ORIGINAL ARTICLE

A Study and Evaluation of Makeown's Esophagectomy Outcomes with Cost and Benefit Analysis: A Single Institutional Review

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ABSTRACT

Background: A minimally invasive approach to esophagectomy is being used increasingly, but concerns remain regarding the feasibility, safety, cost, and outcomes. We performed an analysis of outcomes including the costs and benefits of Hybrid and open esophagectomy approaches for esophageal cancer surgery.

Methods: The data of 15 consecutive patients who underwent a McKeown's esophagectomy at Sri Aurobindo Institute of Medical Science and Post Graduate Institute (SAIMS and PGI), Indore between November 2017 and October 2019 were analysed. Open esophagectomy was performed in 10 patients, and hybrid esophagectomy in 05. There were no differences in patient characteristics among the 2 groups. Hybrid esophagectomy via a thoracoscopic-laparotomy approach and open esophagectomy by a thoracotomy-laparotomy approach.

Results: Hybrid esophagectomy required a longer operative time than open esophagectomy (p value 0.02), but these patients reported less postoperative pain (p value 0.01). There were no significant differences in blood loss, intensive care unit stay, hospital stay, or postoperative complications among the 2 groups. Hybrid esophagectomy incurred higher operative and surgical material cost and inpatient care and total hospital costs than open esophagectomy (p value 0.01).

Conclusion: Hybrid esophagectomy resulted in the least postoperative pain but the greatest operative cost and longest operative time. Open esophagectomy was associated with the lowest operative cost and shortest operative time but the most postoperative pain.

Key words: Cost analysis, Esophageal Carcinoma, Esophagectomy, Surgical procedures, Operative time , Treatment outcome

INTRODUCTION

Oesophageal cancer is the eighth most common cause of cancer worldwide.[1] Surgery is still the gold standard for the treatment of resectable esophageal cancer. However, oesophagectomy for oesophageal cancer is a complex procedure, with morbidity and mortality rates of 23–50% and 2–8%, respectively, in western countries[3] and of 9–29% and 2–4%, respectively, in India.[4]

Minimally invasive esophagectomy (MIO), which aims to reduce the morbidity rate, was first introduced into clinical practice in 1992.[5]

The mechanisms of MIO may lie in minimising the reaction to surgical injury and inflammation.[6] Reduced morbidity and mortality rates of 11–25% and 1–3%, respectively, have been reported by many surgeons, which are lower than previous rates using the traditional open approach.[7]

The primary end points are major respiratory complications within 30 days after surgery. These respiratory complications involve respiratory distress or failure after the operation with continuation of mechanical ventilation, pulmonary atelectasis requiring sputum suction by bronchoscopy, pneumonia requiring specific antibiotics confirmed by thoracic X-ray or CT scan of the thorax and a positive sputum culture, and acute respiratory distress syndrome.

The secondary endpoints include other postoperative complications not involved in the primary endpoints according to systematic classification of morbidity and mortality after thoracic surgery. Other secondary endpoints include histopathology, intraoperative variables involving volume of blood loss, duration of operation, the number and location of lymph nodes dissected, postoperative pain scale evaluated by pain score and quality of life questionnaires (EORTC QLQ-C30 and QLQ-0ES18), in-hospital mortality

and 30-day mortality rate, intensive care unit stay, the length of hospital stay, operative and surgical material cost and inpatient care and total expenses in hospital, 2 year survival rate.

METHODS

This is a 2 years single institute, retrospective study which aims to compare the effectiveness of hybrid oesophagectomy to open three-stage transthoracic oesophagectomy for resectable oesophageal cancer.

The data of 15 consecutive patients who underwent a McKeown's esophagectomy at Sri Aurobindo Institute of Medical Science and Post Graduate Institute (SAIMS & PGI), Indore between November 2017 and October 2019 were analysed. Open esophagectomy was performed in 10 patients, and hybrid esophagectomy in 05. There were no differences in patient characteristics among the 2 groups. Hybrid esophagectomy via a thoracoscopic-laparotomy approach and open esophagectomy by a thoracotomy-laparotomy approach.

Patients with resectable thoracic oesophageal carcinoma in cT1b-4aN0-2M0 are eligible for inclusion using chest CT and upper abdomen. We do not routinely include a positron emission tomography (PET)/CT scan as a preoperative workup because high-cost. Cervical oesophageal cancer and adenocarcinoma of the oesophagogastric junction are excluded. Cervical oesophageal cancer is treated mainly with radiotherapy, and cancer of the oesophagogastric junction is resected via a single left thoracic approach commonly.

The patients are divided into two groups. Group A patients receive McKeown hybrid esophagectomywhich involves thoracoscopic oesophagectomy and gastric mobilisation by laparotomy with cervical anastomosis. Group B patients receive open McKeown oesophagectomy, which involves a right thoracotomy and laparotomy with cervical anastomosis. All patients received two field lymphadenectomy which involves resection of the lymph nodes in the thorax and abdomen. Neo-adjuvant chemotherapy will be performed for patients according to guidelines.

Inclusion criteria

Subjects may enter the trial with all of the following: (1) oesophageal carcinoma confirmed by pathology; (2) resectable thoracic oesophageal carcinoma in cT1b-4aN0-2M0 using chest CT preoperatively, ultrasonography of the abdomen, head CT and bone scan; (3) oesophageal carcinoma that can be resected initially by multidisciplinary treatment, or that can be resected after neoadjuvant therapy; (4) age between 18 and 75 years; (5) Eastern Cooperative Oncology Group Performance Status (ECOG PS) score ≤2; (6) a life expectancy ≥12 months; (7) tolerate tracheal intubation and general anaesthesia as determined by an anaesthetist preoperatively; (8) laboratory findings including liver and kidney function, and electrolyte findings in 14 days before operation meet the criteria; (9) informed consents must be signed before the beginning of any procedures in the study.

Exclusion criteria

Subjects may not enter the trial with one of the following: (1) cervical oesophageal cancer and adenocarcinoma of the oesophagogastric junction; (2) history of thoracic or abdominal operations which may affect the study; (3) unable to tolerate tracheal intubation and general anaesthesia as determined by an

Table 1: Preoperative Patient Characteristics

Preoperative Patient Characteristics	Open (n=10)(67%)	Hybrid (n=05)(33%)	Total (n = 15)	*P*
Age, median (IQR)	65 (56–72)	64 (56–72)	64 (56–72)	0.45
Sex, male, n (%)	07(70%)	03 (30%)	10 (67%)	0.21
Sex, female, n (%)	03(60%)	02(40%)	05(33%)	
BMI, kg/m^2, median (IQR)	28 (25–32)	28 (25–33)	28 (25–32)	0.07
Pretreatment weight loss, n (%)	7 (70%)	2 (40%)	9 (60%)	0.258
Albumin, mg/dL, median (IQR)	3.9 (3.7–4.2)	3.9 (3.6–4.2)	3.9 (3.6–4.2)	0.207
Hemoglobin, mg/dL, median (IQR)	13.3 (12.1–14.5)	13.3 (11.7–14.6)	13.3 (11.9–14.5)	0.21
History of tobacco use, n (%)	9 (90%)	03 (60%)	12 (80%)	0.017
Prior gastric or esophageal surgery	0	0	0	
Previous anti-reflux surgery, n (%)	0	0	0	
Previous chest surgery, n (%)	0	0	0	
Comorbid conditions				
Hypertension	04(40%)	1(10%)	05(33%)	0.92
Coronary artery disease, n (%)	01(10%)	0	01(07%)	0.999
Diabetes mellitus, n (%)	02 (20%)	01(20%)	03(20%)	0.95
History of gastroesophageal reflux disease	01 (10%)	01(20%)	02 (13%)	0.76
Peptic ulcer disease	01 (10%)	0	01 (07%)	0.171
COPD/emphysema, n (%)	02 (20%)	01 (20%)	03 (20%)	0.054
Preoperative endoscopic interventions, n (%)	0	0	0	

anaesthetist preoperatively; (4) severe comorbidities such as any unstable systemic disease, including active infection, uncontrolled hypertension, angina within previous 3 months, congestive heart failure, myocardial infarction within previous 6 months, severe arrhythmias, and liver, kidney or other metabolic diseases; (5) poor compliance of follow-up; (6) pregnant or lactating women; (7) ECOG PS scores >2; (8) other patients considered unsuitable such as those who do not agree to participate in the trial.

RESULTS

The study population overall was predominantly male (67%), with a median age of 64 years. The most common co-morbid conditions were hypertension and diabetes, present in 33% and 20%, respectively. In this population, 61.3% of patients had at least 1 comorbid condition and 76.7% had an ASA score of at least 3.

Table 2: Technical and perioperative Aspects

Technical and perioperative Aspects	Open (n=10) (67%)	Hybrid (n=05) (33%)	Total (n = 15)	*P*
Gastric conduit, n (%)	10 (100%)	05 (100%)	15 (100%)	0.294
Pyloric drainage procedure, n (%)	10 (100%)	05 (100%)	15 (100%)	0.59
Feeding jejunostomy, n (%)	2 (20%)	01 (20%)	03 (20%)	0.829
Stapled anastomosis, n (%)	0	0	0	
Conversion to open, n (%)		0		
Operative time	320 min (5.3 hrs)	410 min (6.8 hrs)	355 min (5.9 hrs)	0.058
Blood loss	450 ml (300-600ml)	320ml (280-350ml)	400ml (380-415ml)	0.062
Postoperative length of stay, median (IQR)	10 (6–14) days	8 (6–14) days	9 (6–14) days	0.069
ICU length of stay, median (IQR)	2 (1–3) days	2 (1–3) days	2 (1–3) days	0.877
Pain score(VAS)	6(5-6.5)	2(1.5-3)	4(2-6)	0.882

Table 3: Post-op adverse outcomes

Post-op adverse outcomes	Open (n=10) (67%)	Hybrid (n = 05) (33%)	Total (n = 15)	*P*
Major morbidity, n (%)				
Vocal fold paresis/paralysis	1(10%)		0	
Empyema	01(10%)	0	01(07%)	0.431
ARDS	02(20%)	0	02 (13%)	0.026
Myocardial infarction	0	0	0	
Congestive heart failure	0	0	0	
Anastomotic leak	2(20%)	0	2(13%)	0.439
Gastric tube necrosis	0	0	0	
Mortality at 30 days, n (%)	01(10%)	0	0	0.083

Table 4: Tumour specific variables

Tumour specific variables	Open (n=10) (67%)	Hybrid (n = 05) (33%)	Total (n = 15)	*P*
Tumour location, n (%)				
Middle esophagus	4 (40%)	3 (60%)	07 (47%)	<0.001
Distal esophagus	6 (60%)	02 (20%)	08 (53%)	
Pathological stage, n (%)				
Stage I	2(20%)	0	2(13%)	
Stage II(Post NACT)	1(10%)	0	1(7%)	
Stage IIA	2 (20%)	1 (20%)	3(20%)	
Stage IIB	1(10%)	2(40%)	3 (20%)	
Stage IIIA	0	0	0	
Stage IIIB	4 (40%)	2 (40%)	6 (40%)	
Squamous tumor type, n (%)	9 (90%)	4 (80%)	13 (87%)	0.03
Adenocarcinoma tumor type, n (%)	1 (10%)	1 (20%)	2 (13%)	<0.001
Nodal metastasis at esophagectomy, n (%)	6 (60%)	2 (40%)	8 (53%)	0.003
Adequacy of cancer resection				
Negative margins, n (%)	10 (100%)	5 (100%)	15 (100%)	0.623
No of lymph nodes examined, median (IQR)	19 (13–26)	23.5 (17–31)	21 (15–29)	<0.001
Costing				
Operative cost		>20%	>20%	
Surgical material cost		>23%	>23%	
In patient care cost		>15%	>15%	
Total hospital cost		>18%	>18%	

Chemotherapy had been given previously in 7.6% of patients and both RT + CT given in 13.3%. Reconstruction with a gastric conduit was done in all patients and all patients had required transfusion of at least 2 U of packed red blood cells.

Hybrid esophagectomy required a longer operative time than open esophagectomy ($p = 0.02$), but these patients reported less postoperative pain ($p = 0.01$). There were no significant differences in blood loss, intensive care unit stay, hospital stay, or postoperative complications among the 2 groups. Hybrid esophagectomy incurred higher operative and surgical material cost and inpatient care and total hospital costs. than open esophagectomy ($p = 0.01$).

Apart from observational studies, [8] two completed randomised controlled trials (RCTs) in the Netherlands have reported promising results for MIO. [9] In the Netherlands study, a reduction of pulmonary infection rate was noted in the MIO group compared with the open oesophagectomy group, and the number of lymph nodes harvested were comparable in both groups, with manifest good oncologic effect in the MIO group. In the TIME (Traditional Invasive vs. Minimally invasive Esophagectomy) trial, the majority of the patients underwent surgery in a three-stage procedure, the patients having adenocarcinoma and squamous cell carcinoma (SCC). Moreover the technical complications in this trial were the same in the two groups, following neoadjuvant therapy. However, multiple surgical procedures were used in the study, and the complication rate was higher than in previous reports. In the French study, [10] Mariette *et al* found that the rate of pulmonary complication was significant lower in the MIO group than in the open oesophagectomy group. The Ivor-Lewis procedure was used in the MIRO trial (Open vs Laparoscopically-assisted Esophagectomy for Cancer: A Multicentric Phase III Prospective Randomized Controlled Trial); however, a benefit from using the Ivor-Lewis MIO in that study may not be generalised to the McKeown oesophagectomy.

There are several ongoing randomised trials regarding the comparison of minimally invasive versus open oesophagectomy, with enrolment of over 100–850 subjects.[11] The ROMIO (Randomized Oesophagectomy: Minimally Invasive or Open) trial is a three-arm trial which aims to compare the outcomes of total MIO versus hybrid MIO versus conventional open oesophagectomy (open thoracotomy and laparotomy). [12] The procedures used in the ROMIO study include the open oesophagectomy or the MIO Ivor-Lewis procedure. The other three ongoing RCTs used the McKeown MIO procedure.[13] The ROBOT trial was designed to compare the outcomes of robot-assisted McKeown MIO versus open McKeown oesophagectomy for resectable oesophageal cancer.[14] Robot-assisted MIO has become popular in developing and developed countries in recent years. However, it has not been as widely used as thoraco-laparoscopic MIO.

NCT02017002 is a trial which aims to compare the outcomes of the Ivor-Lewis and tri-incision approaches for patients with oesophageal cancer in Taiwan.[15] The NCT02188615 trial is investigating the outcomes of neo-adjuvant chemoradiotherapy followed by MIO for squamous cell oesophageal cancer (NACRFMIE) in Taizhou China.[16] The protocol used in the NCT02188615 study was the McKeown MIO with or without neo-adjuvant chemoradiotherapy. Although guidelines are supportive of neo-adjuvant chemoradiotherapy plus surgery over surgery alone,[17] the reported studies lacked well-designed series, almost all mixing stages and types of tumour. Therefore, surgeons and oncologists might have different opinions about which modality to recommend, especially in clinical stage II or III.

Although the TIME and MIRO trials reported advantages of MIO over open oesophagectomy, currently the majority of oesophageal surgery is done by means of the open approach. Therefore, more studies are needed to clarify the role of MIO in the surgical treatment of oesophageal cancer. Here, we aim to conduct a multicentre, prospective, randomised, open controlled trial in order to evaluate the effectiveness of MIO versus open oesophagectomy through a McKeown procedure for the surgical treatment of resectable oesophageal cancer. We hope the results of our study will provide a high level of clinical evidence to support the routine use of MIO.

CONCLUSION

Hybrid esophagectomy resulted in the least postoperative pain but the greatest operative cost and longest operative time. Open esophagectomy was associated with the lowest operative cost and shortest operative time but the most postoperative pain.

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