Sato, et al

Original Article (Clinical Original)

Postoperative pulmonary complications and thoracocentesis in early versus late chest tube removal after thoracic esophagectomy with three-field dissection: a propensity score matching analysis

Takuji Sato¹, Takeo Fujita¹, Naoya Okada¹, Hisashi Fujiwara¹, Takashi Kojima², Ryuichi Hayashi³, and Hiroyuki Daiko¹

This study was conducted and based in Japan.

¹Division of Esophageal Surgery, National Cancer Center Hospital East, Kashiwa, Japan ²Division of Gastroenterological Oncology, National Cancer Center Hospital East, Kashiwa, Japan

³Division of Head and Neck Surgery, National Cancer Center Hospital East, Kashiwa,

Japan

Course of Advanced Clinical Research of Cancer, Juntendo University Graduate School of Medicine

2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan

((Surgery Today))

Corresponding author: Hiroyuki Daiko, MD, PhD, FACS

Division of Esophageal Surgery, National Cancer Center Hospital East, Kashiwa, Japan

6-5-1 Kashiwanoha, Kashiwa 277-8577, Japan

Phone: +81-4-7133-1111, FAX: +81-4-7131-9960, E-mail: hdaikou@east.ncc.go.jp

ee perez

Key words: chest tube management, esophagectomy, esophageal cancers

Sato, et al

Abstract

Purpose

To evaluate the safety of early chest tube removal after thoracic esophagectomy with three-field dissection.

Methods

This prospective cohort study evaluated patients who underwent thoracic esophagectomy with three-field dissection during 2013–2015. Patients were assigned into two groups according to whether they underwent early or late chest tube removal. Propensity score matching in a 1:1 ratio was applied. The two groups were compared regarding incidences of postoperative pulmonary complications and thoracocentesis.

Results

After propensity score matching, 89 patients in each group were analyzed. There was no significant difference between groups in the incidences of pulmonary complications, or thoracocentesis. Significantly more patients achieved first mobilization within 15 hours postoperatively in the early removal group (89.8%) compared with the late removal group (52%, p<0.01). Multivariate analysis revealed that early chest tube removal was not a risk factor for pulmonary complications or thoracocentesis. Independent risk factors for pulmonary complications were previous

((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

Sato, et al

history of pulmonary disease (odds ratio: 0.81 [0.63-0.98]; p=0.02) and neoadjuvant chemotherapy (odds ratio: 0.67 [0.32-0.96]; p=0.04).

Conclusion

Early chest tube removal is feasible and safe compared with late chest tube removal

after thoracic esophagectomy with three-field dissection.

Sato, et al

Introduction

Chest tube drainage after thoracic esophagectomy with three-field dissection for esophageal cancer is performed to prevent and detect postoperative pulmonary complications, such as postoperative bleeding and pneumothorax. However, the optimal duration of chest tube drainage is still controversial [1]. The widely accepted practice has been to remove the chest tube when the daily drainage volume becomes less than 100–200 ml, with no air leakage [2,3]. Another report suggests that the chest tube should routinely be left in place until there is no evidence of chylothorax or anastomotic leakage detected by postoperative contrast study [3]. In thoracic esophagectomy with three-field dissection, the chest tube usually remains inserted for more than 4 days to reduce the drainage volume to the accepted amount or to ensure the absence of chylothorax and anastomotic leakage [3,4].

The enhanced recovery after surgery (ERAS) program recommends that chest tubes should be removed as soon as possible. The efficacy of the ERAS program for perioperative management of esophagectomy has been widely described [1,2]; however, there is little evidence of the effects of early chest tube removal in transthoracic esophagectomy with three-field dissection. Although some reports have investigated the safety and feasibility of early chest tube removal, the duration of chest tube drainage in

Early v.s. late chest tube removal in esophagectomy

these reports was still 2–3 days [5,6].

In clinical practice, the optimal timing and criteria for chest tube removal varies among institutions and physicians, but most physicians use the total drainage volume per day as one of the criteria. Herein, we performed early chest tube removal on postoperative day 1 (POD1) using early removal criteria, regardless of the daily amount of drainage volume being produced. The aim of the present study was to investigate the safety and feasibility of early chest tube removal on POD1 in thoracic esophagectomy with three-field dissection by analyzing the incidence of postoperative pulmonary , perez complications and thoracocentesis.

Methods

Study design and population

This was a prospective cohort study. Comprehensive informed consent regarding the present study were obtained at the first visit of our Division. Data were collected from patients who underwent thoracic esophagectomy with three-field dissection in the Division of Esophageal Surgery of the National Cancer Center Hospital East from December 2013 to December 2015. We excluded patients who underwent transhiatal

Sato, et al

esophagectomy or salvage esophagectomy, and thus included a total of 220 patients. This study was approved by the Institutional Review Board of the National Cancer Center Hospital East (approval number # 2015-183).

Chest tube management

We classified the patients into two groups based on chest tube management. In the first half of the study period (2013 to August 2014), chest tubes were removed when the drainage volume was less than 200 ml/day; the patients treated via this protocol were classified as the late removal group. In the second half of the study period (September 2014 to December 2015), chest tubes were removed based on the following criteria, regardless of the daily total drainage volume: 1) non-turbid drainage volume not exceeding 300 ml for the last 6 hours, 2) no air leakage. If either of these criteria were not fulfilled, the chest tube was not removed until conditions were deemed appropriate. The patients treated via this second protocol were classified as the early removal group.

Study outcomes

The primary outcome was to evaluate the safety and feasibility of early chest tube removal on POD1 by comparing the incidences of pulmonary complications and

((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

Sato, et al

thoracocentesis between the early and late removal groups. The secondary outcome was to compare the early and late removal groups regarding the duration of chest drainage, early removal rate, total drainage volume, and achievement of first mobilization within 15 hours postoperatively. Pulmonary complications were defined as conditions such as pneumonia, pyothorax, pneumothorax, and chylothorax (Clavien-Dindo Class II). The indication for thoracocentesis was dyspnea and peripheral oxygen desaturation due to effusion and atelectasis.

Operative management

Esophagectomy with three-field lymph node dissection was performed via either open thoracotomy or thoracoscopy, followed by the placement of a chest tube for drainage in both thoracic cavities. The area of lymph node dissection was the same regardless of the thoracic approach. Routinely, the left middle and lower mediastinal pleurae were partially resected to enable optimal dissection of the lymph nodes located around the descending aorta and left pulmonary ligament. At the end of the thoracic procedure, a 20 Fr double-lumen chest tube (Argyle[™] Trocar Catheter, Nippon Covidien Ltd. Tokyo, Japan) was placed dorsally and apically in both thoracic cavities. All cases were reconstructed by the stomach via the posterior mediastinal route or

Page 10 of 56

Sato, et al

retrosternal route, with cervical anastomosis.

Postoperative management

After surgery, the endotracheal tube was removed in the operating room. All patients with stable vital signs attempted first mobilization in the morning on POD1. However, first mobilization was postponed in patients without stable vital signs during activity. From POD1, the patients received 24-hour continuous enteral feeding of a polymeric formula at an initial speed of 20 ml/h from the jejunum via a nasogastric tube. The feeding speed was increased by 20 ml/h every 24 hours, reaching 80 ml/h on POD4. After the enteral feeding had started, the chest tube was removed on POD1 if the criteria were fulfilled. Enteral feeding was continued at a speed of 80 ml/h until oral intake was started on POD7.

On POD7, all patients underwent a contrast study to identify any anastomotic leakage. If there was no leakage, liquid oral intake was started immediately. Starting on POD8, the oral diet progressed daily from semisolid to solid. When the oral intake was insufficient to provide the daily caloric requirement, peripheral parental nutrition was added. Patients who were able to take in enough nutrition orally were discharged after POD10.

Statistical analysis

Statistical analyses were performed with R (The R Foundation for Statistical Computing, Vienna, Austria). For unmatched comparisons, categorical variables were analyzed using the Fisher exact test, whereas continuous variables were analyzed using a two-sided *t*-test or a Mann-Whitney U test. All differences with a p value of < 0.05were considered statistically significant. The association between the late and early removal groups was analyzed using propensity score matching. Propensity scores to determine the matched pairs between the two groups were created using four variables that could potentially influence the occurrence of pulmonary complications and the persistence of pleural effusion; these four variables were clinical stage, receipt of neoadjuvant chemotherapy, type of surgical approach, and procedure applied to the thoracic duct. Multivariate logistic regression analysis was performed to determine whether these four variables were factors that could determine the duration of chest tube drainage. We matched the propensity scores in a 1:1 ratio using the neatest neighbor method, with no replacements, and a 0.2 caliper width. Multivariate analysis by logistic regression was performed to evaluate categorical variables.

Sato, et al

Results

Patient characteristics in the two groups

A total of 220 patients were divided into the late (n = 110) and early (n = 110) removal groups. All patients underwent curative thoracic esophagectomy with reconstruction of the gastric conduit. The baseline characteristics of the patients before and after propensity score matching are listed in Table 1. After propensity score matching, 89 matched patients remained in each group. The characteristics of the 89 matched cases are shown in Table 1. The two groups had similar clinical features; however, the posterior mediastinal reconstruction route was more frequently performed in the late removal group.

Chest tube drainage volume

The average drainage volume did not significantly differ between the two groups after propensity score matching. Figure 1 shows the average drainage volume in the first 24 hours postoperatively in both thoracic cavities. In the bilateral thoracic cavity, the average drainage volume did not significantly differ between the two groups (712.6 \pm 271.7 ml in the late removal group vs. 773.9 \pm 300.6 ml in the early removal group, p =

((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

0.15). There were also no significant differences between groups in the drainage volumes from the left thoracic cavity (277.4 \pm 178.3 ml in the late removal group vs. 302.7 ± 171.6 ml in the early removal group, p = 0.34) and right thoracic cavity (435.0 \pm 197.4 ml in the late removal group vs. 479.9 \pm 226.6 ml in the early removal group, p = 0.16). The early removal group tended to have a larger drainage volume than the late removal group.

Duration of chest tube drainage and early chest tube removal rate

Figure 2 presents the duration of chest tube drainage. The average duration of drainage significantly differed between the groups. The average duration until bilateral chest tube removal was 3.77 ± 2.3 days in the late removal group and 1.52 ± 1.3 days in the early removal group (p < 0.01). The duration until left chest tube removal was 2.88 ± 1.6 days in the late removal group vs. 1.07 ± 0.4 days in the early removal group (p < 0.01). The duration until right chest tube removal was 3.35 ± 2.2 days in the late removal group vs. 1.51 ± 1.2 days in the early removal group (p < 0.01).

Analysis of potential factors associated with amount of chest drainage volume

To further analyze the potential factors associated with the amount of chest drainage

Sato, et al

volume after thoracic esophagectomy, we investigated the important clinical factors such as ;1) ligation of thoracic duct, 2) liver function before treatment, 3) extent of lymph node dissection (D2 versus D3 lymph node dissection) based on the definition Japanese Classification of Esophageal Cancer (The 11th edition), 4) pathological tumor invasion, and 5) infectious events in thoracic cavity. Tables 2 shown that there were no significant differences of these factors between early and late chest drain removal after propensity-score matched groups.

Incidences of surgical complications after propensity score matching

The rate of early chest tube removal, and the incidences of pulmonary complications and thoracocentesis were compared after propensity score matching (Table 3). After propensity score matching, there were no significant differences between the two groups in patient demographics and type of surgical treatment. In the early removal group, the success rates of early removal of the right and left chest tubes were 70.7% and 96.6%, respectively, while no patient underwent early chest tube removal in the late removal group. There were no significant differences between the early and late removal groups in the incidences of anastomotic leakage (16.9% vs. 20.2%, p = 0.70), pulmonary complications (7.9% vs. 6.7%, p = 1.00), and thoracocentesis (10.1% vs. 13.5%, p =

((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

0.64), and in the postoperative hospital stay (21.4 \pm 14.2 days vs. 19.7 \pm 11.1 days, *p* = 0.39).

The number of patients and duration of chest tube drainage are shown in Figure 3. Early removal on POD1 of the chest tube in the right thorax was performed in 63 of 89 (70.7%) patients, and in the left thorax in 86 of 89 (96.6%) patients in the early removal group. In contrast, no patient underwent chest tube removal on POD1 in the late removal group (p < 0.01). Compared with the late removal group, the early removal group had significantly greater rates of early chest tube removal in the right thorax (92.1% vs. 22.4%, p < 0.01) and the left thorax (97.7% vs. 53.9%, p < 0.01). Overall, the early removal group (Figure 3).

Postoperative first mobilization in the two groups

The efficacy of the fast-track postoperative protocol is widely reported in many fields, including the field of esophageal surgery. Early chest drain removal after thoracic esophagectomy reportedly accelerates patients' postoperative activity [7]. Thus, we compared the timing of postoperative first mobilization in the two groups. As described, the same postoperative analgesic protocol was applied in each group. As shown in

Sato, et al

Figure 4, 89.8% of patients in the early removal group achieved postoperative first mobilization within 15 hours, whereas this early mobilization was only achieved in 58.4% of patients in the late removal group (p < 0.01). In both groups, the remaining patients could not achieve first postoperative mobilization within 15 hours due to reasons such as discomfort, pain, patient refusal, and low blood pressure (data not shown).

Uni- and multivariate analyses of pulmonary complications and thoracocentesis

Potential factors associated with amount of chest drainage volume and the incidences of pulmonary complications and thoracocentesis did not significantly differ between the two groups after propensity score matching (Table 2 and 3). The pulmonary complications that we encountered were pyothorax (n = 3), chylothorax (n = 4), pneumothorax (n = 7), and pneumonia (n = 4). The causes of pyothorax were chylothorax (n = 1) and retrograde infection (n = 2), and did not occur due to anastomotic leakage (data not shown).

Uni- and multivariate analyses were performed to determine whether early chest tube removal was a risk factor for pulmonary complications and thoracocentesis (Tables 4 and 5).

((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

The risk factors for pulmonary complications were history of pulmonary disease (p = 0.02) and neoadjuvant chemotherapy (p = 0.04). In contrast, uni- and multivariate analyses found no significant risk factors for thoracocentesis. These results indicate that early chest tube removal was not a risk factor for pulmonary complications or thoracocentesis.

Discussion

The present study found that early chest tube removal after thoracic esophagectomy was not an independent risk factor for pulmonary complications or thoracocentesis, and promoted early mobilization. This suggests that early chest tube removal may be considered as safe and feasible as late chest tube removal.

In thoracic surgery, the aims of chest tube insertion are to evacuate air and fluid from the pleural space, ensure complete pulmonary re-expansion, and restore respiratory mechanics. In cases with intra-thoracic anastomosis, chest tube insertion also aids in monitoring for anastomotic leakage. Therefore, the criteria for chest tube removal include complete expansion of the remaining lung tissue, and cessation of air leakage and high-volume fluid drainage. Chest tubes can exacerbate postoperative pain, cause

Sato, et al

ineffective ventilation, decrease sputum evacuation, and lead to atelectasis [1]; hence, thoracic surgeons aim to reduce the duration of chest drainage. In thoracic esophagectomy, in general, the widely accepted practice was to remove the chest tube when the drainage volume was less than 100–200 ml per day, with no leakage of air or chyle and no anastomotic problems [2,3]. However, these criteria occasionally lead to a long duration of chest tube drainage, and most patients require more than 4 days of chest tube retention postoperatively [2,3].

Since the ERAS program has been applied to thoracic esophagectomy, the safety and feasibility of relatively early chest tube removal with high drainage volume has been proven [5]. However, even with the acceptance of the ERAS program, there are few clinical trials or multicenter reports regarding chest tube management after thoracic esophagectomy. Thus, the optimal timing of chest tube drainage removal depends on the criteria set by each institution and physician. Therefore, the present study was conducted to evaluate the safety and feasibility of early chest tube removal on POD1 after thoracic esophagectomy with three-field dissection.

Compared with chest tube management in lung surgery, the difficulty in conducting clinical trials for chest tube management after esophagectomy is based on the reconstruction of the resected esophagus, as either intra-thoracic or cervical anastomosis

((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

Sato, et al

can be performed. In cases with intra-thoracic anastomosis, a chest tube inserted intraoperatively may be effective for drainage when anastomotic leakage occurs [8,9]. However, as the anastomosis in thoracic esophagectomy with three-field dissection is located in the cervical area, chest tubes may not be effective for the monitoring and treatment of anastomotic leakage. There were 33 cases of cervical anastomotic leakage in the present study; these patients were successfully managed via the transcervical approach, and no patient required chest tube placement to treat the leakage. Hence, we considered that early chest tube removal was possible in the present study regardless of the evaluation of anastomosis, as all patients underwent thoracic esophagectomy with three-field dissection. Thus, judgment of the appropriate timing of chest tube removal in the present study was based on the daily total drainage volume [2,3,5].

Early chest tube removal after thoracic surgery is reportedly influenced by two parameters: the reported daily drainage amount, and the protein content of the pleural drainage fluid. The maximum amount of daily pleural drainage at which chest tube removal may be attempted is considered to be 450 ml/day of nonchylous drainage [10]; however, several reports failed to validate this recommendation [11]. Therefore, a consensus on the threshold drainage volume for safe chest tube removal has not yet been reached. Previous reports suggest that the protein content of the pleural drainage

Sato, et al

fluid is a more reliable and precise criterion for chest tube removal than drainage amount, due to the poor absorption rate of proteins from the pleural surfaces [11]. Therefore, the appropriate criteria for chest tube removal are drainage volume below the safe threshold, and protein density in the range of the absorption rate. In the present study, we chose removal criteria of non-turbid drainage volume not exceeding 300 ml for the last 6 hours, and no air leakage. Although these criteria did not precisely meet the protein density criterion, the summary of these criteria did not conflict with previous reports.

We successfully removed the chest tubes based on these criteria. The success rate on the early removal group was 97.7% for the left chest tube, and 70.7% for the right. There is no previous report of a chest tube being removed as early as in the present study. In addition, our data showed that the pulmonary complication rate was 6–7%, which was similar to the previously reported rates of 7–38% [12-14]. Also, the rates of thoracocentesis in our study (10–13%) were almost the same as those described by Kosugi et al. (12%) [15]. Therefore, we achieved early chest tube removal with a high success rate and without a significant increase in pulmonary complications or thoracocentesis.

The present study also demonstrated a possible advantage of early chest tube

((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

Sato, et al

removal regarding its effect on first mobilization after esophagectomy. Chest drainage tubes often increase chest pain, and restrict patient mobility after thoracic surgery. A previous report found that early chest tube removal significantly reduced the impairment of 6-minute walking distance after thoracic surgery [16]. The recent ERAS concept supports this advantage. Therefore, we evaluated the potential influence of early chest tube removal on the timing of first mobilization after thoracic esophagectomy. The present study revealed significantly greater achievement of first mobilization within 15 hours postoperatively in the early removal group compared with the late removal group.

The present study has several limitations. The study covered a period of more than 2 years, during which time the thoracic and abdominal surgical devices differed slightly. However, the anesthesia and perioperative patient management procedures were performed consistently with the same clinical management pathway, which may be considered a strength of the study. Further studies on chest tube management should be planned in a prospective, randomized, controlled manner in multiple centers. In addition, although the present patients were all managed with the same analgesics and postoperative mobilization protocol, further exploration is required to determine the best patient support after thoracic esophagectomy.

Sato, et al

In conclusion, the present study revealed that the incidences of postoperative pulmonary complications and repeat chest puncture did not significantly differ between the early and late removal groups. Furthermore, early chest tube removal promoted early first mobilization postoperatively. Thus, the present results indicate that early chest tube removal using early removal criteria may be considered as safe and feasible as late chest tube removal.

Acknowledgment

This research did not receive any specific grant from funding agencies in the public, commercial, or not -for-profit sectors. We greatly appreciate the members of National Cancer Center Hospital East and the Course of Advanced Clinical Research of Cancer at Juntendo University Graduate School of Medicine for their critical discussion of this manuscript. We thank Kelly Zammit, BVSc, from Edanz Group (www.edanzediting.com/ac), for editing a draft of this manuscript.

Conflict of Interest



((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

Sato, et al

All authors declare that they have no conflict of interest.

References

[1] Findlay JM, Gillies RS, Millo J, Sgromo B, Marshall REK, Maynard ND. Enhanced Recovery for Esophagectomy. Ann. Surg. 2014; 259:413-31.

[2] Younes RN, Gross JL, Aguiar S, Haddad FJ, Deheinzelin D. When to remove a chest

tube? A randomized study with subsequent prospective consecutive validation. J. Am.

Coll. Surg. 2002; 195: 658-62.

[3] Lagarde SM, Omloo JNT, Ubbink DT, Busch ORC, Obertop H, van Lanschot JJB.

Predictive factors associated with prolonged chest drain production after esophagectomy.

Dis. Esophagus. 2007; 20: 24-8.

Sato, et al

- [4] Law S, Boey JP, Kwok KF, Wong KH, Chu KM, Wong J. Pleural drainage after transthoracic esophagectomy: Experience with a vacuum system. Dis. Esophagus. 2004; 17:81–6.
- [5] Pan H, Hu X, Yu Z, Zhang R, Zhang RW, Ge J. Use of a fast-track surgery protocol on patients undergoing minimally invasive oesophagectomy: Preliminary results, Interact. Cardiovasc. Thorac. Surg. 2014; 19: 441–7.
- [6] Low DE, Kunz S, Schembre D, Otero H, Malpass T, His A, et al. Esophagectomy-it's not just about mortality anymore: Standardized perioperative clinical pathways improve outcomes in patients with esophageal cancer. J. Gastrointest. Surg. 2007; 11: 1395–402.
- [7] Gao S, Zhang Z, Argón J, Brunelli A, Cassivi S, Chai Y, et al. The Society for

Translational Medicine: clinical pretice guidelines for the postoperative management of chst tube for patients undergoing lobectomy. J. Thorac Dis. 2017; 9: 3255-3264.

[8] Tang H, Xue L, Hong J, Tao X, Xu Z, Wu B. A Method for Early Diagnosis and Treatment of Intrathoracic Esophageal Anastomotic Leakage: Prophylactic Placement of

a Drainage Tube Adjacent to the Anastomosis. J. Gastrointest. Surg. 2012; 16: 722-7.

[9] Schaheen L, Blackmon SH, Nason KS. Optimal approach to the management of intrathoracic esophageal leak following esophagectomy: A systematic review. Am. J. Surg. 2014; 208: 536–43.

((Japan Surgical Society))

Early v.s. late chest tube removal in esophagectomy

- [10] Grodzki T. Prospective algorithm to remove chest tubes after pulmonary resection with high output--is it valid everywhere?. J. Thrac. cardiovasc. Surg. 2008;136: 536-7.
- [11] Olgac G, Cosgun T, Vayvada M, Ozdemir A, Kutlu CA. Low protein content of drainage fluid is a good predictor for earlier chest tube removal after lobectmy. Interact Cardiovasc Thorac Surg. 2014; 19: 650-655.
- [12] Fang W, Kato H, Tachimori Y, Igaki H, Sato H, Daiko H. Analysis of pulmonary complications after three-field lymph node dissection for esophageal cancer. Ann. Thorac. Surg. 2003; 76: 903–8.
- [13] Zingg U, Smithers BM, Gotley DC, Smith G, Aly A, Clough A, et al. Factors Associated with Postoperative Pulmonary Morbidity After Esophagectomy for Cancer. Ann. Surg. Oncol. 2011; 18: 1460–8.
- [14] Ferguson MK, Celauro AD, Prachand V. Prediction of major pulmonary complications after esophagectomy. Ann. Thorac. Surg. 2011; 91: 1494–501.
- [15] Kosugi SI, Kanda T, Yajima K, Ishikawa T, Sakamoto K. Risk factors influencing the pleural drainage volume after transthoracic oesophagectomy. Eur. J. Cardio-Thoracic Surg. 2013; 43: 1116–20.
- [16] Nomori H, Horio H, Suemasu K. Early removal of chest drainge tubes and oxygen support after a lobectomy for lung cancer facilitates earlier recovery of the 6-imuite

Sato, et al

wolking distance. Surg Today. 2001; 31: 395-399.

Early v.s. late chest tube removal in esophagectomy

Early v.s. late chest tube removal in esophagectomy

8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
30 39
39 40
40 41
41 42
42 43
43 44
44

((Japan Surgical Society))

for per perient

Sato, et al

Figure Legends

Fig. 1 Average drainage volume in 24 hours after esophagectomy in the bilateral, left, and right thoracic cavities after propensity score matching

Although the drainage volume tended to be slightly higher in the early removal group than the late removal group, this difference was not significant. In the bilateral thoracic cavity, the average drainage volume did not significantly differ between groups (712.6 \pm 271.7 ml in the late vs. 773.9 \pm 300.6 ml in the early removal group, p = 0.15). There was also no significant difference in the drainage volume from the left (277.4 \pm 178.3 ml in the late vs. 302.7 \pm 171.6 ml in the early removal group, p = 0.34) and right thoracic cavity (435.0 \pm 197.4 ml in the late vs. 479.9 \pm 226.6 ml in the early removal group, p = 0.16).

Early removal group (n = 89): chest tubes were removed on postoperative day 1 regardless of the daily total drainage volume, as long as the non-turbid drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the drainage volume was less than 200 ml/day.

Early v.s. late chest tube removal in esophagectomy

Fig. 2 Average duration of chest tube drainage in the two groups after propensity score matching

The average duration until bilateral chest tube removal was 3.77 ± 2.3 days in the late and 1.52 ± 1.3 days in the early removal group (p < 0.01). The duration until left chest tube removal was 2.88 ± 1.6 days in the late removal group vs. 1.07 ± 0.4 days in the early removal group (p < 0.01). The duration until right chest tube removal was $3.35 \pm$ 2.2 days in the late vs. 1.51 ± 1.2 days in the early removal group (p < 0.01).

Early removal group (n = 89): chest tubes were removed on postoperative day 1 regardless of the daily total drainage volume, as long as the non-turbid drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the drainage volume was less than 200 ml/day.

Fig. 3 Number of patients and duration of drainage in early and late removal groups

In the early removal group, the chest tubes were successfully removed on the first postoperative day from the left thorax in 96.6%, and the right thorax in 70.7%. In

Sato, et al

contrast, no patients in the late removal group underwent chest tube removal on postoperative day 1 (p < 0.01). By postoperative day 2, 92.1% of the right and 97.7% of left chest tubes had been removed in the early removal group, whereas 22.4% and 53.9%, respectively, had been removed in the late removal group.

Early removal group (n = 89): chest tubes were removed on postoperative day 1 regardless of the daily total drainage volume, as long as the non-turbid drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the drainage volume was less than 200 ml/day.

Fig. 4 Number of patients and first postoperative mobilization in the early and late chest tube removal groups after esophagectomy

The number of patients who achieved first postoperative mobilization within 15 hours was significantly greater in the early removal group compared with the late removal group (89.8% vs. 58.4%, p < 0.01). The other patients failed to achieve first postoperative mobilization within 15 hours for several reasons, such as discomfort, pain, low blood pressure, and patient refusal.

Early removal group (n = 89): chest tubes were removed on postoperative day 1

((Surgery Today))

Early v.s. late chest tube removal in esophagectomy

Sato, et al

regardless of the daily total drainage volume, as long as the non-turbid drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the drainage volume was less than 200 ml/day.

for perpension



י ר
2
2 3 4 5 6 7 8 9 10 11 12 13 14
4
5
6
7
8
9
10
11
11
12
13
14
15
16
17
18
10
20
20
21
22
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38
24
25
26
20
27
28
29
30
31
32
33
34
35
26
20
3/
38
39
40
41
42
43
44
44 45
46

4	6
4	7

	Before pro	pensity score matcl	hing	After prop	ensity score matching	5
Factors	Late removal $(n = 110)$	Early removal $(n = 110)$	<i>p</i> value	Late removal $(n = 89)$	Early removal $(n = 89)$	<i>p</i> value
Sex, male/female	93/17	91/19	0.86	73/16	74/15	1.00
Age (years), n (%)			1			0.76
< 65	46 (41.8)	45 (41.7)		39 (43.8)	36 (40.4)	
\geq 65	64 (58.2)	63 (58.3)		50 (56.2)	53 (59.6)	
ASA-PS	× /	. ,	0.24			0.27
1	39 (35.5)	31 (28.2)	••	34 (38.2)	26 (29.2)	••
≥ 2	71 (64.5)	79 (71.8)		55 (61.8)	63 (70.8)	
BMI, mean \pm SD	22.0 ± 3.3	21.8 ± 2.7	0.62	22.0 ± 3.4	21.7 ± 2.7	0.62
Smoking status, n (%)	22.0 - 5.5	21.0 - 2.7	0.76	22.0 - 5.1	21.7 - 2.7	0.80
Smoker	90 (81.8)	85 (78.7)	0.70	71 (79.8)	65 (75.8)	0.00
Never smoked	20 (18.2)	23 (21.3)		18 (20.2)	21 (24.1)	
Heart disease, n (%)	8 (7.2)	7 (6.3)	1	6 (6.7)	5 (5.6)	1.00
Pulmonary disease (%)	14 (12.7)	8 (7.2)	0.26	13 (14.6)	6 (6.7)	1.00
Clinical stage (UICC 7th), n (%)		- ()	0.14	()	• (••••)	0.90
I	44 (40.0)	38 (34.5)	0.11	33 (37.1)	31 (34.8)	0.20
Ĩ	21 (19.1)	13 (11.8)		11 (12.4)	13 (14.6)	
III	38 (34.5)	54 (49.1)		38 (42.7)	40 (44.9)	
ĪV	7 (6.4)	5 (4.5)		7 (7.9)	5 (5.6)	
Location of primary tumor, n (%)	, (, , ,)		0.67			0.49
Upper thoracic	11 (10.0)	16 (14.5)		9 (10.1)	15 (16.8)	
Middle thoracic	55 (50.0)	56 (50.9)		44 (49.4)	44 (49.4)	
Lower thoracic	44 (40.0)	38 (34.5)		36 (40.4)	27 (33.4)	
Neoadjuvant chemotherapy, n (%)	51 (46.3)	52 (47.2)	1	42 (47.1)	42 (47.1)	1.00
Type of surgical approach, n (%)		()	0.08	() (() () () () () () () () (1.00
Thoracoscopy	59 (53.6)	73 (66.4)		54 (60.7)	54 (60.7)	
Thoracotomy	51 (46.4)	37 (33.6)		35 (39.3)	35 (39.3)	
Thoracic duct, n (%)		()	0.22		()	1.00
Preserved	42 (38.2)	50 (46.3)		36 (40.4)	36 (40.4)	
Resected	68 (61.8)	58 (53.7)		53 (59.6)	53 (59.6)	
Reconstruction route, n (%)		. ,	0.001			0.01
Posterior mediastinal	101 (91.8)	80 (74.1)		82 (92.1)	69 (77.5)	
Retrosternal	9 (8.2)	28 (25.9)		7 (7.9)	20 (22.5)	

ASA-PS: American Society of Anesthesiologists-Physical Status, BMI: body mass index, SD: standard deviation, UICC: Union for International Cancer Control. Early removal group (n = 89): chest tubes were removed on postoperative day 1 regardless of the daily total drainage volume, as long as the non-turbid drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the drainage volume was less than 200 ml/day.

	Propens			
Factors	Late removal $(n = 89)$	Early removal $(n = 89)$	<i>p</i> value	
Ligation of thoracic duct, n (%)			1.00	
Preserved	36 (40.4)	36 (40.4)		
Resected	53 (59.6)	53 (59.6)		
Liver function, n (%)			0.74	
Child-Pugh A	83 (93.2)	85 (95.5)		
Child-Pugh B	6 (6.8)	4 (4.5)		
Extent of lymph node dissection, n (%)			0.41	
D2 LN dissection	12 (13.4)	16 (17.9)		
D3 LN dissection	77 (86.6)	73 (82.1)		
Pathological tumor invasion, n (%)			0.76	
pT1, pT2	41 (46.0)	43 (48.3)		
pT3, pT4	48 (54.0)	46 (52.7)		
Infectious events in thoracic cavity, n (%)	1 (1.1)	2 (2.2)	1.00	

 Table 2. Factors potentially associate with amount of drainage volumes

D2 and D3 LN (lymph node) dissection is based on the definition Japanese Classification of Esophageal Cancer (The 11^{th} edition). Early removal group (n = 89): chest tubes were removed on postoperative day 1 regardless of the daily total drainage volume, as long as the non-turbid drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the drainage volume was less than 200 ml/day.

	Proper	nsity score matching	
Factors	Late removal $(n = 89)$	Early removal $(n = 89)$	<i>p</i> value
Success removal on POD1, n (%) Right chest tube Left chest tube	0 (0) 0 (0)	64 (71.0) 86 (96.6)	< 0.001
Anastomotic leakage, n (%)	15 (16.9)	18 (20.2)	0.70
Pulmonary complications, n (%)	7 (7.9)	6 (6.7)	1.00
Thoracocentesis, n (%)	9 (10.1)	12 (13.5)	0.64
Hospital stay (days), mean \pm SD	21.4 ± 14.2	19.7 ± 11.1	0.39

Table 3 Surgical complications in the two groups after propensity score matching

Continuous variables are listed as the mean \pm SD.

POD1: postoperative day 1, SD: standard deviation. Early removal group (n = 89): chest tubes were removed on postoperative day 1 regardless of the daily total drainage volume, as long as the non-turbid drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the r Perien

drainage volume was less than 200 ml/day.

Factors

1 2

p value

Multivariate analysis

p value

Odds ratio (95% CI)

|--|

Table 4. Uni- and multivariate analyses of pulmonary complications after propensity score matching

Pulmonary

$\begin{array}{c c c c c c c c c c c c c c c c c c c $	i actors	complications (-)	complications (+)	<i>p</i> value		Odds ratio (95% CI)	<i>p</i> value
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			•	0.47	-		
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			12			0.47 (0.16-1.38)	0.17
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		30	1				
≥ 65				0.96			
$\begin{array}{c c c c c c c c c c c c c c c c c c c $						1.54 (0.69–3.45)	0.31
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		96	7				
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	ASA-PS			0.90			
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	1		8			1.85 (0.85-4.02)	0.12
$\begin{array}{c c c c c c c c c c c c c c c c c c c $				<u> </u>			
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		21.9 (±3.0)	$20.6 (\pm 3.5)$			1.44 (0.63–3.29)	0.39
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		126		0.73		0.70(0.27, 1.79)	0.45
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			11			0.70(0.27-1.78)	0.45
With pulmonary disease1450.81 (0.63-0.98)0.02With pulmonary disease15180.61110.611110.611110.61110.61110.73110.73110.73110.73110.73110.731100.020.67 (0.32-0.96)0.040.041100.020.67 (0.32-0.96)0.0410.04100.020.67 (0.32-0.96)0.0410.0510.67 (0.32-0.96)0.0410.650.67 <td></td> <td>37</td> <td>2</td> <td>< 0.01</td> <td></td> <td></td> <td></td>		37	2	< 0.01			
Without pulmonary disease1518Clinical stage (UICC 7 th)632I222II222III707IV102Neoadjuvant chemotherapy822With neoadjuvant chemotherapy8311Type of surgical approach Thoracoscopy0.25Thoracoscopy9810Thoracic duct Preservation0.77Preservation666673Drainage volume in right thoracic cavity, mean \pm SD381.6 (\pm 15.8.5)396.1 (\pm 307.7)0.841.3 (0.82–1.11)0.37Chest tube removal Early removal Late removal10.71 (0.03–14.40)0.82		14	5	< 0.01		0.81 (0.63-0.98)	0.02
$\begin{array}{c c c c c c c c c c c c c c c c c c c $						0.01 (0.05 0.90)	0.02
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		101	, in the second s	0.61			
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Ι	63	2				
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	II	22	2			1.20 (0.42-3.49)	0.73
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			7				
With neoadjuvant chemotherapy 82 2 $0.67 (0.32-0.96)$ 0.04 Without neoadjuvant chemotherapy 83 11 0.25 $1.26 (0.59-2.71)$ 0.55 Thoracoscopy 98 10 0.77 $1.03 (0.47-2.26)$ 0.95 Thoracic duct 0.77 0.77 0.77 0.61 $1.25 (0.38-4.15)$ 0.95 Preservation 80 $455.0 (\pm 211.3)$ $486.6 (\pm 241.6)$ 0.61 $1.25 (0.38-4.15)$ 0.71 Drainage volume in right thoracic cavity, mean \pm SD $381.6 (\pm 158.5)$ $396.1 (\pm 307.7)$ 0.84 $1.3 (0.82-1.11)$ 0.37 Chest tube removal Early removal Late removal 82 7 1 $0.71 (0.03-14.40)$ 0.82		10	2				
Without neoadjuvant chemotherapy 83 11Type of surgical approach 0.25 Thoracoscopy 98 Thoracoscopy 67 Thoracic duct 0.77 Preservation 66 Resection 99 Drainage volume in right thoracic cavity, mean \pm SD $455.0 (\pm 211.3)$ $486.6 (\pm 241.6)$ 0.61 Drainage volume in left thoracic cavity, mean \pm SD $381.6 (\pm 158.5)$ $396.1 (\pm 307.7)$ 0.84 $1.3 (0.82-1.11)$ 0.37 Chest tube removal Early removal Late removal 82 7 1 83 6				0.02			
Type of surgical approach Thoracoscopy 0.25 $1.26 (0.59-2.71)$ 0.55 Thoracotomy 67 3 0.77 Thoracic duct Preservation 0.77 0.77 Preservation Resection 66 6 Preservation mean \pm SD $455.0 (\pm 211.3)$ $486.6 (\pm 241.6)$ 0.61 Drainage volume in right thoracic cavity, mean \pm SD $381.6 (\pm 158.5)$ $396.1 (\pm 307.7)$ 0.84 Drainage volume in left thoracic cavity, mean \pm SD 82 7 1 Chest tube removal Early removal Late removal 82 7 1 83 6 $0.71 (0.03-14.40)$ 0.82		82	2			0.67 (0.32–0.96)	0.04
Thoracoscopy9810 $1.26 (0.59-2.71)$ 0.55 Thoracotomy6730.77Thoracic duct0.771.03 (0.47-2.26)0.95Preservation9971.03 (0.47-2.26)0.95Drainage volume in right thoracic cavity, mean \pm SD455.0 (± 211.3)486.6 (± 241.6)0.611.25 (0.38-4.15)0.71Drainage volume in left thoracic cavity, mean \pm SD381.6 (± 158.5)396.1 (± 307.7)0.841.3 (0.82-1.11)0.37Chest tube removal Early removal Late removal827 6610.71 (0.03-14.40)0.82		83	11	0.05			
Thoracotomy673Thoracic duct0.77Preservation66Resection99Drainage volume in right thoracic cavity, mean \pm SD455.0 (± 211.3)486.6 (± 241.6)0.61Drainage volume in left thoracic cavity, mean \pm SD381.6 (± 158.5)396.1 (± 307.7)0.841.3 (0.82–1.11)0.37Chest tube removal Early removal Late removal8271836		00	10	0.25		1.2((0.50, 2.71)	0.55
Thoracic duct 0.77 Preservation 66 6 Resection 99 7 Drainage volume in right thoracic cavity, mean \pm SD $455.0 (\pm 211.3)$ $486.6 (\pm 241.6)$ 0.61 Drainage volume in left thoracic cavity, mean \pm SD $381.6 (\pm 158.5)$ $396.1 (\pm 307.7)$ 0.84 Chest tube removal Early removal Late removal 82 7 1 0.71 (0.03-14.40) 0.82						1.26 (0.59–2.71)	0.55
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		07	3	0.77			
Resection997Drainage volume in right thoracic cavity, mean \pm SD455.0 (\pm 211.3)486.6 (\pm 241.6)0.611.25 (0.38–4.15)0.71Drainage volume in left thoracic cavity, mean \pm SD381.6 (\pm 158.5)396.1 (\pm 307.7)0.841.3 (0.82–1.11)0.37Chest tube removal Early removal Late removal8270.71 (0.03–14.40)0.82		66	6	0.77		1 03 (0 47-2 26)	0.95
Drainage volume in right thoracic cavity, mean \pm SD455.0 (± 211.3)486.6 (± 241.6)0.611.25 (0.38-4.15)0.71Drainage volume in left thoracic cavity, mean \pm SD381.6 (± 158.5)396.1 (± 307.7)0.841.3 (0.82-1.11)0.37Chest tube removal Early removal Late removal8270.710.82			7			1.05 (0.47 2.20)	0.75
mean \pm SD435.0 (± 211.3)486.6 (± 241.6)0.611.25 (0.38–4.13)0.71Drainage volume in left thoracic cavity, mean \pm SD381.6 (± 158.5)396.1 (± 307.7)0.841.3 (0.82–1.11)0.37Chest tube removal Early removal Late removal82710.71 (0.03–14.40)0.82				0.61		1.05 (0.00 4.15)	0.71
mean ± SD 381.0 (±138.3) 396.1 (±307.7) 0.84 1.3 (0.82–1.11) 0.37 Chest tube removal 1 1 1 1 1 1 Early removal 82 7 0.71 (0.03–14.40) 0.82 Late removal 83 6 0.71 (0.03–14.40) 0.82		455.0 (±211.3)	486.6 (±241.6)	0.61		1.25 (0.38–4.15)	0.71
mean ± SD1Chest tube removal1Early removal82Late removal83		381 6 (+158 5)	3061(+3077)	0.84		13(0.82, 1.11)	0.37
Early removal 82 7 0.71 (0.03-14.40) 0.82 Late removal 83 6 6 6 6	mean \pm SD	501.0 (±150.5)	550.1 (±507.7)	0.04		1.5 (0.62–1.11)	0.57
Late removal 83 6				1			
			7			0.71 (0.03–14.40)	0.82
ASA-PS: American Society of Anesthesiologists-Physical Status, BMI: body mass index, CI: confidence intervals, SD: standard deviation,	Late removal	83	6				
	ASA-PS: American Society of Anesth	esiologists-Physical S	status, BMI: body ma	ss index, CI: c	onfiden	ce intervals, SD: standar	d deviation,

Univariate analysis

Pulmonary

Cancer Control. Early removal group (n = 89): chest tubes were removed on postoperative day 1 regardless of the daily total drainage volume, as long as the non-turbid

((Japan Surgical Society))

drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the drainage volume was less than 200 ml/day.

 For per Periew

Multivariate analysis

p value

0.20

0.11

0.59

0.48

0.91

0.18

0.41

0.62

0.24

0.98

0.96

0.96

0.45

Odds ratio (95% CI)

0.62 (0.30-1.28)

1.86 (0.88-3.94)

1.22 (0.59-2.55)

1.26 (0.66-2.42)

0.86 (0.06-12.10)

0.50 (0.18–1.38)

1.41 (0.63-3.18)

0.79 (0.31-3.90)

0.53 (0.18–1.53)

0.99 (0.53-1.84)

1.02 (0.47-2.21)

0.93 (0.07-11.90)

0.70 (0.27-1.78)

Factors -	Univariate analysis				
	Thoracocentesis (-)	Thoracocentesis (+)	<i>p</i> value		
bex		. –	0.77		
Male	130	17			
Female	27	4			
Age (years)			0.64		
< 65	65	10			
≥ 65	92	11			
ASA-PS†			0.81		
1	103	15			
≥ 2	54	6			
\overline{BMI} , mean \pm SD	21.9 (±3.1)	20.8 (±3.1)	0.11		
Smoking status			0.81		
Smoker	121	5			
Never smoked	36	16			
Pulmonary disease			1		
With pulmonary disease	17	2	1.00		
Without pulmonary disease	140	19			
Clinical stage (UICC 7 th)	110		0.34		
I	54	10			
II	23	1			
III	68	10			
IV	12	0			
Veoadjuvant chemotherapy		,	0.49		
With neoadjuvant chemotherapy	76	8	0.17		
Without neoadjuvant chemotherapy	81	13			
Type of surgical approach	· ·	10	0.81		
Thoracoscopy	96	12			
Thoracotomy	61	9			
Thoracic duct	• -		0.82		
Preservation	63	9			
Resection	94	12			
Drainage volume in right thoracic	-		0.45		
avity, mean \pm SD	453.0 (±205.3)	491.5 (±269.9)	0.45		
Drainage volume in left thoracic	0 00 0 (+1 55 5)		0.05		
avity, mean \pm SD	289.9 (±175.5)	291.4 (±175.2)	0.97		
Chest tube removal			0.64		
Early removal	77	12			
Late removal	80	9			

ence intervals, SD: standard deviation, UICC: Union for International Cancer Control. Early removal group (n = 89): chest tubes were removed on postoperative day 1 regardless of the daily total drainage volume, as long as the non-turbid drainage volume had not exceeded 300 ml over the last 6 hours, and there was no air leakage. Late removal group (n = 89): chest tubes were removed when the drainage

((Japan Surgical Society))

45 46

41 42

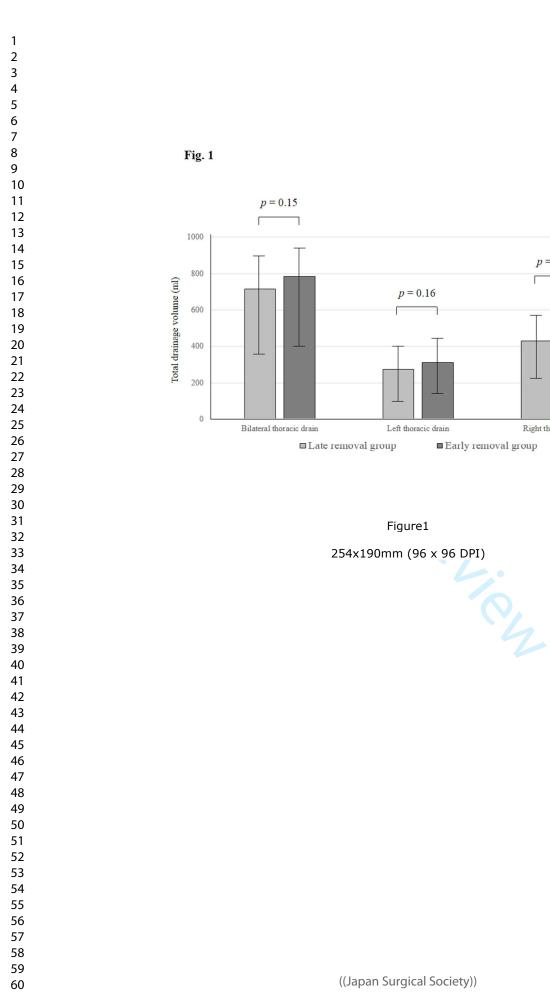
43 44

volume was less than 200 ml/day.

 For peer Periewiew

p = 0.34

Right thoracic drain





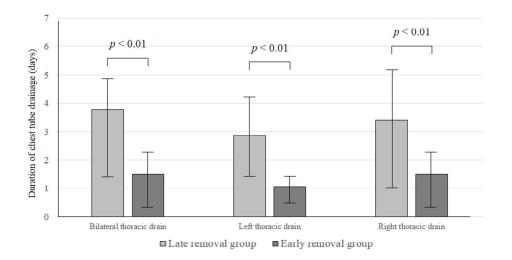
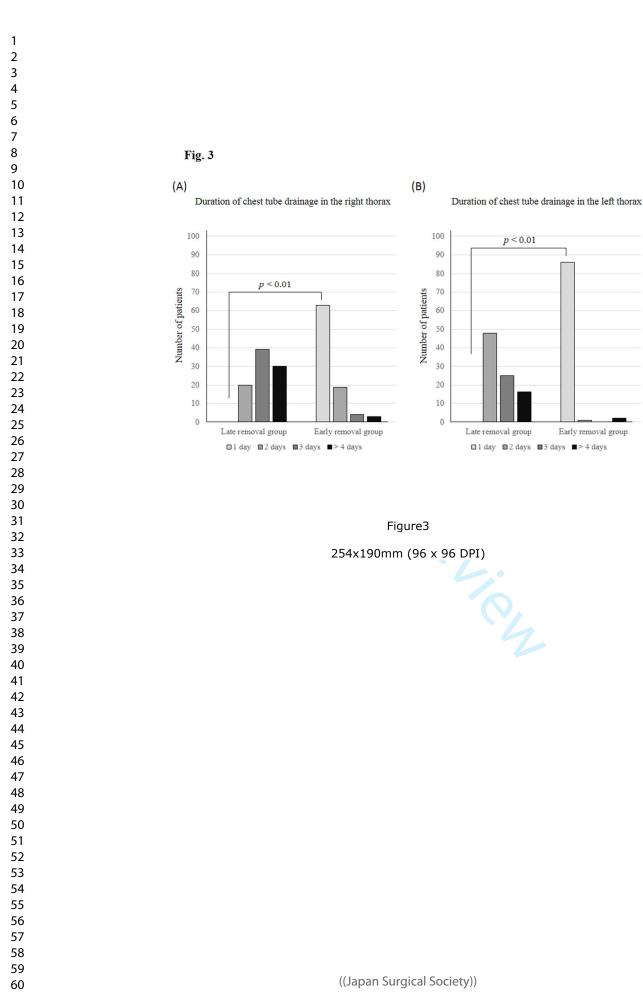


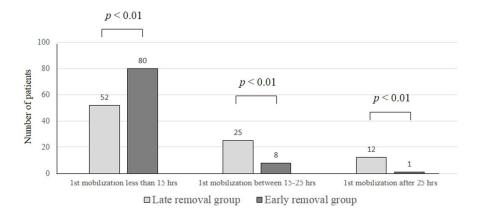
Figure2

254x190mm (96 x 96 DPI)

((Japan Surgical Society))









254x190mm (96 x 96 DPI)