

Perioperative management and outcomes of minimally invasive esophagectomy: case study of a high-volume tertiary center in Taiwan

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Background: Mortality and complication rates for surgical esophagectomy remain high despite progress in surgical techniques and perioperative care. Minimally invasive surgery and intraoperative goal-directed fluid management are gaining popularity in Taiwan; however, perioperative complications and short-term outcomes have been rarely reported. In this retrospective study, we analyzed the surgical procedures performed as well as the perioperative outcomes and treatments after esophagectomy in a high-volume medical center in Taiwan. The goals of this study are to compare the complications and the following treatment between different surgical procedures and to analyze if any preoperative coexisting disease and anesthesia conduct might be associated with postoperative complications and hospitalization course.

Methods: We retrospectively reviewed the data of all patients who had undergone esophagectomy and reconstruction in 2015. Patient characteristics, type of surgery performed, method of anesthesia, postoperative hospitalization course, and additional surgical interventions were reviewed and analyzed.

Results: In total, 64 patients were included. Among them, 58 patients (90.6%) were reported squamous cell carcinoma, 33 patients (51.6%) received McKeown minimally invasive esophagectomy (MIE), and 20 (31.3%) received Ivor-Lewis MIE. The most common postoperative complications were pulmonary complications (18.7%), such as empyema and pleural effusion, dysrhythmias (14.1%), anastomosis leakage (14.1%), vocal cord paralysis (9.4%), gastric tube stenosis (4.7%), chyle leakage (4.7%), and acute kidney injury (AKI, 4.7%). Twenty-five percent of patients received secondary operative interventions for the aforementioned complications. Postoperative arrhythmia ($P=0.042$), pulmonary complications ($P=0.009$), and AKI ($P=0.015$) were significantly associated with prolonged intensive care unit (ICU) stays. Thirty-day and 90-day mortality rates were 3.1% and 4.7% respectively. Patients with preoperative arrhythmias have a higher risk of developing post-operative dysrhythmia ($P=0.013$) and lung complications ($P=0.036$). Patients with an underlying heart disease are at higher risk of post-op AKI ($P=0.002$) and second surgical intervention ($P=0.013$). Chronic kidney diseases are associated with post-op dysrhythmia ($P=0.013$), lung complications ($P=0.036$) and post-op AKI ($P\leq 0.01$). Although McKeown MIE bore a significantly longer surgical time and higher intraoperatively-infused crystalloid than did Ivor Lewis MIE, there were no significant differences regarding postoperative cardiothoracic complications and patient outcomes.

Conclusions: Postoperative outcomes of McKeown MIE and Ivor-Lewis MIE were comparable in our center and short term outcomes were similar to those in previous reports. However, despite neoadjuvant concurrent chemoradiation therapy (CCRT), the use of minimally invasive techniques, and well-controlled anesthesia, the incidence of perioperative complications remains high. Our results suggest that patients with preoperative comorbidity of arrhythmia, heart diseases, and CKD are associated with more common post-operative complications. Furthermore, postoperative dysrhythmias, pulmonary complications, and AKI warrant special anesthetic and surgical care to prevent prolonged ICU stay.

Keywords: Esophagectomy; esophageal neoplasms; outcome assessment

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Introduction

Esophageal cancer is the eighth most common cancer worldwide and the sixth most common cause of cancer-related death (1). The mortality rate of esophagectomy remains high with associated procedural complexity. In addition, with different major histological types, mainly adenocarcinomas and squamous cell carcinomas, the postoperative complications and treatment may differ between Western and Asian countries (2). Recently there are significant progress in surgical techniques (3), intraoperative goal-directed fluid management and perioperative care. Various forms of neoadjuvant concurrent chemoradiation therapy (CCRT) incorporating minimally invasive esophagectomy (MIE) procedures such as McKeown MIE and Ivor Lewis MIE have become the mainstay of surgical treatment for esophageal cancer. However, the perioperative management and short-term outcomes of these procedures have rarely been reported.

In the present study, we used 1-year patient data to analyze the type of surgical procedures, the postoperative complications, short-term outcomes, and postoperative management of patients with esophageal cancer who underwent esophagectomy and reconstruction at a high-volume medical center in Taiwan. The goals of this study are to compare the complications and the following treatment between different surgical procedures and to analyze if any preoperative coexisting disease and anesthesia conduct might be associated with postoperative complications and hospitalization course.

Methods

We retrospectively reviewed data from patients with esophageal cancer who had undergone surgical esophagectomy between January and December 2015. The surgical procedures were performed by either of the two chest surgeons in our center. Patient demographics, disease status, cancer staging, neoadjuvant CCRT, perioperative management, operative technique, and postoperative course were reviewed and extracted from electronic medical records and hand-written anesthetic sheets. The major

postoperative complications and morbidities were recorded and categorized as follows: dysrhythmias, reintubations, acute kidney injury (AKI, defined as an increase in serum creatinine level by ≥ 0.3 mg/dL within 48 hours), pulmonary complications (including pneumonia, empyema, or pleural effusion requiring intervention), gastric(G)-tube complications (including anastomosis leakage, stenosis, or necrosis), chyle leakage, vocal cord paralysis (identified through bronchoscopic examination), iatrogenic hypoparathyroidism, and reoperations. In addition, 30- and 90-day mortality rates were recorded. The two mostly performed procedures, McKeown MIE and Ivor Lewis MIE were isolated for comparison. We also analyzed if major postoperative complications including dysrhythmias, lung complication, AKI, secondary surgical intervention, and 30-day mortality were associated with preexisting comorbidities. Statistical analysis was performed using Student's *t*-test for continuous variables, and the association among the variables and the length of stay was tested using the Kruskal-Wallis test. The chi-squared test was used for categorical variables. In all analyses, $P < 0.05$ was considered statistically significant. SPSS version 22.0 (International Business Machines, Armonk, NY, USA) was used for all analyses.

Results

In total, 64 patients received esophagectomy and reconstruction in 2015 in our hospital. Baseline demographic characteristics are listed in *Table 1*. Perioperative management and surgical procedures are listed in *Table 2*. Anesthesia conduct includes general anesthesia with 8.0 French endotracheal tube or pre-existing tracheostomy, invasive blood pressure monitoring, and central venous catheter placement. One lung ventilation during thoracoscopic stage of MIE was achieved using Coopdech endobronchial blocker tube and patients were positioned into left lateral decubitus position for all of our patients.

Overall, the mean intensive care unit (ICU) stay was 9.6 ± 20.1 days and mean hospital stay was 28.4 ± 25 days. Infusion of 6% hydroxyethyl starch (Voluven, Fresenius/

Table 1 Baseline demographic characteristics of all patients

Characteristics	Mean ± SD/N (%)
Age (y/o)	58.3±10.7
Gender	
Male	57 (89.1)
Female	7 (10.9)
Pathology	
Squamous cell carcinoma	58 (90.6)
Adenocarcinoma	5 (7.8)
Neuroendocrine carcinoma	1 (1.6)
Staging	
IA	1 (1.6)
IB	2 (3.1)
IIA	2 (3.1)
IIB	13 (20.3)
IIIA	19 (29.7)
IIIB	19 (29.7)
IIIC	7 (10.9)
IV	1 (1.6)
ASA classification	
II	17 (26.6)
III	46 (71.8)
IV	1 (1.6)
Neoadjuvant CCRT	56 (87.5)
Underlying disease	
Second primary malignancy	10 (15.6)
Old cerebrovascular accident	4 (6.3)
Heart disease	2 (3.1)
Arrhythmias	1 (1.6)
Hypertension	11 (17.2)
Diabetes mellitus	4 (6.3)
Lung disease	5 (7.8)
Chronic kidney disease	1 (1.6)
Liver/GI disease	19 (29.7)

Data are presented as mean ± SD and N (%). CCRT, concurrent chemoradiation therapy; GI, gastrointestinal.

Table 2 Perioperative management and surgical procedures performed

Perioperative variables	Mean ± SD/N (%)
Induction time (min)	38±16
Surgical time (min)	523±91
Procedure performed	
McKeown MIE	33 (51.6)
Ivor-Lewis MIE	20 (31.3)
Total laryngectomy + tri-incision	6 (9.3)
Laparotomy ileo-colon interposition for eso.; reconstruction with cervical anas.	2 (3.1)
Robotic tri-incision	1 (1.6)
Mis subtotal esophagectomy, G-tube not done since adhesion and suspected perforation	1 (1.6)
Single port VATS total pharyngo-laryngo-esophagectomy	1 (1.6)
Neck lymph node dissection	
Not performed	1 (1.6)
2 fields	7 (10.9)
3 fields	56 (87.5)
Intraoperative fluid management	
Intraoperative urine output (mL)	700±463
Crystalloid infused (mL)	2,592±1,028
Voluven 500 mL infusion	18 (28.1)
Albumin 100 mL infusion	27 (42.2)
Blood transfusion	12 (18.8)
Postoperative analgesia	
Single dose morphine	29 (45.3)
Intravenous PCA	24 (37.5)
Epidural PCA	11 (17.2)
Extubate in the operating room	41 (64.1)

Data are presented as mean ± SD and N (%). PCA, patient-controlled analgesia.

Hospira, Germany), albumin, or blood during the intraoperative period was not associated with the length of ICU or hospital stay. However, postoperative arrhythmia and pulmonary complications were associated with a prolonged ICU stay (P=0.042 and 0.009, respectively) but not hospital stay (P=0.448 and 0.125, respectively).

Table 3 Demographic characteristics and anesthetic management of patients who underwent McKeown MIE and Ivor Lewis MIE

Baseline characteristics	Operation performed		P value
	McKeown MIE (n=33)	Ivor-Lewis MIE (n=20)	
Pathology			0.056
Squamous cell carcinoma	32 (97%)	17 (85%)	
Adenocarcinoma	0 (0%)	3 (15%)	
Neuroendocrine carcinoma	1 (3%)	0 (0%)	
Staging			0.709
ASA classification			0.412
Surgical time (min)	529.5±87.8	474.3±52.3	0.016
Intraoperative fluid management			
Crystalloid (mL)	2,731.5±979.8	2,000±801	0.008
Voluven 500 mL infusion	9 (27.3%)	5 (25%)	0.43
Albumin 100 mL infusion	14 (42.4%)	10 (50%)	0.336
Blood transfusion	3 (9.1%)	5 (25%)	0.111
Extubate in operating room	23 (69.7%)	13 (65%)	0.429

Data were expressed as N (%) and mean ± SD. MIE, minimal invasive esophagectomy; PCA, patient-controlled analgesia.

However, the occurrence of postoperative AKI was associated with both prolonged ICU stay (P=0.015) and hospital stay (P=0.017).

The most common postoperative complications included lung complications (18.7%), dysrhythmias (14.1%), anastomosis leakage (14.1%), vocal cord paralysis (9.4%), G-tube stenosis (4.7%), chyle leakage (4.7%), and AKI (4.7%). In our study, 25% of patients received secondary surgical interventions for the aforementioned complications. The 30- and 90-day mortality rates were 3.1% and 4.7% respectively.

The two most common surgical approaches, namely McKeown MIE and Ivor-Lewis MIE, were analyzed separately (Table 3). McKeown MIE required a significantly longer surgical time and significantly higher total volume of infused intraoperative crystalloid than did Ivor-Lewis MIE. The postoperative complications and patient outcomes of these two approaches are listed in Table 4. Neither major organ complications nor G-tube complications differed significantly between the two groups. However, there is a trend toward higher incidence of vocal cord paralysis McKeown MIE group (P=0.067) and chyle leakage in

Table 4 Comparison of postoperative morbidity and mortality rates of McKeown MIE (minimal invasive esophagectomy) and Ivor Lewis MIE [presented as N (%)]

Postoperative major complications	McKeown MIE (n=33)	Ivor -Lewis MIE (n=20)	P value
Dysrhythmia	6 (18.2)	1 (5.0)	0.169
AKI	1 (3.0)	2 (10.0)	0.287
Lung complication	7 (21.0)	4 (20.0)	0.19
Anastomosis leak	4 (12.1)	4 (20.0)	0.437
G-tube stenosis	2 (6.0)	1 (5.0)	0.52
G-tube necrosis	2 (6.0)	0	
Second surgical intervention	6 (18.2)	6 (30.0)	0.318
Vocal cord paralysis	5 (15.1)	0	0.067
Chyle leak	0	2 (10.0)	0.064
Iatrogenic hypoparathyroidism	1 (3.0)	0	0.432
ICU stay	7.3±15.8	12.5±28.5	0.405
Hospital stay	28.9±23.3	29.6±32.7	0.929
30-day mortality	1 (3.0)	0	0.533
90-day mortality	1 (3.0)	0	

AKI, acute kidney injury; MIE, minimal invasive esophagectomy; ICU, intensive care unit.

the Ivor-Lewis MIE group (P=0.064). In the McKeown MIE group, 30-day mortality was observed in one patient. However, 30-day mortality was not observed in the Ivor Lewis MIE group.

The association between major post-operative complications and pre-operative comorbidity are shown in Table 5. Patients with preoperative arrhythmias have a higher risk of developing post-operative dysrhythmia (P=0.013) and lung complications (P=0.036). Patients with underlying heart diseases are at higher risk of post-operative AKI (P=0.002) and second surgical intervention (P=0.013). Chronic kidney diseases are associated with post-operative dysrhythmia (P=0.013), lung complications (P=0.036) and post-operative AKI (P≤0.01).

Discussion

A total of 64 patients underwent surgical esophagectomy in our center in 2015, and the mortality rate was low (<5%). Hence, our results were consistent with those of

Table 5 Comparison of postoperative morbidity and mortality rates between patients with different preexisting comorbidities [presented as N (%)]

Post-op major complications	Cancer			Old CVA			Heart diseases			Arrhythmia		
	Y (n=10)	N (n=45)	P value	Y (n=4)	N (n=60)	P value	Y (n=2)	N (n=92)	P value	Y (n=1)	N (n=63)	P value
Dysrhythmia	0 (0%)	9 (16.7%)	0.164	1 (25%)	8 (13.3%)	0.516	1 (50%)	8 (12.9%)	0.137	1 (100%)	8 (12.7%)	0.013
Lung complication	1 (10%)	11 (20.4%)	0.44	2 (50%)	10 (16.7%)	0.098	1 (50%)	11 (17.7%)	0.25	1 (100%)	11 (17.5%)	0.036
AKI	0 (0%)	3 (5.6%)	0.445	1 (25%)	2 (3.3%)	0.047	1 (50%)	2 (3.2%)	0.002	0 (0%)	3 (4.8%)	0.823
Second surgical intervention	3 (30%)	13 (24.1%)	0.691	2 (50%)	14 (23.3%)	0.233	2 (100%)	14 (22.6%)	0.013	1 (100%)	15 (23.8%)	0.081
30-day mortality	0 (0%)	2 (3.7%)	0.536	0 (0%)	2 (3.3%)	0.711	0 (0%)	2 (3.2%)	0.796	0 (0%)	2 (3.2%)	0.856

Post-op major complications (cont')	Lung disease			Chronic kidney disease			Liver/GI disease			ASA classification			
	Y (n=5)	N (n=59)	P value	Y (n=1)	N (n=63)	P value	Y (n=19)	N (n=45)	P value	II (n=17)	III (n=46)	IV (n=1)	P value
Dysrhythmia	2 (40%)	7 (11.9%)	0.082	1 (100%)	8 (12.7%)	0.013	4 (21.1%)	5 (11.1%)	0.296	2 (11.8%)	7 (15.2%)	0 (0%)	0.938
Lung complication	1 (20%)	11 (18.6%)	0.941	1 (100%)	11 (17.5%)	0.036	5 (26.3%)	7 (15.6%)	0.314	4 (23.5%)	8 (17.4%)	0 (0%)	0.819
AKI	1 (20%)	2 (3.4%)	0.092	1 (100%)	2 (3.2%)	<0.01	0 (0%)	3 (6.7%)	0.249	1 (5.9%)	2 (4.3%)	0 (0%)	0.978
Second surgical intervention	2 (40%)	14 (23.7%)	0.42	1 (100%)	15 (23.8%)	0.081	5 (26.3%)	11 (24.4%)	0.874	3 (17.6%)	12 (26.1%)	1 (100%)	0.296
30-day mortality	0 (0%)	2 (3.4%)	0.676	0 (0%)	2 (3.2%)	0.856	1 (5.3%)	1 (2.2%)	0.523	1 (5.9%)	1 (2.2%)	0 (0%)	0.869

CVA, cerebrovascular accident.

previous studies in high-volume hospitals (4,5). According to previous investigations, procedural volume is a crucial determinant of the outcome of esophagectomy (6-8). Procedures performed in high-volume centers theoretically have favorable short-term outcomes and low mortality (4). However, hospital stays were longer as the majority of our patients were diagnosed of squamous cell carcinoma and consequently required additional operations on the upper esophagus. With optimal pulmonary protection and fluid management, 64.1% of our patients were extubated in the operation room.

However, pulmonary complications including empyema and pleural effusion remain the most common postoperative complications associated with prolonged ICU stay and the most common indications for further surgical intervention (6.4%). Yet hospital stays were not significantly prolonged by postoperative pulmonary complications. Our results differ from those of previous studies, which have suggested that isolated pulmonary complications are associated with prolonged hospital stays (9).

ICU stays are longer in our center when comparing to previous reports. In our center, all of the patients were transferred to ICU directly after esophagectomy, and 69% of the patients were transferred to general ward within 5 days. However, there are six patients stayed in ICU for more than four weeks, with the longest ICU stay being 125 days to be exact. These patients were all complicated with either anastomosis leakage, empyema, G-tube necrosis, or massive bleeding, and five of them received more than two reoperations. The other patient who had a prolonged ICU course is the oldest man in our cohort who is 81 years old and suffered from a delayed weaning process, leading to his prolonged ICU stay. To some extent, the relative longer ICU and hospital stay in our study can be explained by the whole-coverage national health insurance in Taiwan.

Previous studies have demonstrated that comorbidity influences outcomes with operative time, cardiovascular complications, anastomotic leakage, and overall survival in patients undergoing esophagectomy (5). In our study, preexisting heart disease, arrhythmia, and CKD are

associated with major postoperative complications, whilst ASA classification, preexisting lung disease, presence of a second primary malignancy, and old cerebrovascular accident (CVA) play nonsignificant roles in postoperative complications. Charlson *et al.* had developed a weighed index of comorbidity for mortality, in which moderate to severe renal disease was assigned a weight of 2, whereas myocardial infarct, congestive heart failure, CVA, chronic pulmonary disease were assigned a weight of 1, indicating that chronic kidney disease itself does play a crucial role in morbidity and mortality (10). In our study, CKD is associated with more post-operative dysrhythmias, lung complications, and acute kidney injuries.

Our results suggest that with adequate monitoring and anesthetic management, operation time and infused volume did not affect postoperative outcomes. Although a longer operative duration and higher volume of infused crystalloids were observed with the McKeown MIE than the Ivor Lewis MIE, the postoperative complications and outcomes of both methods were comparable. Goal-directed fluid management guided by pulse pressure variation, stroke volume, or stroke volume variation are routinely used in our center; such management is advantageous for lengthy surgical procedures. However, complications differ with different surgical techniques. More patients were observed to have vocal cord paralysis in the McKeown MIE group; and a higher number of patients with chyle leakage were observed in the Ivor Lewis MIE group. Our results were similar to another retrospective report, in which a significantly higher incidence of vocal cord paralysis was associated with the McKeown MIE (11). For transthoracic esophagectomy, chylothorax is a well-known complication associated with high morbidity and mortality (12). A randomized controlled trial and a meta-analysis have reported that transthoracic esophagectomy is associated with a high incidence of pulmonary complications and chyle leakage and longer hospital stays (13,14).

In Western countries, distal esophageal and gastroesophageal adenocarcinomas account for >70% of upper gastrointestinal malignancies; however, squamous cell carcinomas were the most common type of esophageal malignancy in this study, reflecting the overall prevalence in Asia, according to a previous report (15). Our results showed that 87.5% of our patients received neoadjuvant CCRT and 97% received MIE. In addition, more complex and higher-risk procedures such as combining otolaryngologist for total laryngectomy with McKeown method, or ileo-colon interposition for esophageal reconstruction were performed

for rescue of advanced-stage patients in our center. In addition to surgeon performance and hospital volume, the outcomes of highly complex surgical procedures such as esophagectomy rely heavily on staff from other hospital units and services, including the anesthetic team, ICU caregivers, nurses, nutritionists, and physical therapists (16,17). Strategies to minimize morbidity and mortality should be advocated, from preoperative patient selection to the implementation of standardized perioperative and multidisciplinary care pathways (18).

Our study has some limitations, such as its retrospective design, relatively small sample size, and relatively short-term follow up. Our results might have been more conclusive if we had extended the research period or included a larger number of patients for analysis. Prospective studies must be designed and undertaken to obtain more solid evidences.

Conclusions

Postoperative dysrhythmias, pulmonary complications, and AKI were significantly associated with prolonged ICU stay. Strategies to prevent post-operative AKI should be implemented to reduce the length of hospital stay. Comparable postoperative complications were observed in patients who underwent McKeown MIE and Ivor Lewis MIE despite differences in operative duration, intraoperatively administered fluids, including crystalloids, albumin, and Voluven; and administered blood products. The 30- and 90-day mortality rates in our study were low and were comparable to those reported in previous studies. Our results suggest that patients with preoperative comorbidity of arrhythmia, heart diseases, and CKD are associated with more common post-operative complications and more often require second surgical intervention.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare

Ethical Statement: The study was approved by the National

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