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Original Article

Oncological Outcomes after Minimally Invasive Oesophagectomy for Oesophageal Carcinoma: Experience from a High Volume Centre in Pakistan

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ABSTRACT

Objective: To share the experience of minimally invasive oesophagectomy for oesophageal carcinoma in terms of oncological clearance and number of lymph nodes resected in our setup, being one of the high volume centres in country.
Study Design: Prospective observational study.
Place and Duration of Study: Department of Thoracic surgery, Combined Military Hospital, Rawalpindi Pakistan, from Jan 2018 to Dec 2021.
Methodology: A total number of 83 patients were included in the study who had a histological diagnosis of carcinoma of oesophagus and underwent minimally invasive oesophagectomy. The resection samples were subjected to histopathological analysis at Armed Forces Institute of Pathology. A Pro forma was designed to record all the demographic information as well as information regarding histological diagnosis, margin clearance, number of lymph nodes retrieved and one-year follow-up analysis.
Results: A total of 83 minimally invasive oesophagectomies were performed for carcinoma of oesophagus. Histopathology report confirmed clearance margin and R0 resection in 80 patients (96.38%) while in 3 patients (3.61%) involvement of radial resection margin was found. Lymph nodes were retrieved with a minimum number of 13 and maximum number of 33 lymph nodes. Mean number of lymph nodes retrieved was 22.23+3.68. (Stations of lymph node removed including abdominal nodes).
Conclusion: Satisfactory oncological clearance and adequate lymphadenectomy can be performed with minimally invasive oesophagectomy when performed in experienced hands.

Keywords: Carcinoma Oesophagus, Minimally Invasive Oesophagectomy, Oncological Outcome, Open Oesophagectomy.

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INTRODUCTION

Oesophageal carcinoma is the 8th commonest cancer worldwide and is among the commonest malignant tumours of upper digestive tract associated with poor prognosis.[1] It is second only to pancreatic cancer in fatality rates. The prevalence of esophageal cancer is observed to be rising word wide over the period of last three decades. This substantial increase is considered to be due to a sharp rise in the incidence of oesophageal adenocarcinoma, which in turn is likely to be due to increasing incidence of obesity, gastroesophageal reflux disease, and Barrett's esophagus, which are all proven major risk factors for adenocarcinoma of the oesophagus. The final outcomes after establishing the diagnosis of oesophageal cancer are less than optimal, with an overall 5-year survival rate of 15% to 25%. There is however, a gradual improvement in disease free and overall survival, which is due to better understanding of surgeons, heavier volume of the operating centres, pre-operative optimisation of patients' performance status and detection of early-stage disease.

Surgery is considered to be the key component and corner stone in multimodality treatment for oesophageal cancer. Traditional open oesophagectomy is still considered to be a highly invasive procedure with high rates of complications and mortality.[2] The overall complication rates after oesophagectomy have always remained considerably high despite major improvements in patient selection, cancer staging and improved surgical outcomes during the last decades. This fact encouraged for the exploration of some better operative procedures that could yield satisfactory oncological outcomes and at the same time are associated with lesser morbidity and mortality, therefore providing a better quality of life post-operative. It eventually resulted in a shift of the oncologic oesophageal surgery from a transhiatal or a transthoracic operation, over the period of time, to a minimally invasive approach favouring similar or even better oncologic margin clearance and lymph

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node dissection and also decreasing the surgical stress secondary to a thoracotomy. Minimal invasive technique has gained quite a favour since its first description by Cuschieri, who published the first minimally invasive transthoracic oesophagectomy in 1992. In the recent decade, many centres are increasingly adopting minimally invasive access oesophagectomy, via either totally thoracoscopic laparoscopic, hybrid or robotic surgery. Various published studies now have also proven better short term outcomes with minimal invasive approach in terms of reduced surgical trauma, lesser incidence of surgical site and respiratory complications[3,4] thus providing enhanced post-operative recovery as compared to traditional open surgery through thoracotomy.

Despite any of the surgical approach used, the basic objective of surgery is to achieve satisfactory oncological outcomes while still maintaining a low procedure related mortality and complications. Many studies have reported safety of minimally invasive oesophagectomy and improvement in patient's quality of life[5,6] but there have always been concerns regarding efficacy of minimally invasive oesophagectomy in achieving satisfactory oncological clearance and adequate lymph node dissection as compared to open surgery. Some of the authors strongly advocate that minimally invasive techniques allow better visualisation and magnification and hence can achieve retrieval of more number of lymph nodes as compared to open approach[7,8] while others have raised concerns over adequate tumour clearance and radial nodal clearance.[9]

The objective of this study is to evaluate efficacy of minimally invasive oesophagectomy when performed for oesophageal cancer in terms of oncological clearance and optimal number of lymph nodes being retrieved along with recurrence rate and overall survival.

METHODOLOGY

This was a prospective descriptive study carried out over a period of four years from January 2018 to December 2021, at Combined Military Hospital, Rawalpindi Pakistani, which is a tertiary care hospital. Sample size was calculated by using WHO calculator by keeping power of study 80%, margin of error 5% and number of adenocarcinoma patients 10(19.6%) and number of squamous cell carcinoma patients 41(80.4%).[10] Non probability consecutive sampling technique was used to include the patients.

Inclusion Criteria: All the patients diagnosed with carcinoma of oesophagus who were considered resectable and underwent minimally invasive oesophagectomy during this time period were included in the study.

Exclsuion Criteria: The patients who were irresectable or inoperable or who underwent oesophagectomy for benign disorders were excluded from the study.

Diagnosis of these patients was confirmed histologically in the preoperative workup. All cases were pre-staged using AJCC classification 7th edition with the help of CT scan chest and abdomen and whole body PET CT scan. After diagnosis and staging, all cases were discussed in a multi-disciplinary team meeting and depending on the type of tumour, clinical stage of the disease and performance status of the patient, a comprehensive treatment plan was formulated for each individual patient. Patients with locally advanced disease were given neoadjuvant chemo radiotherapy whereas those with early stage disease or where neoadjuvant treatment was not possible, were considered for upfront surgery. All patients received general anaesthesia with single lumen endotracheal intubation. All patients underwent prone thoracoscopic oesophageal mobilization, supine laparoscopic stomach mobilization and gastric tube formation with neck anastomosis. Each patient had a 3-field lymphadenectomy with removal of abdominal, mediastinal and cervical lymph nodes. The resection samples were subjected to histopathological analysis at Armed Forces Institute of Pathology. Adjuvant treatment was decided based on final histo-pathological report and on the decision of multidisciplinary team meeting post operatively.

The study was approved by institutional review board of the hospital (CMH QTA-IRB/048). Demographic data of the patients like age, gender, comorbidities were recorded. Type of the tumour, location of the tumour and provision or non-provision of neo adjuvant treatment was also recorded. Record was kept for per-operative and post-operative complications and recovery. The histopathological data was recorded for margin clearance and number of lymph nodes retrieved from the specimen. All the patients were then followed up for a period of one year and record of recurrence and death was also kept.

Data was analysed using Statistical Package for the social sciences (SPSS) version 19:00. Categorical variables like gender, type and location of tumour and margins of clearance were expressed in terms of

frequency and percentage whereas quantitative variables like age of the patient and number of retrieved lymph nodes were expressed as Mean with Standard deviation. Kaplan-Meier survival curves were utilised to determine disease free survival, which was calculated from the date of surgery to the date of recurrence.

RESULTS

A total of 83 minimally invasive oesophagectomies were performed during this period for carcinoma of oesophagus. Out of these 83 subjects, 62(74.7%) patients were males while 21(25.3%) were females. Mean age of the patients was 56.71±6.68 years with a range of 43 to 70 years. Out of all the cases diagnosed as carcinoma oesophagus, 59(71.1%) were Squamous cell carcinoma while 24(28.9%) were Adenocarcinoma. Depending on location of tumour, 55(66.26%) were located in lower oesophagus while 15(18.07%) were in mid oesophagus and 3(3.61%) were in upper oesophagus. These demographic details are summarised in Table-I. Various early complications occurring during the procedure or during the same admission are depicted in Figure-1.

Table-I: Demographics of Patients.

Variable		n(%)
Age (years)		56.71±6.68
Gender	Males	62(74.7%)
	Females	21(25.3%)
Type of the tumour	Squamous cell carcinoma	62(74.7%)
	Adenocarcinoma	21(25.3%)
Location of tumour	Lower one third	55(66.26%)
	Middle one third	15(18.03%)
	Upper one third	3(3.61%)
Neoadjuvant chemo-radiotherapy		81(97.6%)
Morbidity		12(14.45%)
Mortality		10(12.04%)

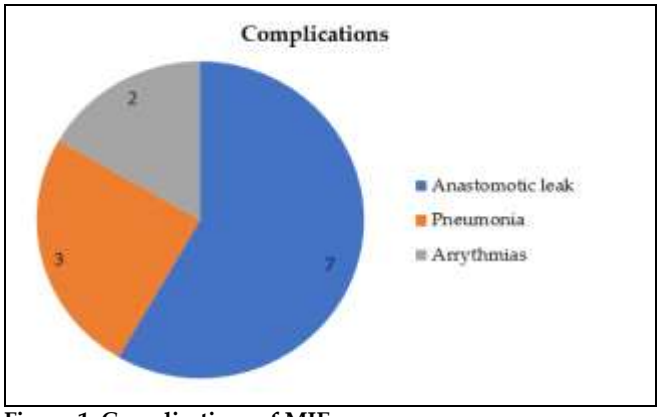

Figure-1: Complications of MIE

All patients underwent minimally invasive oesophagectomy with oesophagogastric anastomosis in neck. Histopathology report confirmed adequate clearance margin and R0 resection in 80(96.38%) cases while in 3(3.62%) cases involvement of radial resection margin was found. Three field lymphadenectomy was done using thoracoscopic and laparoscopic approach and a minimum number of 13 lymph nodes and a maximum number of 33 lymph nodes were retrieved. Mean number of lymph nodes retrieved was 22.23±3.68. These oncological outcomes are summarised in Table-II.

Table-II: Oncological Outcomes

Variable		n(%)
Resection margins	Uninvolved	80(96.38%)
	Involved (Radial)	3(3.62%)
No. of lymph nodes retrieved	Minimum	13
	Maximum	33
	Average	22.23+3.68

All the patients were followed up for a period of one year in order to detect any delayed complication or to diagnose recurrence. In our study recurrence occurred in 7(8.43%) cases. Earliest recurrence occurred 4 months after surgery which was diagnosed on follow up upper gastrointestinal endoscopy. Overall disease free survival is depicted in Figure-2.

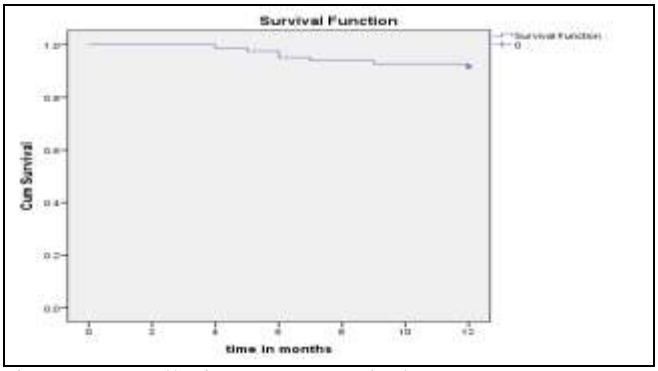

Figure-2: Overall Disease Free Survival

DISCUSSION

Many studies available in the literature clearly establish improved outcomes when minimally invasive surgical techniques are utilised in various surgical procedures. Increasing number of centres across the world are now adopting minimally invasive oesophagectomy as their favoured surgical procedure for oesophageal cancer due to better patient tolerability, lesser complication and mortality rate. It not only reduces the surgical insult to the patient but

also improves patients' prognosis. Various studies such as those published by Mariette *et al.*,[11] and Naffouje *et al.*,[12] have shown short term advantages like less haemorrhage, enhanced recovery and lower complication rates in patients undergoing minimally invasive oesophagectomy when compared with those who have undergone open oesophagectomy. Zhou *et al.*,[13] in his published study also showed fewer complication rate for minimally invasive oesophagectomy. Similarly, a Population-Based Study from Sweden and Finland[14] compared the outcomes after open oesophagectomy and minimally invasive oesophagectomy for oesophageal cancer, and documented a shorter hospital stay, reduced mortality over 90 days and lesser hospital readmission rates over 30 days after minimally invasive oesophagectomy compared to open oesophagectomy. This was also demonstrated in our study and the complication rate was found to be 14.45%, which is less than the complication rate in published literature for open oesophagectomy.

Ever since the introduction of minimally invasive oesophagectomy, there have always been concerns whether minimally invasive oesophagectomy is equally effective in achieving similar oncological outcomes in terms of longitudinal and radial margin clearance as compared to open oesophagectomy. Braghetto *et al.*,[15] in his published study demonstrated R0 resection in 75.36% of patients whereas Wullstein *et al.*,[16] achieved an R0 resection in 92% of patients placed in minimally invasive surgery group as compared to 84% in open oesophagectomy group. Worrell *et al.*,[17] described a higher rate of negative pathologic margin in minimally invasive oesophagectomy then in open oesophagectomy (95 vs. 93.5%). In our study, R0 resection was achieved in 96% of patients. These better results can be due to careful patient selection, neoadjuvant therapy, large number of oesophagectomies being performed at our centre and vast experience of the surgeons performing minimally invasive oesophagectomy.

Another important concern for minimally invasive oesophagectomy is whether adequate lymphadenectomy (Mediastinal as well as abdominal) can be performed via minimally invasive approach or not. The optimal number of lymph nodes that are needed to be harvested during oesophagectomy for malignancy is still debated. It is generally believed that a minimum number of 15 lymph nodes should be recovered for pathologic examination during oesophagectomy, whether it is done in upfront fashion or after administering neo-adjuvant chemo radiotherapy, with an understanding that the more the better especially in early stage tumour. Luketich *et al.*,[3] in their study showed an average of 21 lymph nodes resected during minimally invasive oesophagectomy. Some other series have shown 17±9.62 lymph nodes (range 2-46) were harvested on an average while performing minimally invasive oesophagectomy as compared to open oesophagectomy, in which an average of 16-18 lymph nodes (range1-44) were retrieved.[18,19] Similarly, Dantoc *et al.*,[20] showed a number 16 lymph nodes retrieved on an average during minimally invasive oesophagectomy while Xie *et al.*,[21] retrieved an average of 22 lymph nodes during minimally invasive oesophagectomy as compared to 9 lymph nodes during open oesophagectomy. In our study, an average of 22 lymph nodes were retrieved which are higher than most of the published literature. This can be due to thoracoscopic oesophageal mobilisation being done in prone position rather than lateral decubitus position as shown by Koyanegi *et al.*[22]

Many studies clearly demonstrate improved quality of life and better survival after minimally invasive oesophagectomy.[11,17] Xie *et al.*,[21] found a higher overall 5 year survival for the patients who underwent minimally invasive oesophagectomy over those who underwent open oesophagectomy (69.9% vs 40.4%). Similarly, Lazzarino *et al.*,[23] found an improved likelihood of survival over one year after oesophagectomy with minimally invasive approach when compared to open approach. Müller-Stich *et al.*,[24] in their meta-analysis showed a three year overall survival of 56 per cent for minimally invasive oesophagectomy versus 52 per cent for open oesophagectomy and disease free survival 54 per cent versus 50 per cent, which were comparable. In our study, 91% of patients remained disease free over follow-up period of 1 year following minimally invasive oesophagectomy. Khan *et al.*,[25] also summed up all these findings in their data analysis and showed that minimally invasive oesophagectomy is comparable to open oesophagectomy in achieving equivalent oncological outcomes with regards to the adequacy of specimen and rate of tumour recurrence. Nevertheless, they added that there exists a learning curve to attain similar results comparable with conventional surgery, which was shown to be 1 year in their study. Beyond this time, the rate of positivity of margins was lower and average number of lymph nodes recovered were comparable with conventional open oesophagectomy.

LIMITATION OF STUDY

Limitations of this study are relatively small sample size and all the surgeries being performed by a surgeon with advanced proficiency for these procedures. The reproducibility of the same results therefore may vary based on the expertise of the surgeons performing the procedures.

CONCLUSION

Minimally invasive oesophagectomy is a reliable and safely performed surgical procedure when performed in experienced hands. It is associated with lesser rates of peri-operative complications and in hospital mortality. Minimally invasive oesophagectomy is equally effective in achieving satisfactory oncological clearance and adequate number of lymph nodes can be resected with careful dissection.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MOF & BU: Data acquisition, data analysis, critical review, approval of the final version to be published.

SSC & RH: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RK & FU: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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