# The Influence of Preoperative Smoking Status on Postoperative Complications and Long-Term Outcome Following Thoracoscopic Esophagectomy in Prone Position for Esophageal Carcinoma

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The influence of preoperative smoking status on postoperative complications and long-term outcome following thoracoscopic esophagectomy in prone position for esophageal carcinoma

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**Disclosures:**

Hironobu Goto, Taro Oshikiri, Takashi Kato, Ryuichiro Sawada, Hitoshi Harada, Naoki Urakawa, Hiroshi Hasegawa, Shingo Kanaji, Kimihiro Yamashita, Takeru Matsuda, and Yoshihiro Kakeji have no conflicts of interest or financial ties to disclose.

**Synopsis:**

Influence of preoperative smoking status on short- and long-term outcomes following thoracoscopic esophagectomy in prone position for esophageal carcinoma

## ABSTRACT

**Background**

Esophagectomy for esophageal carcinoma is associated with higher morbidity and mortality rates than other gastrointestinal surgeries. Smoking is an established risk factor for postoperative complications after esophagectomy. This study aimed to retrospectively investigate the impact of smoking status on short-and long-term outcomes of patients undergoing thoracoscopic esophagectomy in the prone position (TEP) for esophageal carcinoma.

**Methods**

In this study, 234 patients with esophageal carcinoma who underwent TEP between 2012 and 2020 were divided into two groups based on smoking status (current or non-current smokers and the Brinkman index) by patients' declarations. Postoperative complications (Clavien–Dindo classification grade II or higher), overall survival (OS), and disease-free survival (DFS) were compared between each smoking status.

**Results**

The rates of postoperative complications were not significantly different between the two groups (current smoker vs. non-current smoker, Brinkman index ≥800 vs. <800). The rate of postoperative pneumonia was higher in the combination group of current and higher Brinkman index (≥800) smokers than in the other group (25.0% vs. 11.8%, *P* = 0.036). Multivariate analysis showed that smoking status was an independent risk factor for postoperative pneumonia (hazard ratio, 0.41; 95% confidence interval: 0.18-0.93; *P* = 0.037). According to the long-term outcomes, no significant differences were observed in OS and DFS between each smoking status.

## Conclusions

The combination of current smoking and heavy smoking history is a risk factor for postoperative pneumonia in patients with esophageal carcinoma treated with TEP, although no correlation was observed between the long-term outcomes and smoking status.

**Key words**: thoracoscopic esophagectomy in the prone position (TEP), esophageal carcinoma, smoking status, Brinkman index, short- and long-term outcomes

## Background

Esophageal carcinoma is one of the most common malignant diseases worldwide. Esophagectomy is a key part of the curative treatment for patients with esophageal carcinoma. However, esophagectomy is associated with higher morbidity and mortality than other gastrointestinal surgeries, due to anastomotic leakage and pulmonary complications [1-3]. Additionally, the impact of postoperative complications such as pneumonia on the recurrence rate and long-term outcomes has been investigated, and a strong correlation has been observed between postoperative complications and poor long-term outcomes [4]. Reducing postoperative complications is important to improve short-and long-term outcomes after esophagectomy for esophageal carcinoma. Therefore, clarifying the risk factors for postoperative complications is important in patients being considered for esophagectomy.

Smoking is an established risk factor for esophageal carcinoma and postoperative complications following esophagectomy, particularly pulmonary complications [5-7]. A recent study using a Japanese nationwide database reported that smoking within 1 year of esophagectomy was an independent risk factor for 30-day mortality [8]. The duration of preoperative smoking cessation should be considered as long as possible to reduce postoperative morbidities [9].

In contrast, thoracoscopic esophagectomy for esophageal carcinoma is widely accepted as a less invasive surgery and is associated with fewer postoperative complications than open esophagectomy [10]. Specifically, thoracoscopic esophagectomy in the prone position (TEP) is less invasive in terms of postoperative respiratory function and reduction of postoperative respiratory complications than thoracoscopic esophagectomy performed in patients in the left lateral decubitus position

[11]. However, no studies have investigated the correlation between short-and long-term outcomes following TEP alone and smoking status.

This study aimed to retrospectively elucidate the impact of smoking status on short-and long-term outcomes in patients undergoing TEP for esophageal carcinoma.

## Patients and Methods

*Patients*

From January 2012 to March 2020, 442 patients underwent TEP at Kobe University Hospital, Hyogo, Japan. Of these, 208 were excluded because 68 patients did not undergo upper mediastinal lymphadenectomy, 27 were not diagnosed with squamous cell carcinoma or adenocarcinoma, 49 underwent non-curative resection, 25 underwent total pharyngo-laryngo-esophagectomy, 15 underwent salvage surgery, and 24 underwent two-stage surgery. In total, 234 patients who underwent TEP were included. None of the patients had undergone preoperative chemoradiotherapy.

The patients were divided into two groups based on their smoking status. For smoking status, which was based on the patients' declarations at initial visit, we used current or non-current smokers and the Brinkman index. Current smokers were defined as smokers until six weeks before surgery [7]. For current smokers, thorough anti-smoking education was given from the initial visit. The Brinkman index was calculated by multiplying the duration of smoking in years by the number of cigarettes smoked per day. The cut-off value of the Brinkman index for postoperative pneumonia was calculated using the receiver operating characteristic (ROC) curve, after which the patients were divided into two groups [12].

In this retrospective study, the diagnosis of esophageal carcinoma was based on the eighth edition of the Union for International Cancer Control tumor–node–metastasis cancer staging system [13]. The patients underwent esophagogastroduodenoscopy, computed tomography, and positron emission tomography for cancer staging.

The clinical, surgical, and pathological records of the patients were obtained from our database and individual electronic medical records. Data collection and analysis were approved by the Institutional Review Board and Ethics Committee of Kobe University on March 1, 2022.

*Surgical procedures*

For esophagectomy, the patient was placed in the prone position using a single-lumen endotracheal tube and balloon blocker. The thoracic procedure was performed with one lung ventilated and the other collapsed. The lung was collapsed using a balloon blocker and an artificial pneumothorax at 8 mmHg. Detailed surgical techniques for thoracic procedures have been previously published [14-16].

After the thoracic procedure, double-lung ventilation was resumed, and the patient was placed in the supine position. The abdominal procedure was performed via laparoscopic or open laparotomy; however, laparoscopic surgery was preferred. Initially, gastric mobilization and abdominal lymph node dissection were performed. Next, a gastric conduit with a width of 3–4 cm was generated and raised via the posterior mediastinum, retrosternal, or antethoracic routes. In some patients who did not receive gastric conduits due to previous gastric resection or synchronous gastric cancer, pedicled jejunal reconstruction via the antethoracic route was performed. Anastomosis was formed in the cervix.

*Outcomes*

We investigated the association between smoking status and clinicopathological characteristics of patients with esophageal carcinoma who underwent TEP. Patients were evaluated according to age, sex, body mass index (BMI), tumor location, clinical T status, clinical N status, clinical stage, histological type, neoadjuvant chemotherapy status, operative time, blood loss, abdominal procedure, conduit, postoperative hospital stay, pathological stage, and postoperative complications (pneumonia, recurrent laryngeal nerve palsy, and anastomotic leakage). Postoperative complications were assessed according to the Clavien–Dindo (C-D) classification [17]. Complications categorized as grade II or higher were considered postoperative complications. Postoperative pneumonia was defined as the presence of clinical manifestations of pneumonia or bronchopneumonia confirmed by diagnostic imaging such as thoracic radiography or computed tomography and a positive sputum culture within the first two weeks after surgery. The 5-year overall survival (OS) and disease-free survival (DFS) rates were compared between the groups. Esophagogastroduodenoscopy and computed tomography were performed during routine follow-up after surgery for esophageal carcinoma. Esophagogastroduodenoscopy was performed annually, whereas computed tomography was performed at least every 6 months. In terms of follow-up after surgery, thorough anti-smoking instruction was given at each visit.

*Statistical analysis*

All statistical analyses were conducted using the JMP software (version 13.0; SAS Institute Inc., Cary, NC, USA). Categorical variables were expressed as numbers. The groups were compared using the chi-square test or Fisher’s exact test. All continuous variables were expressed as medians (range) and were compared using the Mann–Whitney U test. Multivariate logistic regression analysis using a Cox proportional hazards model was performed to identify the independent risk factors for postoperative pneumonia. The 5-year OS and DFS of each group were assessed using the Kaplan–Meier method and compared using the log-rank test. *P*-values less than 0.05 were considered significant.

*ROC curve*

The ROC curve plots the sensitivity of a test versus its false-positive rate (1-specificity) for all possible cut-off points. The area under the ROC curve (AUC) is an indicator of the test accuracy. The precise cut-off level was determined using the AUC and the highest sum value of sensitivity and specificity as indicators [12].

## Results

*Patient characteristics, surgical outcomes, and postoperative complications*

In total, 442 patients with esophageal carcinoma underwent TEP between 2012 and 2020 at Kobe University Hospital. Of these, 234 patients were included in the study. Based on the patients' declarations at initial visit, the current smoker group consisted of 83 patients, while the non-current smoker group consisted of 151 patients. Clinicopathological characteristics of the patients are presented in Table 1. No significant differences were found in sex, tumor location, clinical T status, clinical N status, clinical and pathological stage, neoadjuvant chemotherapy status, histological type, operative time (overall and thoracic procedure), blood loss, abdominal procedure, conduit, lymph node dissection, or postoperative hospital stay. However, significant difference was observed in age and BMI; the current smoker group was younger and lower BMI than the non-current smoker group ($P = 0.001$, $<0.001$). No significant differences in postoperative complications (pneumonia, recurrent laryngeal nerve palsy, and anastomotic leakage; C-D grade II or higher), were observed between the two groups. The mortality rates in the two groups were similar and one patient in the non-current smoker group died of subarachnoid hemorrhage.

The cut-off value of the Brinkman index calculated using the ROC curve was 800 and the AUC was 0.5786. The high Brinkman index (≥800) group consisted of 95 patients, whereas the low Brinkman index (<800) group consisted of 139 patients. Clinicopathological characteristics of the patients according to the Brinkman index are presented in Table 2. No significant differences were found in age, BMI, tumor location, clinical T status, clinical N status, clinical and pathological stage, neoadjuvant chemotherapy status, histological type, operative time (overall and thoracic procedure), blood loss, abdominal procedure, conduit, or lymph node dissection. Significant differences were observed in sex and postoperative hospital stay; the higher Brinkman index group included more men and had a longer postoperative hospital stay than the lower Brinkman index group ($P = 0.016$, $P = 0.016$). With regard to postoperative complications (pneumonia, recurrent laryngeal nerve palsy, and anastomotic leakage; C-D grade II or higher), no significant differences were observed between the two groups. One patient in the lower Brinkman index group died of subarachnoid hemorrhage and the mortality rates in the two groups were similar.

The combination of current smokers and higher Brinkman index (≥800) group consisted of 48 patients, whereas the other group consisted of 186 patients. Clinicopathological characteristics of the patients according to the combination of high

Brinkman index and current smokers are presented in Table 3. No significant differences were found in age, sex, BMI, tumor location, clinical T status, clinical N status, clinical and pathological stage, neoadjuvant chemotherapy status, histological type, operative time (overall and thoracic procedure), blood loss, abdominal procedure, conduit, lymph node dissection, or postoperative hospital stay. With regard to recurrent laryngeal nerve palsy and anastomotic leakage (C-D grade II or higher), no significant differences were observed between the two groups. The rate of postoperative pneumonia (C-D grade II or higher) was higher in the combination of current smokers and higher Brinkman index group than in the other group (25.0% vs. 11.8%, $P$ = 0.036). One patient in the other group died of subarachnoid hemorrhage and the mortality rates in the two groups were similar.

*Risk factor for postoperative pneumonia after TEP*

We evaluated the risk factors for postoperative pneumonia (C-D grade II or higher) after TEP for esophageal carcinoma using a multivariate Cox proportional hazard model. Table 4 shows that a combination of current smoking and a higher Brinkman index (≥800) was an independent risk factor for postoperative pneumonia after TEP in multivariate analysis (hazard ratio= 0.41; 95% confidence interval: 0.18-0.93; $P$ = 0.037).

*Long-term outcomes*

The OS curves are shown in Figure 1. The 5-year OS rates were 63.3% and 58.6% in the current and non-current smoking groups, respectively (Fig. 1A, P = 0.290). According to the Brinkman index, the 5-year OS rate was 60.2% in the high Brinkman index (≥800) group and 60.0% in the low Brinkman index (<800) group (Fig. 1B, P = 0.834). Additionally, the 5-year OS rate was 64.0% in the combination of current smokers and a higher Brinkman index (≥800) group, and 59.3% in the other group (Fig. 1C, P = 0.368). The OS curves for each study were not significantly different. The DFS curves are showed in Figure 2. The 5-year DFS rates in the current and non-current smoking groups were 56.6% and 54.4%, respectively (Fig. 2A, P = 0.289). According to the Brinkman index, the 5-year DFS rates were 52.3% in the high Brinkman index (≥ 800) group and 56.9% in the low Brinkman index (<800) group (Fig. 2B, P = 0.794). Additionally, the 5-year DFS rate was 53.4% in the combination of current smokers and a higher Brinkman index (≥800) group, and 55.8% in the other group (Fig. 2C, P = 0.571). DFS curves for each investigation were not significantly different. The median follow-up period for 234 patients was 43 months. All patients were given thorough anti-smoking instruction in terms of follow-up after surgery.

## DISCUSSION

In the present study, we evaluated the relationship between smoking status and short- and long-term outcomes of patients who underwent TEP for esophageal carcinoma. Our analyses revealed that current smoking or a higher Brinkman index was not a risk factor for postoperative complications. However, the combination of current smoking status and a higher Brinkman index was an independent risk factor for postoperative pneumonia after TEP. According to the long-term outcomes, no significant differences were observed in OS and DFS between each smoking status. Although the problems remain that patients with esophageal carcinoma may refuse to provide real smoking status, we had to build our data from their declarations. We have provided thorough anti-smoking education from the initial visit to follow-up period after surgery. Due to such a education, in terms of follow-up after surgery, there hardly were patients who continued to smoke.

Presently, at multiple institutions, esophagectomy can be performed on patients with esophageal carcinoma using a thoracoscopic approach because a multicenter randomized controlled trial revealed that thoracoscopic esophagectomy resulted in a lower incidence of pulmonary infections after surgery compared with open esophagectomy [10]. However, even with the thoracoscopic approach, past heavy smoking is a risk factor for pulmonary morbidities [18]. In a previous study, smoking within one year of esophagectomy was an independent risk factor for 30-day mortality [8]. Other study reported that the duration of preoperative smoking cessation was necessary to reduce postoperative morbidities [9]. However, only current smoking or a higher Brinkman index were not risk factors for postoperative complications, including pneumonia, in the present study. Therefore, we hypothesized that the effects of a single risk factor would be reduced in when surgery is done in the prone position. Currently, both left lateral decubitus and prone positions have been frequently used during thoracoscopic esophagectomy [19, 20]. Previous studies on the relationship between postoperative complications after thoracoscopic esophagectomy and smoking status were performed in patients treated in the left lateral decubitus position [9, 18]. We previously reported that TEP is less invasive in terms of postoperative respiratory function and reduces postoperative respiratory complications than the left lateral decubitus position [11]. In the prone position, because artificial pneumothorax and gravity improve the operative field view without any compression of the right lung, no mechanical damage occurs. Additionally, the risk of airway secretions flowing into the left lung was lower in the prone position than in the left lateral decubitus position. Moreover, we recently reported that obstructive ventilation failure is also not a risk factor for pneumonia or prognosis in TEP [21].

On the other hand, the combination of current smoking and a higher Brinkman index was an independent risk factor for postoperative pneumonia, even in TEP. Therefore, smoking cessation before affecting esophageal carcinoma is very important. However, six weeks is not sufficient as a period of smoking cessation before surgery. Smoking patients must quit smoking immediately when they are diagnosed with esophageal carcinoma. The standard treatment for patients with locally advanced esophageal carcinoma is neoadjuvant chemoradiotherapy or chemotherapy followed by surgery [22, 23]. Since smoking is contraindicated in neoadjuvant chemoradiotherapy or chemotherapy, patients can be required the duration of smoking cessation before surgery. Additionally, as a premise for smoking cessation, each component of the perioperative care bundle, such as oral hygiene, respiratory training, measurement of physical fitness, swallowing evaluation and rehabilitation, and nutritional support, are essential. These components improve postoperative outcomes after esophagectomy [24]. Thus, we have introduced these components in perioperative management.

Smoking is an established risk factor for esophageal carcinoma; however, little is known about the possible influence of risk factors on survival [5, 7, 25]. In the present study, no correlation was observed between the long-term outcomes and smoking status. Many prognostic factors, such as TNM stage, age, and sex may affect oncological outcomes. In addition, a less invasive approach using TEP may reduce the adverse impact of smoking status on survival. In the future, the prone position will increasingly become principal surgical position during esophagectomy. Regardless of our negative results concerning the long-term outcomes for patients with esophageal carcinoma after TEP, smoking cessation is essential because smoking causes several diseases and cancers [26-28]. Especially, although there is not room for improvement of Brinkman index status, the state of current smoking before surgery could be intervened. The knowledge obtained by this study is very significant for esophageal carcinoma surgery in which the prone position will become principal surgical position.

This study had several limitations. First, this was a single-center retrospective study with a small sample size. However, the surgery quality for all cases was well-controlled by surgeons who were board-certified by the Japan Society for Endoscopic Surgery. Second, these results may not be extrapolated to institutions where open esophagectomy or thoracoscopic esophagectomy is performed in the left lateral decubitus position.

## CONCLUSIONS

The present study demonstrated that the combination of current smoking and heavy smoking history is a risk factor for postoperative pneumonia in patients with esophageal carcinoma, although no correlation was observed between long-term outcomes and smoking status. Smoking cessation and each component of the perioperative care bundle should be considered an important part of esophageal carcinoma treatment.

Acknowledgments

Informed consent was obtained from the patients for the publication of this report and any accompanying data. Patient anonymity was also maintained.

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## Figure legends

**Fig. 1A: Overall survival rates in the current and non-current smoker groups**

The 5-year overall survival rate was 63.3% in the current smoker group. The 5-year overall survival rate was 58.6% in the non-current smoker group. The difference was not significant ($P = 0.290$).

**Fig. 1B: Overall survival rates in the higher (≥800) and lower (<800) Brinkman index groups**

The 5-year overall survival rate was 60.2% in the higher Brinkman index (≥800) group. The 5-year overall survival rate was 60.0% in the lower Brinkman index (<800) group. The difference was not significant ($P = 0.834$).

**Fig. 1C: Overall survival rates in the current smoker and higher Brinkman index (≥800) group and other than them groups**

The 5-year overall survival rate was 64.0% in the current smoker and higher Brinkman index (≥800) group. The 5-year overall survival rate was 59.3% in the other than them group. The difference was not significant ($P = 0.368$).

**Fig. 2A: Disease-free survival rates in the current and non-current smoker groups**

The 5-year disease-free survival rate was 56.6% in the current smoker group. The 5-year disease-free survival rate was 54.4% in the non-current smoker group. The difference was not significant ($P = 0.289$).

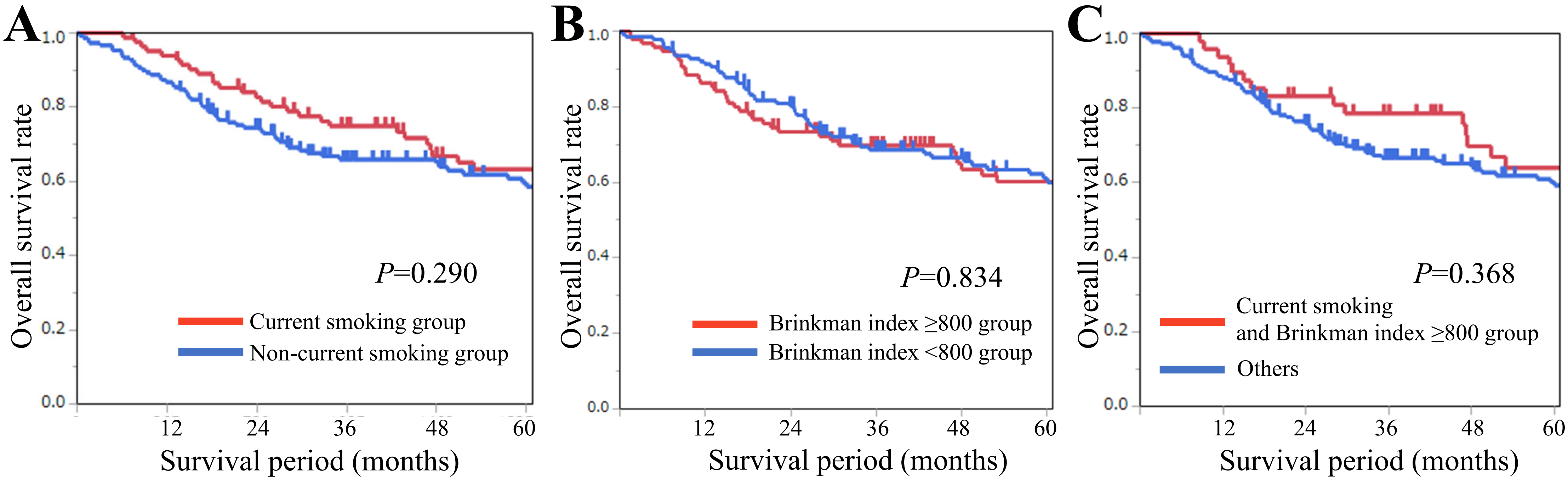
**Fig. 2B: Disease-free survival rates in the higher (≥800) and lower (<800)**

**Brinkman index groups**

The 5-year disease-free survival rate was 52.3% in the higher Brinkman index (≥800) group. The 5-year disease-free survival rate was 56.9% in the lower Brinkman index (<800) group. The difference was not significant ($P$ = 0.794).

**Fig. 2C: Disease-free survival rates in the current smoker and higher Brinkman index (≥800) group and other than them groups**

The 5-year disease-free survival rate was 53.4% in the current smoker and higher Brinkman index (≥800) group. The 5-year disease-free survival rate was 55.8% in the other than them group. The difference was not significant ($P$ = 0.571).

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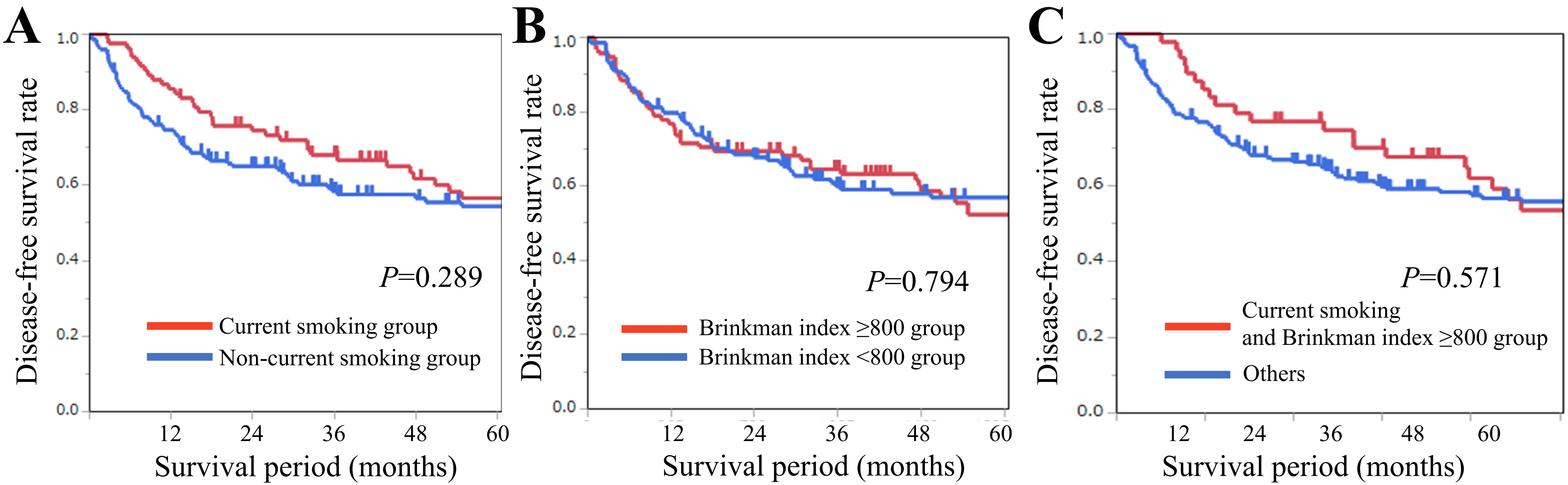


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**Table 1**：Comparison of current and non-current smoking patients who underwent thoracoscopic esophagectomy in prone position

| Parameters | | Non-current (n=151) | Current (n=83) | *P* value |
|---|---|---|---|---|
| Age (years) | | 67 (40-81) | 63 (42-79) | 0.001 |
| Sex | Male / Female | 127 (84%) / 24 (16%) | 71 (86%) / 12 (14%) | 0.851 |
| Body mass index | | 21.9 (15.3-29.1) | 20.3 (13.1-28.1) | <0.001 |
| Tumor location | Ut | 26 (17%) | 10 (12%) | 0.544 |
| | Mt | 75 (50%) | 42 (51%) | |
| | Lt | 50 (33%) | 31 (37%) | |
| Tumor depth (clinical) | cT1 | 62 (41%) | 35 (42%) | 0.943 |
| | cT2 | 22 (15%) | 13 (16%) | |
| | cT3 | 67 (44%) | 35 (42%) | |
| Nodal status (clinical) | cN- / cN+ | 50 (33%) / 101 (67%) | 27 (33%) / 56 (67%) | 1.000 |
| UICC-Stage (clinical) | I | 56 (37%) | 31 (37%) | 0.943 |
| | II | 37 (25%) | 23 (28%) | |
| | III | 52 (34%) | 26 (31%) | |
| | IV | 6 (4%) | 3 (4%) | |
| Histological type | SCC / Adeno | 142 (94%) / 9 (6%) | 79 (95%) / 4 (5%) | 1.000 |
| Neoadjuvant chemotherapy | Yes / No | 111 (66%) / 58 (34%) | 71 (65%) / 38 (35%) | 1.000 |
| Operative time (min) | | | | |
| Overall procedure | | 688 (461-963) | 702 (354-1361) | 0.539 |
| Thoracic procedure | | 317 (198-540) | 320 (207-523) | 0.867 |
| Blood loss (ml) | | 234 (0-1320) | 259 (0-2605) | 0.888 |
| Abdominal procedure | Laparoscopy / Open | 119 (79%) / 32 (21%) | 64 (77%) / 19 (23%) | 0.869 |
| Conduit | Stomach / Jejunum | 144 (95%) / 7 (5%) | 79 (95%) / 4 (5%) | 1.000 |
| Lymph node | Two- / Three- | 108 (72%) / 43 (28%) | 57 (69%) / 26 (31%) | 0.656 |

| | | | | |
|---|---|---|---|---|
| dissection | field | | | |
| Postoperative hospital stay (days) | | 37 (15-296) | 41 (14-257) | 0.559 |
| Complications[a] | Pneumonia | 21 (13.9%) | 13 (15.7%) | 0.703 |
| | Recurrent laryngeal nerve palsy | 12 (7.9%) | 11 (13.2%) | 0.251 |
| | Anastomotic leakage | 22 (14.6%) | 18 (21.7%) | 0.204 |
| Mortality | | 1 (0.6%) | 0 | 1.000 |
| UICC-Stage (pathological) | 0 | 4 (3%) | 2 (2%) | 0.406 |
| | I | 48 (32%) | 33 (40%) | |
| | II | 45 (30%) | 27 (33%) | |
| | III | 34 (22%) | 16 (19%) | |
| | IV | 20 (13%) | 5 (6%) | |

SCC: Squamous cell carcinoma; Adeno: Adenocarcinoma

a Based on the Clavien-Dindo classification, grade II or higher [17]

**Table 2**：Comparison of the patients with the Brinkman index who underwent thoracoscopic esophagectomy in prone position

| Parameters | | Brinkman index <800 (n=139) | Brinkman index ≥800 (n=95) | *P* value |
|---|---|---|---|---|
| Age (years) | | 65 (40-81) | 67 (44-79) | 0.145 |
| Sex | Male / Female | 111 (80%) / 28 (20%) | 87 (92%) / 8 (8%) | 0.016 |
| Body mass index | | 21.4 (13.1-29.1) | 21.2 (15.5-28.1) | 0.645 |
| Tumor location | Ut | 18 (13%) | 18 (19%) | 0.454 |
| | Mt | 72 (52%) | 45 (47%) | |
| | Lt | 49 (35%) | 32 (34%) | |
| Tumor depth (clinical) | cT1 | 59 (42%) | 38 (40%) | 0.581 |
| | cT2 | 18 (13%) | 17 (18%) | |
| | cT3 | 62 (45%) | 40 (42%) | |
| Nodal status (clinical) | cN- / cN+ | 68 (49%) / 71 (51%) | 47 (49%) / 48 (51%) | 1.000 |
| UICC-Stage (clinical) | I | 50 (36%) | 37 (39%) | 0.498 |
| | II | 40 (29%) | 20 (21%) | |
| | III | 45 (32%) | 33 (35%) | |
| | IV | 4 (3%) | 5 (5%) | |
| Histological type | SCC / Adeno | 129 (93%) / 10 (7%) | 92 (97%) / 3 (3%) | 0.250 |
| Neoadjuvant chemotherapy | Yes / No | 92 (66%) / 47 (34%) | 65 (68%) / 30 (32%) | 0.778 |
| Operative time (min) | | | | |
| Overall procedure | | 696 (354-1215) | 689 (471-1361) | 0.348 |
| Thoracic procedure | | 320 (198-523) | 315 (207-540) | 0.389 |
| Blood loss (ml) | | 240 (0-2605) | 248 (0-1680) | 0.506 |
| Abdominal procedure | Laparoscopy / Open | 114 (82%) / 25 (18%) | 69 (73%) / 26 (27%) | 0.107 |
| Conduit | Stomach / Jejunum | 133 (96%) / 6 (4%) | 90 (95%) / 5 (5%) | 0.761 |
| Lymph node dissection | Two- / Three-field | 98 (71%) / 41 (29%) | 67 (71%) / 28 (29%) | 1.000 |

| | | | | |
|---|---|---|---|---|
| Postoperative hospital stay (days) | | 35 (14-168) | 44 (15-296) | 0.016 |
| Complications[a] | Pneumonia | 15 (10.8%) | 19 (20.0%) | 0.059 |
| | Recurrent laryngeal nerve palsy | 10 (7.2%) | 13 (13.7%) | 0.120 |
| | Anastomotic leakage | 20 (14.4%) | 20 (21.1%) | 0.217 |
| Mortality | | 1 (0.7%) | 0 | 1.000 |
| UICC-Stage (pathological) | 0 | 3 (2%) | 3 (3%) | 0.090 |
| | I | 44 (32%) | 37 (39%) | |
| | II | 44 (32%) | 28 (29%) | |
| | III | 37 (26%) | 13 (14%) | |
| | IV | 11 (8%) | 14 (15%) | |

SCC: Squamous cell carcinoma; Adeno: Adenocarcinoma

a Based on the Clavien-Dindo classification, grade II or higher [17]

**Table 3**：Comparison of high Brinkman index, current smoking patients and others who underwent thoracoscopic esophagectomy in prone position

| Parameters | | Current and Brinkman index ≥800 (n=48) | Others (n=186) | *P* value |
|---|---|---|---|---|
| Age (years) | | 66 (53-79) | 66 (40-81) | 0.542 |
| Sex | Male / Female | 45 (94%) / 3 (6%) | 153 (82%) / 33 (18%) | 0.070 |
| Body mass index | | 20.9 (15.5-28.1) | 21.4 (13.1-29.1) | 0.110 |
| Tumor location | Ut | 7 (15%) | 29 (16%) | 0.396 |
| | Mt | 28 (58%) | 89 (48%) | |
| | Lt | 13 (27%) | 68 (36%) | |
| Tumor depth (clinical) | cT1 | 24 (50%) | 73 (39%) | 0.402 |
| | cT2 | 6 (13%) | 29 (16%) | |
| | cT3 | 18 (37%) | 84 (45%) | |
| Nodal status (clinical) | cN- / cN+ | 24 (50%) / 24 (50%) | 91 (49%) / 95 (51%) | 1.000 |
| UICC-Stage (clinical) | I | 19 (40%) | 68 (36%) | 0.978 |
| | II | 12 (25%) | 48 (26%) | |
| | III | 15 (31%) | 63 (34%) | |
| | IV | 2 (4%) | 7 (4%) | |
| Histological type | SCC / Adeno | 47 (98%) / 1 (2%) | 174 (94%) / 12 (6%) | 0.477 |
| Neoadjuvant chemotherapy | Yes / No | 32 (67%) / 16 (33%) | 125 (67%) / 61 (33%) | 1.000 |
| Operative time (min) | | | | |
| Overall procedure | | 705 (471-1361) | 690 (354-1215) | 0.516 |
| Thoracic procedure | | 322 (207-491) | 318 (198-540) | 0.816 |
| Blood loss (ml) | | 257 (0-1680) | 239 (0-2605) | 0.418 |
| Abdominal procedure | Laparoscopy / Open | 36 (75%) / 12 (25%) | 147 (79%) / 39 (21%) | 0.559 |

| | | | | |
|---|---|---|---|---|
| Conduit | Stomach / Jejunum | 45 (94%) / 3 (6%) | 178 (96%) / 8 (4%) | 0.701 |
| Lymph node dissection | Two- / Three-field | 31 (65%) / 17 (35%) | 134 (72%) / 52 (28%) | 0.375 |
| Postoperative hospital stay (days) | | 50 (15-296) | 35 (14-168) | 0.196 |
| Complications[a] | Pneumonia | 12 (25.0%) | 22 (11.8%) | 0.036 |
| | Recurrent laryngeal nerve palsy | 8 (16.7%) | 15 (8.1%) | 0.099 |
| | Anastomotic leakage | 11 (22.9%) | 29 (15.6%) | 0.281 |
| Mortality | | 0 | 1 (0.5%) | 1.000 |
| UICC-Stage (pathological) | 0 | 1 (2%) | 5 (2%) | 0.166 |
| | I | 23 (48%) | 58 (31%) | |
| | II | 15 (31%) | 57 (31%) | |
| | III | 6 (13%) | 44 (24%) | |
| | IV | 3 (6%) | 22 (12%) | |

SCC: Squamous cell carcinoma; Adeno: Adenocarcinoma

a Based on the Clavien-Dindo classification, grade II or higher [17]

**Table 4**：Multivariate analysis of postoperative pneumonia (Clavien-Dindo classification, grade II or higher)

| Parameters | | Odds Ratio (95% CI) | *P* value |
|---|---|---|---|
| Age | | 0.98 (0.93-1.03) | 0.413 |
| Sex, male | | 0.34 (0.07-1.63) | 0.135 |
| Body mass index | | 1.07 (0.93-1.23) | 0.329 |
| Tumor depth (clinical) | | | 0.990 |
| | cT1 | 1.000 | |
| | cT2 | 0.95 (0.24-3.69) | 0.944 |
| | cT3 | 0.97 (0.34-2.73) | 0.951 |
| Nodal status (clinical), positive | | 1.04 (0.39-2.81) | 0.931 |
| Neoadjuvant chemotherapy, yes | | 0.87 (0.24-3.31) | 0.872 |
| Abdominal procedure, Laparoscopy | | 0.81 (0.31-2.18) | 0.683 |
| Thoracic operative time | | 0.99 (0.99-1.01) | 0.889 |
| Blood loss | | 0.99 (0.99-1.01) | 0.182 |
| Current smoker and Brinkman index ≥800 | | 0.41 (0.18-0.93) | 0.037 |

CI: Confidence interval