Ref. No.: AIIMS/JDH/2022/02/512

Date: - 15th February 2022

To

The Dean (Academics)

AIIMS, Jodhpur

(Through Proper Channel)

Subject: Submission of MCh. (Surgical Gastroenterology) thesis.

Respected Sir,

I am a final year MCh. resident in the Department of Surgical Gastroenterology at AIIMS Jodhpur. I am hereby submitting five copies of my thesis, titled "**Lymph node yield in minimally invasive (Robotic and thoracoscopic assisted) esophagectomy in carcinoma esophagus-A prospective descriptive study"**. This thesis was done under the guidance of Dr. Subhash Chandra Soni (Guide) and Co Guides, Dr. Ashok Kumar Puranik, Dr. Vaibhav Kumar Varshney, and Dr. Deepak Vedant. I hereby request you to kindly accept five copies of my thesis and do the needful. I shall be highly obliged.

Thanking You

Yours Sincerely,

Raghav Nayar

Dr Raghav Nayar

MCh resident

Department of Surgical Gastroenterology,

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forwarded

15/02/2022

R2 forms

LYMPH NODE YIELD IN MINIMALLY INVASIVE (ROBOTIC AND THORACOSCOPIC ASSISTED) ESOPHAGECTOMY IN CARCINOMA ESOPHAGUS-A PROSPECTIVE DESCRIPTIVE STUDY

Thesis Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfillment of the requirement for the degree of

Magister Chirurgiae (M.Ch.)

SURGICAL GASTROENTEROLOGY

JUNE, 2022

AIIMS, JODHPUR

DR. RAGHAV NAYAR

All India Institute of Medical Sciences, Jodhpur

DECLARATION BY THE CANDIDATE

I hereby declare that this thesis titled "**LYMPH NODE YIELD IN MINIMALLY INVASIVE (ROBOTIC AND THORACOSCOPIC ASSISTED) ESOPHAGECTOMY IN CARCINOMA ESOPHAGUS-A PROSPECTIVE DESCRIPTIVE STUDY**" is a bonafide and original research work carried out in partial fulfilment of the requirement for the degree of Magister Chirurgiae (M.Ch.) in Surgical Gastroenterology under supervision and guidance, in the Department of Surgical Gastroenterology, All India Institute of Medical Sciences, Jodhpur.

Dr. Raghav Nayar
Department of Surgical Gastroenterology,
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All India Institute of Medical Sciences, Jodhpur

CERTIFICATE

This is to certify that the thesis titled **"LYMPH NODE YIELD IN MINIMALLY INVASIVE (ROBOTIC AND THORACOSCOPIC ASSISTED) ESOPHAGECTOMY IN CARCINOMA ESOPHAGUS-A PROSPECTIVE DESCRIPTIVE STUDY"** is the bonafide work of **Dr. Raghav Nayar**, carried out in partial fulfilment of the requirement for the degree of Magister Chirurgiae (M.Ch.) in Surgical Gastroenterology under our guidance and supervision, in the Department of Surgical Gastroenterology, All India Institute of Medical Sciences, Jodhpur.

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CERTIFICATE BY HEAD OF THE DEPARTMENT

This is to certify that **Dr. Raghav Nayar** has satisfactorily completed his thesis titled **"LYMPH NODE YIELD IN MINIMALLY INVASIVE (ROBOTIC AND THORACOSCOPIC ASSISTED) ESOPHAGECTOMY IN CARCINOMA ESOPHAGUS-A PROSPECTIVE DESCRIPTIVE STUDY"** in partial fulfilment of the requirement for the degree of Magister Chirurgiae (M.Ch.), in Surgical Gastroenterology. He has done the research work under my supervision and guidance. He has fulfilled all the requisites under the regulations laid by the All India Institute of Medical Sciences, Jodhpur and no part of the thesis has been submitted to any other university.

Prof (Col.) Dr. Ashok Kumar Puranik

Professor and Head

Department of Surgical Disciplines

All India Institute of Medical Sciences, Jodhpur

LIST OF ABBREVIATIONS

SCC	Squamous cell carcinoma
OE	Open esophagectomy
MIE	Minimally invasive esophagectomy
THE	Transhiatal Esophagectomy
RA	Robotic-assisted
RLN	Recurrent laryngeal nerve
ILE	Ivor Lewis esophagectomy
RE	Robotic esophagectomy
TA	Thoracoscopic assisted
ARDS	Acute respiratory distress syndrome
MODS	Multiple organ dysfunction syndrome
RAMIE	Robot- assisted minimally invasive esophagectomy
LN	Lymph node
TE	Thoracoscopic esophagectomy
LNY	Lymph node yield
RATE	Robot-assisted transhiatal esophagectomy
VATE	Video-assisted transhiatal esophagectomy
TAILE	Thoracoscopic-assisted Ivor Lewis esophagectomy
RAILE	Robotic-assisted Ivor Lewis esophagectomy
CECT	Contrast enhanced computed tomography
EGD	Esophagogastroduodenoscopy
ERAS	Enhanced recovery after surgery
FJ	Feeding jejunostomy
CAP	College of American Pathologists
AJCC	American Joint Committee on Cancer
ECCG	Esophagectomy Complications Consensus Group
IQR	Interquartile range
ICG	Indocyanine green
ECOG	Eastern cooperative oncology group
SAIO	Subacute intestinal obstruction
NACRT	Neoadjuvant chemoradiotherapy

NACT	Neoadjuvant chemotherapy
RTE	Robotic-transthoracic esophagectomy
TTE	Transthoracic esophagectomy
RAE	Robot-assisted esophagectomy
VATS	Video assisted thoracoscopic surgery

LIST OF TABLES

SUMMARY

Background: Minimally Invasive Esophagectomy (MIE) has been gaining popularity especially in carcinoma esophagus. It is associated with less morbidity, complications, shorter duration of hospital stay as well as better post-operative outcomes. With the advent of robotic MIE, there has been debate on the improved outcomes and overall as well as disease free survival compared to thoracoscopic MIE. We aimed to do a prospective descriptive analysis to ascertain the same and compare the 2 modalities.

Objectives: The study aimed to have a descriptive analysis of the 2 types of MIE-Robotic-assisted (RA) and Thoracoscopic assisted (TA) and to describe, the advantage, if any of one technique over the other with respect to lymph node yield (LNY)-thoracic and abdominal, the length of hospital/ICU stay, complications and recurrence at the end of 6 months.

Methods and procedures: Total of 33 patients with biopsy proven carcinoma of the esophagus and meeting inclusion criteria underwent MIE (23 in TA and 10 in RA) with or without neo-adjuvant treatment in accordance with NCCN guidelines in the Department of Surgical Gastroenterology at AIIMS Jodhpur. The recruitment of patients was done from 1st January 2020 to June 30th 2021 and they were followed up till 6 months post-surgery. Baseline and demographic characteristics, mean duration of thoracic phase (robotic or thoracoscopic), the total length of post-operative stay (ICU as well as in-hospital), intraoperative as well as postoperative complications; LN yield (thoracic and abdominal), any recurrence within 6 months as evaluated by CECT neck, thorax and abdomen and upper GI endoscopy at 6 months, was evaluated and compared between the 2 groups (RA and TA) and also with the data from current literature.

Results: Thirty-three patients were recruited with 23 in TA arm and 10 in RA arm with comparable baseline and demographic characteristics. Almost 80% patients in both arms had received some form of neo-adjuvant treatment. The final pathological stage revealed more advanced (stage 2 and 3) tumors in the TA arm (60%) compared to the RA arm (20%). The most common tumor location was the mid-thoracic esophagus in both arms. The mean duration of thoracic phase was more in the RA arm viz a viz TA arm (168$\pm$27 vs 133$\pm$28)

minutes, intra-operative blood loss was comparable with a median of 200 ml. No major intra-operative visceral or vascular injury occurred in any of the cases and 50% patients were extubated immediately post-surgery in RA arm compared to 43.5% in TA arm. The median LNY post neoadjuvant treatment was slightly more in the RA arm [post NACT-21(17,27.3) vs 19(16,27.8); post NACRT 25(18.8,27.5) vs 20(15,26.5)]. Supra and infra-carinal LNY were comparable between 2 arms. Major (Clavien Dindo $\geq$ 3a complications) were seen more in the TA arm (52.4%) vs 30% in RA arm. The incidence of other major peri-operative complications in the RA arm was either less or comparable to the TA arm. There was no major difference in locoregional recurrence (~20%) or distant metastasis (~10%) in the 2 arms.

Conclusions: MIE is feasible with good LNY and peri-operative complications. RAMIE compared to TA-MIE has slightly better lymph nodal yield with fewer major post-operative complications, especially pulmonary. Strict adherence to perioperative standardized protocols and multimodality therapy in the treatment of carcinoma esophagus helps achieve better peri-operative outcomes.

INTRODUCTION

Esophageal cancers are on the rise globally, and it has become the fourth leading cause of cancer death in the Indian population. Squamous cell carcinomas (SCC) are the most common sub-type in the Asian subcontinent(1). Surgical intervention is the mainstay of treatment for carcinoma esophagus is surgery. However, esophagectomy is a morbid procedure with a high risk of complications and may require intensive care unit admission after surgery. All these can increase the length of hospital stay and the cost of treatment. At the present time, there is no standard technique for esophageal resection. It is governed by several factors, including the surgeon's experience, tumor location, and patients' affordability. Open esophagectomy (OE) was associated with significant morbidity and mortality due to greater pulmonary complications, longer intensive care unit (ICU) stay, and increased pulmonary complications(2). Minimally invasive esophagectomy (MIE) is the recommended procedure for carcinoma esophagus. It is associated with less morbidity without compromising oncological outcomes(3). Radical resection of the esophagus along with lymph nodes is seen to be an indicator of long-term survival in patients with localized esophageal carcinoma(4). Although the mortality from esophageal cancers has fallen over the last 20 years, it still carries a high risk, almost 10 % of in-hospital mortality(5). The overall complication rate of esophagectomy varies from 17 to 74 %. Cushieri first introduced a minimally invasive thoracoscopic or laparoscopic approach in 1992 to minimize the pulmonary complications and also to reduce the morbidity associated with open esophagectomy. The first totally laparoscopic Transhiatal Esophagectomy (THE) was performed by DePaula et al. in 1995(6). The transthoracic approach is the preferred approach, but the complications, especially cardiopulmonary, are very high (50-70%)(2). The advantages include en-bloc resection of paratracheal, subcarinal, and paraesophageal lymph nodes(2). Also, MIE is associated with better global quality of life, functional aspect, and less pain three months post-procedure compared to open esophagectomy(7).

In 2003, the first case of a robotic-assisted (RA) thoracoscopic esophagectomy was performed(8). Since then, robotic surgery has come a long way, and completely robotic esophagectomies are being performed. Robotic esophagectomies have a better exposure of upper mediastinum along with better lymph nodal yields, especially along Recurrent laryngeal nerve (RLN) along with high definition view and tremor suppression and also reduced blood loss, shorter ICU stay, and pulmonary complications(9,10). Another advantage

is that there is decreased pain in robotic surgery as the instruments are longer and the fulcrum of the instruments is inside the body, and it helps in precise dissection and management in a limited space(11). Robotic-assisted surgery is an improvement over conventional methods as it provides 7 degrees of movement, better visualization, more magnification, and tremor suppression. The surgeon can perform complex procedures comfortably with better optics. The mortality rate after open esophagectomy ranges from 4 to 16 % (12). Studies that compared thoracoscopic versus robotic esophagectomy showed lesser blood loss in the robot-assisted group with a similar rate of complications, hospital stay, and mortality(12).

Hence it holds great promise for the future.

Types of robotic esophagectomies(11)

1. Complete robotic THE (neck anastomosis)

2. Complete robotic Ivor Lewis esophagectomy (ILE) - Intra-thoracic anastomosis

3. Complete robotic McKeown esophagectomy (neck anastomosis)

4. Combination of the abdominal and thoracic phases of the operation (combined robotic esophagectomy)

Types of thoraco-laparoscopic esophagectomy(11)

1. Combined transthoracic and laparotomy (ILE)

2. Combined laparoscopic with thoracoscopy-assisted/thoracotomy ILE

3. Complete thoraco-laparoscopic ILE

4. Complete laparoscopic THE

5. Combined thoracoscopic with laparotomy/hand-assisted laparoscopic three-field McKeown esophagectomy

6. Combined laparoscopic with thoracotomy McKeown esophagectomy

7. Complete thoraco-laparoscopic three-field McKeown esophagectomy

9. Complete laparoscopic Vagus-sparing esophagectomy

Several studies including meta-analysis have shown that increased lymph nodal yield, especially thoracic lymph nodes in esophagectomy, is associated with more accurate staging and improved disease-free and overall survival (13,14). Robotic esophagectomy is thought to be associated with improved lymph nodal yield and hence may have an impact on the disease-free as well as the overall survival. It may become the standard of care for resectable carcinoma esophagus in a few years. Robotic esophagectomy (RE) with two-field lymphadenectomy is feasible, safe with less post-surgery morbidity in terms of pulmonary complications, length of hospital stay, and oncologically effective with respect to the incidence of R0 resection, lymph node retrieval, and local recurrence. RE has also been found to have a shorter learning curve than conventional thoraco-laparoscopic surgery and lesser assistant dependence for camera vision and instrument control. However, studies on robotic approach to esophagectomy are technically diverse, with variable quality in reporting of technique and outcomes with lack of standard definitions for complications

Very few studies have been done comparing the lymph nodal yield between robotic-assisted and thoracoscopic assisted esophagectomy, and this is one of the first Indian studies comparing RA and TA esophagectomy.

REVIEW OF LITERATURE

In 2003, Luketich et al published the initial series on MIE and showed meager morbidity rates with excellent patient outcomes (as detailed later), and this led to its widespread acceptance compared to its open counterpart. A meta-analysis comparing MIE and OE showed a trend towards less blood loss, longer operative time, shorter hospital stay, and lower pulmonary complications in the MIE arm compared to OE(table 1)(1).

Table 1-Comparison of peri-operative outcomes in OE and MIE; NR-Not recorded

Study	**Year**	**No. of patients**	**Intraoperativeblood loss**	**Duration**	**Hospital stay**	**Total complications**	**Pulmonary complications**
Xiong et al	2017	488	More in OE p=0.001	More in MIE p<0.001	Shorter in MIE p<0.001	NR	Less in MIE
Yibulayin et al	2016	15790	More in OE p=0.05	More in MIE p<0.001	Shorter in MIE p<0.05	Less in MIE p<0.05	Less in MIE
Lv et al	2016	6025	More in OE p=0.0009	More in MIE p<0.001	NR	NR	Less in MIE
Guo et al	2016	1549	More in OE p=0.001	NR	NR	Lower in MIE p<0.001	Less in MIE
Nagpal et al	2010	1284	More in OE p<0.01	Longer in OE p<0.01	Less in MIE p=0.004	Lower in MIE p<0.007	Less in MIE P=0.04
Biere et al	2009	1061	More in OE	Longer in MIE p NR	Less in MIE P<0.01	Equivalent	Equivalent

Initially, during the evolution of MIE, the thoracic phase was performed in the lateral decubitus position. However, MIE in the prone position, as published by Palanivelu et al., established the prone position as being less morbid and ergonomically better for the operating surgeon. In this study, Palanivelu et al. (2) studied 130 patients undergoing minimally invasive esophagectomy for SCC of the middle third of the esophagus, out of which only one received neoadjuvant chemotherapy, and all surgeries were completed by laparoscopic technique without any conversions with two field lymphadenectomies in the entire cohort. Mean operative time in this study was 220 minutes with a mean lymph node yield of 18 lymph nodes, mean ICU stay of 1 day, time to oral intake four days, mean post-operative hospital stay eight days, and 30-day post-operative mortality of 1.54 % (2/130). The mortalities were attributed to an acute cardiac event in one case and anastomotic leak with ARDS and MODS in the other case. Major complications seen in this series included anastomotic leak-2.3 %, myocardial infarction-1.54%, delayed gastric emptying-2.31%, and deep venous thrombosis (2.31%). The study revealed that the stage-specific survival was comparable to the open and other manually invasive surgeries after a mean follow-up of 20 months. However, further studies argued that prone position did not allow for an easy conversion to open thoracotomy, if necessary, and a modified semi-prone position was found to be beneficial in this respect. The study also revealed that minimally invasive procedures result in reduced or total loss of the haptic feedback, which is a necessary tool to ensure adequate margin during transection.

Goel et al. (1) presented their experience with 27 patients after neoadjuvant chemoradiation followed by McKeown esophagectomy. The mean time for robot thoracic mobilization and total surgical procedure in this study was 108.4 and 342.7 minutes, respectively. R0 resection rate was 96.3%, and the average LN yield was 18. Node negativity and pathological complete response rates were 66.6 and 44.4 %, respectively. 4 cases underwent conversion due to various reasons. Similar ICU stay in these patients, low overall morbidity and mortality established the feasibility of RAMIE post neoadjuvant treatment in carcinoma esophagus.

Ruurda et al(2) analyzed 16 studies and 118 patients of RAMIE. The operating duration varied from 231 to 312 minutes, blood loss of 54-350 ml, ICU stay of median one day(range 0-3.5 days). The number of harvested LNs varied from 18 to 38, and the R0 rates were above 90%. The conversion rates in this study varied from 0 to 21%, with a total length of hospital stay of 7-21 days.

Luketich et al. (4) reported their review of MIE of over 1000 patients over 15 years, both McKeown type 3-incision (MIE-Chest) and Ivor Lewis (MIE-neck), in which they found 30-day mortality of 1.68 % with 0.9% in the MIE ILE group and 2.5% in the MIE-Neck group, median ICU stay of 2 days, and a median stay of 8 days. The incidence of RLN palsy in this study was lower in the ILE MIE-chest group (1%) than in the MIE-Neck group. Comparing anastomosis, they found that neck anastomosis had a more proximal resection margin and lower morbidity associated with cervical leaks. In contrast, an intrathoracic anastomosis had lesser tension at the anastomotic site, a lower incidence of anastomotic leak, and also of RLN palsy. The most frequent reasons for conversion to an open operation (45/101; 4.5 %) were better assessment of tumor margin (n=5), adhesions (n=10), and inadequate conduit length/need for more mobilization (n=2). The major unanticipated adverse events included MI, bleeding, and splenectomy. The median lymph node yield was 21 and was slightly higher in the MIE chest group.

Another study by Park et al(3), who examined 136 patients undergoing MIE, both early and advanced esophageal cancer, showed that the one-lung ventilation time was significantly higher in the robotic esophagectomy (RE) group compared to the thoracoscopic esophagectomy(TE) group, however, the total blood loss and the total operative time was not significantly different between the two groups. The mean of dissected LNs was significantly greater in the RE group than in the TE group (37.3±17.1 versus 28.7±11.8). The Lymph node yield (LNY) was significantly higher in the upper mediastinum and abdomen in the RE arm than TE (p=0.032 for upper mediastinum and 0.007 for the abdominal phase). Furthermore, the 30-day mortality in the RE group was 1.6 % versus 0 in the TE group. The difference in respiratory complications, anastomotic leak, or vocal cord paralysis was not statistically different between the two groups. The incidence of major complications i.e., more than Clavien Dindo grade IIIa was also not significantly different between the two groups (16.1 % vs. 20.9 %).

Zhang et al(4) compared robotic-assisted versus thoracoscopic assisted Ivor Lewis esophagectomy for esophageal cancer. They found that there was no conversion in TE, whereas two patients in RE were converted to open. The overall complication rate (both major and minor) was comparable between the two groups. There was no significant difference in the length of stay between the two groups (9 days in both the groups). They found no statistically significant difference between the lymph node yield between the two types (19.7 ± 9.8 vs. 20.3 ± 9.7, p = 0.689) and also no difference in region-wise lymph nodes

(thoracic, abdominal, right and left RLN). There was no significant variability between the two groups in terms of blood loss [200.0 ml (100.0–262.5 ml) vs. 200.0 ml (150.0–245.0 ml); p = 0.100], three-month mortality rates (1.5% in both the groups) and complication rate (28.8 vs. 24.2%, P = 0.554).

ROBOT trial, which is a randomized control trial comparing Robot-assisted MIE versus open transthoracic esophagectomy for resectable esophageal cancer(7), patients undergoing robotic-assisted MIE (RAMIE) had fewer post-operative complications compared to OE (59% vs. 80%; p = .02). RAMIE resulted in lower blood loss compared to open esophagectomy (400 ml vs 568 ml; P<0.001), lower pulmonary complications (32% vs 58%; P = .005), lower cardiac complications (22% vs 47%; P = .006) and a lower mean post-operative pain score.

van Hillegersberg(8) published his experience of 18 cases of robot-assisted thoracoscopic esophago-lymphadenectomies in 2006. The mean operating time for the thoracoscopic phase was 180 min, median blood loss 400 ml, median lymph node yield was 20, median ICU stay was four days, and hospital stay 18 days. Pulmonary complications occurred in 10 patients (48%).

Puntambekar et al. (9) published their experience with robotic esophagectomy in 32 patients. The most common site of involvement in the esophagus (60% cases) was the lower thirds with predominant histology SCC (80% cases). The average surgical duration in this experience was 204.94 minutes (range 180-300 minutes) and mean blood loss 86.75 ml (range 50-200 ml). The mean lymph node yield in this study was 18.36 (range 13 to 24). 2 patients had a positive circumferential margin, and the conversion rate was 0. Post-operative morbidity occurred in 20 % of cases, amongst which dysphagia was the most common (7.23 %), followed by pleural effusion (3.61 %). Anastomotic leak was seen in 3 cases, and chyle leak in one case. 2 cases of RLN palsy were also seen. About 80 % of patients were disease free at ten months follow-up period.

P.C. Sluis et al. (10) studied the long-term results of 108 cases of robotic-assisted MIE with two-field lymphadenectomy. The majority of patients (78%) were stage cT3 and higher, and almost 70 % had a clinically positive nodal disease. The conversion was required in 20 patients (19%). The median duration of the procedure was 381 minutes (range 264-550 min), with the median duration of the thoracoscopic phase being 175 minutes (range 108 to 241 min). The postoperative complications were observed in 66% of patients, with pulmonary

complications being the most common subtype (33%) followed by Anastomotic leak in 19%, chylothorax in 18%, vocal cord palsy cardiac complications in 9%. The median (range) ICU stay in this study was 1(1-76), and hospital stay [median(range)] was 16(9-123).

Weksler et al(11) presented a retrospective review of a prospective database analyzing 37 patients (11 RA and 26 MIE) in which they found no significant differences in operative duration, blood loss, LNY, postoperative complications, length of ICU, and hospital stay between the two modalities.

Chao et al(12) presented a single centre retrospective propensity matched analysis of esophageal SCC patients who underwent McKeown esophagectomy via robotic-assisted(37) and video-assisted (107) techniques. Using propensity matching analysis, 34 matched pairs were identified. They concluded that the number of lymph nodes amongst the two groups were comparable except the left RLN area (5.32 in the robotic-assisted group vs. 3.32 in the video assisted group; p=0.007). The incidence of both RLN palsy as well as pulmonary complications and need for blood transfusions were comparable in both the RATE group and the VATE group. The study revealed that the dissection of nerves located ventrally to the left RLN was frequently the most difficult part of the VATE procedure. Moreover, the operating time was 30 minutes longer in the RATE arm.

ElsVisser et al published a meta-analysis that included 26 studies from 2017-2019 with a follow-up of 15-94 months and found that overall survival significantly improved in the high lymph node yield group [$p < 0.01$]. Ten studies also described improved disease-free survival with increased lymph node yield ($p < 0.01$)(13).

NP Rizk et al(5) analysed 4627 patients undergoing esophagectomy to find an optimum number of lymph nodes that need to be resected for a better five years and overall survival in these patients. They found that for node-negative non-metastatic moderately and poorly differentiated cancers and all node-positive cancers, five years survival greatly improved by increasing the LNY. According to their published work, optimum lymph node yield stage-wise is depicted below-

S. no.	Pathological T stage	Optimum LN yield
1.	pT1N0M0	10-12
2.	pT2N0M0	15-22
3.	pT3/4N0M0	31-41
4.	pT1N+M0	10
5.	pT2N+M0	15
6.	pT3/4N+M0	29-50

A review on the evolution of MIE by Hasson et al also commented on the learning curve in MIE with the optimum number ranging from 20-80 depending on the outcome parameter being measured(14). Zhang et al quoted this number at 26 to gain proficiency in the thoracoscopic phase and at 14 for the abdominal dissection(15). The number of cases needed to increase the LN yield from 25 to 40 was quoted as a minimum of 30 by Park et al(16).

Zhang et al(4) conducted a retrospective analysis of 184 patients, out of which 76 were in the RA-ILE group, and 108 were in the TA-ILE group between December 2014 to June 2018. Propensity score matching analysis was performed between 66 matched pairs, and perioperative outcomes were compared. The study revealed two conversions to thoracotomy in the RAILE group and significantly longer operating time which was consistent with most other studies comparing robot-assisted and thoracoscopic esophagectomy. However, no statistically significant difference was noted in the overall complications, length of stay, blood loss, number of total dissected lymph nodes, as well as detailed categories of lymph nodes. The study concluded that early outcomes are comparable in the two arms.

RESEARCH QUESTION AND AIMS AND OBJECTIVES

3.1 Research question and aims: This study aims to have a descriptive analysis of the two types of minimally invasive esophagectomies (MIE), i.e., Robotic-assisted (RA) and thoracoscopic assisted (TA) in patients of resectable carcinoma esophagus fulfilling inclusion criteria and describe the outcomes with special reference to thoracic lymph nodal yield in patients undergoing MIE from 1st January 2020 to 31st December 2021. This study also aims to describe, if feasible, whether anyone type has the advantage over the other with respect to the length of hospital/ICU stay, complications and recurrence at the end of 6 months.

3.2 Objectives

3.2.1 Primary objective:

To study the lymph node yield of modified two-field MIE, i.e., RA and TA with respect to thoracic (supracarinal, infracarinal) and abdominal lymph nodes.

3.2.2 Secondary objectives:

To describe MIE with respect to-

1.) Duration of thoracoscopic/robotic phase

2.) Length of ICU and hospital stay

3.) Intraoperative and post-operative complications

4.) To evaluate for recurrence at 6 months by contrast-enhanced CT scan neck, thorax and abdomen, and upper GI endoscopy

MATERIALS AND METHODS

4.1. Study setting

Thirty-three consecutive patients undergoing minimally invasive esophagectomy, either thoracoscopic assisted or robotic-assisted for carcinoma esophagus and meeting inclusion criteria during the study period, were recruited from the Department of Surgical Gastroenterology at AIIMS, Jodhpur.

4.2. Duration of study

The duration of our study extended from 1st January 2020 to 31st December 2021. Patients were recruited till June 30, 2021 and followed up for 6 months in person (post-discharge every 15 days till 2 months and monthly after that). CECT neck, thorax and abdomen, and upper GI endoscopy were done at 6 months post-surgery.

4.3. Sample size

Based on a previous study conducted by Park S et al(17) and keeping in mind the primary end point of lymph nodal yield in MIE, the following formula was used for calculating sample size (n)

$$n = \frac{(Z_{\alpha/2}+Z_{\beta})^2 \times 2 \times}{\sigma^2 d^2}$$

where $Z_{\alpha/2}$ is the critical value of the Normal distribution at $\alpha/2$ or the standard normal variance (e.g., for a confidence level of 95%, α is 0.05 and the critical value is 1.96), $Z\beta$ is the power of the standard normal variance (e.g., for a power of 80%, β is 0.2, and the critical value is 0.842), σ^2 is the pooled variance, and d is the expected difference or the affect size (d in this case=0.687).

Using this calculation, n=34 in each arm i.e., RA and TA. **Limitations-** Based on a retrospective analysis of the database of our department from 1st January 2017 to 31st December 2019, 14 cases of MIE were done. Hence keeping in view the patient load, non-availability of robotic surgery during the COVID 19 pandemic, and the limited duration of this study for the thesis, we had decided to keep a minimum sample size

of 10 patients in each arm, i.e., RA and TA. We recruited 23 patients in the TA arm and 10 patients in the RA arm.

4.4. Study design

It was a single-centre descriptive study. All the patients undergoing minimally invasive esophagectomy within the study period without any exclusion criteria were included. The mean duration of thoracic phase (robotic or thoracoscopic), the total length of post-operative stay (ICU as well as in-hospital), intraoperative as well as postoperative complications; LN yield (thoracic and abdominal), any recurrence within 6 months as evaluated by CECT neck, thorax and abdomen and upper GI endoscopy at 6 months, was evaluated and compared with the data from current literature.

4.5. Inclusion criteria

1. Age of 18 to 80 years
2. Histology proved primary esophageal carcinoma
3. GE junction tumors (Siewert I and II)
4. Managed by minimally invasive esophagectomy, either robotic-assisted or thoracoscopic assisted
5. With or without neoadjuvant treatment
   Written informed consent taken
6. All patients shall strictly follow ERAS protocol for esophagectomy (attached in annexures)

4.6. Exclusion criteria

1. Esophagectomy for benign disease
2. Severe cardiopulmonary comorbidity
3. ASA 3 or higher
4. ECOG performance status $\geq$ III

4.7 Preoperative evaluation

All patients underwent an intensive pre-operative evaluation-endoscopy and biopsy, neck, thorax, and abdominal CT, Pulmonary function tests, screening echocardiography, and bronchoscopy if necessary. CT was performed preoperatively and post-operatively at 6 months. Endoscopic examination was performed at 6 months post-operatively. Grading of dysphagia was done using the modified Takita's grading attached in annexures (22).

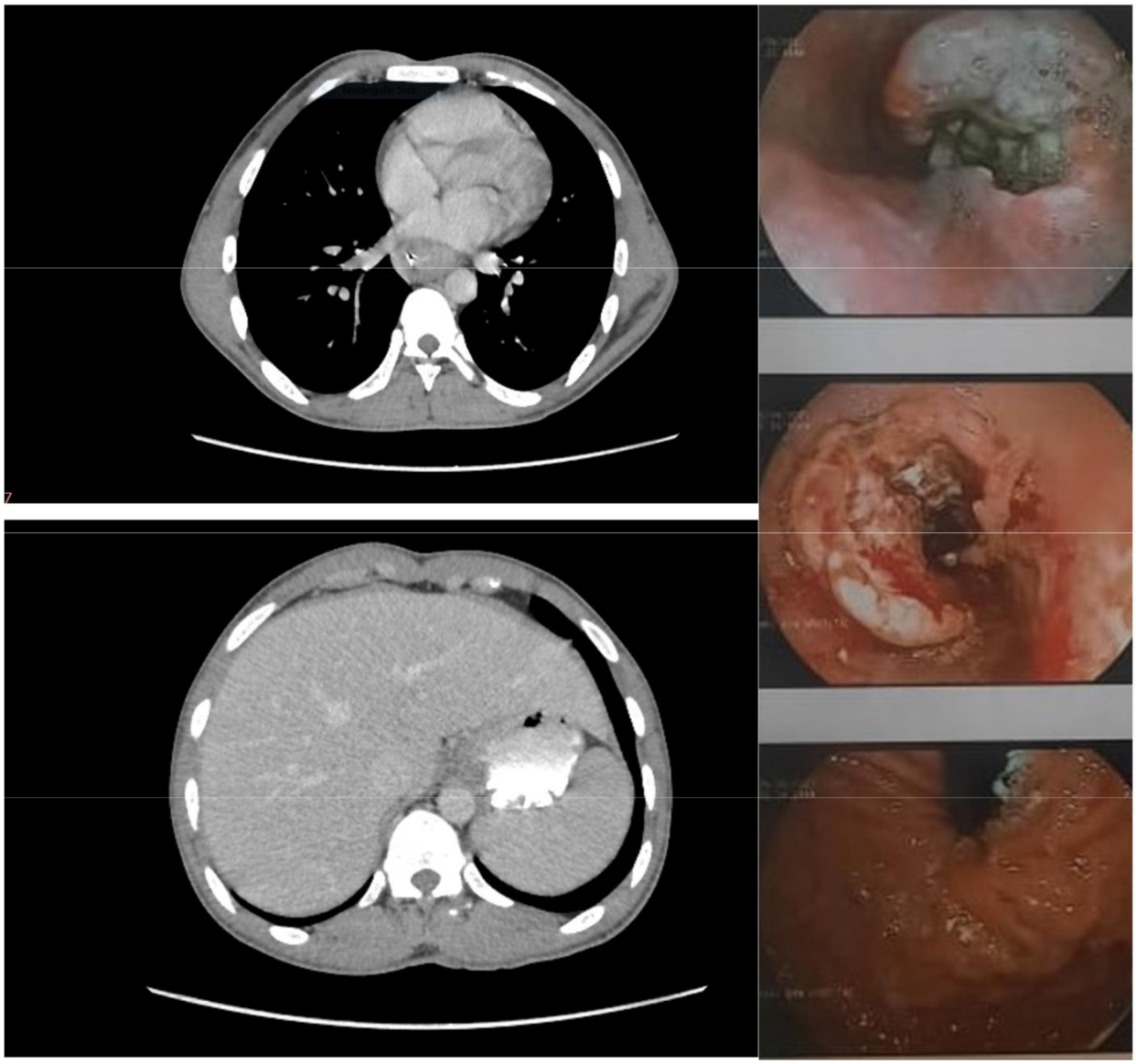

Figure 1-Preoperative evaluation with (a) and (b) showing growth in lower esophagus extending upto GE junction and (c) EGD showing circumferential ulcerative growth

4.8. Surgical procedure:

Patients underwent esophagectomy with thoracic phase done either thoraco-laparoscopically or robotic-assisted with gastric pull through and cervical esophagogastric anastomosis. All patients, whether RA or TA, had strict adherence to peri-operative ERAS (Enhanced recovery after surgery) protocol.

4.8.1 Surgical technique of thoracoscopic esophagectomy

4.8.1.1 Thoracic phase (thoracoscopic)

1. Patient is intubated with a single-lumen endotracheal tube in a standard conventional manner in the supine position.
2. After intubation, the patient is changed to prone position with bean bags under the chest and pelvis.
3. The surgeon stands on the right of the patient, the camera surgeon to the left of the surgeon, and the assistant to the left of the patient. The scrub nurse also stands on the right of the patient. The laparoscopic cart with the monitor is placed on the left of the patient.
4. After painting and draping, under strict aseptic precautions, ports are placed after creating pneumothorax on the right side of the chest maintaining insufflation pressure of 6 to 8 mm Hg.

Mobilization of esophagus and control of Azygous vein

5. Azygous vein, esophagus, and pleura are inspected, and resectability is assessed. The inferior pulmonary ligament is divided to retract the inferior lobe of the right lung.
6. Thoracic esophagus along with periesophageal tissue is mobilised; Azygous vein is dissected and cut after applying Weck's® hem-o-lok.
7. The esophagus is encircled with an umbilical tape for retraction and periesophageal lymph nodal clearance was achieved.
8. The mediastinal pleura and esophagus are excised en bloc.
9. Laterally, dissection was carried down from the supracarinal area to the left pleura. Then the lower third of the pleura is mobilised and the esophagus dissected from diaphragmatic hiatus.

Lymph nodal clearance

10. A thorough lymph nodal clearance is first achieved in the infracarinal space. The LNs are dissected according to Japanese classification and sent for histopathology after labelling separately.

11. Once the inferior pulmonary vein is identified and dissected, lymph nodal clearance is achieved in the supracarinal space especially to the right of right recurrent laryngeal nerve.
12. Haemostasis is achieved, and 24F ICD is placed through the camera port.
13. Port sites are closed with skin stapler and dressing done.

    Then the position is changed for the abdominal phase to modified Lloyd-Davis position with reverse Trendelenburg/ supine position.

4.8.1.2 Abdominal phase (laparoscopic) and neck phase (open)-

1. The patient is positioned in reverse Trendelenburg position. Ports are placed as follows- supraumbilical port 10 mm for the camera, 5 mm epigastric port for liver retraction; 5 mm ports-right and left midclavicular port. The left anterior axillary port can be inserted for stomach retraction.
2. The surgeon stands between the legs of the patient. Camera surgeon and scrub nurse to the right and assistant to the left of the surgeon. Laparoscopic cart with monitor towards the head of the patient.
3. Pneumoperitoneum created by closed Veress needle/open Hasson cannula technique maintaining 12 to 14 mm Hg insufflation pressure. The left liver lobe is retracted using Nathanson's retractor.
4. The gastrocolic omentum is then divided close to the liver, and the left gastric artery and vein are then divided. All lymphofatty tissue around the stomach is then dissected and the esophagus is separated from the right crura of diaphragm. The stomach is completely mobilized. Note is made of accessory left Hepatic artery arising from left gastric artery and is preserved, if present.
5. Pneumoperitoneum is deflated, and cervical dissection started. Through a small, 4 to 6 cm cervical incision, the esophagus is taken out, dissected, transected, and a NG tube is attached to this end of the specimen.
6. Then the esophagus is pulled at its lower end by applying traction, and then after sealing the cervical incision with pads, pneumoperitoneum is again created, and the specimen is pulled into the abdomen.
7. The specimen is taken out through the abdominal incision by enlarging the incision.
8. The gastric conduit is attached to one end of the NG, which was in the stomach and is pulled up through the neck incision.

9. The specimen is retrieved, haemostasis checked, and the gastric tube is placed in native bed
10. Cervical esophago-gastric anastomosis is done via semi-mechanical/ completely stapled/ hand-sewn manner as decided by the chief operating surgeon
11. Sutures and ryles tube is placed in gastric tube
12. Neck wound is closed with a skin stapler after approximating strap muscles
13. Feeding jejunostomy(FJ) is done using Witzel's technique 40 cm from DJ flexure
14. Rectus sheath is closed, skin is closed with skin staplers, and dressing applied

4.8.1.3 Abdominal Phase (Robotic)-

1. Supine position
2. 8mm robotic port is placed 15 cm from xiphisternum in the midline, right, and left midclavicular line.
3. 10mm assistant port is placed in the left lumbar region
4. Rest of the steps are the same as in the laparoscopic approach

4.8.1.4 **Abdominal Phase and neck phase (Open)-**

1. Midline abdominal incision given
2. Gastrocolic ligament divided close to the liver
3. Gastric artery and vein ligated and cut
4. Lesser sac is opened, greater omentum divided preserving gastroepiploeic arcade
5. Stomach is mobilised completely and esophagus separated from right crura
6. Oblique left anterior to sternocleidomastoid incision given, strap muscles are divided
7. Oesophagus is then dissected, cut at lower cervical level
8. Gastric tube is prepared with four fires of 55 mm green linear cutting staplers NTLC after doing stretching of pylorus
9. Specimen is retrieved, haemostasis checked and gastric tube is placed in native bed
10. Cervical esophago-gastric anastomosis is done in hand sewn single layer interrupted
11. Sutures and ryles tube is placed in gastric tube
12. Neck wound is closed with skin stapler after approximating strap muscles and romovac suction drain is placed
13. FJ is done using witzel technique 40 cm from DJ
14. Abdominal drain no. 28 is placed near hiatus from left side
15. Abdomen is closed after placing drain in upper abdomen

16. Skin is closed with skin staplers

4.8.1.5 **Surgical technique of Robotic esophagectomy**

4.8.1.5.1 Thoracic phase (Robotic)-

1. Patient is placed in prone/ modified prone position
2. Three 8mm robotic ports are placed in 5^{th}, 7^{th} and 9^{th} ICS in mid axillary line, posterior axillary line and midscapular line on right side
3. One 12mm assistant port is placed in 9 th ICS in anterior axillary line
4. Robotic arms 2,3 and 4 are draped and docked in position
5. Thoracic esophagus along with periesophageal tissue is mobilised (rest of steps similar as above)
6. Azygous vein is dissected and cut after applying Weck's ®hem-o-lok.
7. Meticulous LN dissection is done as mentioned above
8. Haemostasis is achieved and 24F ICD is then placed through assistant port
9. Port sites are closed with skin stapler and dressing is done
   Abdominal and neck phases same as described above.

4.8.2. Pathological analysis

Pathological analysis of the resected specimen was done as follows-

Fixation:

Specimens were fixed in 10% formalin.

Gross Examination:

Specimens were grossly examined for dimensions and tumor location. The distance of the margins was measured. Detailed lymph node gross examination was done. The total number of lymph nodes dissected out was noted, and representative sections taken.

Processing of histopathology specimens

Representative sections were processed as per the routine histopathology processing. Routine hematoxylin and eosin staining was done on the sections.

Reporting of histopathology specimens

Specimen were reported as per the latest College of American Pathologists (CAP) protocol. Pathological stage classification was done as per American Joint Committee on Cancer (AJCC) 8^{th} edition manual (attached in Annexure).

4.9. Data collection

Demography, clinicopathological characteristics, radiological parameters, intraoperative findings and complications, histopathological characteristics with particular reference to LN yield, length of hospital stay, intraoperative and post-operative complications, morbidity, recurrence, and mortality were recorded in the Microsoft Excel database. The complications of esophagectomy were recorded according to Esophagectomy Complications Consensus Group (ECCG) (24) (Attached in Annexures).

4.10. Discharge criteria

1. Vital signs within normal limit
2. Patient taking oral semisolids/ feeding jejunostomy feeds
3. Passed stool and flatus
4. No tubes or catheters (except FJ tube)
5. Able to ambulate without assistance
6. Pain controlled on oral analgesics

4.11. Follow up

All patients were followed up in person at an interval of every 15 days for 3 months and monthly thereafter. A contrast-enhanced CT scan neck, thorax, and abdomen was performed after the completion of 6 months post-surgery along with an esophagogastroduodenoscopy to check for recurrence and anastomotic stricture if any.

4.12. Statistical analysis

All data was acquired in a specified format as in proforma and entered in SPSS v 26/MS-Excel software for analysis. Measured data were expressed as median with interquartile range (IQR) at the 25^{th} and 75^{th}percentiles or as percentages. Proportions were compared using Chi-square or Fisher's exact test, whichever is applicable and numerical data were compared using the Mann Whitney u test. P-value ≤ 0.05 was considered significant in all statistical evaluations. Time to event will be analysed by the Kaplan Meier curve. P-value ≤ 0.05 was considered significant in all statistical evaluations. As the protocol was changed owing to

COVID 19 pandemic, mainly descriptive statistics was used and no comparisons were made due to small numbers in the robotic assisted arm

4.13. Ethical considerations

All the patients enrolled in the study received the standard care management, and the participation in the study did not lead to change in their usual diagnostic workup, follow up, or management. All personal data collected during the study was kept strictly confidential.

IMAGES

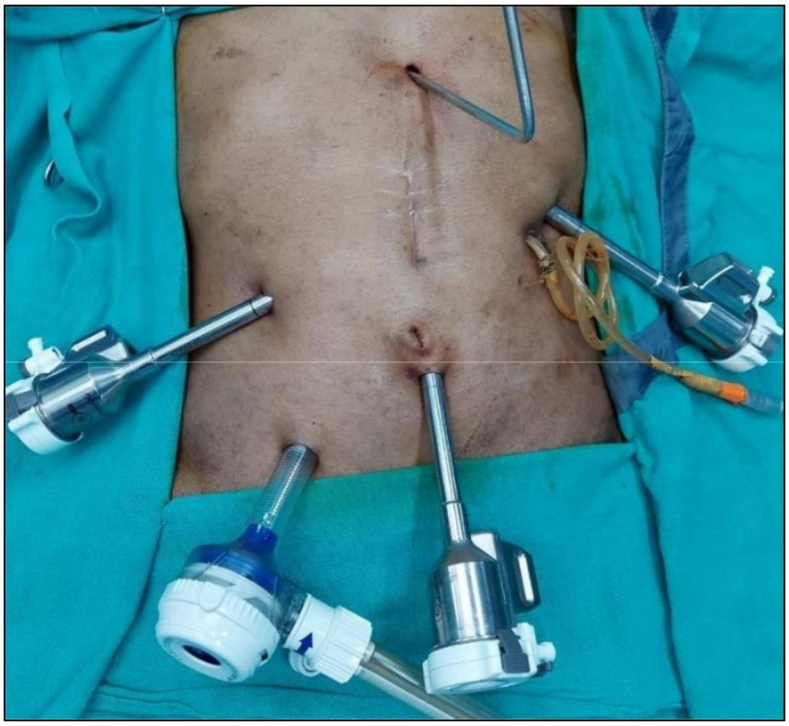

Figure 2-Port position of RAMIE (abdominal phase)

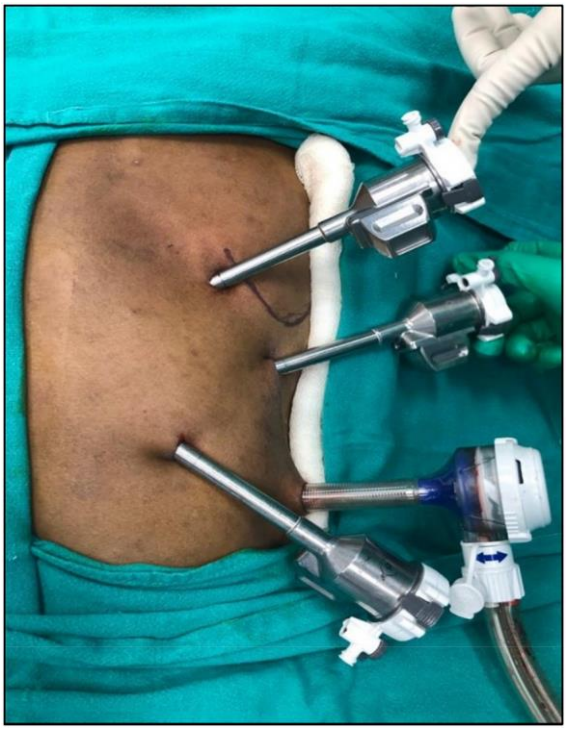

Figure 3- Port position of RAMIE (thoracic phase)

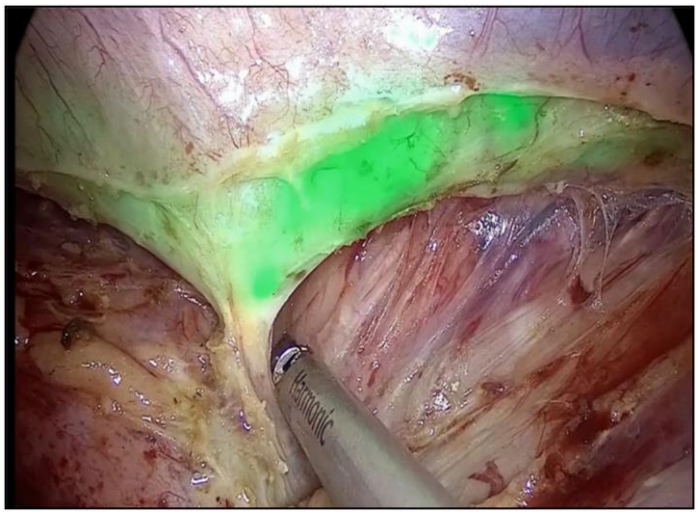

Figure 4-Thoracoscopic dissection keeping thoracic duct in view

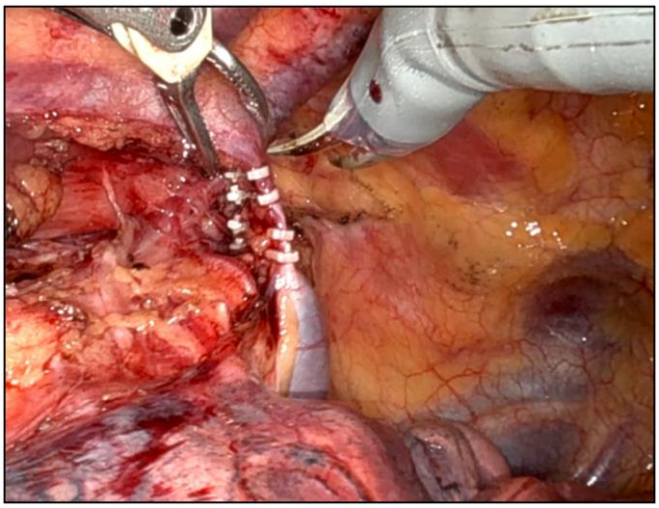

Figure 5-Clipping and dividing Azygous vein

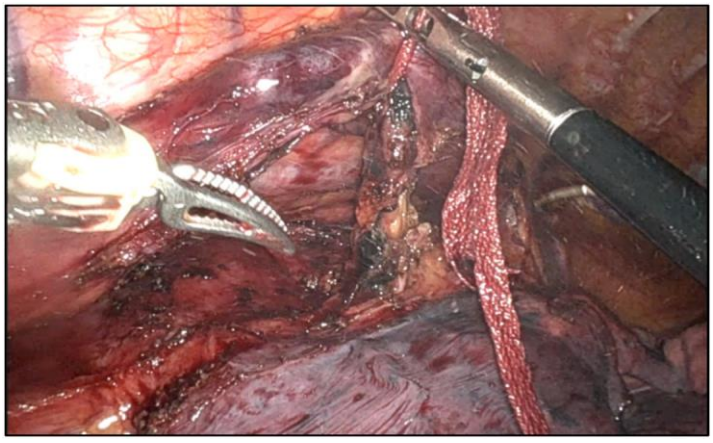

Figure 6-Dissection of 106rtb LN station with retracted esophagus

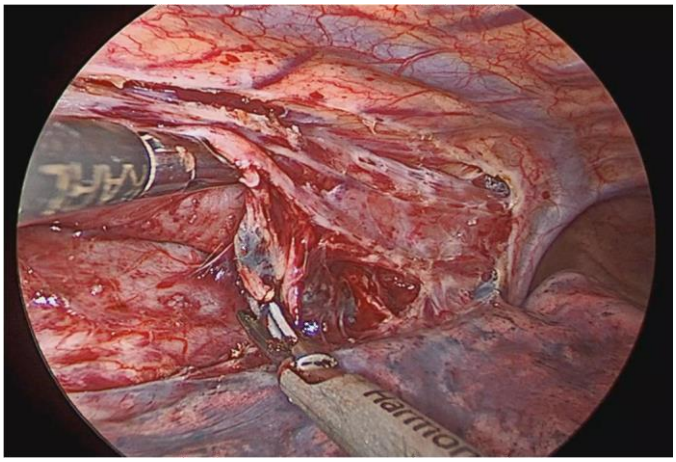

Figure 7-Dissection of peri-esophageal LNs (station 108)

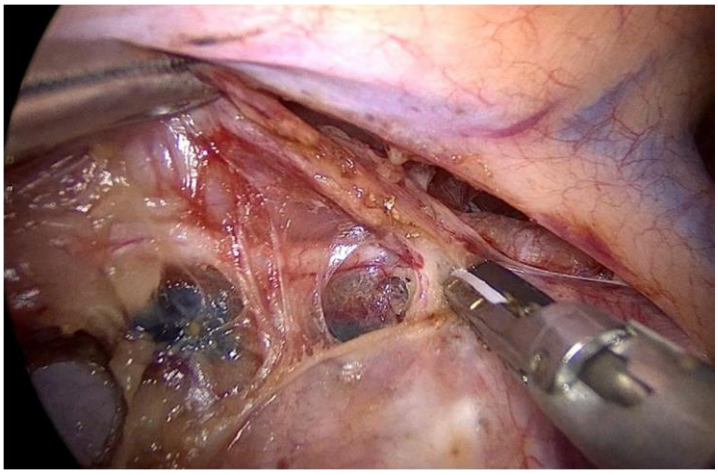

Figure 8-Dissection of station 109 bronchial LNs

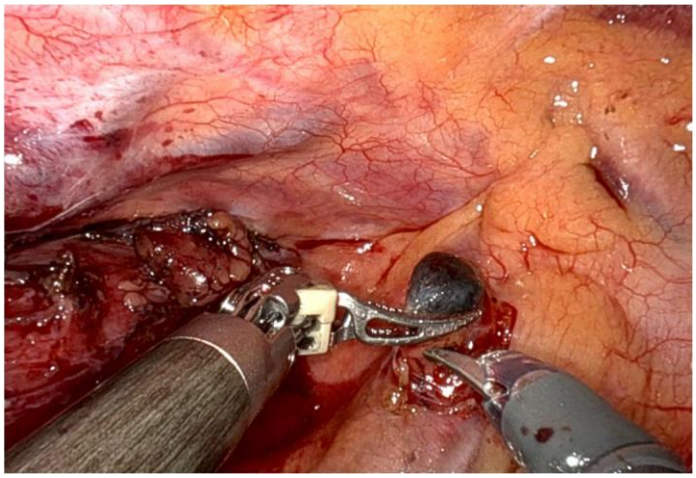

Figure 9-Dissection of station 106 rt RLN LN

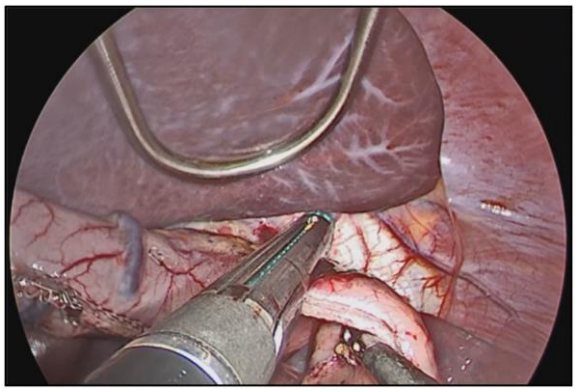

Figure 10-Laparoscopic creation of gastric conduit

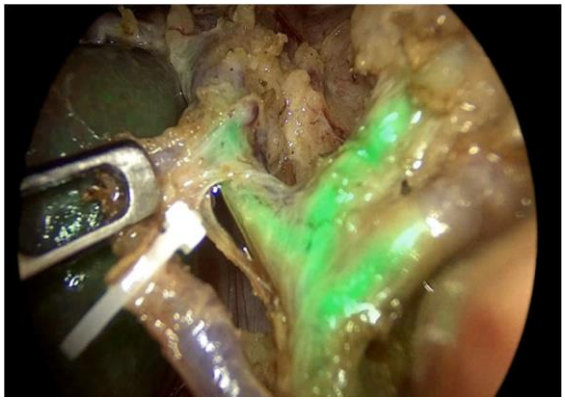

Figure 11-Preserving replaced Left Hepatic from Left gastric artery

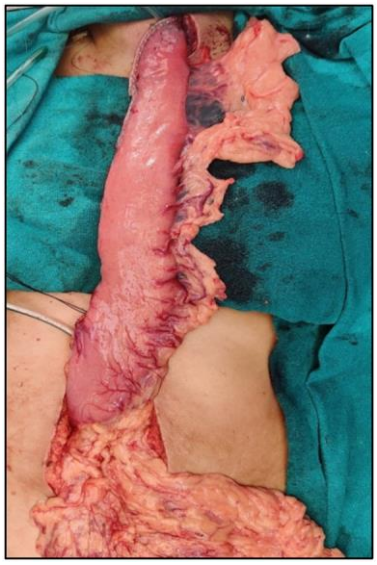

Figure 12-Checking adequacy of conduit length

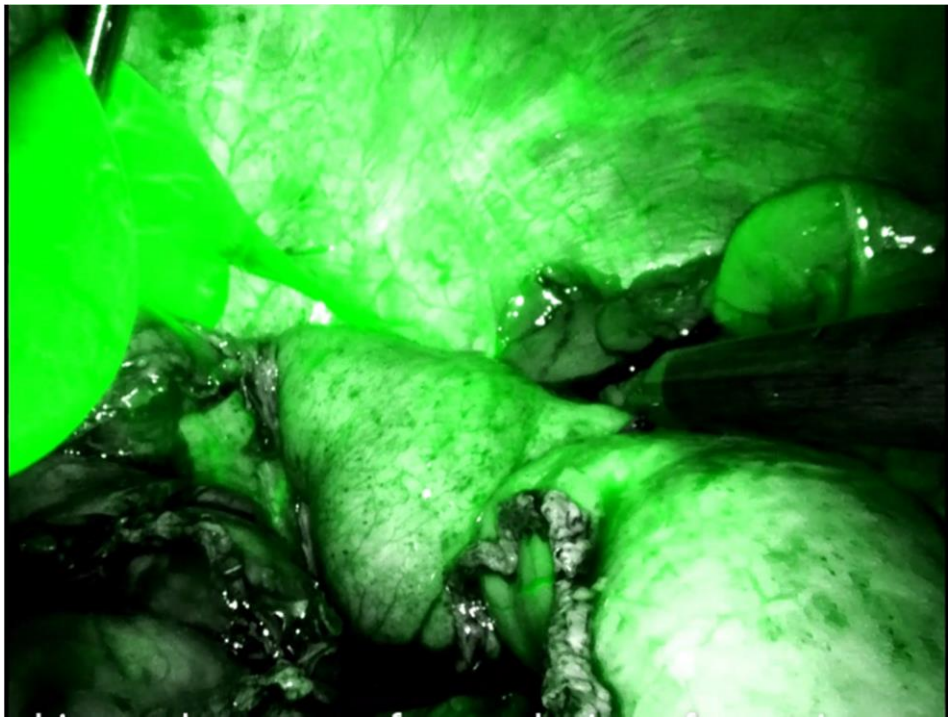

Figure 13-Assessment of conduit vascularity using ICG dye

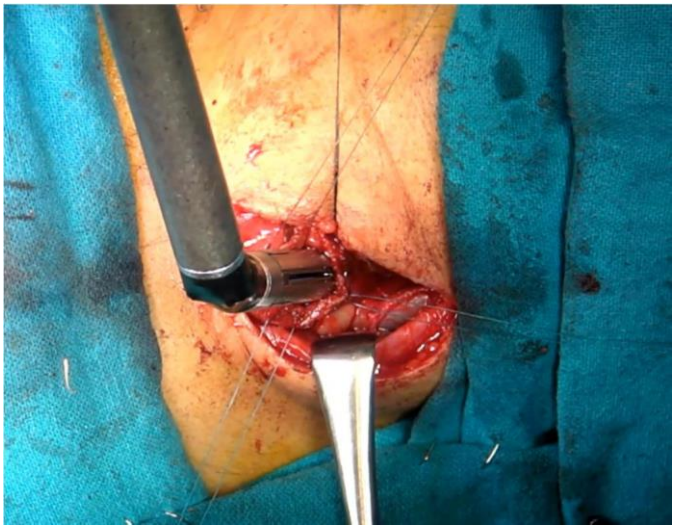

Figure 14-Semi-mechanical cervical esophago-gastric anastomosis

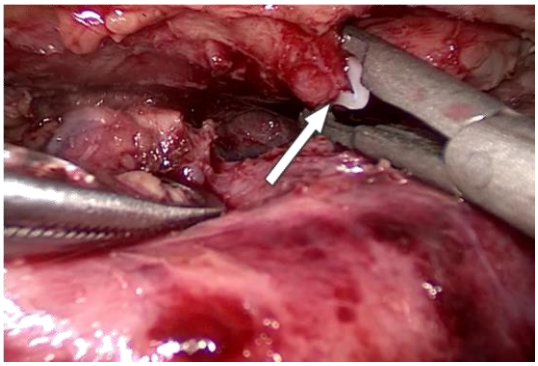

Figure 15-Clipping of thoracic duct in a case of post-operative chylothorax

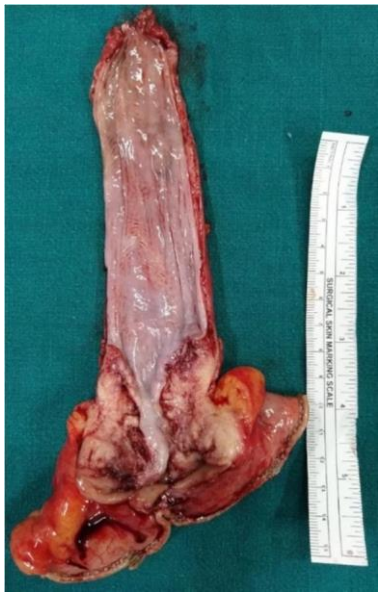

Figure 16-Resected specimen showing GE junction growth

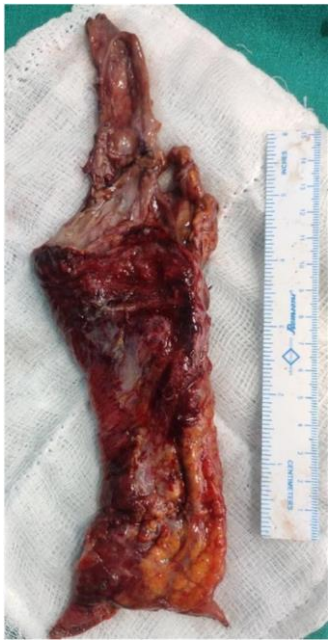

Figure 17-Resected conduit in case of conduit necrosis

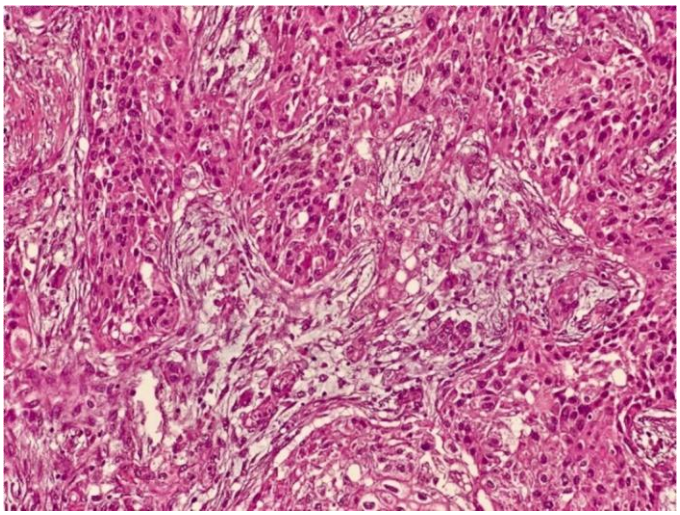

Figure 18-Islands of squamous cell carcinoma. H.E. 40X

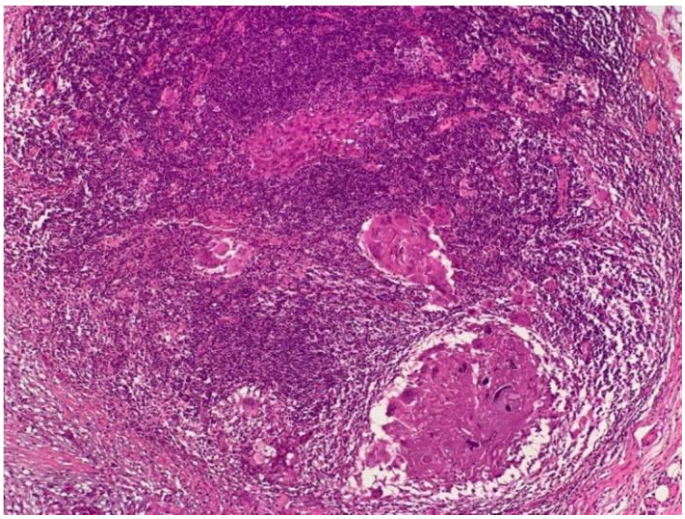

Figure 19-Metastatic deposits of squamous cell carcinoma in LN

RESULTS

Thirty-eight patients of biopsy-proven carcinoma esophagus were screened for inclusion during the study recruitment period extending from January 2020 to June 2021. Out of 38 patients, five were excluded from the study due to various reasons (two were found to be metastatic intra-operatively on staging laparoscopy, 2 were found to be locally advanced and underwent salvage esophagectomy without LN dissection, and one required performance of the esophagectomy via transhiatal route due to dense adhesions in the right hemithorax).

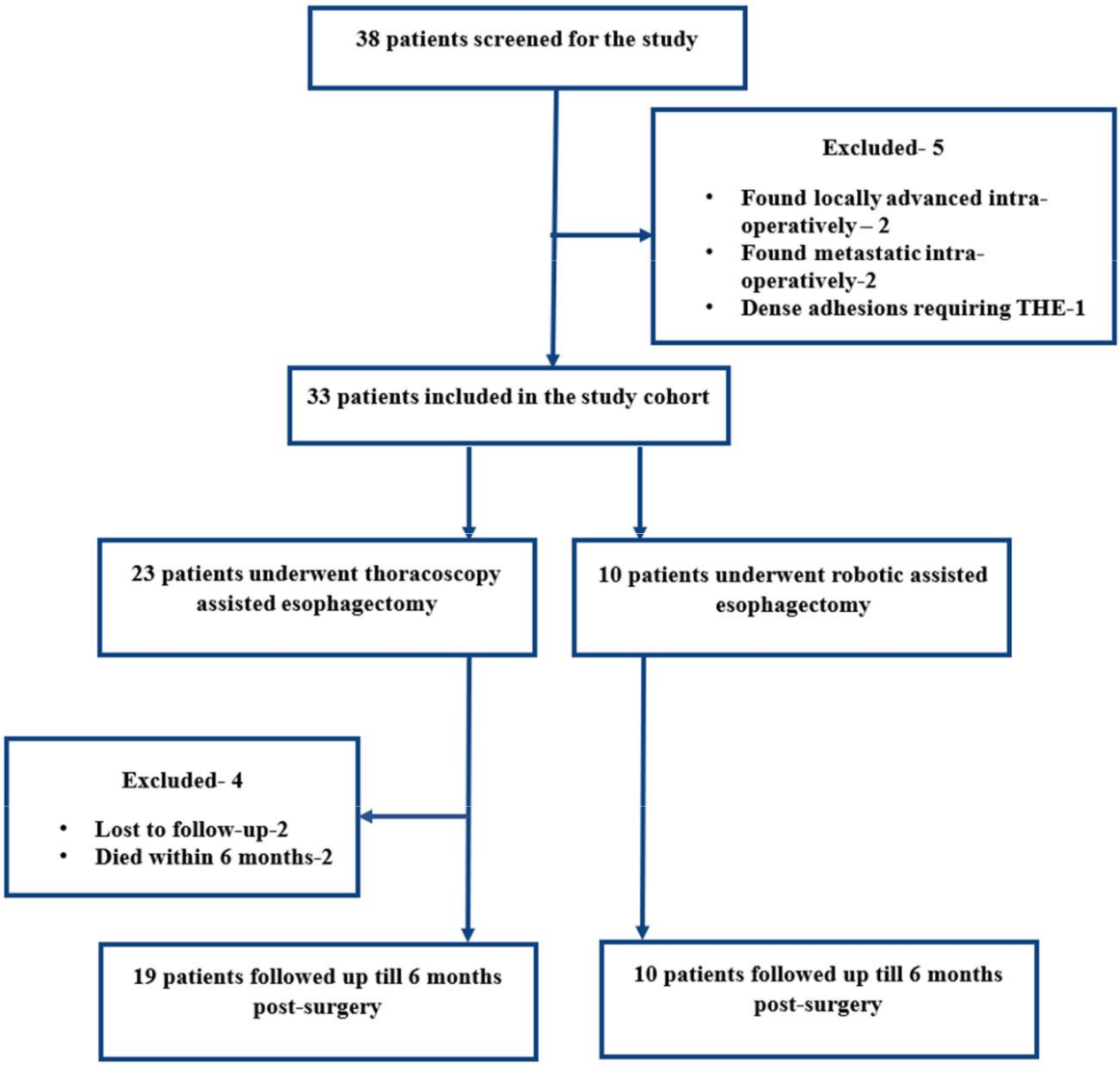

Figure 20-CONSORT diagram of the study

6.1 Baseline characteristics (Table 3)

Out of 33 patients included in the final analysis, 16 patients (48.5%) were females. The median age (IQR) of the study population was 50 (45, 58) years. 11 of 33 (33.3%) patients had a history of smoking, and three patients (9.1%) had a history of alcohol consumption. The most common presenting complaints were dysphagia (100%), loss of weight (60.6%), and loss of appetite (39.4%) of patients. The median grade of dysphagia was grade 3 (IQR 2,3) [modified Takita's classification], and the median duration of symptoms was 2 months (IQR 2, 3). Squamous cell carcinoma was the type of malignancy in all patients (33; 100%), and the majority of tumors were located in the middle third of the esophagus (n=17; 51.5%). Majority of patients had an ECOG performance status of grade 1 (n=29, 87.9%) and median (IQR) body mass index (BMI) was 21 (19,22) kg/m^2 [21.4(19.3, 22.8)in the TA arm versus 21.4(19.3, 22.3) in the RA arm]. The median (IQR) preoperative albumin level was 3.7 (3.6, 4) gm/dl, and preoperative nutritional intervention through NG tube or FJ was done in 4 patients (12.1%). Neoadjuvant treatment was received by 27 out of 33 patients (81.8%). Fifteen patients received neoadjuvant chemotherapy (Carboplatin-paclitaxel based), and 12 received chemoradiotherapy (carboplatin-paclitaxel and 41.4 Gy in 23 fractions). The median (IQR) number of days between neoadjuvant treatment and surgery was 41 (31.5, 62.5) days. Thirty-three patients underwent minimally invasive esophagectomy (MIE), out of which 23 patients (69.7%) underwent thoracoscopic dissection, and 10 (30.3%) underwent robotic-assisted dissection in the thoracic phase. In the assessment of response to therapy, the median (IQR) Ryan's tumor regression grade was 2(1,3). The final pathological stage was stage 0 in 9 patients (27.3%), stage I in 8 patients (24.2%), stage II in 7 patients (21.2%), and stage III in 9 patients (27.3%).

Table 2-Baseline characteristics

Characteristic	**Overall (n=33)**	**Thoracoscopic assisted (n=23)**	**Robotic assisted(n=10)**
Age [years, median (IQR)]	50 (45,58)	50 (45, 58.5)	50.5 (44.75, 59)
Gender Male, n (%) Female, n (%)	 17 (51.5) 16 (48.5)	 12 (52.2) 11 (47.8)	 6 (60) 4 (40)
Presenting symptoms			

Dysphagia, n (%)	33 (100)	23 (100)	10 (100)
Loss of weight, n (%)	20 (60.6)	15 (65.2)	5 (50)
Loss of appetite, n (%)	13 (39.4)	10 (43.5)	3 (30)
Addictions, n (%)			
Alcohol	3 (9.1)	2 (8.7)	1 (10)
Smoking	11 (33.3)	10 (4.3)	1 (10)
Comorbidity, n (%)			
Hypertension	5 (15.1)	3 (13)	2 (20)
Diabetes mellitus	3 (9.1)	2 (8.7)	1 (10)
Psychiatric illness	1(3)	1 (4.3)	0
Hepatitis C	1 (3)	1 (4.3)	0
Histology			
SCC, n (%)	33 (100)	23 (100)	10 (100)
Tumor location			
Mid thoracic, n (%)	17 (53.5)	12 (52.2)	5 (50)
Lower thoracic, n (%)	12 (36.4)	7 (30.4)	5 (50)
EGJ, n (%)			
Siewert 1, n (%)	2 (6.1)	2 (8.7)	0
Siewert 2, n (%)	2 (6.1)	2 (8.7)	0
ECOG score			
I	29 (87.9)	20 (87)	9 (90)
II	4 (12.1)	3 (13)	1 (10)
Grade of dysphagia, n (%) [Modified Takita]			
I	6 (18.2)	4 (17.4)	2 (20)
II	6 (18.2)	5 (21.7)	1 (10)
III	15 (45.5)	10 (43.5)	5 (50)
IV	4 (12.1)	2 (8.7)	2 (20)
V	2 (6.1)	2 (8.7)	0 (0)
Duration of dysphagia [months, Median (IQR)]	2 (2,3)	2 (2, 3.5)	2 (2, 4)

BMI [Kg/m2, median (IQR)]	21 (19,22)	21.4(19.3, 22.8)	21.4(19.3, 22.3)
Preoperative albumin level [g/dl, mean ± SD]	3.74 ± 0.38	3.78 ± 0.36	4 ± 0.38
Preoperative tube feeding, n (%)	4 (12.1)	3 (13)	1 (10)
Neoadjuvant therapy, n (%)	27 (81.8)	19 (82.6)	8 (80)
NACT, n (%)	15 (45.5)	11 (47.8)	4 (40)
NACRT, n (%)	12 (54.5)	8 (34.8)	4 (40)
Interval between neoadjuvant therapy and surgery [days, median (IQR)]	41 (31.5, 62.5)	41 (32, 64)	41(31.3, 63.3)
TNM (pathological stage)			
0	9 (27.3)	5 (21.2)	4 (40)
I	8 (24.2)	4 (17.4)	4 (40)
II	7 (21.2)	7 (30.4)	0
III	9 (27.3)	7 (30.4)	2 (20)

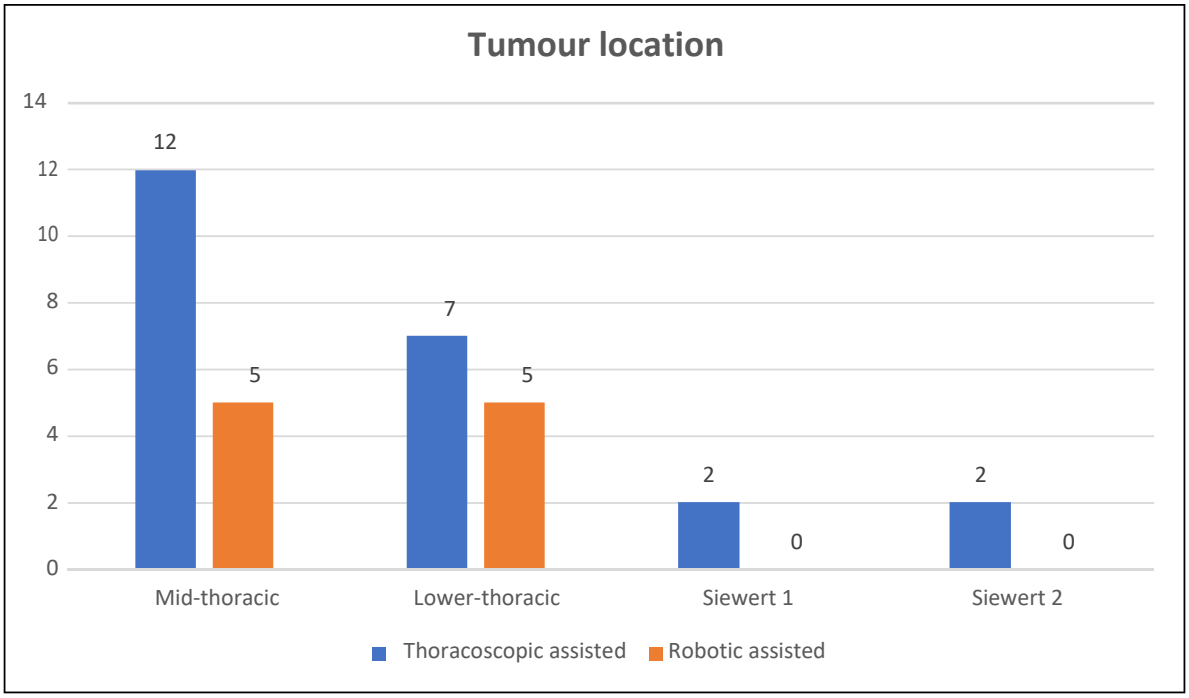

Figure 21-Distribution of tumor in the two arms

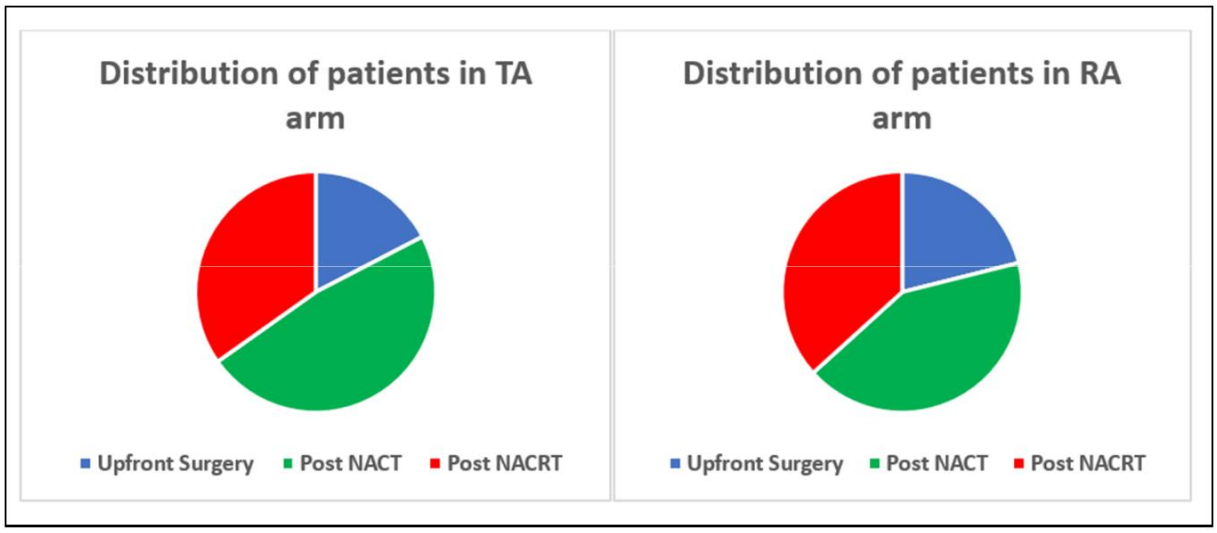

Figure 22-Multimodality treatment distribution in the two arms

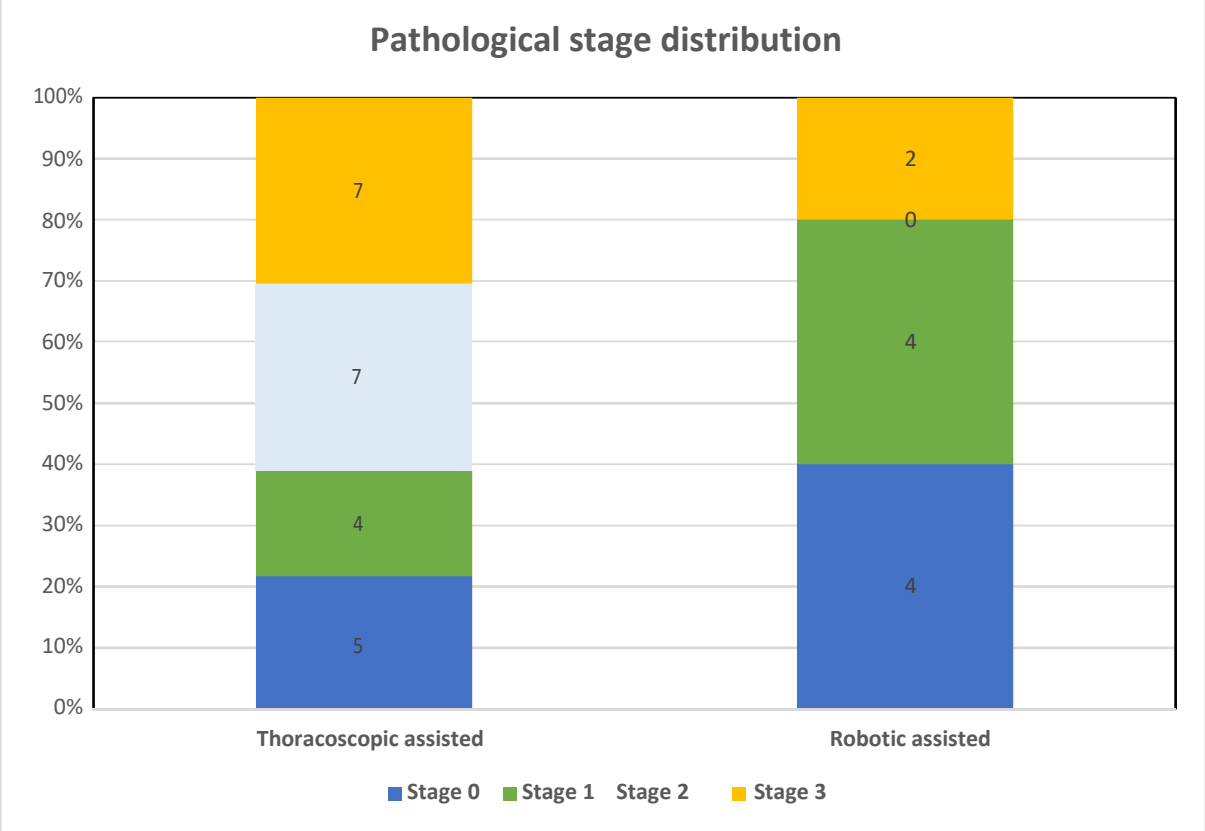

Figure 23-Pathological stage of tumors in the two arms

6.2 Intra-operative characteristics (Table 4)

Twenty-three patients underwent thoracoscopic assisted (TA) dissection, and 10 underwent robotic-assisted (RA) dissection in the thoracic phase, and all patients underwent a Mckeown esophagectomy with modified two-field lymph node (LN) dissection. The abdominal phase was performed by open laparotomy in 25 patients (75.8%), laparoscopic in 5 (15.2%), and robotic in 3 patients (9.1%). The mean duration of the thoracic phase was 133±28 minutes in the TA arm and 168±27 minutes in the RA arm. The median (IQR) blood loss (in ml) was 200 (200,250) in the TA arm and 200 (200,225) in the RA arm. The cervical esophago-gastric anastomosis was performed hand-sewn in 15 patients and semi-mechanical in 18 patients. The thoracic duct was electively clipped in 2 patients (6.1%) to achieve oncological radicality, and thoracic duct injury occurred in 1 patient, which was identified intra-operatively using Indocyanine green dye and near-infrared spectroscopy (OPAL1® technology, Karl Storz), and the thoracic duct was clipped in the thorax to prevent post-operative chylothorax. No intra-operative airway, bronchial, or major vascular injury was

reported in any of the cases. Eighteen patients (54.5%) could not be extubated post-surgery immediately, and required elective ventilation and ICU stay for at least one day.

Table 3-Intraoperative characteristics

Characteristic	**Overall**	**Thoracoscopic assisted (n=23)**	**Robotic assisted(n=10)**
Abdominal phase Open, n (%) Laparoscopic, n (%) Robotic, n (%)	 25 (75.8) 5 (15.2) 3 (9.1)	 18 (78.3) 5 (21.7) 0	 7 (70) 0 3 (30)
Duration of thoracoscopic phase (Mean±SD) minutes	140±27	133±28	168±27
Blood loss in thoracoscopic phase [Median (IQR)] ml	200 (200,250)	200 (200,250)	200 (200,225)
Neck anastomosis Handsewn, n (%) Semi-mechanical, n (%)	 15 (45.5) 18 (54.5)	 8 (34.8) 15 (65.2)	 7 (70) 3 (30)
Intra-operative airway/ bronchus injury	0	0	0
Intra-operative major vascular injury	0	0	0
Intra-operative Thoracic duct injury	1 (3.1)	1 (4.3)	0
Immediate extubation post-surgery, n (%)	15 (45.5)	10 (43.5)	5 (50)

6.3 Lymph node yield (Tables 5-8)

All patients underwent a modified two-field lymphadenectomy. The median (IQR) lymph node yield (LNY) was 20 (17, 27) in the TA group and 21 (17, 21,25) in the RA group. On comparing the thoracic and abdominal LNY separately, the median (IQR) thoracic LNY was 15 (11.5, 22.5) in the TA group and 15 (10.75, 20.25) in the RA group. The median (IQR)

abdominal LNY was 6 (4, 7) in the open group [n=25], 5.5 (4, 7) in the laparoscopic group [n=5] and 5 (3.25, 7.5) [n=3] in the robotic group.

The median (IQR) LNY post neoadjuvant chemotherapy is 21 (17, 27.25), post neoadjuvant chemoradiotherapy is 20 (16, 27.25) and for upfront surgery is 21 (15.75, 26.5) (table 6). The LNY according to thoracic stations (Japanese Classification-Annexures) is depicted in table 4.

Table 4-Percentage of cases in which thoracic and abdominal LN stations were retrieved

Station number	**Thoracoscopic yield (n, %)**	**Robotic yield (n, %)**
105	7 (30.4)	5 (50)
106	17 (73.9)	7 (70)
107	21 (91.3)	9 (90)
108	18 (78.3)	10 (100)
109	13 (56.5)	4 (40)
110	16 (69.6)	9 (90)
111	2 (8.7)	0
112	1 (4.3)	0
Abdominal LNs (station 1 to 6)	23 (100)	9 (90)

Table 5-Comparative median LNY with and without neo-adjuvant therapy

Lymph node yield	**Upfront surgery**	**Post NACT**	**Post NACRT**
LNY [Median (IQR)])	21(15.75,26.5)	21(17,27.25)	20 (16,27.5)

Table 6-Comparison of LNY after neoadjuvant treatment

Region of LNY	**Post neoadjuvant therapy**	**Post-NACT**	**Post-NACRT**
Thoracoscopic assisted [median, IQR]	19 (13,26); n=19	19 (16,27.75); n=11	20 (15,26.5); n=8
Robotic assisted [median, IQR]	20 (17,26.75); n=8	21 (17,27.25); n=4	25 (18.75,27.5); n=4

Table 7-Yield of LNs according to area of dissection in thorax

Region of LNY	**Thoracoscopic assisted [median, IQR]**	**Robotic-assisted [median, IQR]**
Supra-carinal	5 (1,6.5)	5 (1,7.25)
Infra-carinal	11 (7,15.5)	11 (5.75,15)

The median number of positive LNs (range) was 0 (range 0 to 6) overall, 0 (0 to 6) in the TA arm and 0 (0 to 3) in the RA arm. 10 (43.5%) patients had positive LNs in the TA group, while two patients (20%) had positive LNs in the RA group.

The final histopathology was squamous cell carcinoma in all 33 (100%) patients. The differentiation pattern was well-differentiated in 2 patients (6.1%), moderately differentiated in 24 patients (72.7%), and poorly differentiated in 7 patients (21.2%). The proximal and distal margin was free in all cases. The circumferential resection margin was involved in 3 patients (9.1%)-all in the TA arm. Lymphovascular invasion was seen in 2 patients (20%) in the RA group, and 8 patients (34.8%) in the TA group, and perineural invasion was seen in 1 patient (10%) in the RA group and 7 patients (30.4%) in the TA group.

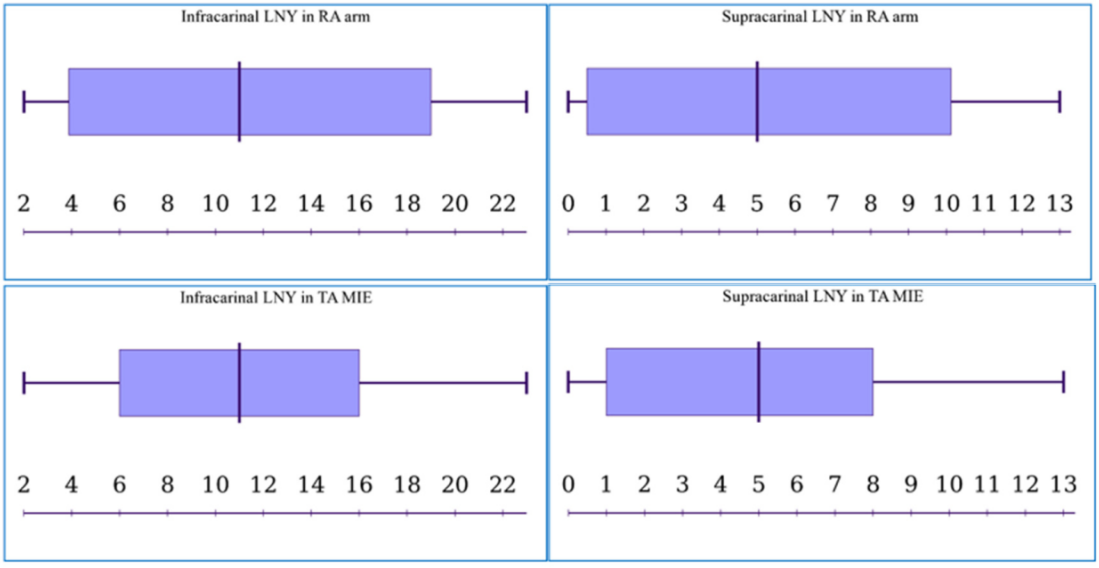

Figure 24-Supra and infra-carinal Lymph node yield in RA and TA arms

6.4 Length of ICU and hospital stay

Eighteen patients (54.5%) [13 in the TA arm-56.5% and 5 in the RA arm-50%] were shifted to ICU and not extubated in the immediate post-operative period. Sixteen patients were extubated on POD 1, one on POD 2(3.1%), and one patient died on POD 2 due to pulmonary complications (both in the TA arm). The median (IQR) post-operative ICU stay was 1 (0,1) day in both the TA and RA arm. The main reasons for post-operative elective ventilation were-prolonged operative time in 10 patients (30.4%), raised lactates in 4 patients (12.1%), and high dose inotropes in 4 (12.1%).

The median (IQR) post-operative length of hospital stay was 6(6,7) days both in the TA and RA arm. Reasons for prolonged post-operative hospital stay (>8 days) in 6 patients (18.2%) [1 in RA arm-10% and 5 in TA arm-21.7%] were pulmonary complications in 3 patients, anastomotic leak in 1, conduit necrosis in 1 and thoracic duct injury requiring re-surgery in 1 patient.

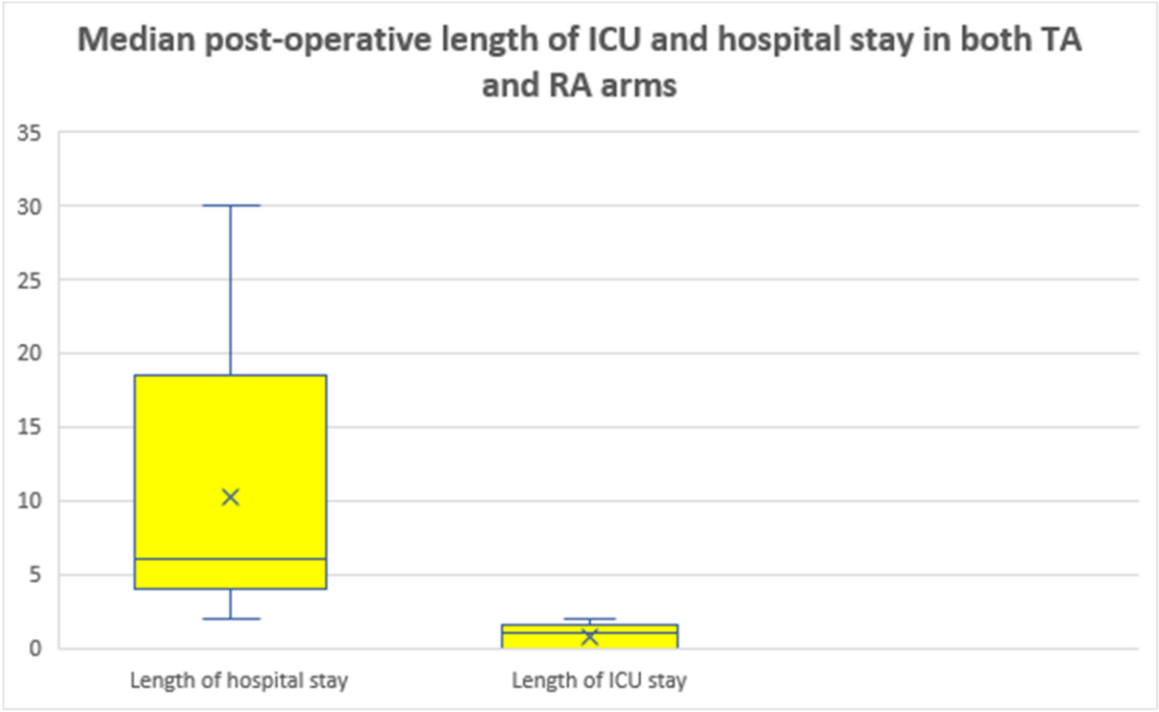

Figure 25-Length of hospital stay

6.5 Post-operative course (Table 9)

The median (IQR) day of extubation in both TA and RA arms was 1(0,1). FJ feeds were commenced on a median (IQR) POD 1 (1,2) in both arms. Median (IQR) POD of ICD removal was 4(3,5). Oral feeds were commenced on a median (IQR) POD of 4(4,5) in the TA arm and 5(4,5) in the RA arm.

Table 8-Post-operative characteristics

Post-operative course	**Overall POD [Median (IQR)]**	**TA arm (n=23) POD [Median (IQR)]**	**RA arm (n=10) POD [Median (IQR)]**
Extubation POD	1 (0,1)	1 (0,1)	1 (0,1)
FJ feed commencement	1 (1,2)	1 (1,2)	1 (1,2)
OGS study	4 (4,5)	4 (4,5)	4 (4,5)
ICD removal	4 (3,5)	4 (3,5)	4 (3,5)
Oral feed commencement	5 (4,5)	4 (4,5)	5 (4,5)
Discharge	6 (6,7)	6 (6,7)	6 (6,7)

6.6 Outcomes (Table 10)

Major complications (Clavien-Dindo $\geq$ 3a) were seen in 11 out of 21 patients in the TA arm followed up till 6 months (52.4%) and in 3 out of 10 patients in the RA arm (30%).

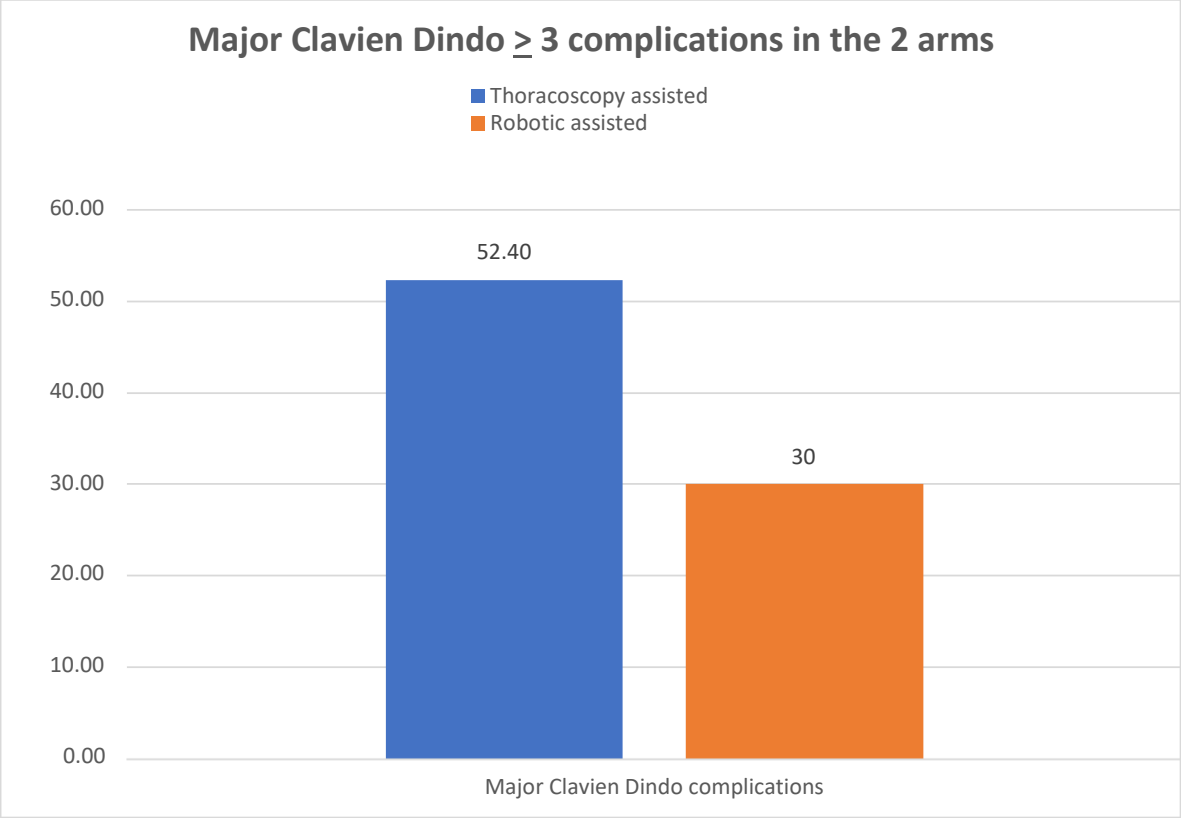

Figure 26-Major Clavien-Dindo complications (≥ 3a)

The most common complication included pulmonary complications as defined by the Esophagectomy Complications Consensus Group (Annexures) were seen in 11 patients in the TA group (47.8%) compared to 3 patients in the RA group (30%). Anastomotic strictures requiring endoscopic dilatation were seen in 10 patients out of 31 patients (31.25%).

The overall incidence of anastomotic leak was 24.2% (8 out of 33) with seven leaks in the TA arm (30.4%) and one leak in the RA arm (10%). 2 of these leaks (6.9%) were delayed AL (>15 days post-surgery; patient discharged on a semi-solid diet). Six of these patients (75%) (5 in the TA arm and 1 in the RA arm) went on to develop an AS requiring endoscopic dilations. Out of the remaining 2, one patient was lost to follow-up, and the other patient had a delayed leak on POD 20th, was resumed on an oral semi-solid diet by POD 30, and continues to do well at 6-month follow-up.

One thoracic duct injury occurred in the TA arm (4.3%) compared to none in the RA arm, which was of type 3b requiring thoracoscopic ligation of thoracic duct following a failed lymphangiographic embolization trial. RLN palsy characterized by post-operative hoarseness of voice or immobility of vocal cords on extubation was seen in 9 patients in the TA group

(39.1%) compared to none in the RA group. All these patients were type 1 requiring only modification of diet to a slurpy diet to prevent repeated aspiration episodes. Six of these patients (66.7%) had an improvement in voice and repeated aspiration episodes on 6 months follow-up. Conduit necrosis occurred in 1 patient in the TA arm (4.3%) compared to 0 in the RA arm and it was a type 3 conduit necrosis requiring excision of the conduit and proximal esophagostomy. Gastric stasis in the conduit causing conduit distension, vomiting, and delayed return of motility occurred in 3 patients in the TA arm (13.04%) viz a viz 1 patient in the RA arm (10%). Subacute intestinal obstruction (SAIO) occurred in 2 patients within 6 months in the TA arm (8.6%), one resolved following conservative management, whereas the other required a redo surgery owing to intussusception at the site of feeding jejunostomy tip. One patient in the TA arm required redo surgery 10 days following esophagectomy owing to compression by a narrowed hiatus on the gastric conduit causing mechanical obstruction. One patient in the RA arm required re-surgery for acute appendicitis 1-month post esophagectomy.

Table 9-Post operative complications

Complication	**Overall, n (%)**	**Thoracoscopic assisted, n (%)**	**Robotic-assisted n (%)**
Anastomotic leak	8 (24.2)	7 (30.4)	1 (10)
Thoracic duct injury	1 (3.03)	1 (4.3)	0
RLN palsy	9 (27.3)	9 (39.1)	0
Pulmonary	14 (42.4)	11 (47.8)	3 (30)
Conduit necrosis	1 (3.03)	1 (4.3)	0
Gastric stasis	4 (12.1)	3 (13.04)	1 (10)
SAIO	2 (6.1)	2 (8.6)	0
Reoperation within 90 days	4 (12.2)	3 (13.04)	1 (10)

6.7 Follow up at 6 months (Table 10)

31 patients out of 33 (93.9%) were alive at the end of 6 months, and 29 (87.9%) patients underwent contrast-enhanced computed tomography and esophagogastroduodenoscopy examination at 6 months. Two patients were lost to follow-up both from the TA arm, owing to a change of telephone numbers and location in a distant state of India.

Anastomotic stricture on upper GI endoscopy at 6 months was seen in 8 patients in the TA arm (34.8%) and 3 patients in the RA arm (30%). On further analysis, AS occurred within 6 months in 6 out of 13 patients (46.1%) undergoing hand-sewn anastomosis (1 lost to follow-up and 1 died) and in 5 out of 16 patients (31.2%) (1 lost to follow up and 1 died). All of them underwent repeated dilations, and 5 out of the 11patients (45.5%) were able to accept a semi-solid diet at 6 months. Anastomotic intraluminal recurrence was seen in none of the cases within 6 months.

Out of 29 patients undergoing CT scan at 6 months, 6 patients (20.7 %) developed locoregional lymph-nodal recurrence (21.1% in the TA arm versus 20% in the RA arm). Distant metastases were seen in 3 patients (10.3%) [10.5% in the TA arm and 10% in the RA arm] till the 6 month follow-up period-one had chest wall metastasis, one had lung metastasis and one had porto-caval lymph nodal metastasis.

Table 10-Follow up at 6 months with EGD and CT scan

Follow up at 6 months	**Overall, n=29**	**Thoracoscopic assisted, n=19**	**Robotic-assisted, n=10**
Anastomotic stricture on endoscopy within or at 6 months, n (%)	11 (37.9)	8 (42.1)	3 (30)
Anastomotic recurrence on endoscopy within or at 6 months, n (%)	0	0	0
Locoregional lymph nodal recurrence on CT at 6 months, n (%)	6 (20.7)	4 (21.1)	2 (20)
Distant metastasis on CT at 6 months, n (%)	3 (10.3)	2 (10.5)	1 (10)

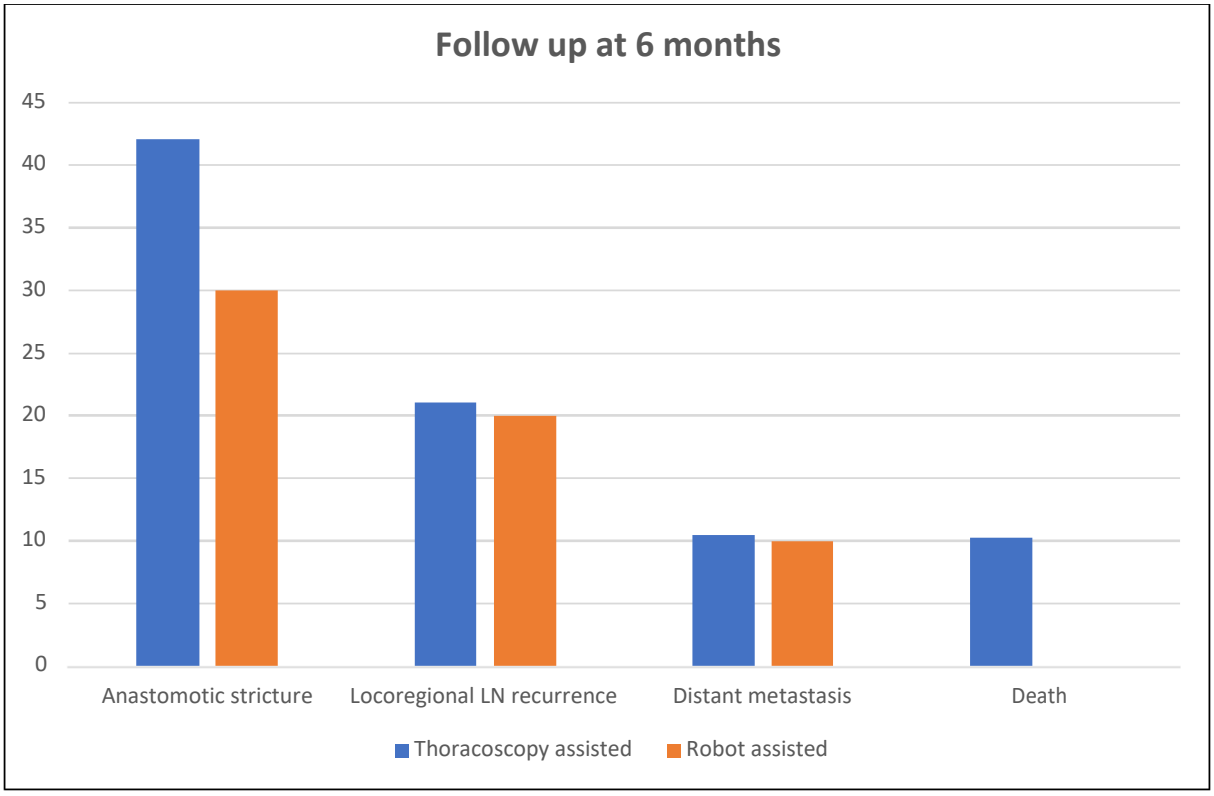

Figure 27-Follow up of patients at 6 months with EGD and CT scan

DISCUSSION

Our study aimed to have a prospective comparison between the two types of MIE: Thoracoscopy assisted (TA) and robotic-assisted (RA) with special reference to the LNY in the thoracic and abdominal compartments. All patients in the study cohort (n=33) underwent transthoracic esophagectomy with modified two-field lymphadenectomy. Twenty-seven out of 33 patients (81.8%) received neo-adjuvant treatment, while 6 underwent upfront surgery and followed a strict peri-operative ERAS protocol. We also compared the two types of MIE for the duration of the thoracic phase, perioperative outcomes, and recurrence with a follow-up period of 6 months.

Lymph node yield (LNY)

The median (IQR) LNY in our cohort was 20 (17, 27) in the TA and 21 (17, 21.3) in the RA group. On comparing the thoracic LNY separately, the median thoracic LNY was 15 in both groups. However, on comparing the post neoadjuvant treatment LNY, the median yield in the post NACT arm was 19 for the TA and 21 for the RA arm and in the post-NACRT arm was 20 for the TA and 25 in the RA arm with a trend towards increasing LNY in the RA arm especially post NACRT. This revealed a distinct advantage of RAMIE, especially in patients post neoadjuvant therapy where indistinct fat planes may be present due to radiotherapy-induced changes making dissection further difficult. A wide range of wrist-articulated motion, greater degrees of freedom, and a magnified view enable more oncological radicality in RAMIE than the thoracoscopic counterpart. Besides the added comfort to the operating surgeon, the robotic arms allow better maneuverability in the confined space of the thoracic cavity.

NCCN guidelines recommend a retrieval of a minimum of 16 LNs for accurate staging and prognostication of the disease. The lymph node retrieval is significantly better with the robotic arms in the published literature. The mean lymph node yield was 18 to 38(1,4,6–10), with a mean retrieval of 27.75 $\pm$ 8.6 nodes comparable to the average LNY during TTE (19.3- 32.6). The LNY is further decreased post neoadjuvant therapy (4,8,11). Parke et al. examined 136 patients comparing robotic and thoracoscopic esophagectomy and concluded that the LNY was greater in the robotic arm than the thoracoscopic arm (37.3 $\pm$ 17.1 versus 28.7 $\pm$ 11.8). The yield was significantly greater in the upper and lower mediastinum and comparable in the middle mediastinum. The abdominal LNY was significantly greater in the

robotic than the laparoscopic arm in the cohort (10.9 versus 5.4; p=0.01)(3). Chao et al. performed a propensity-matched analysis for RA versus TA MIE, with almost 50% of patients in either arm receiving neo-adjuvant therapy. They showed similar LNY in the mediastinum and along RLN except to the left of RLN, where the RA arm had a higher yield in the propensity-matched groups (5.32 versus 3.38; p<0.007)(10). However, this entails a more aggressive LN dissection not routinely practiced at all centres. However, like the one by Zhang et al. (10), a few studies found no statistically significant difference between the lymph node yield between the two types robotic and thoracoscopic (19.7 ± 9.8 vs. 20.3 ± 9.7, p = 0.689). Also, they found no difference in region-wise lymph nodes (thoracic, abdominal, right, and left RLN), but they excluded all patients undergoing neo-adjuvant treatment where the major benefit of robotic-assisted dissection comes in.

Similarly, Weksler et al. (8) analysed a retrospective database comparing 26 patients of MIE against 11 patients of RAMIE and found a comparable LNY in the two arms (23 $\pm$ 10) without any significant difference in the post-operative complications but only 38% of patients in their study received neo-adjuvant treatment in any form. Our study is not sufficiently powered to comment on the superiority of RAMIE over TA MIE, but it does show the non-inferiority of the two arms with respect to LNY with the added advantage of fewer post-operative complications. Moreover, almost 80% of our patients received neoadjuvant treatment, which is now the standard of care. The LNY in RAMIE is significantly more than the thoracic counterpart with comparable post-operative complications, especially post NACRT, which is the standard of care following the landmark CROSS trial(12).

Among the various stations, L.N. retrieval is better in the upper mediastinum, especially along RLN with RTE(3). Oncological clearance of the right and posterior part of the trachea and periesophageal tissue was done. RLN palsy was relatively high (19%) attributable to extensive en-bloc lymph node dissection. The higher pulmonary morbidity (pneumonia, atelectasis, and ARDS) was attributed to more extensive lymphadenectomy. Protecting this nerve is imperative as bilateral injury to this nerve may cause life-threatening dyspnea and aspiration. Rates of RLN palsy are less in RTE compared to TTE(3)(13)(14). Duan et al. compared RTE with TTE, a greater lymph node yield, and lymph nodal metastasis around left RLN with a lower incidence of nerve injuries (7.4 versus 22.5%)(15). REVATE trial is ongoing, which will provide insight about the ease of lymph nodes retrieval along the

recurrent laryngeal nerve (106recR and 106recL) through robotic esophagectomy vis a vis laparoscopic approach, results of which are expected in 2026(13).

Goel et al. reviewed 27 patients undergoing RAMIE post chemoradiotherapy with an acceptable complications rate, LNY but a slightly higher conversion rate (15%). This could be attributed to the higher number (92.5%) of T3/T4 tumors (1). Hernandez et al. report a series of 52 patients undergoing RTE, out of which 30 patients had undergone neo-adjuvant chemo-radiotherapy with comparable and acceptable oncological outcomes without an increase in the complication rate(16). This also helped conclude the feasibility and oncological efficacy of RTE post chemoradiotherapy. Furthermore, transhiatal esophagectomies are associated with worse LNY as compared to their transthoracic counterparts, especially in cases of SCC, which is the predominant subtype in the Asian subcontinent. Moreover, the incidence of upper mediastinum LN positivity even in cases of adenocarcinoma of the distal esophagus is up to 10%(17). This mandates the need for a complete lymphadenectomy to achieve survival and oncological benefit. The 7 degrees of freedom as offered by robotic arms allows improved mobility and tremor filtration in confined spaces enabling better LNY, especially in the upper mediastinum. Better LNY as evidenced in RAMIE, translates into better overall and disease-free survival, and this evidence is more pronounced in patients receiving neoadjuvant therapy(18). Besides, all our patients underwent a R0 resection.

Intraoperative duration and blood loss

The mean duration of the thoracic phase was 133$\pm$28 minutes in the TA arm and 168$\pm$27 minutes in the RA arm in our study. In the published literature, the overall mean operative time for thoracic dissection (in minutes) for RTE varies from 104 to 335 minutes (7,19,20) with a median operating time of 146.6 minutes for the thoracic phase. This is slightly higher than that for the thoracoscopic group (120.1$\pm$68.5 minutes), but several studies have shown that the difference is not statistically significant(3,8,21). The overall operating time (in minutes) for RTE was 231-311 with a median operating duration of 267 minutes(22–24) which is comparable to and in some instances less than that described for thoracoscopic esophagectomy (259-410 minutes)(3,8,25–27). Our thoracic phase timing in both the arms lie within the expected range, and in the robotic-assisted surgery is slightly higher than the thoracoscopic assisted intervention. This could be attributed to the learning curve in the robotic surgeries as the primary team performing the surgeries were within the described

learning curve of 20 cases needed to attain proficiency in RAMIE(16). This could also be due to the frequent instrument change required in the early phase of robotic training owing to a lack of familiarity and experience with this platform.

However, the console time, excluding docking and undocking is shorter, which is expected to reduce with experience. In centers with experience, the docking and undocking time has been reduced to less than 10 minutes (19,28). Hence, in these centers, it is desirable to develop a focussed robotic operating team familiar with the procedures and equipment and the use of an experienced surgical assistant. Also, the importance of precise port positioning should not be downplayed as it contributes to better ergonomics and a decrease in the frequency of instrument change(6). Our docking time ranged from 10-30 minutes.

Furthermore, the duration of the thoracic phase in robotic surgery decreases with experience post the shorter learning curve. Kim et al showed that the overall time of the thoracic phase reduced from 176.3$\pm$12.3 minutes in the initial 6 cases to 81.7$\pm$16.5 minutes in the latter 15 cases ($p<0.001$). Sluis et al also reported similar observations with a decrease in operating time from 199 to 166 minutes ($p<0.001$) during the transition from the first group of 43 patients to their next lot of 42 patients(29). This also resulted in significantly higher proportions of immediate extubations following the procedure(20). Similarly, Fuchs et al also showed a reduction in the total mean operating time of RTE from 445 minutes to 403 minutes from the initial 10 to the subsequent 10 cases(30). Similar outcomes were seen of RTHE with a reduction of mean operating time of 342 minutes for the first 6 cases and 216 minutes for the next 6 as shown by Espat et al(31). Familiarity with handling the robotic instruments and docking as well as undocking helps significantly reduce the surgical time. The operative duration has a significant bearing on the post-operative outcomes as longer times in esophagectomy correlate with more pulmonary complications, prolonged hospital stay, reintubation, and mortality(32).

The median (IQR) blood loss (in ml) was 200 (200,250) in the TA and 200 (200,225) in the RA arm and was comparable. The mean blood loss encountered during the procedure, according to published literature, is 94 to 400 ml which is in concordance with our findings(1,4,7,8,10,22,33). The blood loss encountered during RTHE (in mL) varies from 53 to 100 ml (23,24,31) and is not significantly different from the thoracoscopic group(3). Jin et al in their cumulative meta-analysis of 8 studies, showed that robotic dissection had a lower blood loss than the thoracoscopic dissection in experienced hands(21). It has been

conclusively proven that more blood loss leads to more post-operative blood transfusions, which is associated with a significantly worse prognosis following radical esophageal resections(34). Pneumo-thorax in MIE has a direct hemostatic effect preventing minor bleeds. Open surgery causes more tissue trauma and the consequent blood loss and release of inflammatory markers leading to increased morbidity. MIE helps overcome these obstacles and contributes to better patient outcomes and less need for blood transfusion.

Post-operative ICU and hospital stay

In our study population, 18 patients (54.5%) [13 in the TA arm-56.5% and 5 in the RA arm-50%] were not extubated immediately and shifted to ICU. Sixteen patients were extubated on POD 1 (48.5%), one patient on POD 2(3.1%), and one patient died on POD 2 due to pulmonary complications (both in the TA arm). Previous studies by Weksler et al and Boone et al cited median ICU stays of 3.5 and 3 days, respectively(8)(9). Goal-directed fluid therapy intra-operatively and minimally invasive approach to esophagectomy helped reduce the ICU stay in our patients.

The median (IQR) post-operative ICU stay was 1 (0,1) day in both the TA and RA arm. The median (IQR) post-operative length of hospital stay was 6(6,7) days both in the TA and RA arm. The short hospital stay in our study cohort could be attributed to strict adherence to ERAS protocols besides the advantages of minimally invasive surgery. Reasons for prolonged post-operative hospital stay (>8 days) in 6 patients (18.2%) [1 in RA arm-10% and 5 in TA arm-21.7%] were pulmonary complications in 3 patients, anastomotic leak in 1, conduit necrosis in 1 and thoracic duct injury requiring re-surgery in 1 patient. In the available literature, the average LOS after MIE was 8 days(5). Dutch upper GI cancer audit describes a median hospital stay of 9 days (range 6.5 to 12.5) after an uncomplicated esophagectomy with considerable variability and heterogeneity amongst different hospital data due to lack of standardized protocol(35). One of the strengths of our study was strict adherence to peri-operative protocols enabling us to have a shorter hospital stay and fewer post-operative complications.

A retrospective study of patients undergoing MIE by Pan et al(17) found that LOS could be reduced from a median (IQR) of 12 (10, 16.5) to 7 (6, 9) days with the introduction of ERAS protocol and fewer perioperative complications. However, they excluded patients who received pre-operative radiotherapy or chemotherapy, and it is these patients who have the maximum incidence of peri-operative complications and consequently increased hospital

stay. In a retrospective analysis of the NSQIP database for factors associated with prolonged hospital stay after esophagectomy, in addition to technical complications, pneumonia, urinary tract infection, need for ventilatory support for more than 48 hours, deep space infection, and progressive renal failures were associated with prolonged LOS. Somashekhar et al evaluated 35 patients who underwent RAMIE and described median (range) post-operative stay of 8(6-13) days(36). This is one day more than our median LOHS. Smithers et al reported median duration of hospital stay 14 days for open esophagectomy, 13 days for thoracoscopic assisted, and 11 days for thoraco-laparoscopic esophagectomy(37). Studies have proven that increased duration of surgery is associated with increased peri-operative complications (especially septic, pulmonary, and renal) and delayed extubation. Intra-operative blood transfusion requirement is further associated with increased operative times(32).

In a study by Kim et al, almost 50% of patients who underwent RAMIE were not extubated immediately post-operatively. This is similar to our rates of prolonged intubation (50% of patients).

Morbidity and complications

Morbidity rates after esophagectomy vary from 26-71% (12,17,22,23,26,28). The most commonly reported post-operative complications are pneumonia and arrhythmia (2). Chylothorax though rare, is a dreaded complication after esophagectomy. Its incidence ranges from 0.5% to 12%, and factors like an incomplete response to neoadjuvant therapy, difficult mediastinal dissection, location of tumor were associated with the risk of postoperative chylothorax(38). Our data showed major post-operative complications (Clavien-Dindo $\geq$ 3a) in 52.4% of the TA arm and 30% of the RA arm with a follow-up period of 6 months. The most commonly encountered complication was pulmonary complications seen in 45.1% of patients of our cohort followed by RLN palsy in 39.1%, AS requiring dilatation seen in 31.2%, AL in 24.2%, and gastric conduit stasis in 13%. Post-operative chylothorax was seen in one patient (3%), which was given a trial of lymphangiographic thoracic duct embolization, failing which thoracoscopic exploration and ligation of the thoracic duct was done. Post-operative complications occur in 6-48% of patients undergoing RTE(4,23,24,39) with major complications occurring in 10-32% patients(19,28,33,40,41) Pneumonia is the most frequently observed complication following RAE seen in 6-18 % cases(8,10,14,22,23,29,41) This is slightly less compared to our incidence of 30% but in view of the small sample size it is not possible to draw concrete conclusions. This could also be

attributable to the following stringent protocol, reporting, and close monitoring of all complications. The incidence of respiratory complications in RTE is almost the same as seen in the VATS group (9.3-41%)(4,8,11). A part of these complications were related to RLN palsy related aspirations.

Postoperative chyle leak is seen in 0 to 12.7%(1,9,14,23,42) of MIE. A magnified view, better maneuverability and the use of ICG-NIRS Firefly imaging or pre-operative oil emulsion all helped contribute to better identification and preservation of thoracic duct resulting in only one thoracic duct injury (type 3) and that too in a case where these adjuncts were not used. This was in contrast to the study by Sluis et al who described rates of upto 33% in RAMIE with the majority being type 2(43). Meticulous dissection and use of the above-mentioned adjuncts helped us achieve low rates of thoracic duct injury.

The cervical anastomotic leak depends on a multitude of factors, including the type of anastomosis, skill of the surgeon, site of anastomosis, vascularity of the conduit, and less dependent on the method of esophagectomy. Still, rates of AL vary from 3.6 to 21%(1,6,8,19,33,42) Galvani et al in their experience with Robotic esophagectomy, observed that the AL rates declined from 33 to 18% when a completely stapled anastomosis was performed(23). This is comparable to other series on TE, where the leak rates vary from 0 to 33%(44). The AL rates in our study were 24.2% in all, with two patients out of 29 patients (6.9%) having a delayed leak (>15 days post-surgery; patient discharged on a semi-solid diet). Most of our leaks were type 2 leaks requiring opening of the neck wound and drainage of the collection with upgradation of antibiotics and daily dressing. This was in contrast to the study by Sluis et al. who leak rates of 22% majority of which were type 3 managed by surgical intervention.

Early post-operative outcomes of RE are comparable with VATS, as the invasiveness of treatment arms is similar. Overall, complication grade more than IIIa as per Clavien-Dindo classification(46) is better with RAMIE, especially regarding pulmonary complications and post-operative infections(45). Kwon Joong et al. conclusively showed no significant difference in major complications between a total RAMIE and a hybrid-RAMIE (10.4% versus 10%)(41).

Vocal cord palsy or RLN injury occurs in 7.4 to 28.6 % of patients(1,3,8,20,29). It is an independent predictive factor for pulmonary complications, aspirations, and prolonged stay at the hospital(46). The incidence varied with the type of esophagectomy with a rate of 14% in

Mckeown versus 2% in THE(46). This was permanent in 20-30 % of patients and required some form of surgical intervention, whereas it was reversible in the other patients (29,46). In our cohort, 66.7% of patients had recovery of voice and aspiration episodes with a follow-up of up to 6 months. Other complications included urinary tract infections, wound infection, cardiac complications, conduit or anastomotic fistulas, and prolonged intubation(8,33).

Post-operative complications can have both short- and long-term impact. A recent meta-analysis found that post-operative complications were associated with significantly decreased 5-year overall and 5-year cancer-specific survival. Post-operative pulmonary complications and anastomotic leaks were associated with lower 5-year overall and disease-free survival(38). Technical complications associated with esophagectomy like anastomotic leak, chylothorax, vocal cord palsy etc. were associated with increased post-operative mortality, almost twice increase in the LOS, need for second or third surgery and increased in other medical complications and ultimately associated with decreased OS(5). Our study also observed that the incidence of major complications was associated with prolonged LOHS. A modified esophagectomy surgical Apgar score using the lowest intraoperative pulse rate, mean arterial pressure, and blood loss has been suggested by Janowak et al. (47), and a score of less than 6 is strongly associated with increased 30-day morbidity. Chen et al. (48) found a trend towards more complications in the conventional treatment arm than fast-track protocol (12.1% vs. 8.6%) though the difference was not statistically significant.

The 30-day mortality of RTE varies from 0-6.4%(3,7,9,42), which is comparable to the 0 to 4% mortality rate observed in thoracoscopic esophagectomy(44). We had one mortality within 30 days post-surgery owing to pulmonary complications (3.2%).

The outcomes of esophagectomy greatly depend on the case load and dedicated training of the surgeons involved in the operative and peri-operative management as it has a long learning curve associated with it (5). Immediate post-operative mortality rate in esophagectomy ranges from 0% to 4% (12,17,20,23). Studies have described a learning curve of 20 cases for a decrease in the operative times and 10 cases to decrease peri-operative complications(16). A large retrospective analysis of more than 1000 MIE found the overall peri-operative mortality rate to be 1.6%, with a mortality rate of 0.9% for minimally invasive Ivor Lewis esophagectomy and 2.5% for minimally invasive Mckeown esophagectomy. The mortality rate after MIE was comparable to that of open esophagectomy. Post-operative ARDS or respiratory failure was significantly associated with mortality after esophagectomy.

MIE and thoracic epidural analgesia were found to be associated with decreased mortality(49).

Long term survival

Five-year overall survival (OS), as estimated by Park et al. was not significantly different between the two groups (69% in RTE versus 59% in TTE)(3). A trend towards a higher 5-year survival (37 versus 27%) has been observed with the transthoracic approach compared to the transhiatal approach(50). The median survival in the RAMIE group is estimated to be around 48 months compared to 44 months in the open cohort but was not statistically significant according to a propensity-matched analysis performed by Weksler et al. Similarly, the disease-free survival (28 versus 26 months) and recurrence pattern were also similar between the two groups in the analysis (51).

Overall recurrence rates varied from 21-64%(6,9,29), comparable to the open procedure(29). The ongoing RAMIE trial aims to compare robotic-assisted versus MIE with regards to survival and quality of life and shall be able to shed more light on the long-term outcomes of RTE(52).

Follow-up till six months

There is no consensus on follow-up of these patients post-surgery, and most guidelines are based on expert recommendations and NCCN guidelines. Since most locoregional relapses occur within 2 years, it is prudent to follow up with these patients more vigorously during the first 2 years. Due to the limited time period of our study, we decided on a follow-up of up to 6 months. For all patients undergoing esophagectomy and final pathological stage of T2 and beyond with/without node-positive disease, imaging studies (CT chest and abdomen) are considered every 6 monthly till two years and then annually. EGD surveillance is not routinely recommended for these patients and is required only in cases with a high degree of clinical suspicion(53). We followed up with our patients (29) with EGD at 6 months and found no local recurrence in any of our patients. EGD was recommended earlier if the patient had AS and required endoscopic dilation which was seen in 11 cases (38%) [42.1% in the TA arm versus 30% in the RA arm]. This is consistent with long-term results of the CROSS trial showing recurrence at the anastomotic site in 2.8% of patients only after multimodality treatment, including esophagectomy(53). Locoregional LN recurrence alone was seen in 20.7% of our patients (similar in TA and RA arms). This is in contrast to 9.3% of patients

who have isolated locoregional recurrence and 16.5% of patients who had combined locoregional and distant recurrence in the study by Oppedijk et al(53). This may be attributable to the shorter follow-up (6 months) in our study and the fact that all patients were SCC in our study compared to 75% adenocarcinomas in the CROSS trial(12).

Drawbacks of MIE

The primary drawbacks of the robotic platform are the cost and the loss of tactile feedback resulting in inadvertent tearing of tissues due to increased shear stress, more so in cases where important visceral manipulation is required. At present, robotic surgery is free of cost to the patients, and the institute bears the cost.

The prolonged operative times, device weight, and subsequent difficulty in changing port location and operating table may hamper its potential benefits. Thus, robotics may not prove especially beneficial in surgeries requiring a wider area and coarse movements. Sometimes, due to overzealous nodal dissection, the increased chylous output is seen in the chest tubes during the initial few post-operative days in MIE, but these have been found to reduce with careful ligation of visible lymphatic tributaries(54). A thoracic duct injury occurred in one patient.

Other drawbacks include lack of standardized technique, steeper learning curve and longer operating time, and the consequent changes in patient's physiology which is especially detrimental in MIE esophagectomies as patients are unable to tolerate single–lung ventilation for long(39). We avoided this complication by performing MIE in a prone/semi-prone position in all our patients allowing the lung to fall under the effect of gravity and the blood to clear out of the field, enabling better view and no requirement for single lung ventilation.

Moreover, in RAMIE, the surgeon is separated from the patient and placed outside the sterile field, thus requiring an additional trained surgeon close to the patient to intervene in case of an emergency. The individual control of the robotic console also hampers learning and teaching(8)

Also, at first glance, it may appear RAMIE has more complications than conventional MIE, but many articles do not have a universal definition for these complications. Our study tried to standardize the complication reporting by adhering to the Esophagectomy Complications Consensus Group. Also, the anastomotic site, technique, and administration of neoadjuvant

therapy may play a major role in determining the outcomes and complications, especially the anastomotic complications(2).

Robotic surgery in the abdominal phase requires excessive visceral manipulation and multiple applications of mechanical devices by many assistants. The challenging initial obstacles include the operating room staff and the patient set-up, which will go a long way in improving outcomes if overcome with a dedicated team. In comparison to the laparoscopic approach, the dexterity and ease of dissection can be achieved after fewer cases with robotic arms. Hence, the learning curve is small in RTE, which is further desirable in complicated procedures so as to help avoid the learning curve associated morbidity(55).

STRENGTHS AND LIMITATIONS

8.1. Strengths of the study:

1. Strict adherence to standardized peri-operative protocols.
2. Standardized follow-up schedule followed by all patients for early detection and management of complications if any.
3. Reporting of complications according to Esophagectomy Complications Consensus Group guidelines (attached in Annexures).
4. Patients who underwent upfront esophagectomy and after neoadjuvant therapy were analyzed separately.
5. All patients underwent CT and upper GI endoscopy at six months to document locoregional and distant recurrence/ metastasis.

8.2. Limitations of the study:

1. Small sample size.
2. Reduction in the sample size owing to COVID-19 pandemic and closure of operation theatres.
3. A short follow-up of 6 months did not allow us to calculate overall or disease-free survival in all cases.
4. Not a randomized control trial.
5. Quality of life was not assessed post-surgery.

CONCLUSIONS

MIE is feasible in carcinoma esophagus patients with good lymph nodal yield and fewer post-operative complications. Robotic esophagectomy compared to thoracoscopic esophagectomy has slightly better lymph nodal yield with fewer major (Clavien Dindo $\geq$ 3a complications) post-operative complications, especially pulmonary. Strict adherence to perioperative standardized protocols and multimodality therapy in the treatment of carcinoma esophagus helps achieve better peri-operative outcomes.

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11. Annexures

11.1 ETHICAL CLEARANCE CERTIFICATE

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2020/3369 Date: 11/12/2020

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2019-20/948**

Project title: **"Lymph node yield in minimally innvasive (Robotic and thoracoscopic assisted) esophagectomy in carcinoma esophagus-A prospective descriptive study"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**M.Ch. Dissertation**
Student Name:	**Dr. Raghav Nayar**
Guide:	**Dr. Subhash Chandra Soni**
Co-Guide:	**Dr. Vaibhav Kumar Varshney, Dr. Deepak Vedant & Dr. Ashok Kumar Puranik**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary

Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

Basni Phase-2, Jodhpur, Rajasthan-342005; **Website:** www.aiimsjodhpur.edu.in; **Phone:** 0291-2740741 Extn. 3109
E-mail : ethicscommittee@aiimsjodhpur.edu.in; ethicscommitteeaiimsjdh@gmail.com

11.2 PARTICIPANT INFORMED CONSENT FORM (PICF)

Participant identification number for this trial: _____

Title of project: **LYMPH NODE YIELD IN MINIMALLY INVASIVE(ROBOTIC AND THORACOSCOPIC ASSISTED) ESOPHAGECTOMY IN CARCINOMA ESOPHAGUS-A PROSPECTIVE DESCRIPTIVE STUDY**

Name of Principal Investigator: Dr Raghav Nayar Tel.No(s). 9811159575

The contents of the information sheet dated …….. that was provided have been read carefully by me / explained in detail to me, in a language that I comprehend, and I have fully understood the contents. I confirm that I have had the opportunity to ask questions.

The nature and purpose of the study and its potential risks / benefits and expected duration of the study, and other relevant details of the study have been explained to me in detail. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal right being affected.

I understand that the information collected about me from my participation in this research and sections of any of my medical notes may be looked at by responsible individuals from AIIMS. I give permission for these individuals to have access to my records.

I agree to take part in the above study.

---------- Date:

(Signatures / Left Thumb Impression)
Place:

Name of the Participant: _____

Son / Daughter / Spouse of: _____

Complete postal address: _____

This is to certify that the above consent has been obtained in my presence.

Signatures of the Principal Investigator
Date: Place:

1) Witness – 1

Signatures

Name:

Address:

2) Witness – 2

Signatures

Name:

Address:

11.3 **सहभागी सुचित सहमति पत्र**

इस जाचं के लिए सहभागी पहचान नमबर_____

अनुसन्धान शीर्षक : **LYMPH NODE YIELD IN MINIMALLY INVASIVE(ROBOTIC AND THORACOSCOPIC ASSISTED) ESOPHAGECTOMY IN CARCINOMA ESOPHAGUS-A PROSPECTIVE DESCRIPTIVE STUDY**

मुख्य अन्वेषक का नाम : Dr Raghav Nayar फोन नंबर:9811159575

मैंने दिनांक_____ के सूचना पत्र में दिये गए सभी तथ्यो को पड़ लिया हैं। मुझे समझ आने वालीं भाषा मैं विस्तार पूर्वक बत्ता दिया है और मैनें तथ्यो को भलीभांति समझ लिया है। मैं पुष्टि करता हूँ कि मुझे प्रशन पुछने का अवसर दिया गया है।

मुझे अध्ययन की प्रकृति, उद्देश्य और इसके सम्भावित लाभ/जोखिमों और अध्ययन की सम्भावित अवधि अन्य प्रासंगिक जानकारी के बारे में विस्तार पुर्वक समझा दिया गया है। में समझाता हूँ कि इस अध्ययन में मेरी भागिधारी स्वेछिक है और इस अध्ययन से किसी भी समय बिना कोई कारण बताए, बिना मेरी चिकित्सा देखभाल या कानूनी अधिकारों के प्रभावित हए अपना नाम वापिस ले सकता/सकती हूँ।

मैं समझता हूँ कि इस अनुसन्धान में मेरी सहभागिता से मेरे बारे में एकत्र जानकारी और चिकित्सीयनोटों को एम्स अस्पताल के जिम्मेदार लोगो द्वारा देखा जायेगा। मैं इन व्यक्तियों को अपने रिकोर्ड देखने कि अनुमति प्रदान करता/करती हूँ।

मैं उपयुर्क्त अध्यन में भाग लेने के लिए अपनी सहमति प्रदानकरता /करती हूँ।

सहभागी के हस्ताक्षर / बाएं अंगूठे का निशान दिनांक: स्थान:

सहभागी का नाम

पिता/पति का नाम

पूरा पता

यह प्रमाणित किया जाता हे कि उपयुर्क्त सहमति मेरी उपस्थति में ली गईं हैं।

मुख्य अन्वेषक के हस्ताक्षर दिनाक: स्थान:

१) गवाह के हस्ताक्षर	२) गवाह के हस्ताक्षर
नाम	नाम
पता	पता

11.4 INFORMATION TO PARTICIPANTS

Title: **LYMPH NODE YIELD IN MINIMALLY INVASIVE(ROBOTIC AND THORACOSCOPIC ASSISTED) ESOPHAGECTOMY IN CARCINOMA ESOPHAGUS-A PROSPECTIVE DESCRIPTIVE STUDY**

Name of Participant: .....

You are invited to take part in this research study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.
You are being asked to participate in this study being conducted in AIIMS, Jodhpur because you satisfy our eligibility criteria.

What is the purpose of research?

This study compares the 2 types of minimally invasive esophagectomy-robotic assisted and thoracoscopic assisted. All the patients shall be following ERAS protocol. The lymph nodal yield in the 2 modalities shall be compared. If you enroll in it you will be benefitted by better perioperative outcomes. We have obtained permission from the Institutional Ethics Committee for conducting this study.

The study design

The study will be a single centre prospective descriptive study and patients will be recruited from Department of Surgical Gastroenterology, AIIMS Jodhpur.

Study Procedures

The study involves evaluation of short term outcomes of MIE in patients undergoing esophagectomy for carcinoma esophagus. You will be counseled about the entire perioperative care before surgery. You will be advised to regular respiratory exercise, early mobilization after surgery and all tubes and drain will be removed as soon as possible. All the events will be recorded. The histopathology specimen shall be processed and all findings with special reference to lymph nodal yield shall be recorded. Complications, if any shall be prospectively recorded. You shall be followed up at 6 weeks and 3 months and recurrence/morbidity shall be recorded.

Possible risks to you.

There is no added risk other than the risk involved due to surgery and disease.

Possible benefits to you
You shall have all the benefits of minimally invasive esophagectomy and the proven benefit of ERAS protocol.

Compensation
Nil

Possible benefits to other people

The results of the research may provide benefits to the society in terms of advancement of medical knowledge and/or therapeutic benefit to future patients.

The alternatives you have

If you do not wish to participate, you still will get the standard treatment for your condition.

Reimbursement

You will not be paid to participate in this research study.

What should you do in case of injury or a medical problem during this research study?

Your safety is the prime concern of the research. If you are injured or have a medical problem as a result of being in this study, you should contact one of the people listed at the end of the consent form. You will be provided the required care/treatment.

Confidentiality of the information obtained from you

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, institutional ethics committee and any person or agency required by law like the Drug Controller General of India to view your data, if required. The results of clinical tests and therapy performed as part of this research may be included in your medical record. The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

How will your decision to not participate in the study affect you?

Your decision not to participate in this research study will not affect your medical care or your relationship with the investigator or the institution. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

Can you decide to stop participating in the study once you start?

The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during the course of the study without giving any reasons.

Can the investigator take you off the study?

You may be taken off the study without your consent if you do not follow instructions of the investigators or the research team or if the investigator thinks that further participation may cause you harm.

Right to new information

If the research team gets any new information during this research study that may affect your decision to continue participating in the study, or may raise some doubts, you will be told about that information.

Contact persons

For further information / questions, you can contact us at the following address:

Principal Investigator:
Dr. Raghav Nayar
Senior resident Ph: 9811159575
Dept. of Surgical Gastroenterology

Principal guide and Co-Investigator Ph: 8447440689
Dr. Subhash Soni
Assistant Professor
Department of GI Surgery
AIIMS Jodhpur

11.5 भागीदारों के लिए सूचना

अनुलग्नक:-2

भागीदारों के लिए सूचना:

आदिलेख:

शीर्षक: अन्नप्रणाली के कैंसर के लिए न्यूनतम इनवेसिव एसोफेगेटॉमी में लसीका ग्रंथि प्राप्ति -भावी वर्णनात्मक

अध्ययन

मूल्यांकन

प्रतिभागी का नाम: ....

आपको इस शोध अध्ययन में भाग लेने के लिए आमंत्रित किया जाता है। इस दस्तावेज़ में दी गई जानकारी यह तय करने मेंI आपकी सहायता करने के लिए है कि भाग लेना है या नहीं। कृपया पूछें अगर आपके पास कोई प्रश्न या चिंता है।आपको एम्स, जोधपुर में आयोजित इस अध्ययन में भाग लेने के लिए कहा जा रहा है क्योंकि आप हमारे योग्यता मान दंडों को पूरा करते हैं।

शोध का उद्देश्य क्या है?

इस अध्ययन में 2 प्रकार के न्यूनतम इनवेसिव एसोफागेक्टोमी- रोबोट असिस्टेड और थोरैकोस्कोपिक असिस्टेड की तुलना की गई है। सभी मरीज ई आर ए एस प्रोटोकॉल का पालन करेंगे। 2 तौर-तरीकों में लिम्फनोडल उपज की तुलना की जाएगी। नामांकन करते हैं तो आपको बेहतर पेरी ओपरेटिव परिणामों से फायदा होगा। हमने इस अध्ययन के संचालन के लिए संस्थागत नैतिकता समिति से अनुमति प्राप्त की है.

अध्ययन डिजाइन

अध्ययन एक एक लकेंद्र भावी वर्णनात्मक अध्ययन होगा और रोगियों को सर्जिकल गैस्ट्रोएंटेरोलॉजी विभाग से भर्ती कराया जाएगा।

अध्ययन प्रक्रियाएं

अध्ययन में कार्सिनोमा अन्नप्रणाली के लिए घुट की के दौर से गुजर रोगियों में न्यूनतम इनवेसिव ग्रासनलीशोथ के अल्पकालिक परिणामों का मूल्यांकन शामिल है। सर्जरी से पहले आपको पूरी देख भाल के बारे में परामर्श दिया जाएगा। आपको नियमित श्वसनव्यायाम, सर्जरी के बाद जल्दी जुटने और सभी नलियों और नाली को जल्द से जल्द हटाने की सलाह दी जाएगी। सभी घटनाओं को दर्ज किया जाएगा। हिस्टोपैथोलॉजी के नमूने को संसाधित किया जाएगा और लिम्फनोडल उपज के विशेष संदर्भ के साथ सभी निष्कर्षों को दर्ज किया जाएगा।

जटिलताओं, यदि कोई संभावित रूप से दर्ज की जाएगी। आपको 6 सप्ताह और 3 महीने तक पालन किया जाएगा और पुनरावृत्ति / रुग्णता दर्ज की जाएगी।

आपके लिए संभावित जोखिम

शल्यचिकित्सा और बीमारी के कारण जोखिम के अलावा कोई अति रिक्त जोखिम नहीं है। आपके लिए संभावित लाभ आपके पास न्यूनतम इनवेसिव एसोफेगेटोमी के सभी लाभ और ई आर ए एस प्रोटोकॉल के सिद्ध लाभ उपलब्ध होंगे।

नुकसान भरपाई- शून्य

अन्य लोगों के लिए संभावित लाभ

शोध के नतीजे भविष्य के मरीजों को चिकित्सा ज्ञान और / या चिकित्सकीय लाभ के उन्नयन के मामले में

समाज को लाभ प्रदान कर सकते हैं।

आपके पास विकल्प हैं

यदि आप भाग लेना नहीं चाहते हैं, तो भी आपको अपनी हालत के लिए मानक उपचार मिलेगा।

अदायगी इस शोध अध्ययन में भाग लेने के लिए आपको भुगतान नहीं किया जाएगा।

इस शोध अध्ययन के दौरान चोट या चिकित्सा समस्या के मामले में आपको क्या करना चाहिए?

आपकी सुरक्षा अनुसंधान की प्रमुख चिंता है। यदि आप इस अध्ययन में होने के परिणामस्वरूप घायल हो गए हैं या चिकित्सा समस्या है, तो आपको सहमति फॉर्म के अंत में सूचीबद्ध लोगों में से एक से संपर्क करना चाहिए।

आपको आवश्यक देख भाल / उपचार प्रदान किया जाएगा।

आपसे प्राप्त जानकारी की गोपनीयता

आपको अपनी चिकित्सा जानकारी (व्यक्तिगत विवरण, शारीरिक परीक्षाओं के परिणाम, जांच, और आपके चिकित्सा इतिहास) की गोपनीयता के संबंध में गोपनीयता का अधिकार है। इस दस्तावेज़ पर हस्ताक्षर करके, आप अनुसंधान टीम जांच कर्ताओं, अन्य अध्ययन कर्मियों, प्रायोजकों, संस्थागत नैतिकता समिति और कानून के अनुसार आवश्यक किसी भी व्यक्ति या एजेंसी को भारत के ड्रग कंट्रोलर जनरल की आवश्यकता होगी, यदि आवश्यक हो तो आपका डेटा देखने के लिए। इस शोध के हिस्से के रूप में किए गए नैदानिक परीक्षण और चिकित्सा के परिणाम आपके मेडिकल रिकॉर्ड में शामिल किए जा सकते हैं। इस अध्ययन की जानकारी, यदि वैज्ञानिक पत्रिकाओं में प्रकाशित या वैज्ञानिक बैठकों में प्रस्तुत की गई है, तो आपकी पहचान प्रकट नहीं होगी।

अध्ययन में भाग लेने का आपका निर्णय आपको कैसे प्रभावित करेगा?

इस शोध अध्ययन में भाग लेने के आपके निर्णय से आपकी चिकित्सा देख भाल या जांचकर्ता या संस्थान के साथ आपके संबंध प्रभावित नहीं होंगे। आपका डॉक्टर अभी भी आपकी देख भाल करेगा और आप किसी भी लाभ को खो देंगे नहीं जिस के लिए आप हकदार हैं।

क्या आप शुरू करने के बाद अध्ययन में भाग लेने से रोकने का फैसला कर सकते हैं?

इस शोध में भागीदारी पूरी तरह से स्वैच्छिक है और आपको बिना किसी कारण बताए अध्ययन के दौरान

किसी भी समय इस अध्ययन से वापस लेने का अधिकार है।

क्या जांच कर्ता आपको अध्ययन से बाहर ले जा सकता है**?**

यदि आप जांचकर्ताओं या शोध दल के निर्देशों का पालन नहीं करते हैं या यदि जांचकर्ता सोचता है कि आगे की भागीदारी से आपको नुकसान हो सकता है तो आपको अपनी सहमति के बिना अध्ययन से बाहर ले जाया जा सकता है।

नई जानकारी का अधिकार

यदि इस शोध अध्ययन के दौरान शोध दल को कोई नई जानकारी मिलती है जो अध्ययन में भाग लेने के आपके फैसले को प्रभावित कर सकती है, या कुछ संदेह उठा सकती है, तो आपको उस जानकारी के बारे में बताया जाएगा।

संपर्क करें

अधिक जानकारी / प्रश्नों के लिए, आप निम्नलिखित पते पर हमसे संपर्क कर सकते हैं**:**

मुख्यजाँचकर्ता**:**

डॉ राघव नायर फ़ोन नंबर**: 9811159575**

सर्जिकल गैस्ट्रोएंटेरोलॉजी विभाग

प्रिंसिपल गाइड और सह-जांच कर्ता- डॉ सुभाष सोनी फ़ोन नंबर**: 8447440689**

11.6 PROFORMA Patient ID:

1. BASIC INFORMATION OF PATIENT

Name	
Age (in years)	
Sex	
Hospital No.	
Address	
Phone number	
Index Diagnosis	

2. CHIEF COMPLAINTS

COMPLAINTS	**YES**	**NO**	**DURATION**
Dysphagia			
Change in Voice			
Breathlessness			
Cough			
Loss of weight			
Abdominal Pain			
Others			

Dysphagia grade at admission (Modified Takita's grading):

ADDICTION

NATURE	**YES**	**NO**	**DURATION**	**ABSTINENCE**
Alcohol				
Smoking				
Tobacco chewing				

Patient ID:

3. CO MORBIDITIES

ILLNESS	**YES**	**NO**	**DURATION**
Systemic Hypertension			
Diabetes Mellitus			
CAD			
COAD/ Bronchial Asthma			
Others			

Ht..... Wt.....BMI……. ECOG…….

4. UPPER GI SCOPY

Esophagus	Growth	From(cm from incisors)	
		To(cm from incisors)	
	Negotiable (Yes/No)		
Biopsy			

5. Pre op CECT (STAGE):

6. PREOPERATIVE PERIOD

	YES	**NO**
Neoadjuvant therapy(CT/RT/CRT)		
Pre operative spirometry		
Carbohydrate drink		
Preoperative counseling		

Type of neoadjuvant therapy (CT/RT/CTRT):

Patient ID:

7. ESOPHAGECTOMY AND GASTRIC PULL THROUGH

Date of surgery	
Date of discharge	
Length of hospital stay (days)	

8. OPERATIVE DETAILS

PARAMETERS	
Thoracoscopy assisted(TA)/ Thoracolaparoscopy(TL)/Robotic assisted(RA)/Robotic (R)	
Sinle lung ventilation/Double lung ventilation	
Thoracotomy Conversion (Yes/No) and Reason	
Type of esophagogastric anastomosis (St/HS)	
Injury to trachea/bronchus	
Intraoperative blood loss (ml)	
Input/Output (ml)	
Restrictive fluid strategy	
Intraoperative blood transfusion (units)	
Intraoperative major cardiac event	
Duration of surgery(hours)	
Duration of thoracoscopic phase(hours)	
Duration of ICU stay(hours)	
Duration of hospital stay(days)	
Ionotrops (Yes/No)	
Extubated (Yes/No)	
Normal vocal cord mobility at time of extubation	
Lactate levels at end of surgery	

St- Stapled; HS- Hand Sewn

9. POSTOPERATIVE PERIOD

	NO. OF POSTOPERATIVE DAY
Extubation	
ICU Stay	
Inotropes	
Mobilisation initiation	
Chest physiotherapy	
FJ feed initiation	
Urinary catheter removal	
Epidural removal	
Neck drain removal	
Chest tube removal	
Abdominal drain removal	
Central line removal	
Antibiotic last dose	
Contrast study	
Oral liquids/ Soft diet	
Discharge	

Patient ID:

	N	AN
Post OP CXR [normal(N)/abnormal(AN)]		

11.7 Postoperative Complications (Esophageal Complications Consensus Group)

Complication	**Yes/No**	**Clavien Dindo Grade**
1. Pulmonary a.) Pneumonia b.) Pleural effusion requiring additional drainage procedure c.) Pneumothorax requiring treatment d.) Atelectasis mucous plugging requiring bronchoscopy e.) Respiratory failure requiring reintubation f.) Acute respiratory distress syndrome g.) Acute aspiration h.) Tracheobronchial injury i.) Chest tube maintenance for air leak for >10 d postoperatively 2. Cardiac a.) Cardiac arrest requiring CPR b.) Myocardial infarction c.) Dysrhythmia atrial requiring treatment d.) Dysrhythmia ventricular requiring treatment e.) Congestive heart failure requiring treatment f.) Pericarditis requiring treatment 3. Gastrointestinal a.) Esophagoenteric leak from anastomosis, staple line, or localized conduit necrosis. b.) Conduit necrosis/failure. c.) Ileus defined as small bowel dysfunction preventing or delaying enteral feeding d.) Small bowel obstruction e.) Feeding J-tube complication		

f.) Pyloromyotomy/pyloroplasty complication g.) *Clostridium difficile* Infection h.) Gastrointestinal bleeding requiring intervention or transfusion i.) Delayed conduit emptying requiring intervention or delaying discharge or requiring maintenance of NG drainage >7 d postoperatively j.) Pancreatitis k.) Liver dysfunction 4. Urologic a) Acute renal insufficiency (defined as doubling of baseline creatinine) b) Acute renal failure requiring dialysis c) Urinary tract infection d) Urinary retention requiring reinsertion of urinary catheter, delaying discharge, or discharge with urinary catheter 5. Thromboembolic a) Deep venous thrombosis b) Pulmonary embolus c) Stroke (CVA) d) Peripheral thrombophlebitis 6. Neurologic/psychiatric a) Recurrent nerve injury b) Other neurologic injury c) Acute delirium d) Delirium tremens 7. Infection a) Wound infection requiring opening wound or antibiotics b) Central IV line infection requiring removal or antibiotics		

c) Intrathoracic/intra-abdominal abscess d) Generalized sepsis e) Other infections requiring antibiotics 8. Wound/diaphragm a) Thoracic wound dehiscence b) Acute abdominal wall dehiscence/hernia c) Acute diaphragmatic hernia 9. Other a) Chyle leak 10. Reoperation for reasons other than bleeding, anastomotic leak, or conduit necrosis		

11. Final Biopsy:

Total number of LNs-

Thoracic LNs	**Supracarinal**	
	Infracarinal	
Abdominal	**Abdominal**	

Resection margins clear-

Proximal-Y/N

Distal-Y/N

12. Follow up at 6 weeks

12.1

Obvious clinical recurrence-Yes/No

Survival-Yes/No

Any complications-

13. Follow up at 3 months

Obvious clinical recurrence-Yes/No

Survival-Yes/No

Any complications-

Vocal cord palsy-

Need for dilatation-

14. Follow up at 6 months

CECT meck, thorax and abdomen-

UGI endoscopy-

Any complications-

Survival-Yes/No

15. Abbreviations

ARDS	Acute Respiratory Distress Syndrome
ERAS	Enhance Recovery After Surgery
ERP	Enhanced Recovery Pathways
ICD	Intercostal Drainage
ICU	Intensive Care Unit
IVF	Intravenous Fluid
NPO	Nil Per Oral
MIE	Minimally Invasive Esophagectomy
POD	Post Operative Day

11.7 ERAS protocol

1. Preoperative
    a. Pre operative counselling for minimum 20 minutes
    b. Inspiratory muscle training including incentive spirometry 15 times 4th hourly 1 week before surgery
    c. Pre operative isotonic carbohydrate drink 800 ml 12 hours and 400 ml 2-3 hours (to be drunk in 20 minutes time)before surgery in all patients except uncontrolled diabetes mellitus(HbA1c >7)
2. Intra operative
    a. Preemptive epidural analgesia
    b. Minimally invasive esophagectomy with thoracic phase done with robotic assistance or thoracoscopy with or without laparoscopic abdominal phase
    c. Goal directed fluid therapy 5-6 ml/kg/hour intra operatively and adding vasopressor when mean blood pressure drops by 20%
3. Post operative
    a. Immediate extubation after surgery or extubation as early as possible
    b. Shifting patient to high dependency unit and then to ward where the patient is on continuous monitoring of vitals
    c. POD 0
        i. Propped up position 30-45 degrees
        ii. Negative fluid balance keeping urine output >0.3ml/kg/hour and MAP >65
        iii. Sitting on bed 4 hours after shifting to ward
        iv. Epidural analgesia
        v. FJ feed 5% dextrose at 20 ml/hour 6 hours after surgery
    d. POD 1
        i. Negative fluid balance
        ii. FJ feed 1 liter at 40 ml/hour
        iii. Saline nebulisation and steam inhalation 6th hourly
        iv. Incentive spirometry 10 times each hour while awake
        v. Out of bed 1 hour morning and 1 hour evening
        vi. Assisted walking
        vii. Stop antibiotics after 3 post operative doses
        viii. Start LMWH

e. POD 2
    i. Remove urinary catheter
    ii. Remove neck drain
    iii. Remove epidural catheter
    iv. FJ 2 liters full strength at 60-80 ml/ hour
    v. Negative fluid balance
    vi. Stop intravenous fluids
    vii. Out of bed for 4 hours
    viii. Assisted walking 2 walks 100 meters
    ix. Incentive spirometry 10 times / hour while awake
    x. Steam inhalation and saline nebulisation 6^{th} hourly
f. POD 3
    i. Remove central line
    ii. Remove ICD if output <200 ml/24 hours and serous in character
    iii. Remove nasogastric tube
    iv. Remove abdominal drain
    v. FJ feed 2 liter at 80 ml/hour
    vi. Out of bed 4 hours
    vii. Assisted / non assisted 3-4 walks 150 meters
    viii. Incentive spirometry 10 times / hour while awake
    ix. Steam inhalation and saline nebulisation 6^{th} hourly
g. POD 4
    i. Oral contrast study (POD 5 if POD 4 is Sunday)
    ii. Allow oral clear liquids if contrast study shows no leak
    iii. FJ 2 liters at 80 ml/hour
    iv. Non assisted 3-4 walks 150 meters
    v. Incentive spirometry 10 times / hour while awake
    vi. Steam inhalation and saline nebulisation 6^{th} hourly
    vii. Stop LMWH
h. POD 5
    i. Oral liquids/semi solids
    ii. FJ 1 liters at 80 ml/hour
    iii. Non assisted 3-4 walks 150 meters
    iv. Incentive spirometry 10 times / hour while awake

v. Steam inhalation and saline nebulisation 6th hourly

vi. Discharge the patient

A margin of 1-2 days allowed for each component

11.8 Dysphagia grading (modified Takita's classification)

I: able to eat normally

II: requires liquids with meals

III: able to take only semisolid food

IV: able to take only liquids

V: able to swallow saliva but not liquids

VI: complete *dysphagia*

11.9 Esophagectomy Complications Consensus Group

1. Pulmonary
    a.) Pneumonia
    b.) Pleural effusion requiring additional drainage procedure
    c.) Pneumothorax requiring treatment
    d.) Atelectasis mucous plugging requiring bronchoscopy
    e.) Respiratory failure requiring reintubation
    f.) Acute respiratory distress syndrome
    g.) Acute aspiration
    h.) Tracheobronchial injury
    i.) Chest tube maintenance for air leak for >10 d postoperatively
2. Cardiac
    a.) Cardiac arrest requiring CPR
    b.) Myocardial infarction
    c.) Dysrhythmia atrial requiring treatment
    d.) Dysrhythmia ventricular requiring treatment
    e.) Congestive heart failure requiring treatment
    f.) Pericarditis requiring treatment
3. Gastrointestinal
    a.) Esophagoenteric leak from anastomosis, staple line, or localized conduit necrosis.
    b.) Conduit necrosis/failure.
    c.) Ileus defined as small bowel dysfunction preventing or delaying enteral feeding
    d.) Small bowel obstruction
    e.) Feeding J-tube complication
    f.) Pyloromyotomy/pyloroplasty complication
    g.) Clostridium difficile Infection
    h.) Gastrointestinal bleeding requiring intervention or transfusion
    i.) Delayed conduit emptying requiring intervention or delaying discharge or requiring maintenance of NG drainage >7 d
    postoperatively
    j.) Pancreatitis
    k.) Liver dysfunction
4. Urologic
    e) Acute renal insufficiency (defined as doubling of baseline creatinine)

f) Acute renal failure requiring dialysis
g) Urinary tract infection
h) Urinary retention requiring reinsertion of urinary catheter, delaying discharge, or discharge with urinary catheter

5. Thromboembolic
e) Deep venous thrombosis
f) Pulmonary embolus
g) Stroke (CVA)
h) Peripheral thrombophlebitis

6. Neurologic/psychiatric
e) Recurrent nerve injury
f) Other neurologic injury
g) Acute delirium
h) Delirium tremens

7. Infection
f) Wound infection requiring opening wound or antibiotics
g) Central IV line infection requiring removal or antibiotics
h) Intrathoracic/intra-abdominal abscess
i) Generalized sepsis
j) Other infections requiring antibiotics

8. Wound/diaphragm
d) Thoracic wound dehiscence
e) Acute abdominal wall dehiscence/hernia
f) Acute diaphragmatic hernia

9. Other
b) Chyle leak
c) Reoperation for reasons other than bleeding, anastomotic leak, or conduit necrosis

11.10 AJCC 8th edition staging of esophageal carcinoma

T Category	T Criteria
TX	Tumour cannot be assessed
T0	No evidence of primary tumour
Tis	High-grade dysplasia, defined as malignant cells confined to the epithelium by the basement membrane
T1 T1a T1b	Tumor invades the lamina propria, muscularis mucosae, or submucosa Tumor invades the lamina propria or muscularis mucosae Tumor invades the submucosa
T2	Tumor invades the muscularis propria
T3	Tumor invades adventitia
T4 T4a T4b	Tumor invades adjacent structures Tumor invades the pleura, pericardium, azygos vein, diaphragm or peritoneum Tumor invades other adjacent structures, such as the Aorta, vertebral body, or airway

N Category	N criteria
NX	Regional LNs can't be assessed
N0	No regional LN metastasis
N1	Metastasis in 1-2 regional LNs
N2	Metastasis in 3-6 regional LNs
N3	Metastasis in 7 or more regional LNs

M Category	M criteria
M0	No distant metastasis
M1	Distant metastasis

Histological grade	**Definition**
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated

Staging for SCC

T	N	M	Stage
T0-2	N0	M0	I
T3	N0	M0	II
T0-2	N1	M0	IIIA
T3	N1	M0	IIIB
T0-3	N2	M0	IIIB
T4a	N0	M0	IIIB
T4a	N1-2	M0	IVA
T4a	NX	M0	IVA
T4b	N0-2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

11.11 Esophagectomy Complications Consensus Group Definitions

1. Anastomotic Leak

Full thickness GI defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification

a) Type I: Local defect requiring no change in therapy or treated medically or with dietary modification
b) Type II: Localized defect requiring interventional but not surgical therapy, for example, interventional radiology drain, stent or bedside opening, and packing of incision
c) Type III: Localized defect requiring surgical therapy

Conduit Necrosis

a) Type I: Conduit necrosis focal Identified endoscopically Treatment—Additional monitoring or non-surgical therapy
b) Type II: Conduit necrosis focal Identified endoscopically and not associated with free anastomotic or conduit leak Treatment—Surgical therapy not involving esophageal diversion
c) Type III: Conduit necrosis extensive Treatment—Treated with conduit resection with diversion

Chyle Leak

a) Type I: Treatment—enteric dietary modifications
b) Type II: Treatment—total parenteral nutrition
c) Type III: Treatment—interventional or surgical therapy

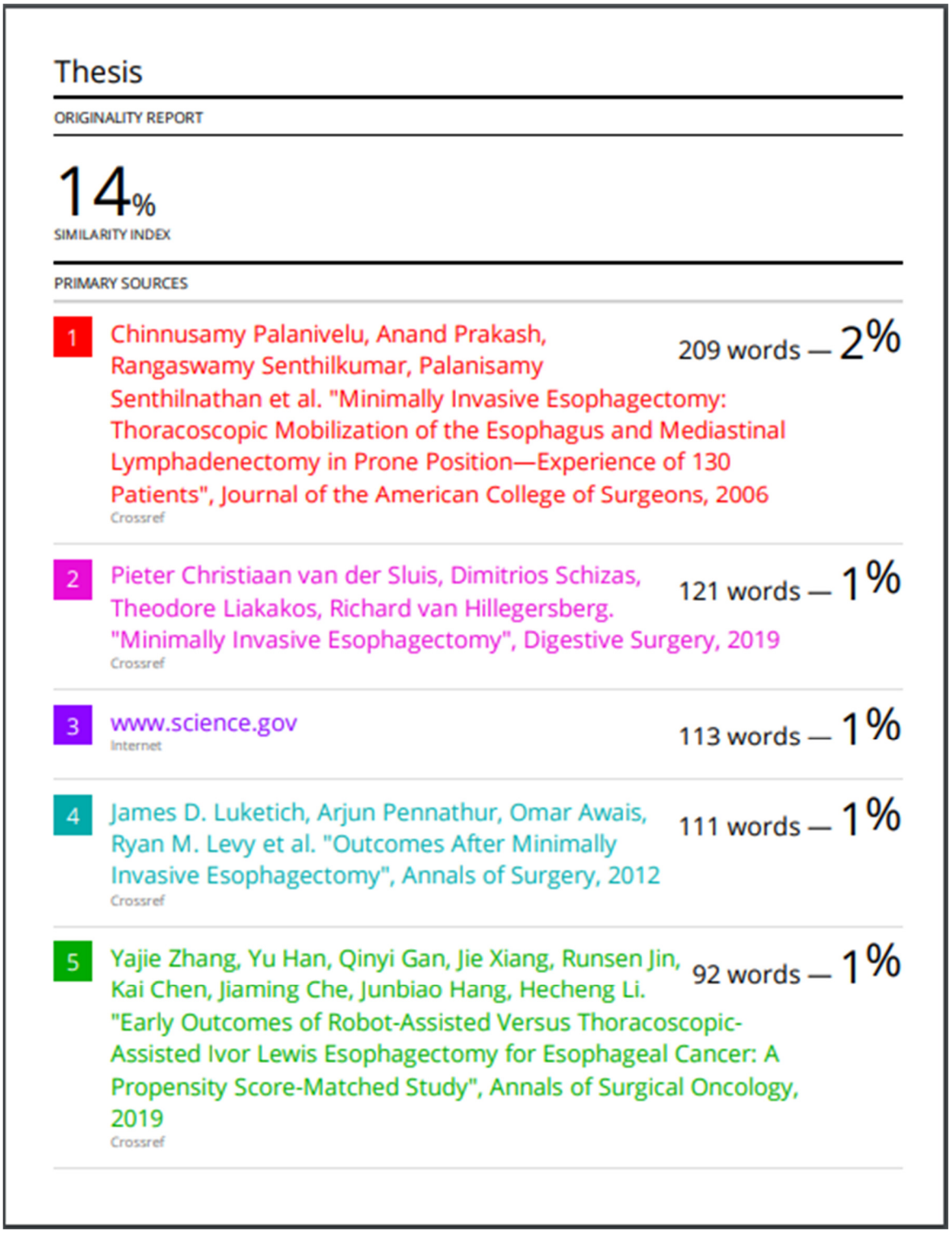
Vocal Cord Injury/Palsy Defined

Vocal cord dysfunction post-resection. Confirmation and assessment should be by direct examination

a) Type I: Transient injury requiring no therapy Dietary modification allowed
b) Type II: Injury requiring elective surgical procedure, for example, thyroplasty or medialization procedure
c) Type III: Injury requiring acute surgical intervention (due to aspiration or respiratory issues)

Severity Level (A) Unilateral (B) Bilateral

11.12 **PLAGIARISM REPORT**



Thesis

ORIGINALITY REPORT

14%

SIMILARITY INDEX

PRIMARY SOURCES

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2 Pieter Christiaan van der Sluis, Dimitrios Schizas, Theodore Liakakos, Richard van Hillegersberg. "Minimally Invasive Esophagectomy", Digestive Surgery, 2019
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5 Yajie Zhang, Yu Han, Qinyi Gan, Jie Xiang, Runsen Jin, Kai Chen, Jiaming Che, Junbiao Hang, Hecheng Li. "Early Outcomes of Robot-Assisted Versus Thoracoscopic-Assisted Ivor Lewis Esophagectomy for Esophageal Cancer: A Propensity Score-Matched Study", Annals of Surgical Oncology, 2019
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92 words — 1%

11.13 KEY TO MASTER CHART

S. No.	Serial Number				
Age	In years				
Gender	1=Male	2=Female			
BMI	In kg/sq. m.				
Smoking	Yes=1	No=0			
Alcohol	Yes=1	No=0			
Family_ho	Yes=1	No=0			
Comorb	1=Diabetes Mellitus	2=Hypertension	3=Psychiatric illness	4=HCV	
Dys_dur	Duration of dysphagia				
Dys_Gr	Grading of dysphagia	Modified Takita classification			
LOIS	Length of ICU stay				
LOHS	Length of hospital stay				
Thorax_phase	1=Thoracoscopic assisted		2=Robotic assisted		
Abdo_phase	1=Laparoscopic	2=Open	3=Robotic		
Duration_TP	Duration of thoracic phase in minutes				
Bld_loss	Blood loss in ml				
Anastomosis	Neck anastomosis	1=Handsewn	2=Semi-mechanical		
Albumin	in gm/dl				
TRG	Tumour regression grade (Modified Ryan's)	0=Complete	1=Near complete	2=Partial	3=Poor or no response
Location	1=Middle thoracic	2=Lower thoracic	3=EGJ Siewert 1	4=EGJ Siewert 2	
NACT	1=Yes	0=No			
NACRT	1=Yes	0=No			
Cycle_CT	Number of cycles of chemotherapy				
Cycle_RT	Number of cycles of radiotherapy				
PODANT	Post operative days after neoadjuvant therapy and before surgery				
T	T stage (AJCC 8)				
N	N stage (AJCC 8)				
Stage	AJCC 8 stage				
M	M stage (AJCC 8)				
Differentiation	1=Well	2=Moderate	3=Poor		
Type	1=SCC	2=Adenocarcinoma	3=Adenosquamous		
LVI	Lymphovascular invasion				
PNI	Perineural invasion				
LNY	Lymph node yield				

LNP	Lymph nodes positive			
LNR	Lymph node ratio			
Pr_margin	Proximal margin	1=Positive	0=Negative	
Dist_margin	Distal margin	1=Positive	0=Negative	
CRM	Circumferential resection margin	1=Positive	0=Negative	
R	Resection status	R0-micro=macroscopic negtaive	R1-Microscopic positive	R2-Macroscopic positive

Supracar_no.	Number of supracarinal LN		
Infracar_no.	Number of infracarinal LN		
Thoracic_LNY	Thoracic LN yield		
Abdomen_LNY	Abdominal Lymph node yield		
Oral_POD	Orals started on POD		
ICD_POD	ICD taken out on POD		
EGD_6m	Esophagogastroduodenoscopy done at 6 months	1=Yes	0=No
EGD6m_AS	Anastomotic stricture at 6 months on EGD	1=Yes	0=No
EGD6m_Rec	Recurrence identified on EGD	1=Yes	0=No
CT_6m	CT scan done at 6 months	1=Yes	0=No
LR_mets	Locoregional metastasis on CT at 6 months	1=Yes	0=No
Distant_mets	Distant metastasis on CT at 6 months	1=Yes	0=No
Adjuvant	Adjuvant therapy	1=Yes	0=No
OGS	Oral gastrograffin study	1=Abnormal	0=Leak
AL	Anastomotic leak	1=Yes	0=No
AS	Anastomotic stricture	1=Yes	0=No
TDI	Thoracic duct injury	1=Yes	0=No
RLN_pal	Recurrent Laryngeal nerve palsy	1=Yes	0=No
Pulmo	Pulmonary complications	1=Yes	0=No
CN	Conduit necrosis	1=Yes	0=No
90_DM	Mortality within 90 days	1=Yes	0=No
Gas_stasis	Gastric stasis	1=Yes	0=No
SAIO	Subacute intestinal obstruction	1=Yes	0=No
Resurg_90d	Resurgery within 90 days	1=Yes	0=No
Clavien_Dindo	Clavien Dindo grading (1-5)		

S. No.	Age	Gender	BMI	Smoking	Alcohol	Family_ho	Comorb	Dys_dur	Dys_Gr	LOIS	LOHS	Thorax_phase	Abdo_phase	Duration_TP	Bld_loss	Anastomosis	Albumin	TRG	Location	NACT	NACRT	Cycle_CT	Cycle_RT	PODANT	T	N	Stage	M	Differentiation	Type	LVI
1	49	1	19.1	0	0	0	0	3	3	0	5	1	0	120	200	2	4.2	1	2	0	1	4	23	44	0	0	0	0	2	1	0
2	63	1	22	0	0	1	0	2	2	0	4	2	3	180	100	2	3.9	2	2	1	0	3	0	31	1b	0	1	0	1	1	0
3	32	2	20	0	0	0	0	1	5	1	7	1	0	150	300	1	3.7	NA	1	0	0	0	0	NA	3	0	1	0	2	1	1
4	20	2	21.3	0	0	0	0	2	1	1	7	2	3	180	100	1	4.1	NA	2	0	0	0	0	NA	2	0	1	0	2	1	0
5	45	1	22.4	1	0	0	3	4	3	1	4	1	0	120	100	1	3.7	NA	2	0	0	0	0	NA	3	1	3	0	2	1	1
6	46	1	18.2	0	0	0	0	2	4	1	6	1	0	120	100	1	3.8	NA	2	0	0	0	0	NA	3	0	2	0	2	1	0
7	50	1	18.1	1	0	1	0	3	3	1	6	1	0	150	100	1	4.6	3	1	0	1	2	23	78	3	2	3	0	2	1	1
8	40	1	19.3	0	0	0	0	2	3	1	6	2	0	180	300	1	3.7	NA	1	0	0	0	0	NA	2	2	3	0	2	1	1
9	44	1	23	0	0	0	1, 2	6	3	0	15	1	1	180	300	1	4	2	1	1	0	3	0	27	2	0	2	0	2	1	0
10	45	1	22.1	0	0	0	0	2	2	0	6	1	1	120	200	1	3.7	1	1	0	1	4	23	24	0	0	0	0	3	1	0
11	53	2	23.2	0	0	0	0	5	4	1	7	2	3	180	200	1	3.5	2	1	1	0	3	0	25	3	1	3	0	2	1	1
12	51	2	20.1	1	0	0	0	2	3	0	8	1	0	120	200	2	3.5	3	1	1	0	6	0	32	2	2	3	0	2	1	1
13	62	2	18.6	1	0	1	1	6	1	0	6	1	0	120	200	2	3.7	3	1	1	0	3	0	34	2	2	3	0	2	1	1
14	48	1	25.8	0	0	0	0	2	4	0	5	1	0	120	200	1	4	NA	4	0	0	0	0	NA	2	1	2	0	2	1	0
15	67	2	19.7	1	0	0	0	4	4	1	6	1	0	120	200	2	3.3	3	3	1	0	1	0	205	3	0	2	0	2	1	0
16	54	1	18.6	0	0	0	0	2	3	0	10	1	0	120	400	2	4.1	0	1	0	1	3	23	36	0	0	0	0	2	1	0
17	54	1	18.2	0	0	0	0	2	3	0	6	1	0	90	200	2	3.5	3	4	1	0	2	0	41	3	2	3	0	2	1	0
18	55	2	19.2	1	0	0	0	2	5	2	2	1	0	180	400	2	3.1	3	1	1	0	2	0	73	3	2	3	0	3	1	1
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22	66	2	19.2	0	0	0	1, 2	2	1	1	7	1	1	150	200	2	4.5	3	2	1	0	2	0	32	2	2	3	0	3	1	1
23	51	2	22.1	1	1	1	1	1	2	1	30	1	0	150	300	1	3.9	2	2	1	0	2	0	41	2	1	2	0	2	1	0
24	52	2	22.6	1	1	0	0	1	2	0	6	1	0	150	200	2	3.6	NA	1	1	0	2	0	46	2	0	2	0	2	1	0
25	69	1	23.4	1	0	1	1	4	3	1	6	1	1	120	300	2	3.7	1	1	0	1	4	23	64	0	0	0	0	2	1	0
26	45	2	21.7	1	0	0	1	1	3	0	13	1	0	120	200	2	3.5	3	2	0	1	4	23	65	2	0	2	0	2	1	0
27	49	1	20.6	0	0	0	0	3	3	1	6	2	0	180	300	1	3.9	0	1	0	1	4	23	13	0	0	0	0	2	1	0
28	66	1	19.4	0	0	0	1, 2	8	3	0	6	2	0	120	200	1	3.6	0	1	0	1	4	23	167	0	0	0	0	3	1	0
29	47	2	19.7	0	0	0	0	6	3	0	8	2	0	180	200	1	4.6	2	2	1	0	4	0	34	1	0	1	0	3	1	0
30	67	2	23.1	0	0	0	0	1	1	1	6	2	0	180	200	1	4.4	1	2	0	1	5	23	64	1a	0	1	0	2	1	0

31	42	1	22.9	0	0	0	0	3	3	1	6	1	0	150	200	2	3.9	0	1	0	1	5	23	47	0	1	1	0	2	1	1
32	58	2	22.3	0	1	0	0	2	3	0	6	2	0	150	200	2	3.5	0	1	0	1	3	23	61	0	0	0	0	3	1	0
33	37	2	21.4	1	0	0	1	8	4	0	11	2	0	150	200	2	4.6	0	2	1	0	3	0	28	0	0	0	0	2	1	0

PNI	LNY	LNP	LNR	Pr_margin	Dist_margin	CRM	R	Supracar_no.	Infracar_no.	Thoracic_LNY	Abdomen_LNY	Oral_POD	ICD_POD	EGD_6m	EGD6m_AS	EGD6m_Rec	CT_6m	LR_mets	Distant_mets	Adjuvant	OGS	AL	AS	TDI	RLN_pal	Pulmo	CN	90_DM	Gas_stasis	SAIO	Resurg_90d	Clavien_Dindo
0	10	0	0	0	0	0	0	0	8	8	2	4	4	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
0	4	0	0	0	0	0	0	1	3	4	0	4	4	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
0	23	0	0	0	0	0	0	2	13	15	8	5	5	1	1	0	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	3
1	12	0	0	0	0	0	0	3	5	8	4	5	6	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	2
1	45	2	0.04	0	0	0	0	12	22	34	11	4	4	1	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	3
1	31	0	0	0	0	0	0	10	15	25	6	5	4	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
0	20	6	0.18	0	0	1	1	5	5	10	10	4	4	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	2
0	25	3	0.12	0	0	0	0	0	20	20	5	4	4	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
0	17	0	0	0	0	0	0	7	5	12	5	4	12	1	1	0	1	0	0	1	0	1	1	1	1	1	0	0	0	0	1	4
0	3	0	0	0	0	0	0	0	3	3	0	4	4	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
0	11	1	0.09	0	0	0	0	0	8	8	3	5	6	1	1	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	1
1	31	6	0.19	0	0	1	0	8	17	25	6	4	4	1	1	0	0	0	1	1	0	0	1	0	1	1	0	0	0	1	0	3
1	22	3	0.14	0	0	0	0	0	15	15	7	4	3	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
0	19	1	0.05	0	0	0	0	1	10	11	8	5	5	0	NA	NA	NA	NA	NA	0	0	0	0	0	1	0	0	0	0	0	0	1
0	17	0	0	0	0	0	0	1	11	12	5	5	5	0	NA	NA	NA	NA	NA	0	0	0	0	0	0	0	0	0	0	0	0	2
0	27	0	0	0	0	0	0	4	16	20	7	4	3	1	0	0	1	0	0	0	0	1	0	0	1	1	0	0	0	0	0	2
1	17	4	0.24	0	0	0	0	5	8	13	4	4	3	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
1	13	6	0.46	0	0	1	0	5	4	9	4	NA	0	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	0	0	1	0	1	0	0	0	5
0	30	0	0	0	0	0	0	1	23	24	6	4	4	1	1	0	1	0	0	0		1	1	0	0	1	0	0	0	0	0	3
0	38	0	0	0	0	0	0	6	23	29	8	11	3	1	1	0	1	0	0	0	0	1	1	0	1	1	0	0	0	0	0	3
0	11	0	0	0	0	0	0	5	2	7	4	4	3	1	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	1	0	1
1	26	4	0.15	0	0	0	0	4	15	19	7	15	3	1	1	0	1	0	1	1		1	1	0	1	1	0	0	0	0	0	3
0	19	1	0.05	0	0	0	0	5	10	15	4	NA	15	NA	NA	NA	NA	0	0	0	1	1	NA	0	1	1	1	0	0	0	1	4
0	31	0	0	0	0	0	0	9	17	26	5	4	3	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
0	20	0	0	0	0	0	0	8	6	14	6	4	3	1	1	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	3
0	19	0	0	0	0	0	0	5	12	17	2	5	3	1	0	0	1	0	0	0		0	0	0	0	0	0	0	0	0	0	2
0	26	0	0	0	0	0	0	6	14	20	6	5	4	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
0	17	0	0	0	0	0	0	2	12	14	3	6	4	1	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1
0	6	0	0	0	0	0	0	0	4	4	2	5	5	1	0	0	1	0	0	0		0	0	0	0	1	0	0	0	0	0	1
0	24	0	0	0	0	0	0	9	11	20	4	15	5	1	1	0	1	0	0	0	1	0	1	0	0	1	0	0	0	0	0	3
0	28	2	0.07	0	0	0	0	13	8	21	7	6	3	1	0	0	1	0	0	0	0	0	0	0	1	1	0	0	1	0	1	3

0	28	0	0	0	0	0	0	12	11	23	5	5	3	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
0	22	0	0	0	0	0	0	7	8	15	7	6	4	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1