Comparing Perioperative Mortality and Morbidity of Minimally Invasive Esophagectomy Versus Open Esophagectomy for Esophageal Cancer

A Nationwide Retrospective Analysis

Takashi Sakamoto, MD,†✉ Michimasa Fujiogi, MD,* Hiroki Matsui, MPH,* Kiyohide Fushimi, MD, PhD,‡ and Hideo Yasunaga, MD, PhD**

Objective: We compared the surgical outcomes of minimally invasive esophagectomy (MIE) and open esophagectomy (OE) for esophageal cancer.
Summary Background Data: MIE has become a widespread procedure. However, the definitive advantages of MIE over OE at a nationwide level have not been established.
Methods: We analyzed patients who underwent esophagectomy for clinical stage 0 to III esophageal cancer from April 2014 to March 2017 using a Japanese inpatient database. We performed propensity score matching to compare in-hospital mortality and morbidities between MIE and OE, accounting for clustering of patients within hospitals.
Results: Among 14,880 patients, propensity matching generated 4572 pairs. MIE was associated with lower incidences of in-hospital mortality (1.2% vs 1.7%, $P = 0.048$), surgical site infection (1.9% vs 2.6%, $P = 0.04$), anastomotic leakage (12.8% vs 16.8%, $P < 0.001$), blood transfusion (21.9% vs 33.8%, $P < 0.001$), reoperation (8.6% vs 9.9%, $P = 0.03$), tracheotomy (4.8% vs 6.3%, $P = 0.002$), and unplanned intubation (6.3% vs 8.4%, $P < 0.001$); a shorter postoperative length of stay (23 vs 26 days, $P < 0.001$); higher incidences of vocal cord dysfunction (9.2% vs 7.5%, $P < 0.001$) and prolonged intubation period after esophagectomy (23.2% vs 19.3%, $P < 0.001$); and a longer duration of anesthesia (408 vs 363 minutes, $P < 0.001$).
Conclusion: MIE had favorable outcomes in terms of in-hospital mortality, morbidities, and the postoperative hospital stay.

Keywords: esophageal cancer, esophagectomy, minimally invasive surgery

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Minimally invasive esophagectomy (MIE) has become a widespread procedure, but its advantages over open esophagectomy (OE) have not been established. Esophagectomy is still the main treatment for esophageal cancer, although multimodality treatment is usually implemented. Because OE is associated with high mortality and morbidity, MIE is expected to provide patients with preferable surgical outcomes over OE. However, the definitive advantages of MIE over OE at a national level, including both high- and low-volume centers, remain unestablished.

Luketich et al[1] reported the feasibility of MIE with a low perioperative mortality rate of 2.9%. Some previous studies have demonstrated comparable mortality between MIE and OE.[2–5] With respect to morbidity, pulmonary complications are a major concern after esophagectomy. Discrepancies exist among previous reports; one randomized control study demonstrated that MIE had a lower pulmonary infection rate than OE (9% vs 29%, $P = 0.005$),[2] but some retrospective studies showed a similar incidence of pulmonary complications between the 2 procedures.[3,5] A recent meta-analysis showed superiority of MIE over OE in terms of both mortality (odds ratio, 0.67; 95% confidence interval, 0.54–0.83) and morbidity (odds ratio, 0.70; 95% confidence interval, 0.63–0.78).[6] However, most of these previous studies used data from highly experienced hospitals. Even if a well-designed prospective trial is conducted, it may be difficult to understand the impact of MIE or OE at a nationwide level.

Analysis of a nationwide database is reasonable to gain an understanding of the real-world impact of MIE and OE. Different types of institutions have various levels of experience. In addition, the indications for MIE or OE vary among facilities. Thus, it is important to account for clustering of patients within each hospital to omit cluster-level confounders when comparing the impact of MIE and OE.

Determination of the real-world impact of MIE and OE on patient outcomes using current data is clinically important. The primary objective of this study was to evaluate the short-term surgical outcomes on a nationwide level. In this study, we analyzed patients with stage 0 to III esophageal cancer using a Japanese inpatient database to compare the surgical outcomes of MIE and OE for esophageal cancer.

METHODS

We extracted data of patients who underwent esophagectomy for esophageal cancer from April 2014 to March 2017 from the Diagnosis Procedure Combination database in Japan. The database contains administrative claims and discharge data from >1000 hospitals. All 82 university hospitals are required to participate in the database, and community hospitals participate in the database on a voluntary basis. The database includes unique identifiers for hospitals; age, sex, height, and weight on admission; diagnoses, comorbidities, and complications clearly differentiated from comorbidities recorded with Japanese text data and the *International Classification of Diseases, Tenth Revision* (*ICD-10*) codes[7]; clinical cancer stage and Tumor, Node, Metastasis classification for malignant tumors (Seventh Edition of the Union for International Cancer Control classification); procedures (with Japanese original codes);

From the *Department of Clinical Epidemiology and Health Economics, School of Public Health, The University of Tokyo, Tokyo, Japan; †Department of Surgery, Tokyo Bay Urayasu Ichikawa Medical Center, Chiba, Japan; and ‡Department of Health Policy and Informatics, Tokyo Medical and Dental University Graduate School, Tokyo, Japan.
✉sakamoto-kob@umin.ac.jp
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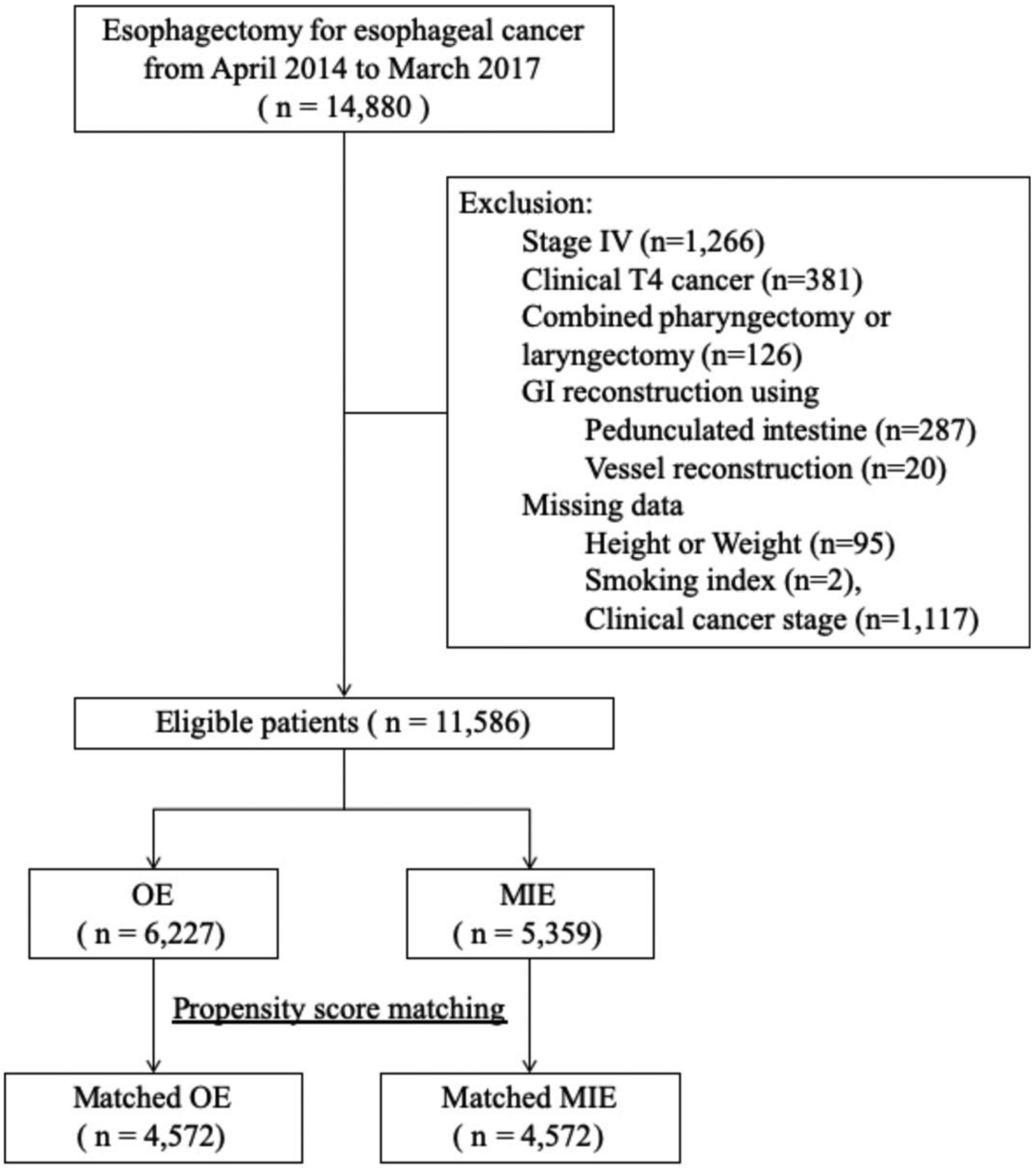

FIGURE 1. Study flow chart. GI indicates gastrointestinal.

duration of anesthesia and use of blood transfusion; and discharge status. The details of the database have been reported elsewhere.[8] We categorized the patients into 3 groups according to their body mass index (<18.5, 18.5–24.9, 25.0–29.9, and ≥30.0 kg/m^2) and smoking index (0–5, 6–20, 21–40, and ≥41 pack-years). We defined diabetes as a requirement for diabetic medications during hospitalization. Using Quan et al's[9] protocol, we calculated the Charlson comorbidity index and summed all *ICD-10*, codes for 17 comorbidities to obtain a score for each patient. In Quan el's protocol, each comorbidity category is given a weighting of 1 to 6 points. The sum of all weightings for a patient provides a single patient comorbidity score. A score of 0 indicates that no comorbidities are present. The Charlson Comorbidity Index is reportedly associated with postoperative complications in gastrointestinal cancer surgeries.[10,11] The clinical cancer stage was divided into 2 categories (0–I and II–III). The field of esophagectomy was either 2-field (thoracic and abdominal approach) or 3-field (cervical, thoracic, and abdominal approach). Hospital volume was calculated as the average number of esophagectomies performed per year in each hospital, with hospitals sorted into 3 grossly equal groups (low, middle, and high) defined by the tertile cutoff points for annual volume. The hospital type was classified as either a teaching hospital or nonteaching hospital. MIE was defined as a total thoracoscopic and laparoscopic approach or a combined approach of thoracoscopy and open laparotomy for esophagectomy. OE was defined as thoracotomy and laparotomy for esophagectomy. Selection of MIE or OE depended on each facility or surgeon. We did not include transhiatal esophagectomy in this study.

We excluded patients with clinical stage IV cancer, clinical stage T4 cancer, combined performance of pharyngectomy or laryngectomy, reconstruction using the pedunculated intestine or vessel reconstruction, or missing data (height, weight, smoking index, or clinical cancer stage).

The study outcomes were in-hospital mortality, morbidities, blood transfusion, duration of anesthesia, continuous intubation for

≥2 days after surgery, unplanned intubation, reoperation during the same admission, and 30-day readmission. The morbidities analyzed in the study were surgical site infection (T793, T813, T814, T941), anastomotic leakage (L021, J853, K20, T810, T813, T814, and long drainage tube placement), anastomotic stenosis (T818, procedure for esophageal dilation), vocal cord dysfunction (J830, G522, G978), empyema (J860, J869), chylothorax (I898, S278, T812), respiratory failure (J12–18, J690, J691, J958, J959, J96, J80), pulmonary embolism (I26), ileus and bowel obstruction (K560, K562, K565–567, K913), acute coronary syndrome (I21-25), stroke (I60–66), acute renal failure (N17), urinary tract infection (N10, N30, N390), and sepsis (A021, A227, A241, A267, A282, A327, A394, A40, A41, A548, B007, B349, B377, P36). *ICD-10* codes that originally included different conditions were checked by Japanese texts. Long drainage tube placement was defined as placement of a drainage tube for ≥3 weeks after surgery. We defined continuous intubation as intubation without a ≥2-day interval between each intubation period. Reoperation included surgery for wound dehiscence; tracheotomy; and abdominal, lung, and thoracic surgery. Blood transfusion was defined as the use of blood products during admission.

The requirement for informed consent was waived for this study because of the anonymous nature of the data. Study approval was obtained from the Institutional Review Board at the University of Tokyo.

Statistical Analysis

We used one-to-one propensity score matching without replacement to compare the surgical outcomes of OE and MIE. We used a logistic regression model to calculate propensity scores. The model was based on the following potential cofounding variables: sex, age, body mass index, smoking index, hypoalbuminemia, diabetes, chronic obstructive pulmonary disease, Charlson comorbidity index, type of hospital (teaching or nonteaching), clinical cancer stage (0–I, II–III), and field of esophagectomy (2- or 3-field). We described the distribution of propensity scores in the MIE and OE groups.

We used nearest-neighbor matching within a caliper of 0.20 standard deviation of the logit of the propensity scores. We calculated standardized differences to compare the confounders of patients between the OE and MIE groups. An absolute standardized difference (ASD) of <0.10 denoted a negligible difference between the 2 groups.[12]

We compared categorical variables with the χ^2 test and continuous variables with the Mann–Whitney test. For in-hospital mortality and total morbidity, we analyzed all patients with a generalized estimating equation (GEE), accounting for hospital clustering of patients to calculate adjusted odds ratios for the independent variables [surgery type (OE or MIE), age, sex, body mass index, smoking index, clinical cancer stage, hypoalbuminemia, diabetes, chronic obstructive pulmonary disease, Charlson comorbidity index, field of esophagectomy, hospital type, and hospital volume]. The significance level was set at $P < 0.05$ for all statistical tests, and all P values were 2-sided. All statistical analyses were conducted using Stata/MP 15.0 (StataCorp, College Station, TX).

RESULTS

We extracted the data of 14,880 patients who underwent esophagectomy for esophageal cancer from April 2014 to March 2017. Among them, we excluded patients with clinical stage IV cancer (n = 1266), clinical stage T4 cancer (n = 381), combined pharyngectomy or laryngectomy (n = 126), reconstruction using the pedunculated intestine (n = 287), vessel reconstruction (n = 20), missing data for height or weight (n = 95), missing data for the smoking index (n = 2), and missing data for the clinical cancer stage (n = 1117). As a result, we identified 11,586 eligible patients (OE, n = 6227; MIE, n = 5359). Propensity score matching generated 4572 pairs of patients (Figure 1). Figure 2 shows the distribution of the propensity scores in the MIE and OE groups.

Table 1 shows the characteristics of all patients and the propensity score-matched patients. Before propensity score matching, there were imbalances in the clinical cancer stage, field of

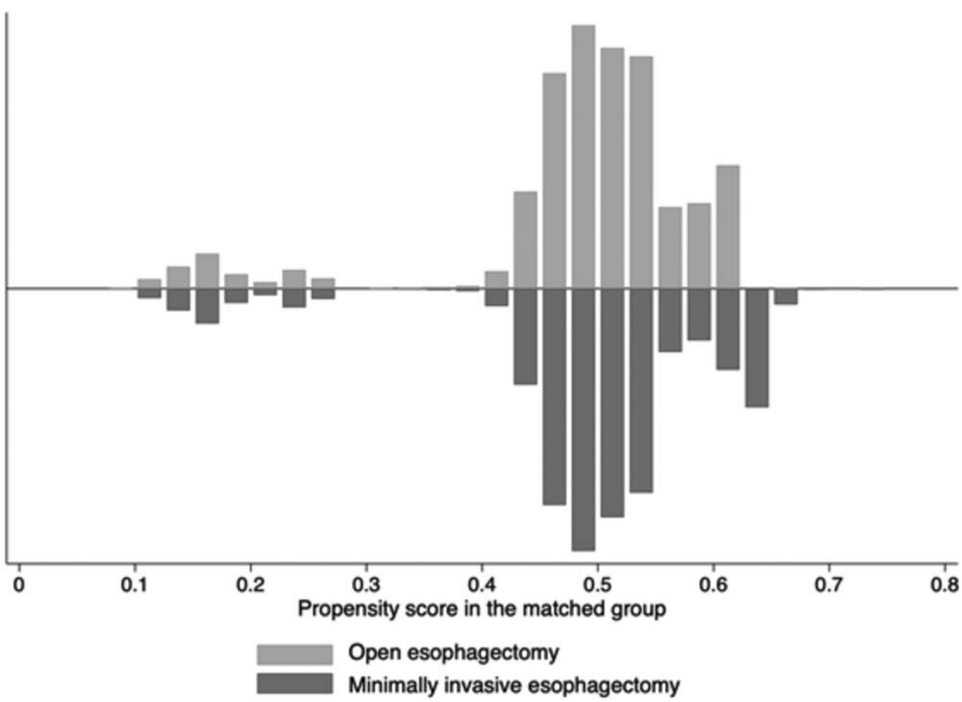

FIGURE 2. Distribution of propensity scores in the minimally invasive esophagectomy and open esophagectomy groups.

TABLE 1. Demographic and Clinical Characteristics of all Patients and Propensity Score-Matched Patients

	All Patients			Propensity Score-Matched Patients		
Factor	**OE (n = 6227)**	**MIE (n = 5359)**	**ASD**	**OE (n = 4572)**	**MIE (n = 4572)**	**ASD**
Sex						
Male	5165 (82.9%)	4403 (82.2%)	0.02	3787 (82.8%)	3791 (82.9%)	0.00
Female	1062 (17.1%)	956 (17.8%)	0.02	785 (17.2%)	781 (17.1%)	0.00
Age, y						
≤64	2053 (33.0%)	1895 (35.4%)	0.05	1619 (35.4%)	1562 (34.2%)	0.03
65–74	2954 (47.4%)	2530 (47.2%)	0.01	2181 (47.7%)	2195 (48.0%)	0.01
≥75	1220 (19.6%)	934 (17.4%)	0.06	772 (16.9%)	815 (17.8%)	0.03
Body mass index, kg/m^2						
<18.5	1157 (18.6%)	895 (16.7%)	0.05	807 (17.7%)	861 (18.8%)	0.03
18.5–24.9	4293 (68.9%)	3776 (70.5%)	0.03	3237 (70.8%)	3203 (70.1%)	0.02
25–29.9	777 (12.5%)	688 (12.8%)	0.01	495 (10.8%)	476 (10.4%)	0.01
≥30.0	53 (0.9%)	53 (1.0%)	0.01	33 (0.7%)	32 (0.7%)	0.00
Smoking index, pack-years						
0–5	1795 (28.8%)	1449 (27.0%)	0.04	1270 (27.8%)	1301 (28.5%)	0.02
6–20	724 (11.6%)	667 (12.4%)	0.03	548 (12.0%)	532 (11.6%)	0.01
21–40	1415 (22.7%)	1262 (23.5%)	0.02	1078 (23.6%)	1048 (22.9%)	0.02
≥41	2293 (36.8%)	1981 (37.0%)	0.00	1676 (36.7%)	1691 (37.0%)	0.01
Clinical cancer stage						
0–I	1451 (23.3%)	1725 (32.2%)	0.20	1101 (24.1%)	947 (20.7%)	0.08
II–III	4776 (76.7%)	3634 (67.8%)	0.20	3471 (75.9%)	3625 (79.3%)	0.08
COPD	431 (6.9%)	364 (6.8%)	0.01	303 (6.6%)	321 (7.0%)	0.02
Hypoalbuminemia	132 (2.1%)	92 (1.7%)	0.03	76 (1.7%)	92 (2.0%)	0.03
Diabetes	464 (7.5%)	388 (7.2%)	0.01	318 (7.0%)	350 (7.7%)	0.03
Charlson comorbidity index						
0	2986 (48.0%)	2733 (51.0%)	0.06	2281 (49.9%)	2183 (47.7%)	0.04
1	1572 (25.2%)	1381 (25.8%)	0.01	1158 (25.3%)	1164 (25.5%)	0.00
≥2	1669 (26.8%)	1245 (23.2%)	0.08	1133 (24.8%)	1225 (26.8%)	0.05
Field of esophagectomy						
Two-field	1719 (27.6%)	363 (6.8%)	0.57	364 (8.0%)	363 (7.9%)	0.00
Three-field	4508 (72.4%)	4996 (93.2%)	0.57	4208 (92.0%)	4209 (92.1%)	0.00
Hospital type						
Nonteaching hospital	2626 (42.2%)	2044 (38.1%)	0.08	1945 (42.5%)	2044 (44.7%)	0.04
Teaching hospital	3601 (57.8%)	3315 (61.9%)	0.08	2627 (57.5%)	2528 (55.3%)	0.04
Hospital volume, procedures per year						
Low (<13)	2213 (35.5%)	1566 (29.2%)	0.14	1384 (30.3%)	1356 (29.7%)	0.01
Middle (13–37)	1937 (31.1%)	1877 (35.0%)	0.08	1508 (33.0%)	1587 (34.7%)	0.04
High (≥37)	2077 (33.4%)	1916 (35.8%)	0.05	1680 (36.7%)	1629 (35.6%)	0.02

Data are presented as n (%). COPD indicates chronic obstructive pulmonary disease.

esophagectomy, and hospital volume (ASD > 0.10). The proportion of patients with an advanced cancer stage (II–III) was higher in the OE group (76.7%) than in the MIE group (67.8%). The proportion of patients who underwent 3-field esophagectomy was higher in the MIE group (93.2%) than in the OE group (72.4%). The proportion of low-volume hospitals was smaller in the MIE group (29.2%) than in the OE group (35.5%). After propensity score matching, each factor between the OE group and MIE group was well balanced (ASD <0.10).

Table 2 shows the in-hospital mortality, morbidities, reoperation during the same admission, and readmission within 30 days after surgery. In the all-patient analysis, in-hospital mortality (1.1% vs 1.9%, $P < 0.001$) and total morbidities (40.7% vs 47.7%, $P < 0.001$) were significantly lower in the MIE than OE group. The MIE group had more favorable outcomes than the OE group in terms of surgical site infection (1.9% vs 2.7%, $P = 0.004$) and anastomotic leakage (12.9% vs 16.9%, $P < 0.001$), although vocal cord dysfunction was more likely to occur in the MIE than OE group (9.3% vs 6.2%, $P < 0.001$). MIE had favorable outcomes with regard to blood transfusion, duration of anesthesia, continuous intubation for >2 days after esophagectomy, unplanned intubation, reoperation, postoperative hospital stay, and readmission within 30 days.

In the propensity score-matching analysis, in-hospital mortality was significantly lower in the MIE than OE group (1.2% vs 1.7%, $P = 0.048$). There was no significant difference in total morbidities between the 2 groups (40.8% vs 42.8%, $P = 0.06$). In a comparison of each complication, we found favorable outcomes in the MIE group with respect to surgical site infection (1.9% vs 2.6%, $P = 0.04$) and anastomotic leakage (12.8% vs 16.8%, $P < 0.001$). In contrast, vocal cord dysfunction was more likely to occur in the MIE group than OE group (9.2% vs 7.5%, $P < 0.001$). We found no significant difference in respiratory failure between the 2 groups (16.8% vs 18.1%, $P = 0.08$). A lower proportion of patients had heart failure in the MIE than OE group (1.6% vs 2.2%, $P = 0.03$). Fewer patients had conditions requiring blood transfusion in the MIE group than OE group (21.9% vs 33.8%, $P < 0.001$). The duration of anesthesia was significantly longer in the MIE group than OE group (408 vs 363 minutes, $P < 0.001$). The reoperation rate was lower in the MIE group than OE group (8.6% vs 9.9%, $P = 0.03$). Fewer patients underwent tracheotomy in MIE group than OE group (4.8% vs 6.3%, $P = 0.002$). The proportion of patients who underwent continuous intubation for >2 days after esophagectomy was higher in the MIE group than OE group (23.2% vs 19.3%, $P < 0.001$); however, fewer patients underwent unplanned intubation in the MIE group than OE

TABLE 2. Outcomes of all Patients and Propensity Score-Matched Patients Undergoing MIE or OE

	All Patients			Propensity Score-matched Patients		
Factors	**OE (n = 6227)**	**MIE (n = 5359)**	***P***	**OE (n = 4572)**	**MIE (n = 4572)**	***P***
In-hospital mortality	120 (1.9%)	61 (1.1%)	<0.001	80 (1.7%)	57 (1.2%)	0.048
Total morbidities	2949 (47.4%)	2181 (40.7%)	<0.001	1955 (42.8%)	1867 (40.8%)	0.06
Surgical site infection	167 (2.7%)	101 (1.9%)	0.004	117 (2.6%)	88 (1.9%)	0.04
Anastomotic leakage	1051 (16.9%)	689 (12.9%)	<0.001	767 (16.8%)	587 (12.8%)	<0.001
Anastomotic stenosis	373 (6.0%)	358 (6.7%)	0.13	312 (6.8%)	301 (6.6%)	0.65
Vocal cord dysfunction	385 (6.2%)	498 (9.3%)	<0.001	345 (7.5%)	422 (9.2%)	0.004
Empyema	63 (1.0%)	42 (0.8%)	0.20	31 (0.7%)	41 (0.9%)	0.24
Chylothorax	63 (1.0%)	58 (1.1%)	0.71	52 (1.1%)	54 (1.2%)	0.85
Ileus and bowel obstruction	51 (0.8%)	51 (1.0%)	0.45	39 (0.9%)	45 (1.0%)	0.51
Respiratory failure	1118 (18.0%)	897 (16.7%)	0.09	829 (18.1%)	766 (16.8%)	0.08
Pulmonary embolism	18 (0.3%)	25 (0.5%)	0.12	16 (0.3%)	20 (0.4%)	0.50
Acute coronary syndrome	14 (0.2%)	9 (0.2%)	0.49	11 (0.2%)	7 (0.2%)	0.35
Heart failure	127 (2.0%)	84 (1.6%)	0.058	100 (2.2%)	72 (1.6%)	0.03
Stroke	23 (0.4%)	14 (0.3%)	0.30	19 (0.4%)	13 (0.3%)	0.29
Acute kidney injury	36 (0.6%)	25 (0.5%)	0.41	26 (0.6%)	23 (0.5%)	0.67
Urinary tract infection	24 (0.4%)	15 (0.3%)	0.33	17 (0.4%)	14 (0.3%)	0.59
Sepsis	104 (1.7%)	73 (1.4%)	0.18	75 (1.6%)	71 (1.6%)	0.74
Blood transfusion	2155 (34.6%)	1068 (19.9%)	<0.001	1545 (33.8%)	1003 (21.9%)	<0.001
Duration of anesthesia, min	352 (280–445)	408 (321–570)	<0.001	363 (292–458)	408 (320–571.5)	<0.001
Postoperative intubation ≥2 days	1212 (19.5%)	1209 (22.6%)	<0.001	881 (19.3%)	1062 (23.2%)	<0.001
Unplanned intubation	512 (8.2%)	333 (6.2%)	<0.001	385 (8.4%)	289 (6.3%)	<0.001
Reoperation during the same admission	595 (9.6%)	439 (8.2%)	0.01	454 (9.9%)	393 (8.6%)	0.03
Tracheotomy	374 (6.0%)	242 (4.5%)	<0.001	286 (6.3%)	218 (4.8%)	0.002
Postoperative length of stay	25 (18–41)	23 (17–35)	<0.001	26 (19–42)	23 (17–36)	<0.001
Readmission within 30 days	1018 (16.3%)	785 (14.6%)	0.01	732 (16.0%)	702 (15.4%)	0.39

Data are presented as n (%) or median (interquartile range).

group (6.3% vs 8.4%, $P < 0.001$). The postoperative length of stay was shorter in the MIE group than OE group (23 vs 26 days, $P < 0.001$).

Table 3 shows the results of the GEE analysis of all patients for in-hospital mortality. OE, older age, hypoalbuminemia, a higher Charlson comorbidity index score, and low hospital volume were significant risk factors for in-hospital mortality.

Table 4 shows the results of the GEE analysis of all patients for total morbidities. OE, older age, male sex, hypoalbuminemia, a higher Charlson comorbidity index score, 3-field esophagectomy, and low hospital volume were significant risk factors for total morbidities.

DISCUSSION

Among 11,586 eligible patients who underwent esophagectomy for esophageal cancer, propensity score matching analysis of 4572 pairs indicated that compared with the OE group, the MIE group had significantly favorable outcomes in terms of in-hospital mortality, surgical site infection, anastomotic leakage, blood transfusion, reoperation, tracheotomy, unplanned intubation, and postoperative length of stay , whereas it had unfavorable outcomes in vocal cord dysfunction, the duration of anesthesia, and the postoperative intubation period. GEE analyses of all patients indicated that OE, older age, preoperative hypoalbuminemia, a higher Charlson comorbidity index score, and lower hospital volume were associated with higher in-hospital mortality and morbidities; and 3-field esophagectomy was associated with higher total morbidities.

Previous studies demonstrated comparable mortality between OE and MIE,[2,3,5,13–16] and a meta-analysis of 15,790 cases suggested lower in-hospital mortality in MIE than OE.[6] One of the first and largest reports from a single institution (University of Pittsburgh) showed a low mortality rate associated with MIE (1.7%); this rate has since acted as a benchmark of MIE.[17] In the present study, the in-hospital mortality rate was only 1.2% in MIE and 1.7% in OE, which are similar to the data in the report from the University of Pittsburgh,[17] but lower than those of previous reports from other countries.[1,3,18] This lower mortality in Japan than in other countries was also shown in a previous report from Japan.[13] Our study also demonstrated that the mortality of MIE was significantly lower than that of OE. This discrepancy can be partially explained by the fact that previous reports had lower statistical power because of the smaller number of patients and lack of accounting for hospital-level confounding factors. Our study involved a large number of patients and a newer dataset than in previous reports. However, this difference in mortality between the 2 groups in our study may have very low clinical importance.

Notably, there was no difference in total morbidities between MIE and OE among the propensity score-matched patients. This discrepancy between in-hospital mortality and morbidity may be explained by the difference in proportions of lethal complications between the 2 groups.

Previous studies showed no significant difference in anastomotic leakage between the 2 groups.[15,19,20] However, our study showed that MIE was superior to OE in terms of anastomotic leakage. This can be attributed to the fact that we used a unique definition of anastomotic leakage as long-term placement of a drainage tube. In addition, technical improvements in MIE may have resulted in the reduction of anastomotic leakage.

Pulmonary complications are a major concern after esophagectomy. Some observational studies have shown inconsistent results regarding the advantages of MIE over OE with respect to pulmonary complications.[3,14,16,20] One retrospective study of a relatively large number of patients showed no significant difference in pulmonary complications between the 2 groups[13]; however, 2

TABLE 3. Generalized Estimating Equation Analysis of all Patients for In-hospital Mortality

In-Hospital Mortality	Odds Ratio	P	95% CI
Surgery type			
OE	Reference		
MIE	0.65	0.008	0.47−0.89
Age, y			
≤64	Reference		
65−74	1.87	0.004	1.23−2.85
≥75	3.66	<0.001	2.35−5.72
Sex			
Female	Reference		
Male	1.41	0.16	0.87−2.27
Body mass index, kg/m^2			
<18.5	1.31	0.16	0.90−1.89
18.5−24.9	Reference		
25.0−29.9	0.73	0.25	0.43−1.24
≥30.0	1.30	0.72	0.31−5.43
Smoking index, pack-years			
0−5	Reference		
6−20	0.96	0.88	0.54−1.69
21−40	0.99	0.96	0.62−1.57
≥41	1.34	0.13	0.92−1.96
Clinical cancer stage			
0−I	Reference		
II−III	1.44	0.055	0.99−2.10
Hypoalbuminemia	2.20	0.04	1.06−4.58
Diabetes	0.96	0.86	0.57−1.60
COPD	1.06	0.81	0.64−1.75
Charlson comorbidity index			
0	Reference		
1	1.67	0.01	1.13−2.46
≥2	2.23	<0.001	1.54−3.22
Field of esophagectomy			
Two-field	Reference		
Three-field	1.08	0.70	0.74−1.57
Hospital type			
Non-teaching hospital	Reference		
Teaching hospital	1.19	0.28	0.87−1.63
Hospital volume, procedures per year			
Low (<13)	Reference		
Middle (13−37)	0.69	0.04	0.48−0.98
High (≥37)	0.72	0.08	0.50−1.04

CI indicates confidence interval; COPD, chronic obstructive pulmonary disease.

TABLE 4. Generalized Estimating Equation Analysis of all Patients for Total Morbidities

Total morbidities	Odds ratio	P	95% CI
Surgery type			
OE	Reference		
MIE	0.88	0.006	0.80−0.96
Age, y			
≤64	Reference		
65−74	1.22	<0.001	1.12−1.32
≥75	1.29	<0.001	1.16−1.44
Sex			
Female	Reference		
Male	1.18	0.002	1.06−1.31
Body mass index, kg/m^2			
<18.5	1.08	0.12	0.98−1.20
18.5−24.9	Reference		
25.0−29.9	1.02	0.69	0.91−1.15
≥30.0	1.42	0.07	0.97−2.08
Smoking index, pack-years			
0−5	Reference		
6−20	1.00	0.98	0.88−1.14
21−40	0.99	0.80	0.88−1.10
≥41	1.10	0.053	1.00−1.22
Clinical cancer stage			
0−I	Reference		
II−III	1.04	0.35	0.96−1.13
Hypoalbuminemia	1.52	0.002	1.16−1.99
Diabetes	0.98	0.75	0.84−1.13
COPD	0.95	0.48	0.81−1.10
Charlson comorbidity index			
0	Reference		
1	1.15	0.004	1.05−1.26
≥2	1.25	<0.001	1.14−1.38
Field of esophagectomy			
Two-field	Reference		
Three-field	1.58	<0.001	1.41−1.76
Hospital type			
Non-teaching hospital	Reference		
Teaching hospital	1.05	0.29	0.96−1.15
Hospital volume, procedures per year			
Low (<13)	Reference		
Middle (13−37)	0.72	<0.001	0.62−0.84
High (≥37)	0.58	<0.001	0.46−0.73

CI indicates confidence interval; COPD, chronic obstructive pulmonary disease.

randomized controlled trials showed a significantly lower incidence of respiratory complications after MIE than OE.[2,15] In our comparison of the 2 groups, we found a comparable incidence of respiratory failure between MIE and OE, a lower incidence of unplanned intubation and tracheotomy in MIE, and a higher incidence of long-term postoperative intubation in MIE. This may indicate that surgeons experienced more hesitation to perform early extubation for patients with MIE than OE.

Mixed results have been obtained regarding the incidence of recurrent laryngeal nerve palsy among previous studies, partially because these studies used various definitions of recurrent laryngeal nerve palsy.[2,14,20] A previous report from Japan showed 8.1% and 10.3% rates of recurrent laryngeal nerve palsy for OE and MIE, respectively, which are similar to our results.[20]

In the present study, we observed a higher incidence of vocal cord dysfunction in MIE than OE using the definition based on ICD-10 codes. A previous report speculated that pneumatic dissection from the thoracic cavity to the neck simplified the neck dissection, leading to less morbidity in MIE.[21] In contrast, the clearer view in MIE may have led surgeons to perform more intense dissection, which led to the higher incidence of vocal cord dysfunction in MIE in our study.

The data from 2014 to 2017 in the present study showed that the reoperation rate was lower in MIE than OE. However, a previous report using Japanese nationwide data from 2011 to 2012 showed a higher rate of reoperation in MIE than in OE.[19] It is plausible that technical improvements in MIE were made between these 2 study periods.

Some reports have demonstrated smaller amounts of bleeding in MIE than in OE.[13,14,19,20] Our results showed that fewer patients undergoing MIE required a blood transfusion than those undergoing OE. These results are compatible with previous reports.

It is biologically plausible that older age, hypoalbuminemia, and a higher Charlson comorbidity index score increase the risk of in-hospital mortality and morbidities in our study. Additionally, 3-field esophagectomy was associated with total morbidities. A previous report suggested that there was no relationship between the field of lymphadenectomy and pulmonary complications.[15] However, a larger extent of dissection might lead to higher incidence of complications.

Our study has several limitations. First, the Diagnosis Procedure Combination database does not include information on the severity of each complication or information regarding neoadjuvant chemotherapy or radiotherapy, which may have caused selection bias with respect to the surgery type; however, a previous randomized controlled trial showed that neoadjuvant chemoradiotherapy did not increase the incidence of postoperative complications.[22] Second, we had no data regarding the tumor location, proportion of R0 resection, details of surgical procedures such as anastomosis and the proportion of conversion, or the number of harvested lymph nodes. Third, in our study, MIE included both totally minimally invasive approaches (thoracoscopy and laparoscopy) and hybrid approaches (thoracoscopy and laparotomy); however, data on the proportions of these approaches were unavailable from the database. Compared with laparoscopy, laparotomy can cause postoperative pain that results in decreased functional residual capacity and respiratory effort. Thus, inclusion of a hybrid approach in MIE may have influenced the insignificant difference in the proportions of pulmonary complications between the MIE and OE groups in the present study. Finally, our data lacked long-term oncologic outcomes, including disease-free survival and overall survival.

In summary, our analysis provided real-world results by using a nationwide database, which showed grossly favorable outcomes of MIE over OE with respect to in-hospital mortality, morbidities, and postoperative length of stay. It may be reasonable to establish MIE as a mainstream esophagectomy technique from the viewpoint of in-hospital mortality and morbidities.

REFERENCES

1. Luketich JD, Pennathur A, Franchetti Y, et al. Minimally invasive esophagectomy: results of a prospective phase II multicenter trial-the eastern cooperative oncology group (E2202) study. *Ann Surg*. 2015;261:702–707.
2. 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;379:1887–1892.
3. Sihag S, Kosinski AS, Gaissert HA, et al. Minimally invasive versus open esophagectomy for esophageal cancer: a comparison of early surgical outcomes from The Society of Thoracic Surgeons National Database. *Ann Thorac Surg*. 2016;101:1281–1288. discussion 1288-1289.
4. Yerokun BA, Sun Z, Yang CJ, et al. Minimally invasive versus open esophagectomy for esophageal cancer: a population-based analysis. *Ann Thorac Surg*. 2016;102:416–423.
5. Zingg U, McQuinn A, DiValentino D, et al. Minimally invasive versus open esophagectomy for patients with esophageal cancer. *Ann Thorac Surg*. 2009;87:911–919.
6. Yibulayin W, Abulizi S, Lv H, et al. Minimally invasive oesophagectomy versus open esophagectomy for resectable esophageal cancer: a meta-analysis. *World J Surg Oncol*. 2016;14:304.
7. International Classification of Diseases (ICD) Tenth Revision. Available at: http://apps.who.int/classifications/icd10/browse/2016/en. Accessed August 8, 2018.
8. Yamana H, Moriwaki M, Horiguchi H, et al. Validity of diagnoses, procedures, and laboratory data in Japanese administrative data. *J Epidemiol*. 2017;27:476–482.
9. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43:1130–1139.
10. Yasunaga H, Horiguchi H, Kuwabara K, et al. Outcomes after laparoscopic or open distal gastrectomy for early-stage gastric cancer: a propensity-matched analysis. *Ann Surg*. 2013;257:640–646.
11. Yasunaga H, Horiguchi H, Matsuda S, et al. Body mass index and outcomes following gastrointestinal cancer surgery in Japan. *Br J Surg*. 2013;100:1335–1343.
12. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46:399–424.
13. Takeuchi H, Miyata H, Gotoh M, et al. A risk model for esophagectomy using data of 5354 patients included in a japanese nationwide web-based database. *Annals of Surgery*. 2014;260:259–266.
14. Tapias LF, Mathisen DJ, Wright CD, et al. Outcomes with open and minimally invasive ivor lewis esophagectomy after neoadjuvant therapy. *Ann Thorac Surg*. 2016;101:1097–1103.
15. Nozaki I, Mizusawa J, Kato K, et al. Impact of laparoscopy on the prevention of pulmonary complications after thoracoscopic esophagectomy using data from JCOG0502: a prospective multicenter study. *Surg Endosc*. 2018;32:651–659.
16. Mamidanna R, Bottle A, Aylin P, et al. Short-term outcomes following open versus minimally invasive esophagectomy for cancer in England: a population-based national study. *Ann Surg*. 2012;255:197–203.
17. Luketich JD, Pennathur A, Awais O, et al. Outcomes after minimally invasive esophagectomy: review of over 1000 patients. *Ann Surg*. 2012;256:95–103.
18. Weksler B, Sullivan JL. Survival after esophagectomy: a propensity-matched study of different surgical approaches. *Ann Thorac Surg*. 2017;104:1138–1146.
19. 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;24:1821–1827.
20. Xie MR, Liu CQ, Guo MF, et al. Short-term outcomes of minimally invasive Ivor-Lewis esophagectomy for esophageal cancer. *Ann Thorac Surg*. 2014;97:1721–1727.
21. Fabian T, Martin J, Katigbak M, et al. Thoracoscopic esophageal mobilization during minimally invasive esophagectomy: a head-to-head comparison of prone versus decubitus positions. *Surg Endosc*. 2008;22:2485–2491.
22. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med*. 2012;366:2074–2084.