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# Outcomes of Right Thoracoscopic Esophagectomy Combined with Laparotomy: a Preliminary Vietnamese Study

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## ABSTRACT

**Background:** Esophageal cancer is the fourth-most-common cancerous disease of the gastrointestinal tract, with increasing incidence rates. **Aim:** The present study aimed to assess the outcomes of right thoracoscopic esophagectomy combined with laparotomy for esophageal cancer treatment in Vietnamese patients. **Methods:** A cross-sectional study of 71 patients was conducted at 108 Military Central Hospital, Hanoi, Vietnam, from January 2010 to December 2017. **Results:** Right thoracoscopic esophagectomy combined with laparotomy was performed in 71 patients with esophageal cancer. The mean patient age was 55.8 years, and 100% were male. Patients were diagnosed with the following cancer stages: Stage 0: 4.2%; Stage I: 14.1%; Stage II: 59.2%; and Stage III: 22.5%. The lymph node metastasis rate was 33.8%. The overall complication rate was 42.3%, which included a pneumonia rate of 12.3%, a respiratory failure rate of 7.0%, an anastomotic leak rate of 11.3%, and a chylothorax rate of 4.2%. The mean postoperative time was 16.4 days. The mean follow-up time was 21.7 months. The median overall survival was 45.7 months. The 1-year, 2-year, 3-year, and 4-year survival rates were 79.7%, 62.3%, 52.3%, and 43.6%, respectively. **Conclusions:** Thoracoscopic esophagectomy combined with laparotomy for esophageal cancer was a safe, effective, and minimally invasive procedure that should play a continued role in cancer treatment.
**Keywords: Esophageal cancer, Thoracoscopic esophagectomy, Outcome, Vietnam.**

## 1. INTRODUCTION

Esophageal cancer (EC) is the fourth-most-common cancerous disease of the gastrointestinal tract, with increasing incidence rates. In 2005, the worldwide burden of esophagogastric cancer was estimated to be 1,500,000 new cases (1,000,000 stomach and 500,000 esophagus). In 2025, it is estimated that the number of new cases will climb up to 2,110,000 cases (1). Currently, EC treatment involves a multidisciplinary therapeutic approach, including surgery, chemotherapy, and radiotherapy, with surgery playing the most important role. However, traditional open esophagectomy represents a major surgery, associated with a high complication rate (60%–80%) and mortality ranging from 5%–10% (2,3). Recently, minimally invasive esophagectomy (MIE) has been rapidly applied and developed, with benefits that include a reduced rate of complications, decreased blood loss, shorter hospital stays, and reduced pain after surgery. Various studies have been performed worldwide to evaluate the effectiveness of this method. However, in Vietnam, thoracoscopic surgery for EC treatment still faces many challenges, such as difficulty learning the technique and complications after surgery. Therefore, this technique is currently only performed at a few large centers, and the outcomes associated with the application of this method in Vietnam must still be evaluated. We performed this study to evaluate the safety, feasibility, and effectiveness of applying this method to Vietnamese EC patients.

## 2. AIM

The present study aimed to assess the outcomes of right thoracoscopic esophagectomy combined with laparotomy for esophageal cancer treatment in Vietnamese patients.

## 3. MATERIALS AND METHODS

### Study design and participants

A cross-sectional study was performed on 71 patients at 108 Military Central Hospital, Hanoi, Vietnam, from January 2010 to December 2017. Participants were EC patients who underwent thoracoscopic esophagectomy combined with laparostomy. The inclusion criteria were as follows: 1) patients diagnosed with EC by endoscopic biopsy; 2) patients diagnosed with Stage I–III thoracic EC; 3) patients with an American Society of Anesthesiologists physical status score ≤ 3, with no contraindications against endotracheal anesthesia. All patients underwent chest-abdominal multi-detector computerized tomography (MDCT) to diagnose pretreatment stage. Patients receiving preoperative chemoradiotherapy (CRT) underwent surgery 6–8 weeks after the completion of CRT. This study was approved by the Scientific Committee in Biomedical Research, 108 Military Central Hospital (Ref: 284/QĐ-V108 dated 10 Sep. 2015).

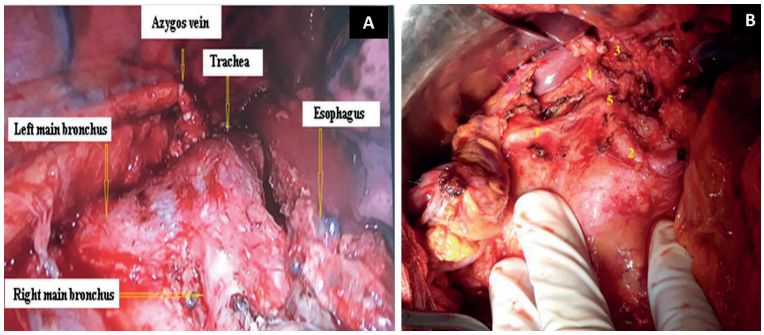


Figure 1. Images showing a 53-year-old man with squamous cell adenocarcinoma. (A) Intrathoracic lymphadenectomy and (B) abdominal lymphadenectomy.

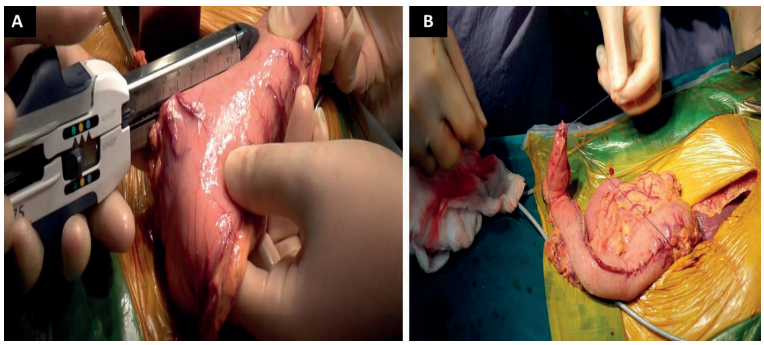


Figure 2. Images showing a 48-year-old man with squamous cell carcinoma of the lower esophagus. (A) Starting from the lesser curvature of the stomach, several loads from a linear cutting stapler were sequentially fired towards the fundus of the stomach to create a 4–5-cm-wide gastric conduit (B).

### MDCT protocol

All patients with EC underwent chest-abdominal MDCT to determine the pretreatment staging. MDCT was performed using a 64-detector-row computed tomography (CT) scanner (SOMATOM DEFINITION AS 64, Siemens Healthineers, Germany). The parameters were as follows: slice thickness, 3 mm; rotation time, 1 second.

### Operative technique

All the patients underwent esophagectomy with three-field right thoracoscopy and laparotomy with cervical anastomosis.

Thoracic phase (Thoracoscopy): The patient was placed in the left lateral decubitus position, using 3 or 4 ports. The camera port was placed at the 8th or 9th intercostal space, just anterior to the scapular line. Working port 1 was placed at the 4th or 5th intercostal space, on the middle or posterior axillary line. Working port 2 was placed at the 6th or 7th intercostal space, on the posterior axillary line. Working port 3 was placed just posterior to the scapula tip (if necessary). Thoracoscopy was performed to exclude metastatic disease and identify relevant anatomic structures.

Next, the inferior pulmonary ligament was divided. The mediastinal pleura overlying the esophagus was divided to the level of the azygos vein to expose the thoracic esophagus, and the azygos vein was divided using 10mm-Click 'AV endoscopic clip appliers (Grena Think Medical, UK). The parietal pleura was incised along the esophagus, medially along the pericardium, and laterally below the aorta. The esophagus was dissected circumferentially and encircled with a gastric tube to facilitate retraction, and the right vagus nerve was divided below the azygos vein. The esophagus was dissected from the hiatal to the inlet after the thoracic esophagus has been completely mobilized by Harmonic scalpel (Ethicon, USA). We performed intrathoracic lymphadenectomy, including lymphadenectomy up to the subcarinal lymph nodes and paratracheal lymphadenectomy on the right side (Figure 1). A thoracic drain tube was placed after the completion of the thoracic phase.

### Abdominal phase (Laparotomy)

A supraumbilical incision was made, and the gastrohepatic ligament was completely opened towards the right crus. The right gastric artery was preserved, the phrenoesophageal ligament was divided, and the right crus was dissected. The course of the right gastroepiploic artery was determined, and the gastrocolic ligament was incised in the avascular portion between the terminal branches of the right and left gastroepiploic vessels to allow entry into the lesser sac. The gastrosplenic ligament was then divided towards the hiatus, dividing the short gastric vessels, using Harmonic scalpel. The greater curvature of the stomach was then mobilized towards the pylorus, dividing the gastrocolic ligament at least 1.5–2 cm away from the vessels while protecting the gastroepiploic vessels with the fingers of the retracting hand.

At approximately the level of the third large vein, along the lesser curvature, lymphatic tissue and vessels were mobilized and divided to expose the gastric wall. The right gastric vessels were preserved, if possible. The gastric conduit is created by using Ethicon linear cutter (Ethicon Endo-Surgery, Inc. US) with 4-5 cm in diameter (Figure 2). Depending on the thickness of the stomach, we chose the right type of linear cutter loads (green, gold, and blue). The gastric conduit stapler line was then overseen with a running 3.0 Vicryl. The upper abdominal lymph nodes

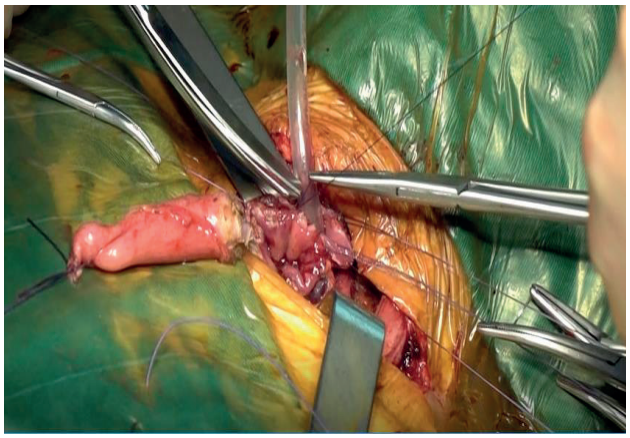

Figure 3. Images of a 48-year-old man with squamous cell carcinoma of the lower esophagus. The cervical anastomosis was handsewn end-to-end using an interrupted suture.

were dissected, and the distal esophagus and the rest of the stomach were mobilized. The Kocher maneuver was seldom necessary.

**Cervical phase**

A 6-cm skin incision was made along the anterior border of the left sternocleidomastoid muscle, starting at the sternal notch and extending to the level of the cricoid cartilage. The deep cervical fascia was incised, and further dissection towards the vertebral bodies was performed to identify the esophagus, which was gently mobilized circumferentially and encircled with a Penrose drain. The esophagus was further dissected into the superior mediastinum, using gentle traction and finger dissection until the dissection completed during the chest phase was encountered. The esophagus was divided in the neck incision, preserving as much cervical esophagus as possible. The gastric tube was pulled through the mediastinum to perform a gastroesophageal anastomosis (end to end, handsewn) in the cervical esophagus. During dissection, care was taken to protect the recurrent laryngeal nerve (Figure 3), such as using a finger to retract the trachea instead of a metal retractor. A tube drain was placed near the anastomosis.

**Esophagectomy outcomes**

Patient demographics, paraclinical tests, and operative details were recorded. The staging was performed according to the American Joint Committee on Cancer 7th Edition (2010). Surgical outcomes were abstracted, including postoperative complications, postoperative mortality (30-day), recurrent rate, and survival.

**Preoperative Chemoradiotherapy**

The patients underwent pre-surgical CRT, as described by the CROSS research study (4). On days 1, 8, 15, 22, and 29, carboplatin, targeted at an area under the curve of 2 mg per milliliter per minute, and paclitaxel, at a dose of 50 mg per $m^2$ body surface area, were administered intravenously. All patients were intravenously premedicated with dexamethasone, clemastine, and ranitidine, as well as standard antiemetic agents, before CRT. A total radiation dose of 41.4 Gy was administered, in 23 fractions of 1.8 Gy each, with 5 fractions were administered each week, starting on the first day of the first chemotherapy cycle.

**Statistical analysis**

Statistical analyses were performed using SPSS version 20.0 (IBM Corp., New York, USA). Survival was analyzed by the Kaplan-Meier method. Overall survival curves were compared using the log-rank test. A $P < 0.05$ was considered significant.

## 4. RESULTS

Of 71 EC patients who underwent thoracoscopic esophagectomy combined with laparotomy, from January 2010 to December 2017, 17 (23.9%) patients received preoperative CRT, and 55 (76.1%) were treated with surgery alone. The median age was 55.8 years (range 40–76). Microscopy revealed that squamous cell carcinoma accounted for 69 (97.2 %) cases, and the following stages were observed: stage 0, 3 (4.2%) patients; stage I, 10 (14.1%) patients; stage II, 42 (59.2%) patients; and stage III, 16 (22.5%) patients. Additionally, 3 patients (4.2%) experienced a pathologically complete response after preoperative CRT. The rate of patients with positive lymph nodes was 24 (33.8%).

All patients underwent expanded 2-field lymph node dissection during this study, including 24 (33.8%) patients with nodal metastases (Table 1). Thoracoscopic esophagectomy was successfully completed in 70 (98.6%) patients. Thoracotomy was necessary for 1 (1.4%) patient due to aortic injury, which required con-

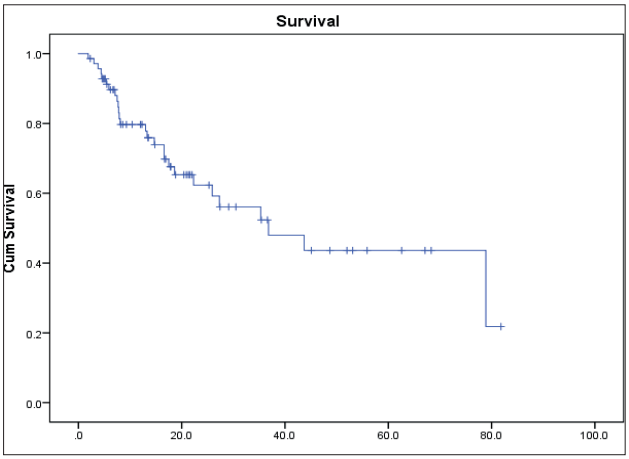


Figure 4. Kaplan-Meier survival curve after thoracoscopic esophagectomy combined with laparostomy.

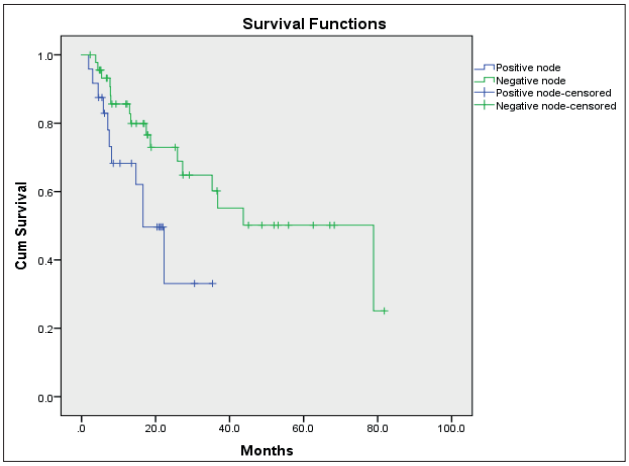


Figure 5. Kaplan-Meier survival curve for overall survival estimates, according to the presence of positive lymph nodes.

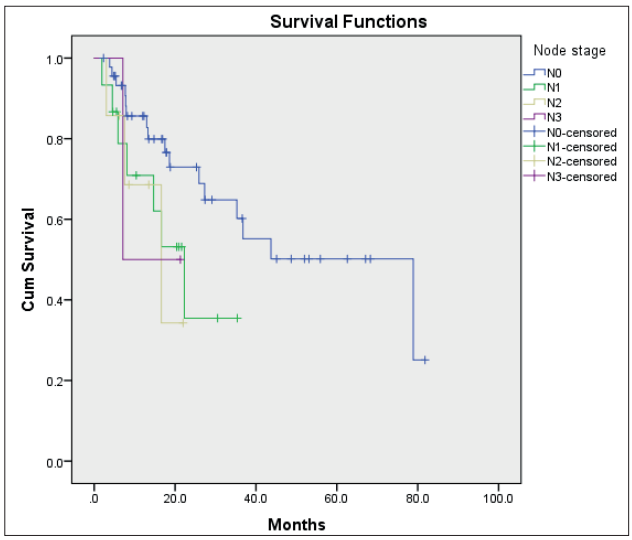


**Figure 6. Kaplan-Meier survival curve for overall survival estimates according to the number of positive lymph nodes.**

| Preoperative patient characteristics | CRT + Surgery n = 17 | Surgery alone n = 54 | Total n = 71 |
|---|---|---|---|
| Age, median | 56.5 | 55.5 | 55.8 |
| Sex, male, n (%) | 17 (100) | 54 (100) | 71 (100) |
| Tumor location, n (%) | | | |
| Middle | 11 (64.7) | 26 (48.1) | 37 (52.1) |
| Lower | 6 (35.3) | 28 (51.9) | 34 (47.9) |
| Pathological stage, n (%) | | | |
| Stage 0 | 3 (17.6) | 0 (0) | 3 (4.2) |
| Stage I | 3 (17.6) | 7 (13) | 10 (14.1) |
| Stage II | 9 (52.9) | 33 (61.1) | 42 (59.2) |
| Stage III | 2 (11.8) | 14 (25.9) | 16 (22.5) |
| Stage IV | 0 | 0 | 0 |
| Squamous tumor type, n (%) | 17 (100) | 52 (96.3) | 69 (97.2) |
| Adenocarcinomas tumor type, n (%) | 0 | 2 (3.7) | 2 (2.8) |
| Positive lymph nodes harvested | 5 (29.4) | 19 (35.2) | 24 (33.8) |

**Table 1. Characteristics of patients who underwent right thoracoscopic esophagectomy. * CRT: Chemoradiotherapy**

| Minor complications | Number (%) | Major complications | Number (%) |
|---|---|---|---|
| Atrial fibrillation | 5 (7.0) | Anastomotic leak | 8 (11.3) |
| Wound infection | 4 (5.6) | Anastomotic stricture | 2 (2.8) |
| Pleural effusion requiring tubes | 8 (11.3) | RLN injury | 13 (18.3) |
| Pneumothorax | 5 (7.0) | Chylothorax | 3 (4.2) |
| | | Tracheal tear | 1 (1.4) |
| | | Pneumonia | 9 (12.3) |
| | | Respiratory failure | 5 (7.0) |
| | | Bleeding* | 1 (1.4) |

**Table 2: Minor and major complications. RLN: Recurrent laryngeal nerve. * The patient experienced bleeding due to thoracic aorta injury and was converted to open thorax surgery.**

version to open thorax surgery. One patient experienced a tracheal tear, which was sewn closed by thoracoscopy. No patient died within 30-days of the operation.

All major and minor surgical complications are shown in Table 2. The most common minor complications included pleural effusion (11.3%), wound infection (5.6%), and atrial fibrillation (7.0%). Major complications included anastomotic leak (8 cases, 11.3%), recurrent laryngeal nerve injury (13 cases, 18.3%), pneumonia (9 cases, 12.3%), chylothorax (3 cases, 4.2%), and anastomotic stricture (2 cases, 2.8%). Most patients with anastomotic leak received non-surgical treatments, included intravenous feeding, systemic antibiotics, and drainage care. Among patients with pneumonia, 5 patients suffered from respiratory failure.

The median intensive care unit stay was 1.4 days (range 0–8 days), and the mean hospital stay was 16.4 days (range 7–40 days). The mean follow-up time was 21.7 months (range 1.0–81.8 months). The Kaplan-Meier curve for overall survival is shown in Figure 4. Median overall survival was 45.7 months [95% confidence interval (95% CI): 35.0–55.4]; and the 1-, 2-, 3-, and 4-year survival rates were 79.7%, 62.3%, 52.3%, and 43.6%, respectively. The median overall survival times for patients with and without positive node harvests were 20.2 and 51.0 months, respectively (Figure 5), which represented a significant difference (p = 0.0357). The median overall survival times also differed according to the number of positive lymph nodes, with survival times of 51.0, 20.8, 14.9, and 14.2 months for N0-stage, N1-stage, N2-stage, and N3-stage, respectively (Figure 6).

## 5. DISCUSSION

In our study, 17 patients received preoperative CRT, and the complete pathological response rate was 17.6% (3/17), the partial response rate was 70.6% (12/17), and the non-response rate was 11.8% (2/17). Huang *et al* (5) reported a complete response rate of 28.5%, a partial response rate of 65.3%, and a non-response rate of 6%, and Fiorica *et al* demonstrated that preoperative CRT decreases the disease stage (6). Similarly, Val Gebski *et al* (7) reported a significant survival benefit among patients who received preoperative CRT.

Esophagectomy for EC is a complex surgery with a high complication rate. The overall complication rate is approximately 40%–70% (2,3,8). In addition, a meta-analysis of 57 studies (n = 15,790) comparing MIE and open esophagectomy, performed by Yibulayin *et al,* reported an overall complication rate for MIE of 41.2% (3). During surgery, we encountered one patient with bleeding and one patient with a tracheal tear. Bleeding was due to thoracic aorta injury during an attempt to stop bleeding from a branch of the thoracic aorta. We attempted to stop the bleeding using electronic cautery, but this was not effective. Subsequently, we performed stitching. Because the blood pressure was too high to tear the thoracic aorta, this case required conversion to an open thorax surgery. Our experience suggested that in cases of bleeding from branches of the thoracic aorta, a compressive gauze should be used to promote coagulation, rather than clipping or stitching; if bleeding continues, the vascular branch should be identified and clamped. The case of injury to the trachea was due to the

lymph node dissection at the site of the tracheal bifurcation by Harmonic scalpel. Therefore, care should be taken when performing a lymphadenectomy at the tracheal bifurcation. The patient with tracheal injury was managed with a thoracoscopy. Luketich *et al* studied 222 patients and found that 2 patients (0.9%) experienced tracheal perforation during surgery (9).

Patients in the present study experienced complications including pneumonia (9 cases, 12.3%), respiratory failure (5 cases, 7.0%), and pneumothorax (5 cases, 7.0%), which were similar to the complication rates reported by other authors. Smither *et al* (2) reported complication rates of pneumonia at 26%, pleural effusion at 5.8%, and respiratory failure at 4.9%. In addition, Ovrebo *et al* reported pneumonia at 39%, lung abscess at 3%, and respiratory failure at 18% (10). We found that among patients with pneumonia, progression to respiratory failure was quite high. Five of 9 patients with pneumonia progressed to respiratory failure, and most cases of respiratory failure were associated with pneumonia. Therefore, when pneumonia is detected, it must be actively treated, and the patient's condition should be monitored closely. Some measures can be used to reduce postoperative respiratory complications, such as the rehabilitation of preoperative respiratory function (eg smoking cessation and respiratory muscle exercise), oral hygiene, postoperative respiratory rehabilitation (aerosol, vibrations, and breathing exercises), and pain relief. In addition, many studies have demonstrated that thoracoscopic esophagectomy in the prone position reduced the rate of postoperative respiratory complications (11,12).

In our series, the rate of anastomotic leak was 11.3% (8 cases), which typically occurred 7–10 days after surgery. Because anastomosis is performed at the neck, the fistula is generally not serious, and most patients with anastomotic leak were treated non-operatively, including fasting, intravenous and tube feeding, systemic antibiotics, and drainage care. The fistula typically resolved on its own within 2-3 weeks, although 1 patient required reoperation to drain the abscess and was discharged at 3 weeks after 2$^{nd}$ operation. Similarly, Luketich *et al* reported an anastomotic leak rate of 11.7% (26/222) (9). The series by Mao *et al* (8) reported an even higher rate of anastomotic leak (23.7%). Many factors can contribute to anastomotic leak following an esophagectomy, including blood perfusion of the anastomosis, the anastomosis formation technique, the position of the anastomosis (in the neck or chest), the organ used as a tube (stomach, colon, small intestine), and nutritional conditions. According to our experience, to increase blood perfusion to the anastomosis, the preservation of the maximum number of blood vessels nourishing the gastric tube is necessary, and the use of Kocher's maneuver to increase the length of the gastric tube limited the tension of the anastomosis. To avoid manipulations that cause injury to the gastric tube, the gastric tube should be created using a stapler to increase the maximum length. Moreover, the gastric tube is approximately 4-5 cm in diameter, and studies using ICG (indocyanine green) to evaluate the blood perfusion of the gastric tube in the stomach reduced the rate of anastomotic leak following esophagectomy (13,14).

In our series, the rate of RLN nerve injury was 18.3% (13 cases). A meta-analysis of four randomized trials, including 267 patients, found that patients with cervical anastomosis were at significant risk of RLN nerve injury (OR: 7.14; 95% CI: 1.75–29.14) (15). Furthermore, three-field lymph node dissection has also been associated with an increased risk of RLN nerve damage. The risk of RLN paralysis ranges from 20%–28% after three-field lymph node dissection compared with 10%–14% after two-field lymph node dissection (16-18). If only partial nerve injury occurs, the patient may recover after a certain time.

In our series, the rate of chylothorax was 4.2% (3 cases), but no patient with chylothorax required reoperation. In a meta-analysis of 20 studies, Lv *et al* found that the rate of chylothorax was 3.7% (19). In the study by Smither *et al,* the rate of chylothorax was reported at 5% in the MIE group (2).

During surgery, to avoid chylothorax complications, many surgeons actively seek and ligate thoracic ducts. However, in a study evaluating this issue in 1,804 patients who underwent esophagectomy for cancer treatment, prophylactic thoracic duct ligation did not reduce the rate of postoperative chylothorax, and this procedure was, instead, significantly associated with poorer postoperative survival (20).

In this study, 70 patients with EC underwent successful thoracoscopic esophagectomy combined with laparotomy. The mean following up was 21.7 months (1.9–81.8 months). One patient lost to follow up was noticed. The Kaplan-Meier method was used to evaluate survival time, and the mean overall survival time was 45.7 months (95% CI: 35.9– 55.4 months). The overall survival rates after 1 year, 2 years, 3 years, and 5 years were 79.7%, 62.3%, 52.3%, and 43.6%, respectively. Our results are similar to those of other studies.

According to Nguyen *et al* (21), the 3-year survival rate was 57%, with an average follow-up time of 26 months. The study by Beasley *et al,* examining 165 patients, showed that the 1-year, 2-year, and 5-year survival rates were 77%, 42%, and 36%, respectively (22). Similarly, Smither *et al* (2) reported a median survival rate of 31 months and a 3-year survival rate of 46%. The survival time for EC patients depends strongly on the disease stage (the degree of invasion, the state of lymph node metastasis). The median overall survival times for patients with and without positive node harvests were 20.2 and 51.0 months, respectively, which represents a significant difference ($p = 0.0357$). Median overall survival times also differed according to the number of positive lymph nodes, with survival times of 51.0, 20.8, 14.9, and 14.2 months for N0-stage, N1-stage, N2-stage, and N3-stage, respectively (Figure 5).

Recently, Zhang H *et al* showed that the 5-year survival rates for pN0, pN1, pN2, and pN3 were 47.7%, 31.4%, 19.7%, and 7.0%, respectively (23). In addition, Zhang HL *et al* (24) reported that the number of metastatic lymph nodes was closely related to survival times in

squamous cell carcinoma, and the 5-year survival rates associated with metastasis to 0, 1, and ≥ 2 lymph nodes were 59.8%, 33.4%, and 9.4%, respectively.

Studies have demonstrated that the number of metastatic nodes is a more important prognostic indicator for EC than metastatic node location (23-26). Higher numbers of metastatic lymph nodes are associated with a worse prognosis. The use of 2-field vs. 3-field lymph node dissection remains controversial. Extended 2-field or 3-field lymph node dissections are typically selected by Western authors, whereas authors from Japan and Korea tend to support 3-field lymph node dissections. Research by Akiyama *et al* showed that the 5-year survival rate for 3-field lymph node dissection was 55% compared with the 35% 5-year survival rate of 2-field lymph node dissection (27). Studies have shown that 3-field lymph node dissection is more radical and associated with an increased rate of complications, especially complications associated with RLN damage (17,18). Therefore, the application of the 3-field lymph node dissection technique should be evaluated for each specific patient.

This study has some limitations. First, our hospital has only performed preoperative CRT since 2015; therefore, the group of patients who received preoperative CRT was small, and the follow-up time was not long. Second, this study was not a randomized clinical trial. Further studies should be performed using larger numbers of patients and longer follow-up durations to compare between the 2 groups of patients.

## 6. CONCLUSION

In our study, the findings showed that thoracoscopic esophagectomy, combined with laparotomy for EC treatment, represents a safe, effective, minimally invasive procedure that should remain a prominent treatment method. Although our preoperative CRT group was small, an effect of preoperative CRT on tumor downstaging and tumor size.

- **Ethical approval and Declaration of patient consent:** The study was approved by the Ethics Committee of 108 Military Central Hospital (Ref: 284/QĐ-V108 dated 10 Sep 2015). Every patient signed an informed consent form before inclusion in the study.
- **Author's contribution:** Trieu Trieu Duong and Nguyen Minh Duc contributed equally to this article as co-first authors. Trieu Trieu Duong and Ho Huu An gave a substantial contribution to the acquisition, analysis, and data interpretation. Each author had a part in preparing the article for drafting and revising it critically for important intellectual content. Each author gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Conflicts of interest:** There are no conflicts of interest to declare.
- **Financial support and sponsorship:** Nil.

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