Table 5 Multivariate analyses of factors associated with pulmonary complications

Factors	Objective variables	control	Odds ratio	95 % CI	*p* value
Smoking	Brinkman index ≥800	Brinkman index <800	2.23	1.14–4.35	0.019
Clinical T	T3, T4	T1, T2	1.83	0.84–395	0.127
Clinical N	N (+)	N (−)	1.21	1.21–2.63	0.630
Salvage esophagectomy	Yes	No	2.51	1.04–6.04	0.040
Bleeding (blood loss/body weight)			1.08	1.04–1.07	0.040

CI confidence interval

meta-analysis. However, there was a possibility that high-risk patients with severe obesity, severe respiratory impairment or uncontrolled diabetes mellitus were initially excluded from undergoing surgery.

A high level of blood loss and increased blood loss/body weight were associated with pulmonary complications in the present study. As shown in Table 6, only a few reports support the current observations on blood loss [13]. Most of the previous reports suggested that high blood loss was unrelated to the incidence of pulmonary complications. However, most of these studies were from Western countries, where most of the surgeries consisted of the Ivor-Lewis procedure and transhiatal esophagectomy. These are considered to lead to less blood loss and to have lower invasiveness for the patient, compared with radical esophagectomy with wide lymph node dissection. Nakamura et al. [13] reported the results from patients who underwent radical subtotal esophagectomy with two- or three-field lymph node dissection. They reported that greater blood loss was associated with pulmonary complications. However, the association between blood loss/body weight and pulmonary complications after esophagectomy has never been investigated. We believe that the blood loss/body weight could reflect stress in a more

Table 6 Summary of reports on pulmonary complications after esophagectomy

First author	Years	Number of patients	Data origin, period	Objectives	Incidence *n* (%)	Independent factors
Shiozaki [12]	2012	96	Single institution 2007–2009	Pneumonia, ARDS	20 (20.8)	FEVI %, CRP, smoking history
Bakhos [1]	2012	220	2 Institutions 2002.1–2009.1	Pneumonia	52 (23.6)	Age, lack of a pyloric drainage procedure
Paul [2]	2011	112	Single institution 2003.1–2006.12	ARDS	15 (13.4)	Respiratory comorbidities, smoking, FEVI % FiO2, perioperative inotrope use
Furguson [3]	2011	516	Single institution 1980–2009	Pneumonia, respiratory insufficiency needing reintubation	197 (38.2)	Age, FEVI %, DLCO %, PS (2–4), serum creatinine, smoking, thoracotomy
Zingg [4]	2011	858	5 institutions 1998–2008	Pneumonia, pleural effusion needing intervention, respiratory failure, ARDS	235 (27.4)	Smoking, number of comorbidities
Dhungel [7]	2010	1032	ACS-NSQIP database 2005–2008	Pneumonia, unplanned intubation	(27)	Diabetes, smoking, alcohol, operation time
Nakamura [13]	2008	184	Single institution 1991–2005	Pneumonia, respiratory failure requiring ventilation	36 (19.6)	Administering corticosteroids, blood loss greater than 630 mL, not providing respiratory physiotherapy
Law [14]	2004	421	Single institution 1990.1–2001.12	Pneumonia, respiratory failure	67 (15.9)	Age, length of operation, tumor location (upper)
Fang [15]	2003	441	Single institution 1986.1–1998.12	Pneumonia, respiratory failure, empyema, air leak prolonged >7 days	32 (7.3)	History of major surgery, abnormal spirometry, choric renal dysfunction
Avendano [16]	2002	61	Single institution 1994.1–2000.10	Pneumonia, chylothorax, ARDS	22 (36.1)	FEVI.0 % (<65 %)

ARDS acute respiratory distress syndrome, *FEV* forced expiratory volume, *CRP* C-reactive protein, *FiO2* fraction of inspired oxygen, *DLCO* diffusion lung capacity for carbon monoxide, *PS* performance status

individual manner. In fact, the Estimation of Physiologic Ability and Surgical Stress (E-PASS) scoring system, which has been reported to be a predictor of post-surgical risk, adopts not blood loss, but blood loss/body weight as a parameter for surgical stress [31]. We, therefore, believe that this parameters should be considered when predicting the risk of pulmonary complications in such patients.

In the present study, there was no significant association between the length of the operation and pulmonary complications. Although we could not investigate the length of the thoracic operation due to missing data, the limited examination ($n = 215$) suggested that it might have been a predictive factor for pulmonary complications. The relationship between the length of the thoracic operation and pulmonary complications has never been investigated. Although several authors have reported that the length of the operation might be a predictive factor [7, 14], we believe that the length of the thoracic operation under one-lung ventilation might be more important for estimating the risk of pulmonary complications. A long thoracic operation equates to a lot of manipulation of the right lung, and a longer unstable period under one-lung ventilation.

Pulmonary complications after salvage esophagectomy have been reported to be more common (29.6–44.0 %) than those after non-salvage esophagectomy. Moreover, high morbidity and mortality rates (7.4–22.2 %) have also been reported for salvage esophagectomy [32–36]. Preoperative radiotherapy can cause lung damage, and CRT sometimes causes dense fibrosis and thickening of the tissue in the irradiated area [37]. In the presence of radiation-induced fibrosis, it is difficult for surgeons to find the correct layer from which to detach the esophagus from the surrounding organs. Therefore, salvage esophagectomy requires a longer operation than non-salvage esophagectomy, and often results in excessive blood loss. Techniques to improve the procedural outcomes of salvage esophagectomy are currently being investigated [38].

A recent randomized controlled trial which compared MIE with open esophagectomy revealed that the rate of pulmonary infection within the first 2 weeks after surgery was lower in the minimally invasive group than in the open group [39]. In the current study, there were no differences in the incidence of pulmonary complications between the patients treated by the thoracoscopic approach and open esophagectomy. A systematic review of MIE showed that there was no strong trend toward deceased pulmonary complications with MIE [40, 41]. Therefore, whether MIE reduces the occurrence of postoperative pulmonary complications remains controversial. Three-field lymph node dissection is our standard surgical procedure, even in thoracoscopic esophagectomy. This might be the reason why the use of the thoracoscopic approach could not reduce the pulmonary complication rates in our patients.

In conclusion, the current study examined the frequency of pulmonary complications after subtotal esophagectomy with lymph node dissection, and investigated the risk factors for postoperative pulmonary complications. Patients with a history of heavy smoking, preoperative definitive chemoradiotherapy and high blood loss during surgery require careful pulmonary care, and should be carefully monitored during the perioperative period.

Conflict of interest Naoya Yoshida and the co-authors have no conflicts of interest to declare.

References

1. Bakhos CT, Fabian T, Oyasiji TO, Gautam S, Gangadharan SP, Kent MS, et al. Impact of the surgical technique on pulmonary morbidity after esophagectomy. Ann Thorac Surg. 2012;93:221–6.
2. Paul DJ, Jamieson GG, Watson DI, Devitt PG, Game PA. Perioperative risk analysis for acute respiratory distress syndrome after elective oesophagectomy. ANZ J Surg. 2011;81:700–6.
3. Ferguson MK, Celauro AD, Prachand V. Prediction of major pulmonary complications after esophagectomy. Ann Thorac Surg. 2011;91:1494–500.
4. 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.
5. Schieman C, Wigle DA, Deschamps C, Nichols Iii FC, Cassivi SD, Shen KR, et al. Patterns of operative mortality following esophagectomy. Dis Esophagus 2012 (Epub ahead of print).
6. Valentí V, Hernández-Lizoain JL, Marínez-Regueira F, Bellver M, Rodríguez J, Díaz González JA, et al. Transthoracic oesophagectomy with lymphadenectomy in 100 oesophageal cancer patients: multidisciplinary approach. Clin Transl Oncol. 2011;13:899–903.
7. Dhungel B, Diggs BS, Hunter JG, Sheppard BC, Vetto JT, Dolan JP. Patient and peri-operative predictors of morbidity and mortality after esophagectomy: American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP), 2005–2008. J Gastrointest Surg. 2010;14:1492–501.
8. Wright CD, Kucharczuk JC, O'Brien SM, Grab JD, Allen MS. Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model. J Thorac Cardiovasc Surg. 2009;137:587–95.
9. Lagarde SM, Reitsma JB, Maris AK, van Berge Henegouwen MI, Busch OR, Obertop H, et al. Preoperative prediction of the occurrence and severity of complications after esophagectomy for cancer with use of a nomogram. Ann Thorac Surg. 2008;85:1938–45.
10. Rodgers M, Jobe BA, O'Rourke RW, Sheppard B, Diggs B, Hunter JG. Case volume as a predictor of inpatient mortality after esophagectomy. Arch Surg. 2007;142:829–39.
11. Thompson AM, Rapson T, Gilbert FJ, Park KG. Hospital volume does not influence long-term survival of patients undergoing surgery for oesophageal or gastric cancer. Br J Surg. 2007;94:578–84.
12. Shiozaki A, Fujiwara H, Okamura H, Murayama Y, Komatsu S, Kuriu Y, et al. Risk factors for postoperative respiratory complications following esophageal cancer resection. Oncol Lett. 2012;3:907–12.

13. Nakamura M, Iwahashi M, Nakamori M, Ishida K, Naka T, Iida T, *et al. An analysis of the factors contributing to a reduction in* the incidence of pulmonary complications following an esophagectomy for esophageal cancer. Langenbecks Arch Surg. 2008;393:127–33.
14. Law S, Wong KH, Kwok KF, Chu KM, Wong J. Predictive factors for postoperative pulmonary complications and mortality after esophagectomy for cancer. Ann Surg. 2004;240:791–800.
15. 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.
16. Avendano CE, Flume PA, Silvestri GA, King LB, Reed CE. Pulmonary complications after esophagectomy. Ann Thorac Surg. 2002;73:922–6.
17. Atkins BZ, Shah AS, Hutcheson KA, Mangum JH, Pappas TN, Harpole DH Jr, et al. Reducing hospital morbidity and mortality *following esophagectomy. Ann Thorac Surg. 2004;78:1170–6.*
18. Martin DJ, Bessell JR, Chew A, Watson DI. Thoracoscopic and laparoscopic esophagectomy: initial experience and outcomes. Surg Endosc. 2005;19:1597–601.
19. Watson DI, Jamieson GG, Devitt PG. Endoscopic cervico-thoraco-abdominal esophagectomy. J Am Coll Surg. 2000;190: 372–8.
20. Koide N, Takeuchi D, Suzuki A, Miyagawa S. Mediastinoscopy-*assisted esophagectomy for esophageal cancer in patients with* serious comorbidities. Surg Today. 2012;42:127–34.
21. Ando N, Kato H, Igaki H, Shinoda M, Ozawa S, Shimizu H, et al. A randomized trial comparing postoperative adjuvant chemotherapy with cisplatin and 5-fluorouracil versus preoperative chemotherapy for localized advanced squamous cell carcinoma of the thoracic esophagus (JCOG9907). Ann Surg Oncol. 2012;19:68–74.
22. Guinan P, Sobin LH, Algaba F, Badellino F, Kameyama S, MacLennan G, et al. TNM staging of renal cell carcinoma: Workgroup No. 3. Union International Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). Cancer. 1997;80:992–3.
23. Nagai Y, Watanabe M, Kamohara H, Miynari N, Hiyoshi Y, Imamura Y, et al. A preventive effect of sivelestat on postoperative respiratory disorders in patients after thoracic esophagectomy. Surg Today. 2013;43:361–6.
24. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012;307: 2526–33.
25. 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;240: 205–13.
26. Kojima S, Sakakibara H, Motani S, Hirose K, Mizuno F, Ochiai M, et al. Incidence of chronic obstructive pulmonary disease, and the relationship between age and smoking in a Japanese population. J Epidemiol. 2007;17:54–60.
27. Akutsu Y, Matsubara H. Perioperative management for the prevention of postoperative pneumonia with esophageal surgery. Ann Thorac Cardiovasc Surg. 2009;15:280–5.
28. Edgard E, Cécile M. Effect of preoperative single-dose corticosteroid *administration on postoperative morbidity following* esophagectomy. J Gastrointest Surg. 2010;14:788–804.
29. Makino H, Kunisaki C, Kosaka T, Akiyama H, Morita S, Endo I. Perioperative use of a neutrophil elastase inhibitor in video-assisted thoracoscopic oesophagectomy for cancer. Br J Surg. 2011;98:975–82.
30. Kayani B, Okabayashi K, Ashrafian H, Harling L, Rao C, Darzi A, et al. Does obesity affect outcomes in patients undergoing *esophagectomy for cancer? A meta-analysis. World J Surg.* 2012;36:1785–95.
31. Haga Y, Wada Y, Takeuchi H, Kimura O, Furuya T, Sameshima H, et al. Estimation of physiologic ability and surgical stress (E-PASS) for a surgical audit in elective digestive surgery. Surgery. 2004;135:586–94.
32. Morita M, Kumashiro R, Hisamatsu Y, Nakanishi R, Egashira A, Saeki H, et al. Clinical significance of salvage esophagectomy for *remnant or recurrent cancer following definitive chemoradio*therapy. J Gastroenterol. 2011;46:1284–91.
33. Takeuchi H, Saikawa Y, Oyama T, Ozawa S, Suda K, Wada N, et al. Factors influencing the long-term survival in patients with esophageal cancer who underwent esophagectomy after chemoradiotherapy. World J Surg. 2010;34:277–84.
34. Miyata H, Yamasaki M, Takiguchi S, Nakajima K, Fujiwara Y, Nishida T, et al. Salvage esophagectomy after definitive chemoradiotherapy for thoracic esophageal cancer. J Surg Oncol. 2009;100:442–6.
35. Tachimori Y, Kanamori N, Uemura N, Hokamura N, Igaki H, Kato H. Salvage esophagectomy after high-dose chemoradiotherapy for esophageal squamous cell carcinoma. J Thorac Cardiovasc Surg. 2009;137:49–54.
36. Chao YK, Chan SC, Chang HK, Liu YH, Wu YC, Hsieh MJ, et al. Salvage surgery after failed chemoradiotherapy in squamous cell carcinoma of the esophagus. Eur J Surg Oncol. 2009; 35:289–94.
37. Lee HK, Vaporciyan AA, Cox JD, Tucker SL, Putnam JB Jr, Ajani JA, et al. Postoperative pulmonary complications after preoperative chemoradiation for esophageal carcinoma: correlation with pulmonary dose-volume histogram parameters. Int J Radiat Oncol Biol Phys. 2003;57:1317–22.
38. Watanabe M, Yoshida N, Karashima R, Sato N, Hirashima K, Imamura Y, et al. Transcervical superior mediastinal lymph node dissection combined with transhiatal lower esophageal dissection before transthoracic esophagectomy: a safe approach for salvage esophagectomy. J Am Coll Surg. 2009;208:e7–9.
39. Biere SS, van Berge Henegouwen MI, Maas KW, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. Lancet 2012;379:1887–92.
40. Sudarshan M, Ferri L. A critical review of minimally invasive esophagectomy. Surg Laparosc Endosc Percutan Tech. 2012;22: 310–8.
41. Watanabe M, Baba Y, Nagai Y, Baba H. Minimally invasive esophagectomy for esophageal cancer: an updated review. Surg Today 2012 (Epub ahead of print).