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Title: Effects of preoperative psoas muscle index and body mass index on postoperative outcomes after video-assisted esophagectomy for esophageal cancer

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Abstract

Introduction: Preoperative psoas muscle index and body mass index are relevant to postoperative outcomes. We investigated the associations of psoas muscle index, body mass index, and preoperative nutritional and muscular score with postoperative outcomes in patients with esophageal cancer who underwent video-assisted surgery.

Methods: We examined 150 patients (124 men, 26 women) who underwent video-assisted esophagectomy from February 2002 to March 2016. We used the Clavien-Dindo classification to analyze postoperative complications. Because skeletal muscle volume differs significantly between male and female patients, all analyses were performed separately. In male patients, we used the following cut-off values to categorize patients into three groups: psoas muscle index (PMI) = 600 mm^2/m^2, body mass index (BMI) = 18.5 kg/m^2, and preoperative nutritional and muscular (PNM) scores 0 to 2.

Results: Two patients were converted to open thoracotomy. Among male patients, PMI and PNM scores were significant risk factors for complications. Among male patients, in the high PMI group, the number of CD ≥ IIIa complications was significantly lower. In the PNM Score 0 group (both PMI and BMI values exceeded the cut-off values), the number of complications was significantly lower. In both sexes, PMI and BMI were not significantly associated with survival.

Conclusions: PMI and PNM score can be useful for predicting postoperative outcomes in male patients with esophageal cancer having undergone video-assisted surgery.

Key Words: esophageal cancer, preoperative nutritional and muscular score, sarcopenia

Introduction

Esophageal cancer (EC) is the seventh most common cancer and the sixth leading cause of death among cancers worldwide[1]. Esophagectomy for EC is an invasive gastrointestinal surgery. Takeuchi et al. reported that the morbidity rate after esophagectomy was 42.8%.[2] The prognosis of EC also remains poor, in spite of the advancement of therapeutic strategies. Thus, comprehensive interventions are needed to improve postoperative outcomes after esophagectomy for EC.

Preoperative skeletal muscle volume is related to short- and long-term outcomes after esophagectomy for EC.[3–5] The skeletal muscle volume of the whole body correlates with the psoas muscle index (PMI), which is calculated by measuring the psoas muscle mass on computed tomography (CT) images of the cross-sectional area at the third lumbar vertebra and normalizing it to height (m^2) [6].

We previously reported that low preoperative PMI among patients was associated with postoperative complications and low overall survival (OS) after esophagectomy.[7] However, the same association did not apply for female patients. We also proposed that the cut-off points of preoperative PMI and body mass index (BMI) to predict postoperative outcomes in male patients were 600 mm^2/m^2 and 18.5 kg/m^2, respectively. We proposed a new score, known as Preoperative Nutritional and Muscular (PNM) score, which comprises the PMI and BMI cutoff values described above. We showed that the PNM score was significantly correlated with postoperative complications and survival after esophagectomy for EC in male patients and demonstrated that it could be useful as a new risk score. However, the difference of surgical approaches was a limitation because of the low rate of thoracoscopic surgery (33%) in the previous study.

Video-assisted thoracoscopic surgery (VATS) is performed in many institutions because of its lower degree of invasion, lower hemorrhage rates, safety, and lower pulmonary complication rates.[8] We have been performing VATS esophagectomy since 1996. In the present study, we showed the effects of preoperative skeletal muscle volume and body mass index on postoperative outcomes after video-assisted esophagectomy for EC.

Materials and Methods

Patients

From February 2002 to March 2016, 150 consecutive patients underwent radical video-assisted esophagectomy at our institution. We performed hand-assisted thoracoscopic surgery (HATS)[9] as a standard procedure and mediastinoscopic transhiatal esophagectomy (MATHE)[10] as a less-invasive procedure from 2002 to 2011. We performed prone-position video-assisted esophagectomy (PPE) since 2012. Two patients who converted to open surgery owing to tumor invasion of the main organs were included in the analysis. Patients diagnosed with a definitive cT4b (invasion to other organs), distant metastasis, severe organ dysfunction, or had a score of 3–4 on the ECOG (Eastern Cooperative Oncology Group) Score of Performance Status[11] were excluded from surgical intervention. We performed a retrospective analysis using cross-sectional CT of the psoas muscle at the third lumbar vertebral level imaged just before the operations. The clinical characteristics of patients were retrospectively gained from medical records. This study was approved by the institutional review board of Hokkaido University Hospital (Authorization number: 011-0135), and informed consent was gained from all patients.

PMI and BMI

The cross-sectional area of the psoas muscle mass at the third lumbar vertebral level was measured by manual tracing on CT scans obtained from the electronic medical record system “MegaOakHR” (NEC Corporation, Tokyo Japan). PMI (expressed as mm^2/m^2) was calculated by normalizing the psoas muscle area by the square of height (m^2). BMI was calculated by dividing preoperative weight (kg) by the square of height (m^2).

Statistical analysis

Continuous variables are reported as median (range) and analyzed using the Mann–Whitney U test to compare two groups without setting a cut-off value. Categorical variables were analyzed using the chi-square test. Multivariate analysis of postoperative complications was performed using a logistic regression model. Postoperative complications were classified using the Clavien–Dindo (CD) classification.[12]

Survival analyses were performed for overall survival (OS) and recurrence-free survival (RFS) using a Cox proportional hazard model. The validation analysis was performed using the chi-square and log-rank test. All statistical analyses were performed using the EZR software, version 1.35 (Saitama Medical Center, Jichi Medical University, Saitama, Japan).[13]

Results

Patient characteristics

The clinical characteristics of the patients are displayed in Table 1. We included a total of 124 males and 26 females. Operative approaches included HATS (n = 69), PPE (n = 64), MATHE (n = 12), laparoscopic transhiatal lower esophagectomy (LTE) (n = 3) and converted open thoracotomy (n = 2). Reconstruction routes were posterior mediastinal (n = 81), retrosternal (n = 43), and subcutaneous (n = 26). Conduits used for the reconstruction were the gastric tube (n = 140) and other sources (n = 10). The rates of drinking alcoholand smoking were significantly higher in male patients than in female patients ($p = 0.04$ and $p < 0.01$, respectively) (Table 1). PMI was significantly lower in female patients ($p < 0.01$). Furthermore, the percent predicted forced expiratory volume one second (FEV1%) was better in female patients ($p < 0.01$).

Three-year OS and RFS rates were better for female patients, but the difference was not significant (male vs. female: OS: 60% vs. 78%, $p = 0.53$; RFS: 51% vs. 57%, $p = 0.71$). We analyzed postoperative complications and survival separately for each sex because of differences in PMI and other parameters.

Analyses of postoperative complications

Postoperative complications categorized using the CD classification were as follows: no complication, 37% (n = 56); CD I: 9% (n = 13); CD II: 17% (n = 25); CD IIIa: 22% (n = 33); CD IIIb: 5% (n = 8); CD IVa: 7% (n = 11); CD IVb: 1% (n = 1), and CD V: 2% (n = 3). The major postoperative complications were anastomotic leakage (15%, n = 22), pneumonia (26%, n = 39), and recurrent nerve palsy (21%, n = 32).

Postoperative complications reported according to sex are shown in Table 2. Age was lower ($p < 0.01$), PMI was higher ($p < 0.01$), and percentage vital capacity (%VC) was better ($p = 0.04$) in male patients in the CD≤ II group than in the CD ≥IIIa group. Multivariate analysis showed that PMI (OR: 0.995, 95% CI: 0.991–0.998, $p < 0.01$) and subcutaneous reconstruction (OR: 3.00, 95% CI: 1.00–8.96, $p = 0.04$) were independent risk factors. Only %VC was significantly in female patients in the CD ≤II group better than in the CD ≥IIIa group.

OS and RFS analysis

The results of survival analysis are shown in Table 3. Univariate analysis of male OS showed that %VC ($p < 0.01$), intraoperative bleeding ($p = 0.02$), and a pathological stage (pStage) between 2 and 4 ($p < 0.01$) were significantly different among groups. Multivariate analysis showed that %VC (HR: 0.97, 95% CI: 0.95–0.99, $p < 0.01$), intraoperative bleeding (HR: 1.001, 95% CI: 1.000–1.001, $p = 0.02$), and pStage between 2 and 4 (HR: 2.55, 95% CI: 1.14–5.70, $p = 0.02$) were independent prognostic factors, whereas PMI was not associated with male OS.

Univariate analysis of female OS showed that %VC and CD ≥IIIa complications were significant prognostic factors. However, neither of them was significant factors on multivariate analysis.

RFS analyses of both of male and female showed the same tendencies as OS analyses. PMI and BMI were not associated with RFS.

Analyses of PMI and BMI status to postoperative short- and long-term outcomes

We previously reported that the cut-off point of PMI and BMI in male patients should be set at 600 mm^2/m^2 and 18.5 kg/m^2, respectively.[7] The analysis of the PMI and the BMI status, and outcomes are displayed in Table 4. PMIs of three patients could not be calculated because preoperative CT had not been performed in those patients.

In the high PMI group, the rate of postoperative complications (CD ≥IIIa) was significantly lower (high vs. low PMI group: 19% vs. 51%, $p < 0.01$). The three-year OS and RFS were better in the high PMI group than in the low PMI group, although they were not significantly different (high vs. low PMI group; OS: 64% vs. 58%, $p = 0.25$; RFS: 62% vs. 43%, $p = 0.08$).

Postoperative complications were not found to be different in the high or low BMI groups. The three-year OS and RFS were better in the high BMI group than in the low group, although they were not significantly different (high vs. low BMI group; OS: 63% vs. 34%, $p = 0.09$; RFS: 54% vs. 15%, $p = 0.05$).

Analysis of preoperative nutritional and muscular (PNM) score

In male patients, PNM score was derived using the following rule: male patients were allocated 1 point if their BMI was less than 18.5 kg/m^2 and 1 point if their PMI was below 600 mm^2/m^2 (a possible maximum total of 2 points).[7] We proposed the PNM score based on which we categorized male patients into low risk (0 points), moderate risk (1 point), or high risk (2 points) groups, as mentioned previously,[7] We validated the grouping by performing a chi-square test and log-rank test. The result of the PMN validation is shown in Table 5. Postoperative complications (CD ≥IIIa) were significantly less in the low-risk group than in the other group (PNM score 0 vs. 1/2: 17% vs. 55%, $p < 0.01$). In the low-risk group, OS and RFS were better than the other group, although the difference was not statistically significant (PNM score 0 vs. 1/2; OS: 65% vs.58%, $p = 0.28$; RFS: 62% vs. 42%, $p = 0.10$).

Discussion

Recent studies reported that preoperative skeletal muscle volume is related to postoperative outcomes after different type of surgeries.[14–22] Despite the importance of sarcopenia being well known, there are no appropriate cut-off point for various diseases. Previously, in a different cohort from that of this study, we showed that PMI and SMI were correlated, and we could easily infer skeletal muscle mass by measuring the PMI in EC patients. We also reported that, in male patients, the optimal cut-off points to predict short- and long-term outcomes should be 600 mm^2/m^2. We also reported that the PNM score, which comprises a combination of PMI and BMI cut-off points, is a useful predictor for postoperative outcomes in EC patients.[7] In the present study, by analyzing a different cohort of patients who had undergone video-assisted surgery, we validated the 600 mm^2/m^2 cut-off point and further confirmed that PMI is associated with postoperative complications in male patients.

In this cohort, the number of male patients with BMI < 18.5 kg/m^2 was 12 (10%), and the number of patients with PNM scores of 2 was 9 (7%). By contrast, in the previous study, the number of male patients with a BMI < 18.5 kg/m^2 was 46 (12%), and the number of patients with PNM scores of 2 was 42 (11%). Because the number of patients with a low BMI was small, statistical analysis based on BMI status could be underpowered in this study. This might be the same reason why the ability of PNM score to predict survival was not confirmed in this study, though it was helpful to expect postoperative complications.

In female patients, PMI and BMI were not useful predictive factors for postoperative outcomes as they were in our previous study. The Asian Working Group for Sarcopenia criteria consists of muscle mass, muscle strength (grip), and physical performance (walking) measurement.[23] In male patients, the skeletal muscle volume may be dependent on male sex hormones which decline with aging. Therefore, the decrease of skeletal muscle volume in female might not be strongly related with aging as it does in male. In addition, in female patients, sarcopenia tends to decrease the muscle strength and lower physical performance, rather than skeletal muscle volume.[24] Consequently, we concluded that the analysis of the skeletal muscle volume could not be helpful to predict postoperative risks in female patients who undergo the operation.

Our study had some limitations. First, the diagnosis of sarcopenia was performed by assessing only the muscle mass. As mentioned before, the diagnosis of sarcopenia normally requires the assessment of the speed of gait, grip, and muscle volume measured by dual-energy X-ray absorptiometry (DXA) or bioelectrical analysis (BIA). Nevertheless, in this study, we used only PMI which expresses the skeletal muscle volume of the whole body. We could not calculate the speed of gate and grip because this study was retrospective Second, the number of female patients of our study was so small that powerful statistical analysis could not be performed. Further investigations are necessary to evaluate the risk of sarcopenia and malnutrition in female patients. Third, all patients in this study underwent video-assisted surgery. Although PNM score was relevant to postoperative complications and not relevant to survival in this study, it was not clear whether the difference of surgical approach influenced the result. Further investigations of the influences of various surgical approaches are necessary.

In conclusion, we found that, in male patients who underwent video-assisted esophagectomy, PMI was associated with postoperative complications and confirmed that a PMI cut-off point of 600 mm^2/m^2 and the PNM score can predict postoperative complications.

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None

Conflict of Interest

None.

Ethical Considerations

This study was approved by the institutional review board of Hokkaido University Hospital (Authorization number: 011-0135), and informed consent was obtained from all patients.

Informed Consent

Informed Consent was obtained from all the patients.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Yamamoto S, Kato K. Immuno-oncology for esophageal cancer. Future Oncol. 2020; 16: 2673-2681.
2. Takeuchi H, Miyata H, Ozawa S, et al. Comparison of short-term outcomes between open and minimally invasive esophagectomy for esophageal cancer using a nationwide database in Japan. *Ann Surg Oncol*. 2017 Jul 1;24(7): 1821–7.
3. Boshier PR, Heneghan R, Markar SR, Baracos VE, Low DE. Assessment of body composition and sarcopenia in patients with esophageal cancer: a systematic review and meta-analysis. *Dis Esophagus*. 2018 Aug;31(8):1–11.
4. Nakashima Y, Saeki H, Nakanihi R, et al. Assessment of sarcopenia as a predictor of poor outcomes after esophagectomy in elderly patients with esophageal cancer. *Ann Surg*. 2018 Jun 1;267(6): 1100–4.
5. Deng HY, Zha P, Peng L, Hou L, Huang KL, Li XY. Preoperative sarcopenia is a predictor of poor prognosis of esophageal cancer after esophagectomy: a comprehensive systematic review and meta-analysis. *Dis Esophagus*. 2019 Mar;32(3): 1–10.
6. Hamaguchi Y, Kaido T, Okumura S, et al. Proposal for new diagnostic criteria of low skeletal muscle mass based on computed tomography imaging in Asian adults. *Nutrition*. 2016 Nov 1;32(11-12): 1200–5.
7. Shichinohe T, Uemura S, Hirano S, Hosokawa M. The impact of preoperative skeletal muscle mass, and nutritional status on short-term and long-term outcomes after esophagectomy for esophageal cancer: A retrospective observational study. *Ann Surg Oncol*. 2019 May 15;26(5): 1301–10.
8. Shichinohe T, Hirano S, Kondo S. Video-assisted esophagectomy for esophageal cancer. *Surg Today.* 2008 Mar 1;38(3): 206–13.
9. Okushiba S, Ohno K, Itoh K, et al. Hand-assisted endoscopic esophagectomy for esophageal cancer. *Surg Today*. 2003 Feb 1;33(2): 158–61.

10. Noguchi T, Shichinohe T, Hirano S, Kondo S. Minimally invasive esophagectomy for cancer patients with low pulmonary function. *Hepatogastroenterology*. 2010;57(101): 768–71.

11. Cancer Therapy Evaluation Program. Common Toxicity Criteria, Version 2.0 (Published Date April 30, 1999). Available from: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/ctcv20_4-30-992.pdf#search=%278.+Cancer+Therapy+Evaluation+Program.+Common+Toxicity+Criteria%27

12. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004 Aug;240(2): 205–13.

13. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. *Bone Marrow Transplant*. 2013 Mar;48(3): 452–8.

14. Oguma J, Ozawa S, Kazuno A, Yamamoto M, Ninomiya Y, Yatabe K. Prognostic significance of sarcopenia in patients undergoing esophagectomy for superficial esophageal squamous cell carcinoma. *Dis Esophagus*. 2019 Jul;32(7): 1–9.

15. Matsunaga T, Miyata H, Sugimura K, et al. Prognostic significance of sarcopenia and systemic inflammatory response in patients with esophageal cancer. *Anticancer Res*. 2019 Jan 1;39(1): 449–58.

16. Deng HY, Zha P, Peng L, Hou L, Huang KL, Li XY. Preoperative sarcopenia is a predictor of poor prognosis of esophageal cancer after esophagectomy: a comprehensive systematic review and meta-analysis. *Dis Esophagus*. 2019 Mar;32(3): 1–10.

17. Soma D, Kawamura YI, Yamashita S, et al. Sarcopenia, the depletion of muscle mass, an independent predictor of respiratory complications after oncological esophagectomy. *Dis Esophagus*. 2019 Mar;32(3): 1–8.

18. Boshier PR, Heneghan R, Markar SR, Baracos VE, Low DE. Assessment of body composition and sarcopenia in patients with esophageal cancer: a systematic review and meta-analysis. *Dis Esophagus*. 2018 Aug;31(8): 1–11.

19. Nishigori T, Okabe H, Tanaka E, Tsunoda S, Hisamori S, Sakai Y. Sarcopenia as a predictor of pulmonary complications after esophagectomy for thoracic esophageal cancer. *J Surg Oncol*. 2016 May;113(6): 678–84.

20. Kasahara R, Kawahara T, et al. A low psoas muscle index before treatment can predict a poorer prognosis in advanced bladder cancer patients who receive gemcitabine and nedaplatin therapy. *Biomed Res Int*. 2017; 7981549.

21. Tsutsumi S, Kawahara T, Teranishi JI, Yao M, Uemura H. A low psoas muscle volume predicts longer hospitalization and cancer recurrence in upper urinary tract urothelial carcinoma. *Mol Clin Oncol*. 2018 Feb 1;8(2): 320–22.

22. Liu J, Motoyama S, Sato Y, Wakita A, Kawakita Y, Saito H. Decreased skeletal muscle mass after neoadjuvant therapy correlates with poor prognosis in patients with esophageal cancer. *Anticancer Res*. 2016 Dec 1;36(12): 6677–85.

23. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc*. 2014 Feb 1;15(2): 95–101.

24. Sanada K, Miyachi M, Tanimoto M, et al. A cross-sectional study of sarcopenia in Japanese men and women; reference values and association with cardiovascular risk factors. *Eur J Appl Physiol*. 2010 Sep 1;110(1): 57–65.

Table 1. Patient background, postoperative complications, and survival by sex
PMI was significantly higher in male patients than female. Pneumonia occurred more in male patients than female.

Variable	Category	Male (n = 124)	Female (n = 26)	*p*
Age (year)		66 (48-85)	64 (25-82)	0.57
Alcohol	+	37 (31%)	3 (12%)	0.04*
Smoking	+	94 (80%)	13 (50%)	<0.01*
DM	+	13 (13%)	3 (12%)	0.89
HT	+	39 (39%)	7 (28%)	0.29
BMI (kg/m^2)		22.0 (14.1-30.7)	20.4 (15.8-27.2)	0.17
PMI (mm^2/m^2)		536 (251-1037)	335 (183-616)	<0.01*
%VC		107 (70-149)	106 (76-131)	0.84
FEV1.0%		71 (23-98)	90 (62-106)	<0.01*
NAC	+	30 (26%)	6 (23%)	0.75
Tumor location	Ce	4 (3%)	1 (4%)	0.87
	Ut	25 (20%)	4 (15%)	
	Mt	46 (37%)	12 (46%)	
	Lt	39 (32%)	8 (31%)	
	Ae	10 (8%)	1 (4%)	
cStage	0,1	41 (34%)	8 (31%)	0.78
	2,3,4	81 (66%)	18 (69%)	
Bleeding (g)		560 (15-2900)	270 (5-1470)	0.09
Operative time (m)		592 (333-1220)	554 (360-808)	0.07
Conduit	gastric tube	114 (92%)	26 (100%)	0.13
	others	10 (8%)	0	
Approach	HATS	56 (45%)	13 (50%)	0.75
	PPE	52 (42%)	12 (46%)	
	MATHE	11 (9%)	1 (4%)	
	LTE	3 (3%)	0	
	open	2 (1%)	0	
Anastomotic leakage	+	19 (16%)	3 (11%)	0.53
Pneumonia	+	36 (31%)	3 (12%)	0.04
Recurrent nerve palsy	+	29 (25%)	3 (12%)	0.13
CD≥IIIa	+	50 (40%)	6 (23%)	0.1
3y OS		60%	78%	0.53
3y RFS		51%	57%	0.71

DM: diabetes mellitus; HT: hypertension; BMI: body mass index; PMI: psoas muscle index; %VC: percentage of vital capacity; FEV1.0%: forced expiratory volume percentage in one second; NAC: neoadjuvant chemotherapy; HATS: hand-assisted thoracoscopic surgery; PPE: prone-position video-assisted esophagectomy; MATHE: mediastinoscopic transhiatal esophagectomy; LTE: laparoscopic transhiatal lower esophagectomy; open: open converted thoracotomy; CD: clavien-dindo; OS: overall survival; RFS; recurrence-free survival
* statistically significant

Table 2. Analyses of postoperative complications in male and female patients

In male patients, PMI and antethoracic reconstruction were multivariate factors. In female patients, only %VC was different.

Variable	Category	Male						Female		
		Univariate			Multivariate			Univariate		
		CD ≤ II (n =74)	CD ≥ IIIa (n = 50)	*p*	OR	95% CI	*p*	CD ≤ II (n = 20)	CD ≥ IIIa (n = 6)	*p*
Age (year)		65 (48-80)	69 (48-85)	<0.01*	1.05	0.99-1.11	0.12	63 (47-82)	68.5 (25-76)	0.5
Alcohol	+	23 (32%)	14 (30%)	0.8				3 (16%)	0	0.55
Smoking	+	67 (93%)	40 (87%)	0.27				12 (63%)	1 (17%)	0.07
DM	+	7 (12%)	6 (15%)	0.69				2 (11%)	1 (17%)	1
HT	+	22 (37%)	17 (43%)	0.6				4 (21%)	3 (50%)	0.3
BMI (kg/m^2)		22.1 (15.1-30.7)	21.2 (14.1-27.6)	0.69				20.2 (15.8-26.1)	22.0 (19.3-27.2)	0.22
PMI (mm^2/m^2)		593 (289-1037)	500 (251-758)	<0.01*	0.995	0.992-0.998	<0.01*	348 (250-616)	319 (183-404)	0.25
%VC		114 (79-149)	105 (70-141)	0.04*	0.99	0.96-1.01	0.38	115 (89-131)	91 (76-116)	<0.01*
FEV1.0%		72 (36-90)	70 (23-98)	0.83				79 (62-106)	79 (69-87)	0.73
NAC	+	16 (23%)	14 (31%)	0.33				5 (25%)	1 (17%)	1
Tumor location	Ce	3 (4%)	1 (2%)	0.49				0	0	0.86
	Ut	14 (21%)	8 (20%)					3 (16%)	1 (20%)	
	Mt	21 (32%)	19 (46%)					8 (42%)	3 (60%)	
	Lt	21 (32%)	11 (27%)					7 (37%)	1 (20%)	
	Ae	7 (11%)	2 (5%)					1 (5%)	0	
cStage	2,3,4	38 (63%)	30 (70%)	0.96				14 (74%)	3 (50%)	0.34
Bleeding (g)		680 (40-2660)	400 (15-2900)					270 (5-7340)	465 (35-1470)	0.87
Operative time (m)		586 (333-1220)	603 (363-1062)	0.11				547 (388-808)	578 (360-802)	0.68
Conduit	gastric tube	70 (95%)	44 (88%)	0.55				19 (76%)	6 (24%)	
	others	4 (5%)	6 (12%)	0.19				0	0	
Approach	HATS	39 (53%)	17 (34%)	0.15				10 (50%)	3 (50%)	0.35
	PPE	25 (34%)	27 (54%)					10 (50%)	2 (33%)	
	MATHE	6 (8%)	5 (10%)					0	1 (17%)	
	LTE	2 (2.5%)	1 (2%)					0	0	
	open	2 (2.5%)	0					0	0	

CD: clavien-dindo; OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; HT: hypertension; BMI: body mass index; PMI: psoas muscle index; %VC: percentage of vital capacity; FEV1.0%: forced expiratory volume percentage in one second; NAC: neoadjuvant chemotherapy; HATS: hand-assisted thoracoscopic surgery; PPE: prone-position video-assisted esophagectomy; MATHE: mediastinoscopic transhiatal esophagectomy; LTE: laparoscopic transhiatal lower esophagectomy; open: open converted thoracotomy

* statistically significant

Table 3. Analyses of survival in male and female patients

PMI wasn't different in both male and female patients.

		OS												RFS								
		Male						Female						Male						Female		
Variable	Category	Univariate			Multivariate			Univariate			Multivariate			Univariate			Multivariate			Univariate		
		HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*P*	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*
Age (year)		1.02	0.97-1.07	0.47				0.95	0.90-1.01	0.11				1	0.96-1.04	0.92				0.99	0.95-1.06	0.99
Alcohol	+	1.03	0.50-2.14	0.93										1.03	0.53-1.96	0.94						
Smoking	+	0.53	0.18-1.50	0.23				0.38	0.07-1.98	0.25				0.32	0.14-0.72	<0.01*	0.27	0.12-0.62	<0.01*	1.08	0.31-3.76	0.9
DM	+	1.53	0.53-4.42	0.43				3.34	0.34-32.4	0.3				1.29	0.50-3.32	0.6				4.92	0.89-27.2	0.07
HT	+	0.81	0.37-1.78	0.59				2.78	0.50-15.6	0.25				0.85	0.43-1.68	0.64				1.26	0.26-6.06	0.77
BMI		0.92	0.81-1.03	0.15				1.14	0.88-1.47	0.33				0.97	0.87-1.08	0.55				1.17	0.93-1.46	0.18
PMI		0.998	0.996-1.001	0.14				0.99	0.98-1.005	0.35				0.999	0.997-1.001	0.17				0.998	0.99-1.006	0.69
%VC		0.97	0.95-0.99	<0.01*	0.97	0.95-0.99	<0.01*	0.92	0.85-0.99	0.04*	0.95	0.88-1.03	0.2	0.99	0.97-1.01	0.14				0.99	0.95-1.04	0.73
FEV1.0%		1.02	0.99-1.05	0.29				0.99	0.92-1.06	0.75				1.01	0.99-1.04	0.3				0.99	0.94-1.06	0.99
NAC	+	1.15	0.52-2.54	0.73				0.79	0.09-6.79	0.83				1.66	0.85-3.22	0.14				1.38	0.35-5.35	0.64
Bleeding		1.001	1.000-1.001	0.02*	1.001	1.000-1.001	0.02*	1.002	1-1.005	0.05				1	0.999-1.001	0.13				1.001	0.999-1.003	0.08
Operative time		1.002	0.999-1.004	0.08				1.007	0.99-1.01	0.08				1	0.99-1	0.07				1.007	1-1.013	0.04*
CD ≥ IIIa	+	1.67	0.86-3.23	0.13				5.98	1.18-30.3	0.03*	2.91	0.48-17.5	0.24	1.94	1.07-3.53	0.03*	2.29	1.23-4.24	<0.01*	1.39	0.29-6.62	0.68
pStage	2,3,4	3.03	1.38-6.66	<0.01*	2.55	1.14-5.70	0.02*	0.89	0.20-4.03	0.88				2.56	1.31-5.00	<0.01*	2.84	1.39-5.81	<0.01*	0.92	0.26-3.29	0.89

HR: hazard ratio; CI: confidence interval; DM: diabetes mellitus; HT: hypertension; BMI: body mass index; PMI: psoas muscle index; %VC: percentage of vital capacity; FEV1.0%: forced expiratory volume percentage in one second; NAC: neoadjuvant chemotherapy; CD: Clavien-Dindo classification

*statistically significant

Table 4. Comparisons of postoperative complications by the cut-off points of PMI and BMI

Postoperative complications over CDIIIa were significantly less in high PMI group.

Variable	PMI < 600 (n = 78)	PMI ≥ 600 (n = 43)	*p*	BMI < 18.5 (n = 12)	BMI ≥ 18.5 (n = 112)	*p*
Anastomotic leakage	13 (19%)	6 (14%)	0.75	1 (14%)	18 (17%)	1
Pneumonia	26 (37%)	9 (21%)	0.13	2 (29%)	34 (32%)	1
Recurrent nerve palsy	18 (26%)	11 (26%)	1	0	29 (27%)	0.26
CD ≥ IIIa	43 (51%)	7 (19%)	<0.01*	5 (42%)	45 (40%)	1
3y OS	58%	64%	0.25	34%	63%	0.09
3y RFS	43%	62%	0.08	15%	54%	0.05

PMI: psoas muscle index; BMI: body mass index; CD: Clavien-Dindo classification; OS: overall survival; RFS: recurrence-free survival
*statistically significant

Table 5. Comparison of postoperative complications and survival by preoperative nutritional and muscular score

Postoperative complications over CDIII were significantly less in PNM score 0 group than score 1 and 2 group.

PNM score	0 (n=45)	1/2 (n=76)	*P*
anastomotic leakage	6 (15%)	13 (18%)	0.81
pneumonia	8 (20%)	27 (38%)	0.07
recurrent nerve palsy	11 (27%)	18 (25%)	1
CD≥III	8 (17%)	42 (55%)	<0.01
3y OS	65%	58%	0.28
3y RFS	62%	42%	0.1

PNM (Preoperative Nutrition and Muscular) score was derived using the following rule: patients were allocated 1 point if their BMI (body mass index) was less than 18.5 kg/m^2 and 1 point if their PMI (psoas muscle index) was below 600 mm^2/m^2 (a possible maximum total of 2 points). CD: Clavien-Dindo classification; OS: overall survival; RFS: recurrence-free survival

*statistically significant