a single-center, not multiple-center and based on retrospective analysis, not prospective randomized analysis. So we cannot exclude bias from patients and surgical approaches selection by the surgeons. This limitation should be taken into account when interpreting the results. Other factors that may affect long-term outcomes are not completely accounted by this analysis.

In summary, it is reasonable to conclude from our study that laparoscopy-assisted Ivor Lewis esophagectomy performed by dedicated thoracic surgeons is safe and can achieve similar long-term survival to open approach. Further prospective randomized multi-center trials are warranted before incorporating laparoscopy-assisted Ivor Lewis esophagectomy into clinical routine.

## Acknowledgements

This study was supported by Science and Technology Planning Project of Fujian Province, China (grant No. 2014J01405).

## Disclosure of conflict of interest

None.

**Address correspondence to:** Kun-Shou Zhu, Department of Thoracic Surgery, Teaching Hospital of Fujian Medical University, Fujian Provincial Cancer Hospital, No. 420 Fuma Road, Fuzhou 350014, Fujian, People's Republic of China. E-mail: kszhucn@126.com

## References

[1] Zacherl J. The current evidence in support of multimodal treatment of locally advanced, potentially resectable esophageal cancer. Dig Dis 2014; 32: 171-175.

[2] Pennathur A, Gibson MK, Jobe BA and Luketich JD. Oesophageal carcinoma. Lancet 2013; 381: 400-412.

[3] Metzger R, Schütze F and Mönig S. Evidence-based operative details in esophageal cancer treatment: surgical approach, lymphadenectomy, anastomosis. Viszeralmedizin 2015; 31: 337-340.

[4] Abu Arab W. Video-assisted thoracoscopic surgery for non-small cell lung cancer. Minim Invasive Surg Oncol 2017; 1: 1-11.

[5] Allaix ME, Long JM and Patti MG. Hybrid ivor lewis esophagectomy for esophageal cancer. J Laparoendosc Adv Surg Tech A 2016; 26: 763-767.

[6] Cuesta MA, van der Wielen N, Straatman J and van der Peet DL. Video-assisted thoracoscopic esophagectomy: keynote lecture. Gen Thorac Cardiovasc Surg 2016; 64: 380-385.

[7] Fang W and Ruan W. Advances in uniportal video-assisted thoracoscopic surgery for non-small cell lung cancer. Minim Invasive Surg Oncol 2017; 1: 20-30.

[8] Kechagias A, van Rossum PS, Ruurda JP and van Hillegersberg R. Ischemic conditioning of the stomach in the prevention of esophagogastric anastomotic leakage after esophagectomy. Ann Thorac Surg 2016; 101: 1614-1623.

[9] Takahashi Y. Real-time intraoperative diagnosis of lung adenocarcinoma high risk histological features: a necessity for minimally invasive sublobar resection. Minim Invasive Surg Oncol 2017; 1: 12-19.

[10] Jones CE and Watson TJ. Anastomotic leakage following esophagectomy. Thorac Surg Clin 2015; 25: 449-459.

[11] Briez N, Piessen G, Torres F, Lebuffe G, Triboulet JP and Mariette C. Effects of hybrid minimally invasive oesophagectomy on major postoperative pulmonary complications. Br J Surg 2013; 99: 1547-1553.

[12] Yamasaki M, Miyata H, Fujiwara Y, et al. Minimally invasive esophagectomy for esophageal cancer: comparative analysis of open and hand-assisted laparoscopic abdominal lymphadenectomy with gastric conduit reconstruction. J Surg Oncol 2011; 104: 623-628.

[13] Bailey L, Khan O, Willows E, Somers S, Mercer S and Toh S. Open and laparoscopically assisted oesophagectomy: a prospective comparative study. Eur J Cardiothorac Surg 2013; 43: 268-273.

[14] Hou Z, Zhang H, Gui L, Wang W and Zhao S. Video-assisted thoracoscopic surgery versus open resection of lung metastases from colorectal cancer. Int J Clin Exp Med 2015; 8: 13571-13577.

[15] Liu C, Li Z, Bai C, Wang L, Shi X and Song Y. Video-assisted thoracoscopic surgery and thoracotomy during lobectomy for clinical stage I non-small-cell lung cancer have equivalent oncological outcomes: a single-center experience of 212 consecutive resections. Oncol Lett 2015; 9: 1364-1372.

[16] Liu K, Zhao J, Zhang W, Tan J, Ma J and Pei Y. Video-assisted thoracoscopic surgery for non-small-cell lung cancer in elderly patients: a single-center, case-matched study. Int J Clin Exp Med 2015; 8: 11738-11745.

[17] Wang Y. Video-assisted thoracoscopic surgery for non-small-cell lung cancer is beneficial to elderly patients. Int J Clin Exp Med 2015; 8: 13604-13609.

[18] Shu B, Lei S, Li F, Hua S, Chen Y and Huo Z. Short and long-term outcomes after gastrectomy for gastric carcinoma in elderly patients. Int J Clin Exp Med 2015; 8: 13578-13584.
[19] Zhang Y, Qi F, Jiang Y, Zhai H and Ji Y. Long-term follow-up after laparoscopic versus open distal gastrectomy for advanced gastric cancer. Int J Clin Exp Med 2015; 8: 13564-13570.
[20] Luo L, Zou H, Yao Y and Huang X. Laparoscopic versus open hepatectomy for hepatocellular carcinoma: short- and long-term outcomes comparison. Int J Clin Exp Med 2015; 8: 18772-18778.
[21] Sheng W, Zhang B, Chen W, Gu D and Gao W. Laparoscopic colectomy for transverse colon cancer: comparative analysis of short- and long-term outcomes. Int J Clin Exp Med 2015; 8: 16029-16035.
[22] Guo C, Zhang Z, Ren B and Men X. Comparison of the long-term outcomes of patients who underwent laparoscopic versus open surgery for rectal cancer. J BUON 2015; 20:1440-1446.
[23] Zaharie F, Ciorogar G, Zaharie R, Mocan T, Zdrehus C, Mocan L, Berindan-Neagoe I, Achimas P, Iancu C and Tomus C. Laparoscopic rectal resection versus conventional open approach for rectal cancer - a 4-year experience of a single center. J BUON 2015; 20: 1447-1455.
[24] Sahay SJ, Fazio F, Cetta F, Chouial H, Lykoudis PM and Fusai G. Laparoscopic left lateral hepatectomy for colorectal metastasis is the standard of care. J BUON 2015; 20: 1048-1053.
[25] Liu Z, Yang R and Shao F. Anastomosis using complete continuous suture in uniportal video-assisted thoracoscopic bronchial sleeve lobectomy. Minim Invasive Surg Oncol 2017; 1: 31-42.
[26] Emile SH. Evolution and clinical relevance of different staging systems for colorectal cancer. Minim Invasive Surg Oncol 2017; 1: 43-52.
[27] Emile SH. Advances in laparoscopic surgery for colorectal cancer: fluorescence- guided surgery. Minim Invasive Surg Oncol 2017; 1: 53-65.
[28] Mallipeddi MK and Onaitis MW. The contemporary role of minimally invasive esophagectomy in esophageal cancer. Curr Oncol Rep 2014; 16: 374.
[29] Decker G, Coosemans W, De Leyn P, Decaluwé H, Nafteux P, Van Raemdonck D, Lerut T. Minimally invasive esophagectomy for cancer. Eur J Cardiothorac Surg 2009; 35: 13-20; discussion 20-21.
[30] Nomura T, Matsutani T, Hagiwara N, Fujita I, Nakamura Y, Makino H, Miyashita M and Uchida E. Mediastinoscopy-assisted transhiatal esophagectomy for esophageal cancer: a single-institutional cohort study. Surg Laparosc Endosc Percutan Tech 2016; 26: e153-e156.
[31] van Hagen P, Hulshof MC, van Lanschot JJ, Steyerberg EW, van Berge Henegouwen MI, Wijnhoven BP, Richel DJ, Nieuwenhuijzen GA, Hospers GA, Bonenkamp JJ, Cuesta MA, Blaisse RJ, Busch OR, ten Kate FJ, Creemers GJ, Punt CJ, Plukker JT, Verheul HM, Spillenaar Bilgen EJ, van Dekken H, van der Sangen MJ, Rozema T, Biermann K, Beukema JC, Piet AH, van Rij CM, Reinders JG, Tilanus HW, van der Gaast A; CROSS Group. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012; 366: 2074-2084.
[32] Djuric-Stefanovic A, Saranovic D, Micev M, Stankovic V, Plesinac-Karapandzic V, Pesko P, Stojakov D, Sabljak P and Bjelovic M. Does the computed tomography perfusion imaging improve the diagnostic accuracy in the response evaluation of esophageal carcinoma to the neoadjuvant chemoradiotherapy? Preliminary study. J BUON 2014; 19: 237-344.
[33] Li Y, Lin Q, Wang L, Sun L, Dai M, Luo Z, Zheng H, Zhao L and Wu H. Application of sequential (18)F-FDG PET/CT scans for concurrent chemoradiotherapy of non-surgical squamous cell esophageal carcinoma. J BUON 2014; 19: 517-523.
[34] Zhou S, Ye W, Ren J, Shao Q, Qi Y, Liang J and Zhang M. MicroRNA-381 increases radiosensitivity in esophageal squamous cell carcinoma. Am J Cancer Res 2014; 5: 267-277.
[35] Ielpo B, Duran H, Diaz E, Fabra I, Caruso R, Malavé L, Ferri V, Lazzaro S, Kalivaci D, Quijano Y and Vicente E. Colorectal robotic surgery: overview and personal experience. Minim Invasive Surg Oncol 2017; 1: 66-73.
[36] Yu Q, Li B, Li P, Shi Z, Vaughn A, Zhu L and Fu S. Plasma microRNAs to predict the response of radiotherapy in esophageal squamous cell carcinoma patients. Am J Transl Res 2015; 7:2060-2071.
[37] Li Z and Rice TW. Diagnosis and staging of cancer of the esophagus and esophagogastric junction. Surg Clin North Am 2012; 92: 1105-1126.
[38] Emile SH. Laparoscopic intersphincteric resection for low rectal cancer: technique, oncologic, and functional outcomes. Minim Invasive Surg Oncol 2017; 1: 74-84.
[39] Boniface MM, Wani SB, Schefter TE, Koo PJ, Meguid C, Leong S, Kaplan JB, Wingrove LJ and McCarter MD. Multidisciplinary management for esophageal and gastric cancer. Cancer Manag Res 2016; 8: 39-44.
[40] Lu J, Sun XD, Yang X, Tang XY, Qin Q, Zhu HC, Cheng HY and Sun XC. Impact of PET/CT on radiation treatment in patients with esopha-

geal cancer: A systematic review. Crit Rev Oncol Hematol 2016; 107: 128-137.

[41] Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL and Makuuchi M. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009; 250: 187-196.

[42] Ghadyalpatil NS, Supriya C, Prachi P, Ashwin D and Avanish S. Gastrointestinal cancers in India: Treatment perspective. South Asian J Cancer 2016; 5: 126-36.

[43] Chen X, Yang J, Peng J and Jiang H. Case-matched analysis of combined thoracoscopic-laparoscopic versus open esophagectomy for esophageal squamous cell carcinoma. Int J Clin Exp Med 2015; 8: 13516-13523.

[44] Wang W, Zhou Y, Feng J and Mei Y. Oncological and surgical outcomes of minimally invasive versus open esophagectomy for esophageal squamous cell carcinoma: a matched-pair comparative study. Int J Clin Exp Med 2015; 8: 15983-15990.

[45] Zhu Y and Chen W. Very long-term outcomes of minimally invasive esophagectomy for esophageal squamous cell carcinoma. J BUON 2015; 20: 1585-1591.

[46] Jing X, Lin Y, Zhang B and Zhang G. Video-assisted thoracoscopic lobectomy mitigates adverse oncological effects of delayed adjuvant chemotherapy for non-small cell lung cancer. J BUON 2016; 21: 1524-1529.

[47] Li Y, Wang P, Li X and Shi G. Minimally invasive esophagectomy for esophageal squamous cell carcinoma in elderly patients. Int J Clin Exp Med 2016; 9: 13007-13013.

[48] Zeng Y, Tian M. Laparoscopic versus open hepatectomy for elderly patients with liver metastases from colorectal cancer. J BUON 2016; 21: 1146-1152.

[49] Wang W, Shao M and Zhang R. Long-term outcomes after laparoscopic versus open surgery for elderly patients with rectal cancer. Int J Clin Exp Med 2016; 9: 18160-18167.

[50] Lee KG, Lee HJ, Yang JY, Oh SY, Bard S, Suh YS, Kong SH and Yang HK. Risk factors associated with complication following gastrectomy for gastric cancer: retrospective analysis of prospectively collected data based on the Clavien-Dindo system. J Gastrointest Surg 2014; 18: 1269-1277.

[51] Xiao H, Xie P, Zhou K, Qiu X, Hong Y, Liu J, Ouyang Y, Ming T, Xie H, Wang X, Zhu H, Xia M and Zuo C. Clavien-Dindo classification and risk factors of gastrectomy-related complications: an analysis of 1049 patients. Int J Clin Exp Med 2015; 8: 8262-8268.

[52] Wong CH, Ma BB, Hui CW, Tao Q and Chan AT. Preclinical evaluation of afatinib (BIBW2992) in esophageal squamous cell carcinoma (ESCC). Am J Cancer Res 2015; 5: 3588-3599.

[53] Hu L, Wu Y, Guan X, Liang Y, Yao X, Tan D, Bai Y, Xiong G and Yang K. Germline copy number loss of UGT2B28 and gain of PLEC contribute to increased human esophageal squamous cell carcinoma risk in Southwest China. Am J Cancer Res 2015; 5: 3056-3071.

[54] Wu GZ, Pan CX, Jiang D, Zhang Q, Li Y and Zheng SY. Clinicopathological significance of Fas and Fas ligand expressions in esophageal cancer. Am J Cancer Res 2015; 5: 2865-2871.

[55] Chen X, Kong J, Ma Z, Gao S and Feng X. Up regulation of the long non-coding RNA NEAT1 promotes esophageal squamous cell carcinoma cell progression and correlates with poor prognosis. Am J Cancer Res 2015; 5: 2808-2815.

[56] Kikuchi O, Ohashi S, Nakai Y, Nakagawa S, Matsuoka K, Kobunai T, Takechi T, Amanuma Y, Yoshioka M, Ida T, Yamamoto Y, Okuno Y, Miyamoto S, Nakagawa H, Matsubara K, Chiba T and Muto M. Novel 5-fluorouracil-resistant human esophageal squamous cell carcinoma cells with dihydropyrimidine dehydrogenase overexpression. Am J Cancer Res 2015; 5: 2431-2440.

[57] Liu JS, Huang Y, Yang X and Feng JF. A nomogram to predict prognostic values of various inflammatory biomarkers in patients with esophageal squamous cell carcinoma. Am J Cancer Res 2015; 5: 2180-2189.

[58] Guan X, Hu B, Jin X and Zhang J. Short- and long-term outcomes of laparoscopic radical cystectomy for bladder cancer in the elderly. Int J Clin Exp Med 2016; 9: 19644-19653.

[59] Guo S, Tang D, Chen X, Chen M and Xiang Y. Laparoscopic colectomy for serosa-positive colon cancer (pT4a) in patients with preoperative diagnosis of cancer without serosal invasion. J BUON 2017; 22: 679-685.

[60] Chen L, Chen J, Xu B, Wang Q, Zhou W, Zhang G, Sun J, Shi L, Pei H, Wu C and Jiang J. B7-H3 expression associates with tumor invasion and patient's poor survival in human esophageal cancer. Am J Transl Res 2015; 7: 2646-2660.

[61] Zhou X, Wang L and Shen W. Laparoscopic surgery as a treatment option for elderly patients with colon cancer. J BUON 2017; 22: 424-430.

[62] Meng H, Wang K, Chen X, Guan X, Hu L, Xiong G, Li J and Bai Y. MicroRNA-330-3p functions as an oncogene in human esophageal cancer by targeting programmed cell death 4. Am J Cancer Res 2015; 5: 1062-1075.

[63] Singh V, Singh LC, Singh AP, Sharma J, Borthakur BB, Debnath A, Rai AK, Phukan RK, Mahanta J, Kataki AC, Kapur S and Saxena S.

Status of epigenetic chromatin modification enzymes and esophageal squamous cell carcinoma risk in northeast Indian population. Am J Cancer Res 2015; 5: 979-999.
[64] He H, Ding F, Li S, Chen H and Liu Z. Expression of migfilin is increased in esophageal cancer and represses the Akt-β-catenin activation. Am J Cancer Res 2014; 4: 270-278.
[65] Xu Y and Lu S. Regulation of β-catenin-mediated esophageal cancer growth and invasion by miR-214. Am J Transl Res. 2015; 7: 2316-2325.
[66] Levy RM, Trivedi D and Luketich JD. Minimally invasive esophagectomy. Surg Clin North Am 2012; 92: 1265-1285.
[67] Yang B and Li Y. A comparative study of laparoscopic microwave ablation with laparoscopic radiofrequency ablation for colorectal liver metastasis. J BUON 2017; 22: 667-672.
[68] Peyre CG, Peters JH. Minimally invasive surgery for esophageal cancer. Surg Oncol Clin N Am 2013; 22: 15-25, v.
[69] Levy RM, Wizorek J, Shende M and Luketich JD. Laparoscopic and thoracoscopic esophagectomy. Adv Surg 2010; 44: 101-116.
[70] Zhang J and Chen W. Comparison of short- and long-term outcomes of laparoscopic hepatectomy for colorectal liver metastasis in the posterosuperior and anterolateral segments. Int J Clin Exp Med 2017; 10: 8102-8109.
[71] Wu D, Wu W, Li Y, Liang S, Wang J, Yao X and Jian Z. Laparoscopic hepatectomy for colorectal liver metastases located in all segments of the liver. J BUON 2017; 22: 437-444.
[72] Li S, Qin X, Li Y, Zhang X, Niu R, Zhang H, Cui A, An W and Wang X. MiR-133a suppresses the migration and invasion of esophageal cancer cells by targeting the EMT regulator SOX4. Am J Transl Res 2015; 7: 1390-1403.
[73] Li Z1, Liu H, Li L. Video-assisted thoracoscopic surgery versus open lobectomy for stage I lung cancer: A meta-analysis of long-term outcomes. Exp Ther Med 2012; 3: 886-892.
[74] Chen FF, Zhang D, Wang YL and Xiong B. Video-assisted thoracoscopic surgery lobectomy versus open lobectomy in patients with clinical stage I non-small cell lung cancer: a meta-analysis. Eur J Surg Oncol 2013; 39: 957-963.
[75] Puri V, Meyers BF. Video-assisted thoracoscopic surgery lobectomy for lung cancer. Surg Oncol Clin N Am 2013; 22: 27-38, v.
[76] Cai Y, Zhou Y, Li Z, Xiang J and Chen Z. Surgical outcome of laparoscopic colectomy for colorectal cancer in obese patients: a comparative study with open colectomy. Oncol Lett 2013; 6: 1057-1062.
[77] Fang F, Han F, Ding YL, Wang HJ. Comparison of laparoscopy-assisted surgery and laparotomy for treating locally advanced distal gastric antral cancer. Exp Ther Med 2013; 6: 753-758.
[78] Ye T, Sun Y, Zhang Y, Zhang Y and Chen H. Three-field or two-field resection for thoracic esophageal cancer: a meta-analysis. Ann Thorac Surg 2013; 96: 1933-1941.