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Gastrointestinal Cancer

Operative Outcomes of Minimally Invasive Esophagectomy versus Open Esophagectomy for Resectable Esophageal Cancer

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Abstract

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Background There is a recent rise in the incidence of esophageal carcinoma in India. Surgical resection with or without neoadjuvant chemoradiation is the current treatment modality of choice. Postoperative complications, especially pulmonary complications, affect many patients who undergo open esophagectomy for esophageal cancer. Minimally invasive esophagectomy (MIE) could reduce the pulmonary complications and reduce the postoperative stay.

Methodology We performed a retrospective analysis of prospectively collected data of 114 patients with esophageal cancer in the department of surgical oncology at a tertiary cancer center in South India between January 2019 and March 2020. We included patients with resectable cancer of middle or lower third of the esophagus, and gastroesophageal junction tumors (Siewert I). MIE was performed in 27 patients and 78 patients underwent open esophagectomy (OE). The primary outcome measured was postoperative complications of Clavien–Dindo grade II or higher within 30 days. Other outcomes measured include overall mortality within 30 days, intraoperative complications, operative duration and the length of hospital stay.

Results A postoperative complication rate of 18.5% was noted in the MIE group, compared with 41% in the OE group ($p = 0.034$). Pulmonary complications were noted in 7.4% in the MIE group compared to 25.6% in the OE group ($p = 0.044$). Postoperative mortality rates, intraoperative complications, and other nonpulmonary postoperative complications were almost similar with MIE as with open esophagectomy. Although the median operative time was more in the MIE group (260 minutes vs. 180 minutes; $p < 0.0001$), the median length of hospital stay was shorter in patients undergoing MIE (9 days vs. 12 days; $p = 0.0001$).

Conclusions We found that MIE resulted in lower incidence of postoperative complications, especially pulmonary complications. Although, MIE was associated with prolonged operative duration, it resulted in shorter hospital stay.

Keywords
- minimally invasive esophagectomy
- open esophagectomy
- operative outcomes
- pulmonary complications
- esophageal cancer

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Introduction

Esophageal cancer is among the cancers with most rapidly increasing incidence in India.[1] It is expected that this substantial increase in incidence will continue in the years to come, owing to rise in the number of adenocarcinomas diagnosed. Surgical resection with or without neoadjuvant chemotherapy or chemoradiotherapy remains the current curative option for resectable esophageal cancers. Improvements in survival after esophagectomy were observed in recent years due to centralization of practice to high volume centers[2,3] and increased use of multi-modality treatment approaches.[4-6] Minimally invasive esophagectomy (MIE) can reduce the amount of trauma by avoiding thoracotomy and laparotomy. Short-term benefits of minimally invasive surgery over open procedures with similar oncological outcomes were evident in recent studies.[7] The main advantages of minimally invasive surgery include less perioperative complications, shorter hospital stay, and faster postoperative recovery. MIE involves a laparoscopy with or without right thoracoscopy, with either a cervical or an intrathoracic anastomosis. Thoracoscopy can be performed through a right lateral thoracic approach with a selective intubation or in prone position without selective lung block. The prone approach with partial lung collapse, will result in lower percentage of pulmonary complications.[8] The randomized Traditional Invasive versus Minimally invasive Esophagectomy (TIME) trial showed that MIE (both thoracoscopic and laparoscopic) was associated with lower incidence of pulmonary complications than open esophagectomy.[9] MIE may have specific advantages, including a lower rate of pulmonary complications, laparoscopic tumor dissection limiting potential tumor spillage, and easier reproducibility of the technique.[10] In this study, we have evaluated whether MIE would result in a lower incidence of postoperative complications.

Materials and Methods

This study was conducted in the department of surgical oncology at a tertiary cancer center in South India, where we have retrospectively evaluated the data which were collected prospectively from 114 patients. We compared MIE (laparoscopic gastric mobilization ± thoracoscopy) with open esophagectomy (open gastric mobilization ± thoracotomy) in patients with esophageal cancer. We included patients between age 18 and 75 years with World Health Organization (WHO) performance status score of 0, 1, or 2 with squamous cell carcinoma or adenocarcinoma of middle third of esophagus, lower third of esophagus, and gastroesophageal junction tumors (Siewert I) that were considered to be resectable at the time of preoperative evaluation, irrespective of neoadjuvant therapy. Tumors located at the pharyngoesophageal junction, cervical esophagus, upper third of esophagus, and gastro-esophageal junction (Siewert type II or III) were excluded from the analysis. Patients with distant metastases and patients having contraindication to laparoscopy were also excluded from the analysis.

Patients with esophageal cancer were taken up for surgery after a complete preoperative workup. Informed and written consent was taken prior to surgery. Clinical tumor staging (cTNM) was based on data obtained from computed tomography (CT). The use of neoadjuvant therapy was determined according to the guidelines (for cT3 and above or cN1 and above) and applied to all patients. Despite the difference in approach to the abdominal and thoracic component of the surgical procedure, the surgical technique was standardized between groups. All the patients were scheduled to undergo either a transhiatal esophagectomy (THE) or transthoracic esophagectomy (TTE) or McKeown's 3-stage esophagectomy with the use of a gastric conduit in all cases. Pyloric drainage procedures were selectively performed and the anastomosis was either sutured or stapled at the discretion of the operating surgeon. Oral intake was allowed on postoperative day 5 after the removal of the nasogastric tube if no anastomotic leak was suspected.

End Points

The primary end point of the study was postoperative complication within 30 days after surgery. Intraoperative and postoperative complication was defined as a surgical or medical complication with a Clavien–Dindo grade II or higher. The most severe complication in a patient was considered for classification of the outcome. Other end points include postoperative death within 30 days, major pulmonary complications within 30 days, operative duration, and the length of hospital stay.

Statistical Analysis

Discrete variables were described with the use of frequencies and percentages and were compared by using the chi-square test or Fisher's exact *t*-test. Continuous variables were described with the use of means (with standard deviations) and medians (with ranges). All the statistical analyses were performed with the use of SPSS, version 25.0 SPSS version 25.0. Armonk, NY: IBM Corp.

Results

From January 2019 to March 2020, we assessed 118 patients for eligibility. Four patients were excluded, with 2 excluded because of a contraindication to curative surgery, 1 because of poor performance status, and 1 because the patient did not give consent for surgery. Therefore, 114 patients underwent surgery of which 28 patients underwent MIE, 86 patients underwent open esophagectomy, and 9 patients were found to be inoperable on table.

Patient and Tumor Characteristics

The clinical characteristics among both the groups did not differ significantly. The disease was common in males with a median age of presentation at 56 years. Most tumors were distal in location, commonly occurring at lower third of esophagus and gastroesophageal junction (GEJ). The percentage of patients receiving neoadjuvant therapy was similarly high in both the groups (75% in the minimally invasive surgery group and 70% in the open surgery group). Most patients in our study underwent THE. The patient and tumor characteristics were depicted in ►Table 1.

Table 1 Patient and tumor characteristics

Characteristic		Study population (*N* = 114)	Minimally invasive esophagectomy (*N* = 28)	Open esophagectomy (*N* = 86)
Age	Median	56 years	56 years	54 years
	Range	24–75 years	40–75 years	24–75 years
Sex	Male	74 (64.9%)	19 (67.9%)	55 (64%)
	Female	40 (35.1%)	9 (32.1%)	31 (36%)
ASA score	2	75 (65.8%)	20 (71.4%)	55 (64%)
	3	39 (34.2%)	8 (28.6%)	31 (36%)
Clinical tumor stage	cT1	6 (5.3%)	2 (7.2%)	4 (4.7%)
	cT2	34 (29.8%)	9 (32.1%)	25 (29%)
	cT3	74 (64.9%)	17 (60.7%)	57 (66.3%)
Clinical node stage	cN0	39 (34.2%)	9 (32.1%)	30 (34.9%)
	cN1	66 (57.9%)	17 (60.7%)	49 (57%)
	cN2	9 (7.9%)	2 (7.2%)	7 (8.1%)
Location of tumor	Mid 1/3	30 (26.3%)	7 (25%)	23 (26.7%)
	Lower 1/3	48 (42.1%)	12 (42.9%)	36 (41.9%)
	GEJ	36 (31.6%)	9 (32.1%)	27 (31.4%)
Neoadjuvant therapy	Yes	81 (71%)	21 (75%)	60 (69.8%)
	No	33 (29%)	7 (25%)	26 (30.2%)
Surgery performed	THE	90 (79%)	21 (75%)	69 (80.2%)
	TTE	8 (7.0%)	2 (7.2%)	6 (7.0%)
	Mckeown's	16 (14%)	5 (17.8%)	11 (12.8%)

Abbreviations: ASA, American Society of Anaesthesiologists' score; GEJ, gastroesophageal junction; THE, transhiatal esophagectomy; TTE, transthoracic esophagectomy.

Pathological Tumor Characteristics

Nine patients who were found inoperable on table were excluded from the final analysis. One patient in the minimally invasive surgery group did not undergo resection due to aorta invasion. Eight patients in the open surgery group did not undergo resection due to peritoneal disease in three cases, aorta invasion in three cases, and bronchial involvement in two cases that were discovered at the time of surgery. No significant differences between the minimally invasive surgery group and the open surgery group were noted with regard to tumor histology, pathological tumor or nodal stage, total number of lymph nodes retrieved, and the number of positive lymph nodes. No significant differences were noted in the incidence of resection margin involvement (R1 or R2). Circumferential margin (CRM) was positive in one case (3.7%) in minimally invasive surgery group as compared to four cases (5.1%) in open surgery group, whereas distal resection margin (DRM) was positive in one case (3.7%) in minimally invasive group as compared to two cases in open surgery group (2.6%). Pathological tumor characteristics were depicted in ►Table 2.

Operative Outcomes

Outcome analysis showed that MIE was associated with significantly lower postoperative complications at 30 days (18.5% vs. 41%; $p = 0.034$ by the chi-square test; odds ratio: 0.33). Although postoperative complications like chylothorax, anastomotic leak, and cardiovascular complications were similar in both the groups, the pulmonary complications were significantly higher in patients undergoing open esophagectomy. Patients who underwent minimally invasive surgery had a lower incidence of pulmonary complications within 30 days (7.4% vs. 25.6%; $p = 0.044$ by the chi-square test; odds ratio: 0.23). Only 1 out of 7 patients who had undergone thoracoscopy had a pulmonary complication, as compared to 7 out of 17 patients who had pulmonary complications after thoracotomy. Intraoperative complications and 30-day mortality rates were similar in both the groups. Although the median operative time was more in the minimally invasive surgery group (260 minutes vs. 180 minutes; $p < 0.0001$), the median length of hospital stay was shorter in patients undergoing minimally invasive surgery (9 days vs. 12 days; $p = 0.0001$). Operative outcomes were depicted in ►Table 3.

Discussion

In this study, we found that MIE was associated with a significantly lower risk of postoperative complications than open esophagectomy (OE). Especially, minimally invasive esophagectomy was associated with a lower risk of pulmonary complications. Intraoperative complications and other nonpulmonary postoperative complications were almost similar with minimally invasive esophagectomy as with open esophagectomy. Although, MIE was associated with prolonged operative duration, it resulted in shorter hospital stay compared to open esophagectomy.

The first published randomized control trial comparing outcomes after minimallyinvasive and open esophagectomy was the TIME trial,[11] which reported a significant decrease in pulmonary infection rates in MIE group. Similar findings were reported in subsequent meta-analyses.[12,13] Similarly, meta-analyses have shown that patients had significantly lesser respiratory complications with MIE.[14,15] We have documented a significantly lower respiratory complications with MIE (7.4% vs. 25.6%; $p = 0.044$). Previous studies have reported significantly low pulmonary complications rates using the minimally invasive transthoracic approach. Luketich et al in their series of 222 patients in left lateral decubitus MIE has reported a pulmonary complication rate of 18%.[16] Palanivelu et al in their minimally invasive series of 130 patients in prone position has reported a pulmonary complication rate of 2.3%.[8] In our analysis where we routinely used a prone approach for thoracoscopy, the pulmonary complication rate was 14.3%. In contrast, the pulmonary complications in patients undergoing the three-stage open transthoracic esophagectomy were reported to be 57%.[17] In our study, patients undergoing open thoracotomy (two-stage Ivor Lewis procedure and three-stage McKeown procedure) had a pulmonary complication rate of 41.2%. We found that a minimally invasive approach to the abdominal phase of esophagectomy was also associated with substantially lower postoperative complications, specifically pulmonary complications. This was probably due to less postoperative pain and less basal lung atelectasis resulting in fewer major pulmonary complications.

In our study, we have documented a postoperative complication rate of 18.5% in the MIS group, as compared with 41% in the open surgery group ($p = 0.034$). Except for pulmonary related complications, other postoperative complication rates remained the same irrespective of the approach. Anastomotic leak is a common postoperative complication and its incidence ranges from 0 to 12%, with a similar occurrence of leak between MIE and OE groups.[18] In our study, anastomotic leak rates were similar in both the groups and were noted to be 3.7% in the MIE group and 5.1% in the OE group. Meta-analyses have also indicated there is no evidence of reduced anastomotic leak in MIE group.[19,20] Meta-analyses have also concluded that cardiovascular complications like arrhythmia, heart failure, deep vein thrombosis, and pulmonary embolism were less apparent in MIE group.[19,20] In our study, although cardiovascular complications were marginally less in the MIE group, they were not statistically significant.

Oncological outcomes like mortality rate, lymph node retrieval, and R0 resection rate were similar in both the groups. Previous studies have failed to show reduced mortality rates after MIE.[9,11] On the other hand, meta-analysis conducted by Yibulayin et al reported a strong evidence of decreased mortality associated with MIE.[19] In the present study, there was no statistically significant difference in 30-day mortality rates between MIE and OE patients. Studies pertaining to lymph node retrieval during esophagectomy have reported an equal number of lymph nodes with open and MIS techniques.[21,22] Randomized control trial conducted by Biere et al also confirmed these results.[9] On the contrary, recent studies have found a significantly higher number of harvested lymph nodes during MIE compared to OE.[23,24] In our study, the median number of harvested lymph nodes was almost similar in both the groups, with a marginal nonsignificant advantage with MIE (13 vs. 12). Review of literature has revealed R0 resection rate of 92% in MIE and 84% in OE.[25] A retrospective analysis published by Burdall et al has found R1 resection rate of 6.1% in MIE and 15.6% in OE.[26] In our study, R0 resection rates were found to be equally good in

Table 2 Pathological tumor characteristics

Characteristic		Study population ($N = 105$)	Minimally invasive esophagectomy ($N = 27$)	Open esophagectomy ($N = 78$)
Pathological tumor stage	pT1	20 (19.0%)	5 (18.5%)	15 (19.2%)
	pT2	21 (20.0%)	5 (18.5%)	16 (20.5%)
	pT3	54 (51.5%)	15 (55.6%)	39 (50.0%)
	pT4	10 (9.5%)	2 (7.4%)	8 (10.3%)
Pathological node stage	pN0	36 (34.3%)	10 (37.1%)	26 (33.3%)
	pN1	21 (20.0%)	6 (22.2%)	15 (19.2%)
	pN2	30 (28.6%)	6 (22.2%)	24 (30.8%)
	pN3	18 (17.1%)	5 (18.5%)	13 (16.7%)
No. of nodes retrieved	Median (range)	12 (6–25)	13 (6–24)	12 (7–25)
No. of nodes positive	Median (range)	3 (0–9)	2 (0–9)	3 (0–7)
Tumor histology	SCC	60 (57.1%)	15 (55.6%)	45 (57.7%)
	Adenocarcinoma	45 (42.9%)	12 (44.4%)	33 (42.3%)
Margin positive (R1/R2)	CRM	5 (4.8%)	1 (3.7%)	4 (5.1%)
	PRM	0	0	0
	DRM	3 (2.9%)	1 (3.7%)	2 (2.6%)

Abbreviations: SCC, Squamous cell carcinoma; CRM, circumferential margin; PRM, Proximal resection margin; DRM, distal resection margin

Table 3 Operative outcomes

End points (outcomes)		Study population (*N* = 105)	Minimally invasive esophagectomy (*N* = 27)	Open esophagectomy (*N* = 78)
Postoperative complication of grade II or higher within 30 days	Anastomotic leak	5 (4.8%)	1 (3.7%)	4 (5.1%)
	Pneumonia/ARDS	17 (16.2%)	1 (3.7%)	16 (20.5%)
	Arrhythmias	7 (6.6%)	1 (3.7%)	6 (7.7%)
	DVT/PE	3 (2.9%)	1 (3.7%)	2 (2.6%)
	Chylothorax	5 (4.7%)	1 (3.7%)	4 (5.1%)
Pulmonary complication of grade II or higher within 30 days	Total	22 (21.0%)	2 (7.4%)	20 (25.6%)
	Patients undergoing thoracotomy (or) thoracoscopy	8/24 (33.3%)	1/7 (14.3%)	7/17 (41.2%)
Overall mortality within 30 days		4 (3.8%)	1 (3.7%)	3 (3.8%)
Intraoperative complications		9 (8.6%)	2 (7.4%)	7 (8.9%)
Operative duration	Median (range)	200 minutes (120–320)	260 minutes (180–320)	180 minutes (120–260)
	Mean ± SD	199.7 ± 55.7 minutes	258.9 ± 42.5 minutes	179.2 ± 43.9 minutes
Length of hospital stay	Median (range)	11 days (7–21)	9 days (7–16)	12 days (7–21)
	Mean ± SD	12.1 ± 3.7 days	9.9 ± 2.7 days	12.8 ± 3.6 days

Abbreviations: ARDS, Acute respiratory distress syndrome; DVT, Deep vein thrombosis; PE, Pulmonary embolism; SD, standard deviation.

both the groups, with R0 resection rate of about 92.6% in MIE group and 92.3% in OE group.

Previous studies have shown a consistently longer total operative time for MIE than for OE.[27,28] TIME trial reported average operative time to be 329 minutes for MIE-TTE versus 299 minutes for open TTE (p = 0.002).[11] Meta-analyses have also found a longer operative time during MIE when compared to OE.[12,19] In our study, we have also documented a significantly longer operative time associated with MIE (260 minutes vs. 180 minutes; $p < 0.0001$), probably due to surgeons learning curve and the ergonomics associated with the procedure. Another parameter of interest with MIE was the length of hospital stay. Studies have found that patients in the MIE group had reduced hospital stay than those in OE group.[13,29] In our analysis, we found those patients who underwent MIE have left the hospital 3 days earlier on average than those who underwent OE (9 days vs. 12 days; p = 0.0001).

The main shortcoming of this study was the duration of follow-up. Although the data pertaining to the short-term variables evaluated were available for all patients, the long-term follow-up data were not available to assess the long-term complication rates and survival. Another limitation of this study is that the study population was not randomized, but was allocated nonrandomly to both the groups and the data was collected from each patient prospectively. Although nonrandomized in nature, both the groups had similar patient and tumor characteristics in our study.

The results from this study stress upon the importance of minimally invasive surgery in reducing the pulmonary complications especially in patients undergoing upper abdominal and thoracic surgeries like esophagectomy. Although our results depict the role of laparoscopy and thoracoscopy while performing esophagectomy, we also acknowledge the role of robotic assisted minimally invasive esophagectomy (RAMIE). Studies have already proved the superiority of RAMIE over OE in terms of lower pulmonary complications, less blood loss and decreased hospital stay. But till date, no randomized controlled trial has evaluated the superiority of RAMIE over MIE. Although our experience with RAMIE is still in the initial phase, we believe that in future the results with MIE could be easily reproduced with RAMIE.

Conclusion

We found that MIE resulted in significantly lower incidence of postoperative complications, especially pulmonary complications. Although, MIE was associated with prolonged operative time, it resulted in shorter hospital stay.

Ethics Approval

This research study was conducted retrospectively from data obtained for clinical purposes. We consulted extensively with the institutional review board of Kidwai Memorial Institute of Oncology, who determined that our study did not need ethical approval.

Consent

Informed consent was obtained from all individual participants included in the study.

Contribution Details

RC, RA and SA were the primary operating surgeons in this study. CSP has evaluated all the pathology specimens. NR was the primary anesthesiologist for all the cases. RC and AD have done literature search and were involved in designing the study and in manuscript preparation. Data acquisition, data analysis, and statistical analysis were done by AD. All the authors were involved in editing and reviewing the manuscript.

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Conflicts of Interest
None declared.

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