ORIGINAL PAPER

Nagoya J. Med. Sci. **78**. 69 ~ 78, 2016

Short-term outcomes after conventional transthoracic esophagectomy

Yukiko Niwa, Masahiko Koike, Masashi Hattori, Naoki Iwata, Hideki Takami, Masamichi Hayashi, Mitsuro Kanda, Daisuke Kobayashi, Chie Tanaka, Suguru Yamada, Tsutomu Fujii, Goro Nakayama, Hiroyuki Sugimoto, Shuji Nomoto, Michitaka Fujiwara and Yasuhiro Kodera

Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, Nagoya, Japan

ABSTRACT

In our department, we have attempted to reduce the incidence of complications of conventional esophagectomy. The objective of this retrospective study was to report the short-term outcomes of esophagectomy. We reviewed 138 consecutive patients who had undergone subtotal esophagectomy by combined laparotomy via a 12-cm upper abdominal vertical incision combined with right anterior muscle-sparing thoracotomy from August 2010 to August 2014. Most of the cervical para-esophageal lymph node dissection was completed within the thoracic cavity. We performed three-field dissection in patients with tumors in the upper or middle third of the esophagus with clinical lymph node metastases in the superior mediastinum; the others underwent two-field dissection. We performed neck anastomoses in patients undergoing three-field dissection and thoracic anastomoses in those undergoing two-field dissection. Effective postoperative pain management was achieved with a combination of epidural anesthesia and paravertebral block. Postoperative rehabilitation was instituted for early ambulation and recovery. Enteral nutrition via a duodenal feeding tube was administered from postoperative day 2. Median hospital stay after surgery was 15 days (range, 10–129). Rates for both 30-day and in-hospital mortality were 0%. Morbidity rate for all Clavien–Dindo grades was 41.3%, whereas the morbidity rate for Clavien–Dindo grades III and IV was 7.2%. Anastomotic leakage developed in two patients (1.4%), recurrent laryngeal nerve palsy in 11 (8.0%), and pneumonia in nine (6.5%). Good short-term outcomes, especially regarding anastomotic leaks, were achieved by consistent improvements in surgical techniques, optimization of several operative procedures, and appropriate perioperative management.

Key Words: esophagectomy, esophageal cancer, transthoracic, outcomes, complications

INTRODUCTION

Esophageal cancer is the sixth most common cause of cancer-related mortality worldwide.[1] Although it is now supplemented by combined chemoradiotherapy, surgical resection remains the mainstay of curative treatment for esophageal cancer. However, esophagectomy is associated with considerable morbidity, having one of the highest mortality rates of all surgical procedures.[2, 3] Over the past two decades, better patient selection, improved preoperative staging, and improved

Received: May 1, 2015; accepted: December 28, 2015

Corresponding author: Masahiko Koike, MD, PhD

Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

Tel: +81-52-744-2249, Fax: +81-52-744-2255, E-mail: dockoike@med.nagoya-u.ac.jp

perioperative care have resulted in a reduction in postoperative mortality.[3] Moreover, enhanced recovery after surgery programs that aim to accelerate functional recovery have proven effective after esophagectomy, resulting in reductions in morbidity, mortality, and length of hospital stay.[4, 5]

In our department, we have made ongoing efforts to reduce the invasiveness of the procedure by improving the surgical techniques, optimizing the operative procedure, and improving preoperative treatment for conventional subtotal esophagectomy, which we perform by combined laparotomy and thoracotomy. These changes have reduced the incidence and severity of complications. In the present retrospective study, we report the short-term outcomes of conventional esophagectomy at our department.

METHODS

Patients

We retrospectively reviewed 194 consecutive patients who had undergone subtotal esophagectomy by combined laparotomy and thoracotomy from August 2010 to August 2014, that is, before the introduction of thoracoscopic esophagectomy, in the Department of Gastroenterological Surgery (Surgery II) of Nagoya University Graduate School of Medicine. The study included 138 patients in whom esophagogastric anastomoses had been achieved by gastric conduit reconstruction and who had undergone typical lymph node dissection. The patients in whom the jejunum was used for esophageal reconstruction (32 patients) and those in whom partial lymph node dissection had been performed (10 patients) were excluded. Patients who had undergone additional procedures such as laryngectomy or pharyngectomy (four patients) and those who had undergone R2 resection (10 patients) were also excluded. The institutional review board of our institution approved this study.

Clinicopathological, perioperative, and intraoperative data were obtained from patient medical records. The tumors were staged according to the seventh edition of the Union for International Cancer Control TNM staging system.[6]

Preoperative treatment

Most patients with clinical stage IB, II, and III (excluding T4) disease received neoadjuvant chemotherapy regimen with standard-dose cisplatin + 5-fluorouracil (5-FU) (cisplatin 80 mg/m^2 on days 1 and 29, plus 5-FU 800 mg/m^2 on days 1–5 and 29–33), whereas some patients with clinical stage III disease received at our department's trial protocol comprising cisplatin + S-1 (cisplatin 60 mg/m^2 on days 8 and 43, plus S-1 40–60 mg according to the patient's body surface area on days 1–21 and 36–56). Patients with locally advanced clinical T4 tumors that were considered marginally resectable received a chemoradiotherapy regimen of concurrent 40 Gy radiation to the main tumor and chemotherapy (cisplatin 70 mg/m^2 on days 1 and 29 plus 5-FU 700 mg/m^2 on days 1–4 and 29–32).

Operative procedures and indications

Patients with tumors in the upper third of the esophagus or in the lower or middle thirds of the esophagus with clinical lymph node metastases in the superior mediastinum underwent three-field dissection, whereas those with tumors in the lower or middle thirds of the esophagus without clinical lymph node metastases in the superior mediastinum and those with tumors in upper thirds underwent two-field dissection. Of note, in our department two-field dissection does include dissection of the cervical para-esophageal nodes. Because surgical techniques for cervicothoracic lymph node dissection have improved, the cervical para-esophageal nodes were

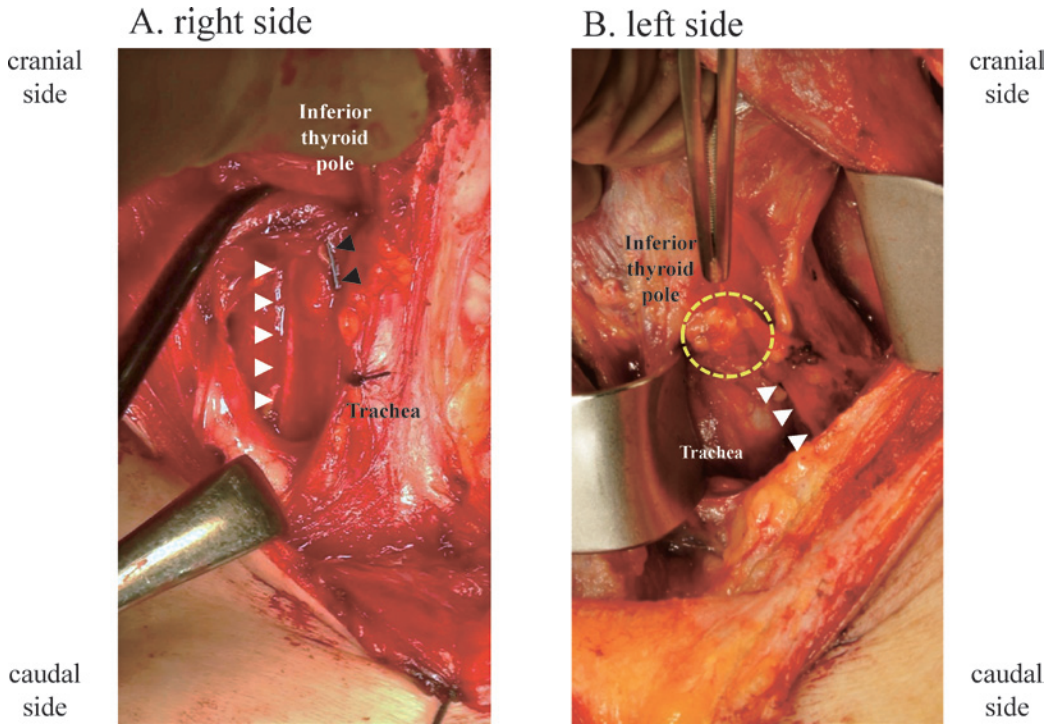

Fig. 1 Intraoperative photograph from the cervical incision after completion of lymph node dissection in the thoracic cavity. White arrowheads indicate the right laryngeal recurrent nerve.
A: The right side. The inferior pole of the right thyroid lobe is lifted to show the entry of the recurrent laryngeal nerve into the larynx. A surgical clip was placed at the superior end of lymph node dissection from the thoracic cavity (black arrowheads indicate surgical clip).
B: The left side. There is only a little fatty tissue remaining anterior to the trachea (enclosed by a dotted line).

almost dissected thorough an intrathoracic approach. The photographs in Fig. 1A and B are taken from the right and left cervical incisions, respectively, after lymph node dissection in the thoracic cavity has been performed. They show that no tissue remains along the right laryngeal recurrent nerve or the cervical paratracheal region on the right side (Fig. 1A) and that the left cervical para-esophageal lymph node dissection is almost complete, only a small amount of fatty tissue remaining anterior to the trachea (Fig. 1B). The wider range of lymphadenectomy, especially in the cervical region, made possible through a thoracic approach enabled omission of the conventional cervical incision, thus reducing invasiveness and pain. Hence, the difference between three-field and two-field dissection is that bilateral dissection of the supraclavicular lymph nodes was not performed during two-field dissection. Patients undergoing three-field dissection underwent neck anastomosis whereas those undergoing two-field dissection underwent thoracic anastomosis.

In an attempt to reduce procedure-related pain, subtotal esophagectomy was performed with right anterior muscle-sparing thoracotomy[7] in the fourth intercostal space accompanied by an anterior axial incision and laparotomy with a 12-cm upper abdominal vertical incision. Esophageal reconstruction consisted of creation of a gastric tube using a rounded and linear stapling device along the greater curvature. We believe that the resultant longer gastric conduit enables creation

of an esophagogastric anastomosis not at the extreme tip of the gastric conduit but lower, where a more abundant blood supply is available for the anastomosis site. Esophagogastric anastomosis was performed by end-to-side anastomosis using a conventional circular stapling device. Pyloroplasty was also performed. A jejunostomy feeding tube was placed in the duodenum (duodenostomy) both to provide nutrition and prevent postoperative ileus.[8] One 15-F Blake drain (Ethicon, Somerville, NJ, USA) was inserted from the right to the left thoracic cavity across the posterior mediastinum to evacuate bilateral pleural effusions.[9]

Perioperative management

Methylprednisolone (250 mg) in saline was administered 2 hours before surgery to reduce the perioperative systemic inflammatory response. For postoperative pain management before April 2013, two epidural anesthesia catheters were inserted for the thoracic and abdominal wounds, whereas after May 2013 one epidural anesthesia catheter was inserted for the abdominal wound and continuous paravertebral block anesthesia administered for the thoracic wound.[10] Postoperative rehabilitation by physical therapists was introduced in 2012 to promote early ambulation and recovery. Nutrients were routinely administered via a duodenal feeding tube to all patients throughout the study period, starting on postoperative day 2 and continuing until the day of discharge. After discharge, home infusion therapy was continued for a few months to maintain adequate nutrition. Detailed descriptions of the clinical pathway for esophagectomy currently followed in our department are shown in Table 1.

Table 1 Clinical pathway for esophagectomy in our department

Day	
POD 0	Direct transfer from operation room to ICU
	Kept intubated in ICU
	Bed rest
	Continuation of paravertebral block and epidural anesthesia
	Continuation of chest tube management (suction 10 cm H20)
	Nasogastric decompression
	Initiation of PPI
POD 1	Extubation
	Transfer to ward
	Initiation of early mobilization
	Continuation of chest tube management (water seal drainage)
POD 2	Removal of nasogastric tube
	Initiation of enteral tube feeding
POD 3	Gradual increase in enteral tube feeding
	Gradual decrease in parental nutrition
POD 4	Discontinuation of antibiotic prophylaxis (cefmetazole sodium)
POD 5	Removal of central venous catheter
POD 7	Removal of chest tube, epidural catheter, paravertebral block catheter and urinary catheter Initiation of oral intake
POD 10-14	Discharge from hospital

POD, postoperative day; ICU, intensive care unit; PPI, proton pump inhibitor.

Definitions of complications

Pneumonia was diagnosed by clinical suspicion of a respiratory infection, usually with associated fever, or a new or progressive infiltrate on chest X-ray films or CT scan. Recurrent laryngeal nerve palsy was diagnosed by fiberoptic laryngoscope examination by an otorhinolaryngologist of patients with hoarseness on postoperative day 3. The severity of postoperative complications was classified using the Clavien–Dindo classification.[11)]

RESULTS

Relevant clinical and pathological characteristics are listed in Table 2. There were 116 men and 22 women, with a median age of 66 years (range, 44–84 years). The histology was squamous cell carcinoma in 126 patients (91%) and adenocarcinoma in 10 (7%); the others were malignant melanoma and basaloid squamous cell carcinoma. Sixty-eight patients (48%) had comorbidities. Eighty-eight patients (64%) received preoperative treatment. Neoadjuvant chemotherapy was administered to 72 patients and neoadjuvant chemoradiotherapy to 16 patients.

Table 2 Relevant clinical and pathological characteristics

Variables		N = 138
Age, median (range; years)		66 (44–84)
Sex	Male	116 (84%)
	Female	22 (16%)
Smoker (preoperative)	Yes	75 (54%)
	No	63 (46%)
Tumor location	Upper thoracic esophagus	18 (13%)
	Middle thoracic esophagus	76 (55%)
	Lower thoracic esophagus	44 (32%)
Histology type	Squamous cell carcinoma	126 (91%)
	Adenocarcinoma	10 (7%)
	Other	2 (2%)
Comorbidity	Hypertension	65 (47%)
	Diabetes mellitus	18 (13%)
	Heart disease	12 (9%)
	COPD	4 (3%)
ASA score	ASA 1	70 (51%)
	ASA 2	52 (38%)
	ASA 3	16 (12%)
Clinical T stage	T1	48 (34%)
	T2	11 (8%)
	T3	78 (57%)
	T4	1 (1%)

Clinical N stage	N0	55 (40%)
	N1	49 (35%)
	N2	30 (22%)
	N3	4 (3%)
Clinical M stage	M0	132 (96%)
	M1	5 (4%)
Preoperative treatment	Yes	88 (64%)
	Chemotherapy	72 (52%)
	Chemoradiotherapy	16 (11%)
	No	50 (36%)

Data are presented as n (%). COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists.

Intraoperative details are presented in Table 3. The median operative time was 476 min (range, 310–682) and the median blood loss 434 mL (range, 67–1370). Cervical, mediastinal and abdominal lymph node dissection was performed in all patients. The commonest reconstruction procedure (63%) was gastric tube conduit reconstruction via a posterior mediastinal route with an esophagogastric anastomosis performed in the thoracic cavity. The median number of lymph nodes retrieved was 46.5 (range, 12–102).

Table 3 Intraoperative variables

Operative time (min), median (range)	476 (310–682)
Blood loss (mL), median (range)	434 (67–1370)
Field of lymph node dissection, n (%)	
Three-field; cervical, mediastinal and abdominal	50 (36%)
Two-field; mediastinal and abdominal	88 (64%)
Level of anastomosis, n (%)	
Cervical	51 (37%)
Thoracic	87 (63%)
Reconstruction route, n (%)	
Posterior mediastinal	106 (77%)
Retrosternal	32 (23%)
Total number of lymph nodes retrieved, median (range)	46.5 (12–102)

Short-term outcomes are listed in Table 4. The median length of stay in the ICU was 1 day (range, 1–8), the median time to ambulation 2 days (range, 1–9), and the median hospital stay after surgery 15 days (range, 10–129). Rates for both 30-day and in-hospital mortality were 0%. Morbidity of any Clavien–Dindo grade occurred in 41.3% of patients and of Clavien–Dindo grades III and IV in 7.2%. The most common complication was arrhythmia (18.8%). Recurrent

laryngeal nerve palsy developed in 11 patients (8.0%) and was permanent in two of them (1.4%). Pneumonia developed in nine patients (6.5%). The incidence of pneumonia did not differ significantly between the two-field dissection and three-field dissection groups (7.9% vs. 4.0%, respectively; p = 0.696). Anastomotic leakage developed in two patients (1.4%), one of whom was treated conservatively whereas the other needed bedside intervention.

Table 4 Short-term outcomes

Days in ICU, median (range)	1 (1–8)	
First ambulatory day (days), median (range)	2 (1–9)	
Hospital stay after surgery (days), median (range)	15 (10–129)	
Mortality rate, n (%)		
30-day mortality	0	
In-hospital mortality	0	
	CD All Grades	CD Grade ≥ 3
Morbidity rates, n (%)	57 (41.3%)	10 (7.2%)
Anastomotic leak	2 (1.4%)	1 (0.7%)
Chyle leakage	3 (2.2%)	1 (0.7%)
Pneumonia	9 (6.5%)	3 (2.2%)
Recurrent laryngeal nerve injury	11 (8.0%)	2 (1.4%)
Tracheal necrosis	1 (0.7%)	1 (0.7%)
Surgical site infection	6 (4.3%)	1 (0.7%)
Arrhythmia	26 (18.8%)	1 (0.7%)

ICU, intensive care unit; CD, Clavien-Dindo classification.

DISCUSSION

In our study, the mortality rate for conventional esophagectomy was 0% and the rate of severe morbidity 7.2%; thus, the outcomes were exemplary and superior to what has previously been reported.[12-17] Our good short-term outcomes are presumably attributable to consistent improvements in surgical techniques, optimization of several operative procedures, and appropriate perioperative management by a team consisting of a wide range of experts.

Anastomotic leakage developed in two patients (1.4%) in this study, which is an excellent result compared with those of previous reports.[12, 15-19] We believe that the low rate of anastomotic leakage was influenced not only by surgical expertise but also by the optimal operative procedure performed. No patients who underwent thoracic anastomosis developed anastomotic leakage in. In our department, the rate of thoracic anastomosis, which was the most frequent site of anastomosis, was 63%. However, selection of the anastomosis site is controversial.[20-23] Anastomotic leakage from a thoracic anastomosis is a life-threatening complication, because of the risk of subsequent development of a pyothorax, fistula between the gastric conduit and lung, or sepsis. Thoracic anastomosis has three advantages. First, the lower anastomotic site on the greater curvature of the stomach provides a blood supply for the anastomotic site. Second, tension at the anastomotic

site is minimized. Third, the gastric tube conduit is not placed through the thoracic inlet, the anatomy of which varies between individuals resulting in a narrow inlet occasionally compressing the gastric tube conduit. Because we consider that these advantages are of paramount importance in formulating the surgical strategy, our first choice is thoracic anastomosis via the posterior mediastinal route. Moreover, dissection of the cervical para-esophageal lymph nodes enables construction of a thoracic anastomosis, which contributes to the reduced rate of anastomotic leakage. We need to put more effort into reducing anastomotic leakage to zero in patients with cervical anastomoses.

Pneumonia developed in nine patients (6.5%) in this study, a rate that is substantially lower than previously reported.[13, 16-18, 24-26] Our low rate of pneumonia can be attributed to optimization of the operative procedure (muscle-sparing thoracotomy and a minimal upper abdominal vertical incision); improvement in surgical technique (the omission of a cervical incision for middle and lower third esophageal cancers); and good perioperative management (adequate pain management for both thoracic and abdominal wounds enabled early ambulation, coughing, and expectoration of secretions). Only five patients (3.6%) in this study needed bedside bronchoscopy for tracheobronchial toilet.

Recurrent laryngeal nerve palsy developed in 11 patients (8.0%) in this study. Of these 11 patients, eight had undergone neck anastomosis. This outcome is more or less the same as previously reported.[15, 16, 24, 27] Although the rate of permanent recurrent laryngeal nerve palsy was only 1.4%, which is low, transient laryngeal nerve palsy adversely affects postoperative recovery by impairing the laryngeal cough reflex and expectoration, potentially resulting in atelectasis or aspiration pneumonia. Transient recurrent laryngeal nerve palsy may have affected the incidence of pulmonary complications in this study. We believe that recurrent laryngeal nerve palsy was caused by excessive stress and traction from pulling the esophagus from the thoracic cavity to the neck operative field or during the use of the circular stapler to perform the anastomotic procedure in the neck. Further effort is needed to reduce the incidence of recurrent laryngeal nerve palsy caused by neck manipulation.

A recent meta-analysis of thoracoscopic esophagectomy versus open esophagectomy[28] and a review[29] have both found that thoracoscopic esophagectomy has benefits regarding length of hospital stay. The length of hospital stay in this study was a little longer than previously reported.[13, 14, 17, 18, 24-26, 30-32] We consider that reduction in complications and adequate perioperative pain management shortened the ambulation time and hospital stay. We introduced thoracoscopic esophagectomy to improve the operative technique by magnifying the surgical view and to enable visualization of the operative field on monitors for the purpose of education. With introduction of thoracoscopic esophagectomy, we expect to further improve short-term outcomes.

Finally, this study has several limitations, namely its retrospective nature and small sample size. These limitations should be considered when interpreting our results.

In conclusion, we believe our good short-term outcomes for conventional esophagectomy, especially regarding anastomotic leaks, were achieved by improvements in surgical techniques, optimization of several operative procedures, and appropriate perioperative management.

Conflict of Interest Statement

The authors have no conflicts of interest.

REFERENCES

1) Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin*, 2011; 61: 69–90.
2) Schieman C, Wigle DA, Deschamps C, Nichols Iii FC, Cassivi SD, Shen KR, Allen MS. Patterns of operative mortality following esophagectomy. *Dis Esophagus*, 2012; 25: 645–651.
3) Jamieson GG, Mathew G, Ludemann R, Wayman J, Myers JC, Devitt PG. Postoperative mortality following oesophagectomy and problems in reporting its rate. *Br J Surg*, 2004; 91: 943–947.
4) Findlay JM, Gillies RS, Millo J, Sgromo B, Marshall RE, Maynard ND. Enhanced recovery for esophagectomy: a systematic review and evidence-based guidelines. *Ann Surg*, 2014; 259: 413–431.
5) Findlay JM, Tustian E, Millo J, Klucniks A, Sgromo B, Marshall RE, Gillies RS, Middleton MR, Maynard ND. The effect of formalizing enhanced recovery after esophagectomy with a protocol. *Dis Esophagus*, 2014.
6) Sobin LH, Gospodarowicz MK, Wittekind C. TNM classification of malignant tumours, 2011, Wiley. com.
7) Miyata K, Fukaya M, Itatsu K, Abe T, Nagino M. Muscle sparing thoracotomy for esophageal cancer: a comparison with posterolateral thoracotomy. *Surg Today*, 2015: 1–8.
8) Oya H, Koike M, Iwata N, Kobayashi D, Torii K, Niwa Y, Kanda M, Tanaka C, Yamada S, Fujii T, Nakayama G, Sugimoto H, Nomoto S, Fujiwara M, Kodera Y. Feeding duodenostomy decreases the incidence of mechanical obstruction after radical esophageal cancer surgery. *World J Surg*, 2015; 39: 1105–1110.
9) Niwa Y, Koike M, Oya H, Iwata N, Kobayashi D, Kanda M, Tanaka C, Yamada S, Fujii T, Nakayama G, Sugimoto H, Nomoto S, Fujiwara M, Kodera Y. Method of bilateral pleural drainage by single Blake drain after esophagectomy. *World J Surg*, 2015; 39: 727–731.
10) Niwa Y, Koike M, Torii K, Oya H, Iwata N, Kanda M, Kobayashi D, Tanaka C, Yamada S, Fujii T, Nakayama G, Sugimoto H, Nomoto S, Fujiwara M, Kodera Y. Combination of continuous paravertebral block and epidural anesthesia in postoperative pain control after esophagectomy. *Esophagus*, 2015: 1–6.
11) 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: 205–213.
12) Blencowe NS, Strong S, McNair AG, Brookes ST, Crosby T, Griffin SM, Blazeby JM. Reporting of short-term clinical outcomes after esophagectomy: a systematic review. *Ann Surg*, 2012; 255: 658–666.
13) Smithers BM, Gotley DC, Martin I, Thomas JM. Comparison of the outcomes between open and minimally invasive esophagectomy. *Ann Surg*, 2007; 245: 232–240.
14) Pham TH, Perry KA, Dolan JP, Schipper P, Sukumar M, Sheppard BC, Hunter JG. Comparison of perioperative outcomes after combined thoracoscopic-laparoscopic esophagectomy and open Ivor-Lewis esophagectomy. *Am J Surg*, 2010; 199: 594–598.
15) Kinjo Y, Kurita N, Nakamura F, Okabe H, Tanaka E, Kataoka Y, Itami A, Sakai Y, Fukuhara S. Effectiveness of combined thoracoscopic-laparoscopic esophagectomy: comparison of postoperative complications and midterm oncological outcomes in patients with esophageal cancer. *Surg Endosc*, 2012; 26: 381–390.
16) Ichikawa H, Miyata G, Miyazaki S, Onodera K, Kamei T, Hoshida T, Kikuchi H, Kanba R, Nakano T, Akaishi T, Satomi S. Esophagectomy using a thoracoscopic approach with an open laparotomic or hand-assisted laparoscopic abdominal stage for esophageal cancer: analysis of survival and prognostic factors in 315 patients. *Ann Surg*, 2013; 257: 873–885.
17) Yatabe T, Kitagawa H, Yamashita K, Hanazaki K, Yokoyama M. Comparison of the perioperative outcome of esophagectomy by thoracoscopy in the prone position with that of thoracotomy in the lateral decubitus position. *Surg Today*, 2013; 43: 386–391.
18) Hong L, Zhang Y, Zhang H, Yang J, Zhao Q. The short-term outcome of three-field minimally invasive esophagectomy for Siewert type I esophagogastric junctional adenocarcinoma. *Ann Thorac Surg*, 2013; 96: 1826–1831.
19) Ganesamoni S, Krishnamurthy A. Three-field transthoracic versus transhiatal esophagectomy in the management of carcinoma esophagus-a single--center experience with a review of literature. *J Gastrointest Cancer*, 2014; 45: 66–73.
20) van Lanschot JJ, van Blankenstein M, Oei HY, Tilanus HW. Randomized comparison of prevertebral and retrosternal gastric tube reconstruction after resection of oesophageal carcinoma. *Br J Surg*, 1999; 86: 102–108.
21) Biere SS, Maas KW, Cuesta MA, van der Peet DL. Cervical or thoracic anastomosis after esophagectomy for cancer: a systematic review and meta-analysis. *Dig Surg*, 2011; 28: 29–35.
22) Klink CD, Binnebosel M, Otto J, Boehm G, von Trotha KT, Hilgers RD, Conze J, Neumann UP, Jansen M. Intrathoracic versus cervical anastomosis after resection of esophageal cancer: a matched pair analysis

of 72 patients in a single center study. *World J Surg Oncol*, 2012; 10: 159.
23) Yasuda T. Optimal reconstruction methods with a gastric substitute after esophagectomy. *Acta medica Kinki University*, 2013; 38: 69–78.
24) Fabian T, Martin JT, McKelvey AA, Federico JA. Minimally invasive esophagectomy: a teaching hospital's first year experience. *Dis Esophagus*, 2008; 21: 220–225.
25) Nguyen NT, Follette DM, Wolfe BM, Schneider PD, Roberts P, Goodnight JE, Jr. Comparison of minimally invasive esophagectomy with transthoracic and transhiatal esophagectomy. *Arch Surg*, 2000; 135: 920–925.
26) Noble F, Kelly JJ, Bailey IS, Byrne JP, Underwood TJ, South Coast Cancer Collaboration O-G. A prospective comparison of totally minimally invasive versus open Ivor Lewis esophagectomy. *Dis Esophagus*, 2013; 26: 263–271.
27) Gao Y, Wang Y, Chen L, Zhao Y. Comparison of open three-field and minimally-invasive esophagectomy for esophageal cancer. *Interact Cardiovasc Thorac Surg*, 2011; 12: 366–369.
28) Nagpal K, Ahmed K, Vats A, Yakoub D, James D, Ashrafian H, Darzi A, Moorthy K, Athanasiou T. Is minimally invasive surgery beneficial in the management of esophageal cancer? A meta-analysis. *Surg Endosc*, 2010; 24: 1621–1629.
29) Takeuchi H, Kawakubo H, Kitagawa Y. Current status of minimally invasive esophagectomy for patients with esophageal cancer. *Gen Thorac Cardiovasc Surg*, 2013; 61: 513–521.
30) Chen B, Zhang B, Zhu C, Ye Z, Wang C, Ma D, Ye M, Kong M, Jin J, Lin J, Wu C, Wang Z, Ye J, Zhang J, Hu Q. Modified McKeown minimally invasive esophagectomy for esophageal cancer: a 5-year retrospective study of 142 patients in a single institution. *PLoS One*, 2013; 8: e82428.
31) Xie MR, Liu CQ, Guo MF, Mei XY, Sun XH, Xu MQ. Short-term outcomes of minimally invasive Ivor-Lewis esophagectomy for esophageal cancer. *Ann Thorac Surg*, 2014; 97: 1721–1727.
32) Martin DJ, Bessell JR, Chew A, Watson DI. Thoracoscopic and laparoscopic esophagectomy: initial experience and outcomes. *Surg Endosc*, 2005; 19: 1597–1601.