IMPACT OF NASOGASTRIC TUBE EXCLUSION AFTER MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER– A PROSPECTIVE OBSERVATIONAL STUDY

THESIS
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CERTIFICATE

This is to certify that the thesis titled **"IMPACT OF NASOGASTRIC TUBE EXCLUSION AFTER MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER"** is the bonafide work of **Dr. VIGNESH N**, 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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This is to certify that **Dr. Vignesh N** has satisfactorily completed her thesis entitled **"IMPACT OF NASOGASTRIC TUBE EXCLUSION AFTER MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER"** in partial fulfillment of the requirement for the degree of Magister Chirurgiae (M.Ch.), in Surgical Gastroenterology. She has done the research work under my supervision and guidance. She 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.

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DECLARATION BY THE CANDIDATE

I hereby declare that this thesis entitled **"IMPACT OF NASOGASTRIC TUBE EXCLUSION AFTER MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER"** 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.

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"If you want to shine like a sun, first burn like a sun."

– Dr A P J Abdul Kalam

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Dr. Vignesh N

Dedicated to my mentor

Prof. Sarath Chandra Sistla

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LIST OF ABBREVIATIONS

ARDS	Acute Respiratory Distress Syndrome
ERAS	Enhance Recovery After Surgery
VATS	Video Assisted Thoracoscopic surgery
ICD	Intercostal Drainage
ICU	Intensive Care Unit
HALS	Hand Assisted Laparoscopic Surgery
LMWH	Low Molecular Weight Heparin
NPO	Nil Per Oral
MIE	Minimally Invasive Esophagectomy
POD	Post–operative Day
RCT	Randomized Control Trials
Vs.	Versus
ASA	American College of Anesthesiologists
CDC	Clavien–Dindo Classification
IQR	Inter quartile range
FBG	Fasting blood glucose
FINS	Fasting insulin
IL–6	Interleukine–6
CRP	C–reactive protein
NGT	Nasogastric tube
FTS	Fast track surgery
LOS	Length of hospital stay
NSAID	Non steroidal anti–inflammatory drug
VTE	Venous thrombo–embolism
ECCG	Esophageal complications consensus group
MAP	Mean arterial pressure
FJ	Feeding jejunostomy
OGS	Oral gastrograffin study
EOF	Early Oral Feeding

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SUMMARY OF THE PROJECT

Background: Nasogastric tube (NGT) is regularly placed across cervical esophagogastric anastomosis (CEGA) after esophagectomy. However, various enhanced recovery after surgery (ERAS) protocols have suggested either early removal or not putting a NGT. However, it is still being used due to the fear of anastomotic leaks and other postoperative complications.

Objectives: This study aims to prospectively evaluate the impact of NGT exclusion in enhanced recovery after surgery **(**ERAS) protocol in patients undergoing minimally invasive esophagectomy (MIE) for esophageal malignancy.

Methods and Procedures: We studied a prospective cohort of 20 consecutive patients from January 2021 to August 2022 who underwent MIE for esophageal malignancy in the Department of Surgical gastroenterology AIIMS, Jodhpur. The primary outcome was the incidence of anastomotic leak, and the other variables compared were post-operative hospital stay, pulmonary complications, and the need for NG tube reinsertion with ERAS protocol followed in all patients.

Results: Median (IQR) age of patients was 48.5 (40-60.5) years, and 55% were males. All 20 patients (100%) received neoadjuvant therapy. Semi-mechanical CEGA anastomosis was done in all –patients. One patient (5%) had an anastomotic leak. Overall morbidity was seen in 40% (n=8) of patients with major complications (Clavien-Dindo≥3) noticed~~seen~~ in 5% (n=1) of patients. There was no mortality during the study period. The median (IQR) length of hospital stay was 6 (6.0 - 7.0) days with a 30-day readmission rate of 5% (n=1). Compliance with the ERAS

protocol was 90%, with major complications being the only factor significantly associated with failure to follow the protocol.

Conclusion: The exclusion of NGT after MIE with CEGA is feasible and safe without an increase in the anastomotic leak rate and other major complications with a reduced length of postoperative hospital stay.

INTRODUCTION

Esophageal cancer is currently the 8th most common cancer worldwide with the 6th highest mortality rate in the world.(1) It is the fourth leading cause of cancer–related mortality in the Indian population and is managed by multimodal therapy, with surgery as the definitive treatment.(2) However, esophagectomy is a procedure with a high risk of complications and may require intensive care unit admission postoperatively. Even in high–volume centers, it is associated with an overall morbidity and mortality rate of 59% and 2.4%, respectively, with an increase in length of hospital stay (LOS) and treatment cost.(3) The introduction of Enhanced recovery after surgery (ERAS) protocol, such as minimally invasive surgery, adequate pain control, nasogastric tube (NGT) early removal, abdominal drains, and early resumption of oral intake, has been found to improve outcomes in upper abdominal surgery.(4) However, the complete exclusion of NGT decompression in esophagectomy patients continues to be debated.

In 1997, Kehlet and Wilmore introduced the fast–track protocol for patients of colorectal surgery to improve postoperative care and decrease the total duration of hospital stay.(5) This has evolved into multidisciplinary teamwork involving surgeons, critical care physicians, anesthesiologists, dieticians, nurses, and physiotherapists. Such ERAS protocol attenuates the trauma and stress associated with surgery, which positively impacts postoperative hospital stay and complications.(6,7) Similarly, fast–track protocol in patients undergoing esophagectomy was first introduced by Cerfolio et al. and was shown to curtail the duration of hospital stay with improved patient satisfaction.(8)

Levin et al. first described NGT for decompression of the gastrointestinal tract in 1921.(9) NGT has been routinely used for decompression and drainage of the stomach to decrease the risk of anastomotic and pulmonary complications. However, a Cochrane review of 37 randomized controlled trials found the routine placement of NGT was associated with inherent risks like throat pain, sinusitis, gastritis, and epistaxis without any added benefit.(10) Exclusion of NGT was most commonly studied in patients undergoing surgical treatment for diseases of the stomach, small bowel, colon, or urogenital tract.(11)

Esophagectomy is considered different from other upper gastrointestinal surgeries because of the use of gastric conduit to restore gastrointestinal continuity, wherein the fluid accumulation and gastric distension increase the risk of pulmonary aspiration and anastomotic leakage if NGT is not used. However, some studies have found that the exclusion of NGT following esophagectomy does not impact outcomes with an ERAS protocol.(12–14) Most of the studies were retrospective and were done in an open transhiatal or transthoracic approach. Randomized controlled trials (RCTs) comparing the conventional NGT group with early removal of NGT on POD 1 or 2 have shown similar postoperative complications with a reduced postoperative hospital stay. However, no RCT has studied complete NGT exclusion post–esophagectomy, and some trials have not reported the effect of NGT exclusion on pulmonary complications or anastomotic leakage.(12–14)

Through this dissertation, we aim to evaluate the impact of NGT exclusion on the postoperative outcomes of patients undergoing minimally invasive esophagectomy (MIE). There are no studies in the Indian population, especially in patients undergoing thoracoscopic or robotic–assisted esophagectomy. This study will provide more evidence regarding such fast–track protocol with NGT exclusion in esophageal surgery.

REVIEW OF LITERATURE

The first study on the ERAS program in esophagectomy was conducted by Cerfolio et al. in 2004.(8) It was a retrospective cohort study of 90 patients who underwent Ivor–Lewis esophagogastrectomy. Preoperative counselling, epidural analgesia, immediate extubation, and early jejunal feeding were given on a postoperative day (POD) 1. In their study, all patients had the removal of urinary catheter, nasogastric tube, and epidural catheter by POD3. Intensive care unit (ICU) stay was routinely avoided. The risk of aspiration was avoided by following head end elevation to 30 degrees, routine NG tube suctioning, and using promotility agents. An oral Contrast study was done on POD 4, and then clear liquids were allowed orally. Out of the 90 patients, 22% did not follow fast–track protocol. They found that the patients who received neoadjuvant chemoradiotherapy had a higher failure rate to follow the fast–track protocol (33% compared to 11% without neoadjuvant chemoradiotherapy). They found that the median LOS was seven days in the fast–track protocol, which was 50% less than in other studies with standard protocol. They found that there was no difference in mortality and morbidity between the two groups.

The first study on fast–track surgery in patients undergoing Minimally invasive Mckeown's esophagectomy was done by Pan et al.(13) It was a retrospective case–control analysis of 80 patients who underwent MIE for esophageal carcinoma. Forty patients in the conventional group were managed according to the standard protocol from January 2012 to June 2012. The other 40 patients were managed with fast–track protocol from January 2013 to April 2013. They included only patients without neoadjuvant therapy. The fast–track protocol consisted of pre–operative patient education, carbohydrate loading where 200 ml of 10% glucose was given

orally, no NGT or peritoneal or neck drain, and restrictive fluid therapy in the perioperative period. Postoperatively the patient was directly shifted to the ward. Enteral feeding through feeding jejunostomy (FJ) was started at a slower rate after 6 hours of surgery and gradually increased in the following days. Patients were educated about chewing and swallowing on POD 2, and clear liquids were allowed orally on POD 2, which was advanced to a semisolid diet by POD 5. They found that patients in the NGT group had 100% sore throat and caused 13% to vomit in the conventional group, whereas in the fast–track group, they caused vomiting in 3% (P >0.05). Patients in the fast–track group received less fluid infusion than the conventional group (p=0.000). The chest tube was removed early in the fast–track group compared to the conventional group (POD3 vs. POD 8, p=0.001). Patients in the fast–track group had early recovery of gastrointestinal function measured by the time to pass the first flatus. They found that excluding NGT had no impact on the anastomotic leak and pulmonary complications on comparing to the conventional group. There was no mortality in the study population. The median LOS was significantly less in the fast–track compared to the conventional group (7 days vs 12 days, p=0.001).

Nguyen et al.(15) evaluated the safety of an MIE by excluding NGT. They did a retrospective cohort study of 124 patients who underwent MIE. They compared two groups, with ninety–eight patients in NGT group placed and 26 patients in no NGT group, with respect to postoperative complications. The anastomotic leak rate was not different between the two groups (9.2% vs. 7.7 %), respectively. Among 26 patients, only one had gastric conduit dilatation, for which NGT was placed under fluoroscopic guidance on POD 1. They concluded that the NGT exclusion during MIE is safe and can be avoided. However, pulmonary complications were not reported in the study.

Daryaei et al.(16) randomized patients undergoing open esophagectomy into NGT group and no NGT group after surgery. All patients underwent either McKeown's or Orringer's transhiatal esophagectomy. Patients in the no NGT group received 10 mg metoclopramide every 8 hours immediately after surgery and continued till the regression of intestinal movements. The rate of pulmonary complications, NGT reinsertion, and wound infection were similar in comparing the groups. The incidence of anastomotic leakage in the NGT group was 6 vs. 0 in no NGT (p=0.02). They found that the postoperative LOS were not different between the groups. They concluded that routine NGT insertion is not recommended for all patients.

Mistry et al.(17) conducted a single–center randomized controlled trial wherein they compared patients undergoing esophagectomy with conventional NGT decompression (6–10 days) vs. early removal of NGT after 48 hours of surgery. They found that the occurrence of anastomotic and pulmonary complications between the early (16 of 75 patients [21.3%]) removal group and delayed (14 of 75 patients [18.7%]) group, respectively (P=.84) was not significant. NGT was reinserted more often (23 of 75 patients [30.7%] vs. 7 of 75 patients [9.3%]) in the early removal group compared to the late removal group (P=.001). Patients in the late removal group (26 of 75 patients [34.7%] vs. 10 of 75 patients [13.3%] in the early removal group; P=.002) had most discomfort due to NGT. The discomfort scores due to NGT were significantly high in the late (1.3; 95% CI, 0.4–2.2; P=.006) than in the early removal group. Their study found that the early NGT removal had no impact on the postoperative complications after esophagectomy.

Shackloth et al.(18) studied the tracheal acid aspiration after esophagectomy and its influence by NGT drainage. They randomized 34 patients into three groups: a single–lumen tube with free drainage and 4–hourly aspiration, no NGT and a sump–type tube on continuous suction drainage. In all three groups, tracheal acid aspiration was present. Respiratory complications were higher in no NGT group after surgery than those with either single–lumen or sump–type tubes (7 cases *versus* 4 cases; P = 0·023). They concluded that NGT was necessary for patients undergoing esophagectomy, and the sump type NGT reduced the incidence of pulmonary complications by preventing tracheal acid aspiration.

Hayashi et al.(19) conducted a single–center prospective RCT of patients undergoing minimally invasive Mckeown's esophagectomy comparing conventional NGT removal group vs. early removal of NGT on POD 1. All patients in both groups had SCC of the esophagus. The thoracic phase of surgery was done by video–assisted thoracoscopic surgery (VATS), and the abdominal phase of surgery by upper midline approach (22.5%) or Hand–assisted Laparoscopic approach (HALS) (77.5%). Around 93% underwent three–field lymphadenectomy. No Fast track protocol was followed among both group of patients. NGT was removed on POD 7 and POD 1 in the conventional and early removal group respectively. They found no difference between the two groups in the incidence of anastomotic leakage, pulmonary complications, NG reinsertion, postoperative hospital stay, and major Clavien–Dindo complications.

ERAS society guidelines for ERAS in esophagectomy were published in 2018.(20) They emphasized the importance of multimodal rehabilitation comprising nutritional assessment and nutritional intervention, preoperative counselling, and optimization of medical comorbidities with a structured exercise program, including

aerobic and strengthening activity in the preoperative setting before major surgery. Multimodal prehabilitation for four weeks was effective and found to have a positive impact on postoperative outcomes, but the data on its effect on esophagectomy was limited. The optimum time interval between chemotherapy or chemoradiotherapy and surgery suggested were 3–6 weeks or 6–10 weeks, respectively. Smoking or alcohol cessation and decreasing the preoperative fasting time were recommended to improve the outcomes. Goal–directed fluid therapy with <2 kg weight gain/day is recommended, maintaining negative fluid balance. There was no specific recommendation on peri–anastomotic drain placement. The guidelines recommend routine NGT placement, but with early removal by day 2. They recommend a single chest tube drain (ICD) with early removal in the absence of chyle or air leak. They recommend early initiation of enteral feeding with target nutrition achieved on days 3–6. Multimodal analgesia with a thoracic epidural was to be followed, avoiding opioids during the period. They recommended the prevention of hypothermia, antithrombotic prophylaxis, and early ambulation in the postoperative period. They also recommended regular audits to know the adherence to protocol.

Apurva et al.(21) have recently reviewed the ERAS protocol in esophagectomy from a tertiary high–volume center in India. All patients were started on a prehabilitation program with smoking cessation, chest physiotherapy and incentive spirometry preoperatively. Cardio–pulmonary exercise tests were done only for patients with borderline functional capacity or high–risk cases. The functional capacity of patients was assessed by 6–min walk test or climbing of stairs. All patients underwent esophageal resection 4–6 weeks after neoadjuvant chemotherapy and 6–8 weeks after neoadjuvant chemoradiotherapy. Oral clear liquids were allowed till 2 hours before surgery. Forty per cent of their cases are done minimally invasively.

Epidural analgesia and goal–directed fluid therapy were used routinely. Forced air warming and fluid warmers were used routinely to prevent hypothermia. Extubation was immediate in 95% of patients. Ambulation of the patients were initiated in the immediate postoperative period. Enteral feed was started on POD 1 and orals on POD 4. After 12 hours of clamping, the NGT was removed on POD 2 if no gastric tube dilatation was evident on the X–ray. The neck drain was not inserted routinely for cervical anastomosis. ICD was removed when output was less than 5 ml/kg/day. They found introduction of ERAS protocol decreased morbidity and mortality (64% and 6.6% before ERAS vs. 43% and 4.9% after ERAS, respectively)

Cao et al.(14) retrospectively evaluated the fast–track protocol in patients underfoing esophagectomy. They excluded patients with ASA III–IV, previous coronary artery disease, moderate COPD, age 65–75 years with hypertension and diabetes. None of the patients received preoperative chemotherapy or radiotherapy. The protocol included pre–operative counselling, fructose and protein drinks up to 2 hours before surgery, thoracic epidural, restrictive fluid strategy, early enteral feed, mobilization, and removal of tubes. NGT was not routinely inserted. Their discharge criteria were the patient tolerating a semisolid diet and walking freely in the ward. Abdominal and neck drains were avoided routinely. The fast–track group had 55 patients, and the conventional arm had 57 patients. Complication rates were 29.1% and 47.4% in the fast–track and conventional groups, respectively, which was statistically significant($p = <0.005$). They found no significant difference in the incidence of anastomotic leaks in the fast–track group compared to the conventional group (9.1% v.s 12.3%, $p=0.58$). The readmission rates were not different (3.6% vs. 5.3%). Median postoperative LOS was significantly less in the fast–track group, 7.7 days (range 6–14 days) and 14.8 days (12–28 days) in the conventional group

(p=0.01). They found compliance to fast–track protocol in about 87.3% of patients, and the main reason for non–compliance was postoperative complications.

Jiang et al.(22) did a retrospective analysis to know the outcomes of enhanced recovery pathways following open transthoracic esophagectomy for esophageal cancer. They analyzed 114 patients who underwent open thoracotomy and esophagectomy. They compared their result with the standard protocol from the literature. They used pre–operative respiratory exercise, intravenous glucose loading 2 hours before surgery, and intra–operative restricted fluid protocol. Early extubation was practised in which 60% of patients were extubated immediately, and another 30% were extubated after a few hours. Urinary catheter and epidural catheter removal was done on POD 2. NGT was kept till POD3 as they thought that gastrointestinal function was in a phase of recovery during the first 48 hours of surgery, and decompression may be useful. They found that both sexes and all stages of the tumor had similar tolerance to protocol. The best results were obtained when the age of the patient was less than 65 years and when the patient had no other comorbidity. They found that postoperative LOS was seven days on average, and the 30–day readmission rate was 4%, with significantly decreased costs without any increase in morbidity or mortality.

Li et al.(23) did a retrospective case–control study to evaluate the impact of ERAS pathways on LOS, morbidity, and readmission. They compared standard protocol with ERAS protocol following open esophagectomy and MIE for esophageal cancer, including Ivor–Lewis and Mckeown's esophagectomy. Of 106 patients, 47 were in the standard and 59 in the enhanced protocol arm. Around 50 % of the patients received neoadjuvant chemotherapy, with a few receiving neoadjuvant

chemoradiotherapy. Complications were expressed using the modification of the Clavien–Dindo grade. (24) Pre–operatively, patients were educated using a booklet and were told that they would be discharged seven days after surgery. Preoperatively patients were instructed to use incentive spirometry ten times per hour with increased physical activity. Feeding jejunostomy was not used routinely. A neck drain was used routinely for cervical anastomosis. Patients were extubated immediately after surgery, and intensive care stay was avoided. Early mobilization was promoted after surgery. The urinary and epidural catheters were removed on POD 2 & 5, respectively. Oral sips were started on POD 3. A barium swallow study was done on POD 5, after which orals were started and progressed to liquids and semi–solids. The neck and chest tube drain were removed after POD 5 after oral contrast study. They found that Clavien–Dindo complications were not different, with the standard protocol group having 62% complication and the enhanced protocol group having 59% complications. The percentage of patients readmitted was also similar (6% vs. 5%). In ERAS group LOS was significantly less compared to standard protocol. 32% of patients in the fast–track protocol could be discharged by their target date. The mean length of hospital stay was 8 (7–17) in the enhanced protocol group compared to 10 (9–17) in the standard group.

Low et al.(25) conducted a retrospective observational study evaluating the effect of standardized pathways in patients undergoing open esophagectomy from May 1991 to May 2006. Forty–one percent of 340 patients in this study underwent neoadjuvant treatment, and they found no difference in complication compared to those without neoadjuvant treatment. They interviewed all patients pre–operatively. An intra–operative restrictive fluid strategy was adopted. Immediate extubation was possible in 99.5% of patients, and mobilization on postoperative day one was done in

85.9% of patients. The nasogastric tube (NGT) was removed on POD 5 after an oral contrast study. Enteral feeding was initiated on POD 3. Thoracic epidural analgesia was administered in 98.5% of patients. Overall morbidity was 45%, of which pulmonary and cardiac complications were the most common, around 17% and 15%, respectively. 4% of patients had an anastomotic leak. They found that the outcome of patients improved over time after implementing the standard protocol.

Gatenby et al.(26) did a retrospective cohort evaluation of an enhanced recovery program in both open esophageal and gastric surgery. They did a pre–operative assessment of patients for fitness for participation in the pathway. Patients were given 750 ml of immunonutrition five days before surgery, and carbohydrate loading with 50g of glucose was given 2 hours before surgery. Epidural analgesia and neutral fluid management protocol were used intra–operatively. All patients underwent either subtotal or total gastrectomy or Ivor–Lewis esophagectomy with two–field lymphadenectomy. Patients were extubated immediately, and early mobilization was done. NGT was inserted routinely in the postoperative period and was removed after POD 4. Enteral nutrition was started on POD 2. A contrast study was not done routinely. Postoperatively urinary catheter and abdominal drain removed on day 4. The chest tube drain was removed on POD 5. Postoperative complications were graded using the Clavien–Dindo classification. Thirty–five patients followed the standard pathway, and 27 were operated on after implementing the enhanced program. Hospital stay was decreased by three days in the intervention group (20.5 vs. 17 days). Stay in the critical care unit, and overall morbidity and death rates were similar.

Giacopuzzi et al.(4) studied the feasibility of ERAS protocol in the Ivor–Lewis and McKeown approach in esophagectomy. The control group was studied retrospectively, and the patients undergoing the ERAS protocol were evaluated prospectively. They compared 17 patients in the control group and 22 in the ERAS group. All patients in the ERAS group and 94.1% in the control group received neoadjuvant treatment. Carbohydrate loading with glucose was given 12 and 2 hours before surgery in the ERAS group. Goal–directed fluid therapy was used intraoperatively in 59.1%, along with epidural analgesia in 72.75% of patients in the ERAS group. Patients were extubated immediately 72.7 % of the time. NGT removal on POD 1 was possible in 50% of patients. In the ERAS group, the oral liquid diet was tolerated by 31.7% of patients on POD 1. Early postoperative ambulation was done, and chest drain and foley's were removed on POD 2. No routine contrast study was done in the ERAS group. They found that the complication rate was less in the ERAS group compared to the standard group(27.4% vs. 44%). However, the LOS was not different between the two groups (9 days vs. 10 days).

Shewale et al.(5) conducted a retrospective case–control study of 708 patients before and after introducing fast–track pathways in patients undergoing esophagectomy for carcinoma. Three hundred and twenty–two patients were included in the standard protocol, and 386 patients in the fast–track protocol. Patients in the fast–track group were extubated immediately, and jejunostomy feeds were started on POD 3. The urinary catheter and epidural catheter was removed on POD 4 and POD 5 respectively. NGT was routinely inserted in the fast–track group and was removed on POD 5. The OGS was done on POD 10, and orals were started on an outpatient basis after POD 10. They found that the patients in the fast–track group had short median LOS (12 vs. 8 days) and ICU stay (4.5 vs. 1.2 days) compared to the conventional

group. They also found a lower rate of pulmonary complications (27 % vs. 20%) and atrial arrhythmia (27% vs. 19%) in the fast–track group. Hospital charges were also lower in the fast–track group.

Munitiz et al.(27) have done a retrospective cohort study to know the effectiveness of clinical pathways in transthoracic Ivor–Lewis esophagectomy. They prepared a written protocol for patients till postoperative day 7. All patients underwent open transthoracic esophagectomy. Immediate extubation was practised along with negative fluid balance till POD 4. The pain was managed by epidural analgesia, and patients were mobilized early. On the 4^{th} postoperative day, the chest tube, epidural and urinary catheters were removed. An oral contrast study was done on POD 5, following which NGT was removed, and orals were allowed. Parenteral nutrition was used till POD 4. Enoxaparin was used for thrombotic prophylaxis from POD 1. They compared the results of 74 patients managed by a clinical pathway from 2003 to 2008 with 74 patients managed by standard protocol from 1998 to 2002, and there was no significant difference in overall morbidity (31% vs. 38%). The anastomotic leak rates were not different, whereas pulmonary complications were more in the standard protocol group (23% vs. 14%) with a p–value of 0.025. The mortality rate was also significantly higher in the standard protocol group (5%), compared to that of the clinical pathway group, with only 1% mortality (p=0.01). Adherence to the protocol was around 59% and was about 86% in patients without complications. No difference was noted in readmission between the two groups.

Blom et al.(28) studied the effectiveness of the ERAS protocol in open esophagectomy patients. There were 103 patients in the ERAS group and 78 in the conventional group. In the pre–operative period, patients were counselled, a

nutritional assessment was done, and necessary nutritional interventions were taken. Epidural analgesia, restrictive fluid management, and prevention of hypothermia were carried out intraoperatively. Postoperatively, patients were mobilized in the immediate postoperative period and enteral feeding were started on POD 1. NGT was removed on POD 2, ICD was removed when output was less than 200 ml, and oral intake was initiated on POD 5. The median (IQR) hospital stay was 15 (12–26) days in the conventional group, whereas it was 14 (11–20) days in the ERAS group. In patients without complications, the hospital stay was 12 (11–15) and 10 (9–12), respectively, which was significantly less in the ERAS group (p=0.005). Readmission rates were similar between the groups (10.3% in the conventional group and 9.7% in ERAS, p=0.903). Overall complication rates were also similar between groups (10.3% vs. 9.75).

Zhao et al.(12) investigated the influence of fast–track pathways on postoperative insulin resistance, recovery of gastrointestinal function, and inflammatory markers. They compared the outcomes in 34 patients who underwent conventional treatment with 34 patients who underwent ERAS protocol between 2009 and 2011. Insulin resistance was measured using fasting blood glucose (FBG), fasting insulin (FINS), C–reactive protein (CRP), and interleukin–6 (IL–6) on POD 1, 3, and 7. The protocol included no routine use of an NGT, abdominal drain, or neck drain, early enteral feeding, and pre–operative carbohydrate loading. Neoadjuvant therapy was given to 50% of patients in the ERAS group. Fast track group had significantly lower time to pass flatus (1.91±1.13 vs. 2.92±1.25 days, p=0.000), time to pass faeces (3.75±1.54 vs. 4.84±1.76 days, p=0.007) and incisional pain score (p=0.05). The protocol was well tolerated, and there was no difference in morbidity. On POD 1 and 3 FINS, CRP and IL–6 levels were significantly lower in the fast–track group, and on

POD 7 CRP level was lower in the fast–track group (p=<0.05). They concluded that the fast–track pathway reduces stress reaction, promotes early recovery of gastrointestinal function, and postoperative insulin resistance.

Tang et al.,(29) did a retrospective case–control study of 108 patients undergoing esophagogastric resections (53 in the conventional group and 55 in the ERAS group). The protocol consists of early extubation and physiotherapy from POD 1. NGT was removed on POD 5, and oral feeds were started on POD 5 and discharged by POD 7. They found that the median hospital stays were reduced from 15 to 11 days after ERAS protocol implementation (p=<0.001). There was no difference in overall morbidity (25.6% vs. 16.7%) or mortality (1.8% vs. 3.6%).

Preston et al.,(30) in their study, assessed the impact of the standardized pathway in esophageal cancer surgery by comparing four groups of patients. Group 1 was before the introduction of the pathway, group 2 after the introduction of the pathway but not included in the pathway, group 3 managed according to the standardized pathway, and group 4 patients from another hospital in the US. The pathway consists of mobilization on POD 1, enteral feeding on POD 1, and oral contrast study on POD 3. NGT removal was done on POD 4, and orals were started on POD 6 or 7. They found reduced complications and LOS [17(12–30) to 7(6–37) days] after introduction of standardized pathway.

In a prospective cohort study by Ford et al.(31) they compared the outcomes of 74 patients in the ERAS group with 41 patients in the non–ERAS and 80 patients in the pre–ERAS group. A significant reduction in LOS from 13 (8–57) to 10 (7–58) was found with ERAS program implementation. The postoperative complications were measured according to Accordion scores and the 30–day readmission rate and

they found there was no difference. On the contrary, in their retrospective case–control study, Findlay et al.(32), in their retrospective case–control study, did not find any benefit in the formalized written pathway of peri–operative care. The adherence rate to the protocol was 47.3% in this study, and no pre–operative characteristics could predict failure to complete the protocol. They used pre–operative carbohydrate loading, restricted intra–operative fluid therapy, early extubation, epidural analgesia, antithrombotic prophylaxis, early enteral nutrition via feeding jejunostomy, a urinary catheter was removed on POD 4, and early oral intake was started on POD 3. LOS was similar between groups, with the protocol group having a median stay duration of 14 days and the standard protocol group having a stay duration of 12 days.

Chen et al.(33) conducted an RCT comparing fast–track surgery (FTS) and conventional surgery. Of the 260 patients, 128 were enrolled in FTS and 132 in the conventional group. The protocol consists of decreasing pre–operative fasting, carbohydrate loading, no routine use of NG, neck drain, abdominal drain, and avoidance of ICU stay. Enteral feeding was started on POD 1, the urinary catheter was removed on POD 1, ICD was removed on POD 3, oral contrast study was done on POD 4, and oral was started on POD 4 if no leak was found. Discharge was planned on POD 7. The postoperative stay was reduced from 12.56 ± 1.92 to 7.62±1.38 days. Hospital expenditure was significantly reduced with FTS. Overall morbidity and mortality were similar with 30–day readmission rate of 2.3%.

A systematic review of 6 studies by Findlay et al.(34) found ERAS for esophagectomy feasible with acceptable morbidity and mortality and improved outcomes. They found that the protocols were not uniform, and there was a dearth of evidence for individual components. Another systematic review by Pisarska et al.(35),

including 1 RCT and 12 comparative studies, found no significant difference in the rate of overall complication rate with ERAS (41% in ERAS vs. 49% in the conventional group), anastomotic leak (9.3% in ERAS vs. 10.8% in the control group), mortality (2.1 % in ERAS vs. 2.9% in the control group), but there was a statistically significant reduction in length of hospital stay(LOS). The mean LOS was 10.76 in the ERAS group, and that of the control group was 14.4 days without any increase in re–admission rate and with decreased non–surgical morbidity. But the included studies were of low quality with a risk of bias and wide variation in protocols followed.

Weijs et al.(36) did a systematic review of 7 studies on nasogastric decompression following esophagectomy. In two RCTs and one retrospective cohort study, peroperative removal of NGT was compared with routine NGT decompression. In the remaining three trials, ERAS protocol without NGT was compared with conventional care with a NGT during the first postoperative days. Pyloromyotomy was routinely performed in studies by Daryaei et al. and was not done by Shackloth et al. and Pan et al. They found that peroperative or early removal of NGT has no impact on the anastomotic leak, pulmonary complications, or mortality. Peroperative or early removal of NGT resulted in a significantly reduced length of hospital stay.

A systematic review by Kaaki et al.(37) investigated the effect of early oral intake (EOI) and or early NGT removal (POD 0–2) in patients undergoing esophagectomy with cervical anastomosis. The meta–analysis included 6 RCTs, 2 for EOI and 4 for early NGT removal. Among the 4 studies for early NGT removal, they found no difference in the rate of anastomotic leak, mortality, pulmonary complications and length of hospital stay.

To evaluate the effect of pre–operative counselling, Betti et al.(38) conducted a prospective study on patients undergoing esophageal and gastrointestinal surgery. Informed consent in writing was taken from all patients, along with detailed verbal and schematic drawing explanations of disease, procedure, and postoperative outcomes. A State–Trait Anxiety Inventory test was done, and anxiety among patients was assessed after informed consent. They found that the anxiety score decreased significantly in most patients with proper pre–operative counselling, and the benefit was more pronounced in elderly patients. In the informed consent, benefits and risk of the procedure were described in detail and was explained to the patient by a trained junior surgeon along with verbal and drawing details of surgery in around 1 hour. They found most of the patients had moderate anxiety at the baseline level. Time taken for consent was a strong predicting factor in patient understanding, and the minimum time required was around 15 to 30 minutes.(39) The LOS can be significantly reduced with appropriate preoperative education.(40)

Normally preoperative fasting lasts more than 12 hours, by which most of the glycogen stored in the liver may be depleted. The body will be in a state of reduced availability of easily usable energy. Surgery, being a state of increased metabolic requirement, done in this state can have much detrimental effect on the body and influence the outcome of surgical care. Carbohydrate loading preoperatively has been found to decrease the early metabolic demand after the surgery, along with decreased insulin resistance.(41) In an RCT by Yuill et al.(42) they gave a carbohydrate drink containing 12.6 g/100 ml of complex carbohydrate, also containing potassium, sodium, magnesium, chloride, and calcium 800 ml 12 hours before surgery and 400 ml 2 hours before surgery over 20 minutes in patients with gastrointestinal surgery. When compared with the placebo group, they found significantly less loss of lean

muscle mass in the carbohydrate–loaded group. There was no increase in aspiration risk, and the total length of stay remained similar between groups.

Hyperosmolar glucose drinks would decrease gastric emptying and increase the risk of aspiration. But when isotonic carbohydrate drink containing 12.5% carbohydrate with an osmolarity of 282 mOsmol/kg was used, it was completely emptied from the stomach within 90 minutes.(43) Noblett et al.(44) noted a significant decrease in the length of in–hospital stay with pre–operative carbohydrate loading in patients undergoing colorectal surgery. They also found that gut function recovered earlier and better grip strength in patients who were carbohydrate loaded orally. A systematic review by Li et al.(45) found that the pre–operative carbohydrate seems to be safe and decreased insulin resistance postoperatively. But the quality of available studies was questionable. Hausel et al.(43) in a randomized control trial (RCT) found that in patients undergoing laparoscopic cholecystectomy preoperative carbohydrate loading was associated with less postoperative nausea and vomiting.

Gustafsson et al.(41) found that pre–operative oral carbohydrate was safe in well–controlled type 2 diabetic patients, and stomach residual volume after 2 hours was similar to that of healthy volunteers. Another study by Can et al.(46) also found that pre–operative oral carbohydrate drinks had all the benefits, as seen in patients without insulin resistance and any risk of aspiration. Intravenous glucose loading in which 1 litre of 5% dextrose was given over 6 hours had a similar effect on blood glucose and insulin level as oral carbohydrate loading. It also decreased the feeling of weakness postoperatively. But the feeling of thirst and hunger was much less with oral carbohydrate loading.(47)

Malnutrition is associated with reduced overall survival and increased toxicity of chemotherapy drugs in colorectal cancer patients.(48) Patients having malignancy of the upper gastrointestinal tract are at higher risk of malnutrition because of poor oral intake. More than 10% weight loss in 6 months has a higher chance of postoperative complications. Protein breakdown and glucose production are found to be increased as a catabolic response in esophageal cancer.(49) The role of immunonutrition in esophagectomy is not proven.(50)

Pulmonary complications are common after esophagectomy and can increase morbidity and stay in the hospital. The role of chest physiotherapy was studied by Dettling et al.(51) in which a 2–week course of respiratory muscle training of 20 minutes was given to patients. They found that the inspiratory muscle function could be improved but did not translate into a reduced postoperative pulmonary complication. Inspiratory exercise using an inspiratory muscle trainer was found to improve postoperative vital capacity and decrease the incidence of pulmonary complications. But incentive spirometry didn't provide any improvement in muscle strength or lung function.(52) The incentive spirometer is a simple device which provides visual feedback and promotes respiratory training. Postoperative pulmonary complications were found to be less with peri–operative use of incentive spirometry in patients undergoing major abdominal surgery. Westwood et al.(53) found that the addition of an incentive spirometer in the peri–operative period decreased the pulmonary complications (6 vs 17%) and ICU stay (3.1 vs. 4 days). Kundra et al.(54) found that pre–operative incentive spirometry better–preserved lung functions than postoperative incentive spirometry. They trained the patients to take 15 times every 4^{th} hour for 1 week in the preoperative period.

Post–surgical pain is a major limiting factor for patient mobilization, coughing to clear secretions, all of which will influence the postoperative outcome. Epidural preemptive analgesia was found to decrease acute post–thoracotomy pain and pain during cough.(55) Preemptive analgesia prevents the central nervous system sensitization to pain, and epidural analgesia was found to decrease postoperative pain intensity by 25%, which was significant when compared to intravenous non–steroid anti–inflammatory drugs and opioids. A study by Saeki et al.(56) found that patient–controlled epidural analgesia in post–esophagectomy patients decreased pulmonary complications and the total length of ICU and hospital stay. The use of epidural analgesia was also associated with decreased risk of anastomotic leak rate (OR 0.13).(57)

Respiratory complications occur in around 50% of esophagectomy patients.(53) Buise et al.(58) did a comparative study between restricted fluid regimens where less than 4 litres of fluid was given intraoperatively and mean arterial pressure (MAP) was maintained above 65 mmHg using noradrenalin infusion whenever needed. They found less pulmonary complication (26 vs. 42%) and similar urine output and anastomotic leak rate when compared with liberal fluid therapy in patients undergoing esophagectomy. A systematic review found that goal–directed fluid therapy was associated with less pulmonary complications with early return of bowel function.(59) Restrictive versus Liberal Fluid Therapy for Major Abdominal Surgery (RELIEF),(60) the largest trial on fluid management, classified the restrictive fluid regimen as 5 ml/kg bolus at induction followed by 5 ml/kg/hr infusion and liberal fluid therapy as 10 ml/kg bolus at induction and 8 ml/kg/hr infusion intra–operative. They found that the restrictive fluid therapy had more acute kidney injury (8.6% vs. 5%), surgical site infection (16.55 vs. 13.6%) and the need for renal

replacement therapy with disability free survival similar at 1 year. These findings suggest that too restrictive a fluid regime could be harmful. The policy in the restrictive group in the RELIEF group was too restrictive in comparison to the study by Brandstrup et al. (61), which showed significant harm in the liberal group, which received more than 6 L fluid on the day of surgery with a weight gain of about 4 kg. With a restrictive fluid regime, overall complications (30% versus 56%, $P = 0.003$), cardiopulmonary (7% versus 24%, $P = 0.007$) and tissue–healing complications (16% versus 31%, $P = 0.04$) were significantly less. This suggests too restrictive a fluid regime may be harmful, and goal–directed or moderately liberal fluid therapy (1–2 litres positive balance) may be the recommended way.(62) On multivariate analysis fluid therapy was the only factor associated with a respiratory complication [P= 0.005 – odds ratio = 1.00).(63) Hikasa et al.(64) studied the impact of fluid therapy on 136 patients who underwent MIE in the prone position. They found that median intra–operative crystalloid administration was 5898 ml vs. 4250 ml in higher and lower fluid balance groups, respectively. They found that complications were more in patients who received higher intra–operative fluid (46% vs. 18%, p <0.001).

Prophylactic ventilation was routine in earlier days after esophagectomy because of fear of fluid shift, airway oedema, and pain of thoracotomy incision. With improvement in surgical techniques along with restrictive fluid therapy, decreased duration of surgery, and epidural analgesia, early extubation is possible after esophagectomy. Lanuti et al.(65) found that early extubation decreases the rate of acute respiratory distress syndrome (ARDS) and ICU stay. Neoadjuvant treatment was not associated with the risk of failure of early extubation. Yap et al.(66) studied factors associated with early extubation after transthoracic esophagectomy. On univariate analysis, better FEV1 and epidural analgesia were associated with early

extubation, and on multivariate analysis, only epidural analgesia was the factor associated with early extubation. There was no difference in pulmonary complications or mortality rate between the early and late extubation groups. Duration of ICU stay was 1 day vs. 2 days in early and late extubation groups, respectively.

Chest tube placement is a routine part of MIE, and it prevents pneumothorax and hemothorax. ICD placed during esophagectomy can be a source of postoperative pain and infection. Yao et al. (67) in a retrospective analysis, found that chest tubes can be safely removed when output is less than 300 ml per day without increasing the chance of hemothorax or pneumothorax. They analyzed patients who had their chest tubes removed when the output was less than 150 ml/day with those whose chest tubes were removed when output became less than 300 ml/day. The chest tube was placed for a minimum of 24 hours postoperatively, and drain fluid character was analyzed before removal, clinically measuring fluid triglyceride level and getting a chest x–ray. The tube was not removed if the triglyceride level was more than 110 mg%. Post chest tube removal, the patient was monitored clinically, and a chest x–ray was done when clinically indicated. In an RCT conducted by Hessami et al.(68) in trauma patients, he found that chest tube removal when output was less than 200 ml rather than 150 ml was associated with less hospital stay and less hospital cost without increasing clinical or radiological pleural effusion. The chest tube can be removed safely in patients without chylothorax or pneumothorax, with lung expansion confirmed on chest x–ray, when the output is less than 5 ml/kg/day.(21)

Lewis et al.(69), in their systemic review, found that there was no benefit in keeping patients nil per mouth after gastrointestinal surgery. Most studies in this review show decreased mortality, infection risk and length of hospital stay in the early

oral feeding group. In a non–inferiority RCT of 280 patients by Sun et al.(70) found that early oral feeding on POD 1 was non–inferior to late oral feeding on POD 7 in patients with McKeown MIE with no impact on cardiac and gastrointestinal complications (30 vs. 32.9%). Early oral feeding allowed early recovery of bowel function (2 vs. 3 days) with a shorter time to pass flatus (2 days vs. 3 days, p=0.001) and better quality of life postoperatively. In the early oral group, patients were asked to drink sips of clear water. The early enteral group underwent an endoscopic examination before a feed to rule out vocal cord palsy. Initially, oral sips were allowed to rule out any aspiration and then liquid diets were allowed on POD 1 and semisolids on POD 2. Parenteral nutrition was supplemented till POD 4. They motioned that the fear of anastomotic leak after early oral intake was not required. A study by Todano et al.(71) in a rat model found that early enteral feeding promotes upper gastrointestinal tract anastomotic healing. The probable mechanism suggested by them was that the mechanical stretch induced by peristalsis promotes healing, and anastomosis healing was also promoted by non–nutrient oral feeds.

When patients of MIE were given enteral feeding through feeding jejunostomy (FJ) 6 hours after surgery at a rate of 20 ml/hour, no adverse effects were observed. Time to flatus was less in the early enteral–fed group.(13) Cerfolio et al.(8) found that ICU stay could be avoided in 77% of esophagectomy patients, and this resulted in high patient satisfaction and decreased cost. None of them had to be resent to ICU. Urinary catheters are usually placed after surgery for urinary output monitoring, but they prevent the patient from being mobilized, and also rate of infection is increased.(34) In one randomized control trial by Zaouter et al.(72) they randomized patients undergoing abdominal and thoracic surgery with an epidural catheter into the early removal group (POD 1), and the standard group on POD 3. They found a

significant decrease in the rate of urinary tract infection in a patient with early removal of the catheter (14% vs. 2%, p = 0.004) with no difference in the rate of catheter reinsertion. Hospital stay was prolonged in patients with urinary tract infections. Chia et al.,(73) in a randomized control trial, found that early removal of Foleys catheter in patients after thoracotomy with epidural analgesia does not increase the risk of catheterization and improves pain scores.

The major preventable cause of death after surgery for malignancy is venous thromboembolism (VTE). Esophagectomy is a high–risk procedure for VTE with a risk rate of 5–7%. In patients with VTE, the in–hospital mortality doubles. Both mechanical and pharmacological prophylaxis is recommended for high–risk procedures. Four–week postoperative course of anti–thrombotic prophylaxis further decreases the risk of VTE.(74) The meta–analysis by Akl et al.(75) showed that no difference in mortality and embolic events between low molecular weight heparin (LMWH) and unfractionated heparin but unfractionated heparin increased the chance of wound hematoma and the need for transfusion intraoperatively. International guidelines for VTE(76) in cancer patients recommend LMWH as the first choice and should be started 12 to 2 hours before surgery and continued 7–10 days postoperatively. They find no evidence to support the use of Fondaparinux in place of LMWH. Mechanical prophylaxis is not recommended as monotherapy. VTE prophylaxis should be used similarly in the laparoscopic procedure as in laparotomy.

To provide the benchmark for reporting outcomes and complications associated with esophageal surgery, a standardized platform was developed by the Esophageal complication consensus group (ECCG).(3) The overall complication rate was 59%, with pneumonia being the most common (14.6%) and atrial dysrhythmia

being the second most common (14.5%) complication. Individual complications like an anastomotic leak, conduit necrosis, chyle leak, and recurrent laryngeal nerve palsy occurred in 11.4%, 1.3%, 4.7%, and 4.2%, respectively. Complications greater than grade IIIb Clavien–Dindo occurred in 17.2% of patients. The Thirty–day and 90–day mortality rates were 2.4% and 4.5%, respectively. The readmission rate in 30 days was 11.2%, of which 77.6% of patients had some postoperative complications. Table 1 shows the protocol and outcomes of studies on ERAS in esophagectomy. Table 2 shows studies on NGT exclusion in esophagectomy.

Table 1: Outcomes of various studies on ERAS protocol in esophagectomy

Author	Design	Program	Findings
Giacopuzzi et al(4) (2017)	Ambispective	ICU stay –1; Mobilization – 1; Enteral feeding – 1 Foley's removal – 1; NG removal – 1; ICD removal – 1 Oral feed – 1	Compliance (%) – 72.7 LOH (days)– 9 Mortality (%) – NA; Morbidity (%) – 27 Readmission (%) – NA
Chen et al(33) (2016)	RCT	ICU stay – avoided Mobilization – 1; Enteral feeding – 1 Foley's removal – 1; NG removal– avoided; ICD removal – 3 Oral feed – 4	Compliance (%) – NA LOH (days)– 7.62 Mortality (%) – 1.6; Morbidity (%) – 8.6 Readmission (%) – 2.3
Shewale et al(5) (2015)	Retrospective case–control	ICU stay – 1.2; Mobilization – 1; Enteral feeding – 3 Foley's removal – 3; NG removal – 5; ICD removal – 5 Oral feed – 10	Compliance (%) – NA LOH (days)– 9 Mortality (%) – 0; Morbidity (%) – 27 Readmission (%) – 0
Pan et al(13) (2014)	Retrospective case–control	ICU stay – avoided; Mobilization –2 Enteral feeding – 0 Foley's removal – 3; NG removal– avoided; ICD removal– 3 Oral feed – 2	Compliance (%) – NA LOH (days)– 7 Mortality (%) – 0; Morbidity (%) – 29 Readmission (%) – 7.5
Ford et al(31) (2014)	Prospective cohort	ICU stay – 1; Mobilization –1 Enteral feeding –1 Foley's removal – 3; NG removal – 5; ICD removal – 5 Oral feed – 6	Compliance (%) – NA LOH (days)– 10 Mortality (%) – 0; Morbidity (%) – 64 Readmission (%) – 13
Cao et al(14) (2013)	Retrospective case–control	ICU stay – avoided Mobilization – 1 Enteral feeding – 1 Foley's removal – 1; NG removal – avoided; ICD removal – 3 Oral feed – 4	Compliance (%) – 73 LOH (days)– 7.7 Mortality (%) – 1.8; Morbidity (%) – 29 Readmission (%) – 3.6

Blom et al(28) (2013)	Retrospective case–control	ICU stay – 1 Mobilization – NA Enteral feeding – 0 Foley's removal – NA; NG removal – 2; ICD removal –2 Oral feed – 5	Compliance (%) – 42–93 LOH (days)– 14 Mortality (%) – 4; Morbidity (%) – 71 Readmission (%) – 9.7
Li et al(23) (2012)	Retrospective case–control	ICU stay – avoided; Mobilization – 1; Enteral feeding – NA Foley's removal – 2; NG removal – 2; ICD removal – 5 Oral feed – 3	Compliance (%) – NA LOH (days)– 8 Mortality (%) – 2; Morbidity (%) – 62 Readmission (%) – 5
Munitiz et al(27) (2010)	Retrospective case–control	ICU stay – 3; Mobilization – 2; Enteral feeding – 5 Foley's removal – 4; NG removal – 5; ICD removal – 4 Oral feed – 5	Compliance (%) – 59 LOH (days)– 9 Mortality (%) – 1; Morbidity (%) – 31 Readmission (%) – 0
Jiang et al(22) (2009)	Retrospective observational	ICU stay – avoided; Mobilization – 2 Enteral feeding – 2 Foley's removal – 2; NG removal – 3; ICD removal – 4 Oral feed – 5	Compliance (%) – 88 LOH (days)– 7 Mortality (%) – 2.6; Morbidity (%) – 64 Readmission (%) – 4
Low et al(25) (2007)	Retrospective observational	ICU stay – 1; Mobilization – 1 Enteral feeding – 3 Foley's removal – NA; NG removal – 5–6; ICD removal – 3–5 Oral feed – 5–6	Compliance (%) – 88 LOH (days)– 7 Mortality (%) – 0.3; Morbidity (%) – 45 Readmission (%) – 4
Cerfolio et al(8) (2004)	Retrospective observational	ICU stay – 1; Mobilization – 1 Enteral feeding – 1 Foley's removal – 3; NG removal – 3; ICD removal – 3 Oral feed – 5	Compliance (%) – 76 LOH (days)– 7 Mortality (%) – 4; Morbidity (%) – 26 Readmission (%) – 4.4

[NG: Nasogastric; RCT: Randomized controlled trial; LOH: Length of hospital stay; ICU: Intensive care unit; NA: Not available]

Table 2: Studies on outcomes of nasogastric tube exclusion in Esophagectomy

Author	Design	Program	Findings
Nguyen et al(15) (2009)	Retrospective	NG tube– 98 No NG tube –26	Anastomotic leak – 7.7% vs. 9.2 % Mortality (%) – NA Pulmonary complications – NA
Daryaei et al (16) (2009)	RCT	NG tube– 22 No NG tube –18	Anastomotic leak – 6 vs 0 Pulmonary complications–no difference Wound infection– no difference NG reinsertion– no difference
Mistry et al(17) (2012)	RCT	Conventional NGT group– POD 6 –10 Early removal NGT group – POD 2	Anastomotic leak – no difference Pulmonary complications – p=0.8 NG reinsertion – 30.7 vs 9.3 % (p=0.006) Patient discomfort – 34.4 % vs 13.3 % (p=0.001)
Hayashi et al(19) (2019)	RCT	Conventional NGT group – POD 7 Early removal NGT group– POD 1	Anastomotic leak – 2.7% vs 8.8 % Pulmonary complications – 21.6 % vs 20.6 % NG reinsertion– 2.7 % vs 2.9 % LOH– 29 days vs 25 days Major Clavien Dindo grade – 24.3 % vs 8.8 %

[RCT: Randomized control trial; NG: Nasogastric; LOH: Length of hospital stay; NA: Not available]

RESEARCH QUESTION AND AIMS AND OBJECTIVES

Research question: Whether Nasogastric tube exclusion in ERAS protocol after minimally invasive esophagectomy increases the risk of cervical esophagogastric anastomotic leak and pulmonary complications without increasing the total length of hospital stay?

Aim of the study: To evaluate the impact of nasogastric tube exclusion under the setting of enhanced recovery pathways on postoperative outcomes following minimally invasive esophagectomy for carcinoma of the esophagus.

Objectives

Primary objective: To evaluate the effect of nasogastric tube exclusion on cervical esophagogastric anastomotic leak

Secondary objectives: To determine the effect of nasogastric tube exclusion on

1. Incidence of Pulmonary complications
2. Commencement of oral feeding
3. Length of hospital stay
4. 30–day readmission rate
5. Incidence of NGT reinsertion
6. 30–day mortality rate

MATERIALS AND METHODS

Study setting

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

Duration of study

From 1st January 2021 to 31st December 2022, patient recruitment was done till October 2022.

Sample size:

Due to the time–bound nature of the study and the influence of the Covid–19 pandemic, 20 patients who underwent esophagectomy for carcinoma of the esophagus with NGT exclusion were prospectively included in the study from 1st January 2021 to October 2022.

Study design

This was a single–center prospective cohort study. All the patients undergoing MIE within the study period without any exclusion criteria features were managed according to the ERAS protocol with NGT exclusion. The data were assessed for the cervical esophagogastric anastomotic leak, length of postoperative stay, postoperative pulmonary complications, the incidence of NGT reinsertion, mortality within 30 days of surgery, and 30–day readmission rates.

Patient evaluation and management:

Patients were evaluated in our outpatient department (OPD). Detailed history, including the onset, grade & duration of dysphagia, loss of weight & appetite, hoarseness of voice, regurgitation, addictions, and comorbidities, were taken. Dysphagia was graded according to modified Takita grading (I– has the ability 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, and VI – complete dysphagia). This was followed by a detailed clinical examination and nutritional assessment.(77)

Upper gastrointestinal tract endoscopy (UGIE) and biopsy were done to confirm the diagnosis. Staging of the tumor was done with contrast–enhanced computed tomography (CECT) of the neck, chest, and abdomen. Enteral nutrition was given through NGT or FJ in patients with more than grade 4 dysphagia and malnourishment or patients planned for neoadjuvant treatment. Patients received neoadjuvant chemotherapy or chemoradiotherapy after a multidisciplinary tumor board discussion according to standard protocol. Patients who underwent neoadjuvant treatment were re–assessed after four weeks of completion of therapy with repeat CECT neck, thorax, and abdomen or whole–body positron emission tomography (PET) –CT scan, and resectability was assessed and planned for surgery.

All patients and their relatives were counselled about the procedure and were given an outline of the protocol, and informed written consent was obtained. A pre–operative evaluation was done with a routine pre–anesthetic checkup, echocardiography, and pulmonary function test. Chest physiotherapy with incentive spirometry was given to all patients. Patients were kept nil per oral for a solid diet 6

hours before surgery. Carbohydrate loading was given with 10% dextrose 12 hours prior (800 ml) and 2 hours prior (400 ml) to surgery or preformed nutritional supplement either orally or through FJ. After placing the thoracic epidural catheter, patients were put in the prone position. Thoracoscopic procedures were done with three ports in the 5^{th}, 7^{th} and 9^{th} intercostals spaces (ICS), while in robotic procedures, an extra port was placed in the 9th ICS (mid–axillary line). Standard minimally invasive McKeown esophagectomy with modified two–field dissection was performed in all patients. The azygos vein was divided routinely, and the thoracic duct was preserved. Once the thoracic phase was completed, an intercostal drainage (ICD) tube was placed, and the patient was repositioned to supine.

The abdominal phase was done through an open, laparoscopic, or robotically assisted approach. The stomach was mobilized along the greater curvature, preserving the gastroepiploic arcade. Left gastric vessels were ligated and divided. A gastric conduit of ~3–4 cm wide was created using a linear cutting stapler (NTLC, Ethicon, J&J, US). The left side of the neck was opened by a 'J–shaped' incision parallel to the sternocleidomastoid muscle. Strap muscles were cut, and the middle thyroid vein, if present, was divided between ligatures. Then, the cervical esophagus was mobilized and cut. The specimen was delivered through the abdomen, and the conduit was taken to the neck orthotopically. The cervical esophagogastric anastomosis (CEGA) was done by semi–mechanical (modified collard technique) in all patients. Feeding jejunostomy was placed by the Witzel technique. Intraoperatively goal–directed fluid therapy was given with a target of around 1 ml/kg/hour urine output and mean arterial pressure of 65 mmHg. ERAS protocols were followed in all patients. NGT was not inserted during CEGA.

Inclusion criteria

1. Biopsy–proven case of carcinoma of the esophagus and gastroesophageal junction (Siewert type I & II)

2. Managed by minimally invasive McKeown esophagectomy, either robotic or thoracoscopic

3. ASA I & II

Exclusion criteria

1. Esophagectomy for benign disease

2. Intraoperative conversion to thoracotomy

3. Ivor–Lewis esophagectomy with intrathoracic anastomosis

4. ASA 3 or higher

5. Siewert type III tumors

ERAS protocol

1. Preoperative

    a. Preoperative counseling for a minimum of 20 minutes

    b. Inspiratory muscle training, including incentive spirometry 15 times fourth hourly one week before surgery

    c. Preoperative isotonic carbohydrate drink 800 ml 12 hours and 400 ml 2–3 hours (to be drunk in 20 minutes) or preformed nutritional

supplement before surgery in all patients except uncontrolled diabetes mellitus (HbA1c >7)

d. Thromboprophylaxis (combined mechanical and pharmacological) – LMWH 12 hr before surgery and TED (thromboembolic deterrent) stockings.

2. Intraoperative

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 intraoperatively and adding vasopressor when mean blood pressure drops by 20%

d. No NGT, neck drain, and abdominal drain inserted at the end of the procedure

3. Postoperative

a. Immediate extubation after surgery or extubation as early as possible

b. Shifting the patient to a high dependency unit and then to a 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. Chest X–ray

iii. FJ feed 1 liter at 40 ml/hour

iv. Saline nebulization and steam inhalation sixth hourly

v. Incentive spirometry ten times each hour while awake

vi. Out of bed 1 hour morning and 1 hour evening

vii. Assisted walking

viii. Start LMWH

e. POD 2

i. Remove urinary catheter

ii. Remove epidural catheter

iii. FJ feed 2 liters' full strength at 60–80 ml/ hour

iv. Negative fluid balance

v. Stop intravenous fluids

vi. Out of bed for 4 hours

vii. Assisted walking 2 walks 100 meters

viii. Incentive spirometry ten times/hour while awake

ix. Steam inhalation and saline nebulization sixth hourly

f. POD 3

i. Remove central line

ii. Remove ICD if output <200 ml/24 hours

iii. FJ feed 2 liters at 80 ml/hour

iv. Out of bed for 4 hours

v. Assisted / non–assisted 3–4 walks 150 meters

vi. Incentive spirometry ten times/hour while awake

vii. Steam inhalation and saline nebulization 6^{th} hourly

g. POD 4

i. Oral contrast study with non–ionic contrast (iohexol) (POD 5 if POD 4 is Sunday)

ii. Allow oral clear liquids if the contrast study shows no leak

iii. FJ feed 2 liters at 80 ml/hour

iv. Non–assisted 3–4 walks 150 meters

v. Incentive spirometry ten times/hour while awake

vi. Steam inhalation and saline nebulization 6th hourly

vii. Stop LMWH

h. POD 5

i. Oral liquids/semi–solids

ii. FJ 1 liter at 80 ml/hour

iii. Non–assisted 3–4 walks 150 meters

iv. Incentive spirometry ten times/hour while awake

v. Steam inhalation and saline nebulization 6th hourly

vi. Discharge the patient

A margin of 1–2 days will be allowed for each component.

Figure 1: Diagrammatic representation of our ERAS protocol

Data collection

Demography, clinicopathological characteristics, radiological parameters, details of all ERAS protocols followed, length of hospital stay, 30–day readmission, and 30–day mortality rates were recorded. The complications of esophagectomy were recorded according to the Esophagectomy Complications Consensus Group (ECCG).

Discharge criteria

1. Vital signs within normal limit
2. Patient is taking oral semisolids
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

All patients were seen at follow–up out–patient clinics 10–14 days and 30 days after the surgery. Patients could contact us telephonically at any time.

Statistical analysis

All data were acquired in a specified format as in proforma and entered in Statistical Package for Social Studies v 23.0 (IBM Corp, United States). 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 was applicable and numerical data were compared

using the Mann–Whitney U test. A two–tailed *p–value* ≤0.05 was considered significant.

Ethical considerations

All the patients enrolled in the study received standard care management, and their participation in the study did not led to any change in their usual diagnostic work up, follow–up, or management. All personal data collected during the study were kept strictly confidential. Patients who refused consent for participation in the study received the standard treatment. There were no additional costs to the patient due to their participation in the study.

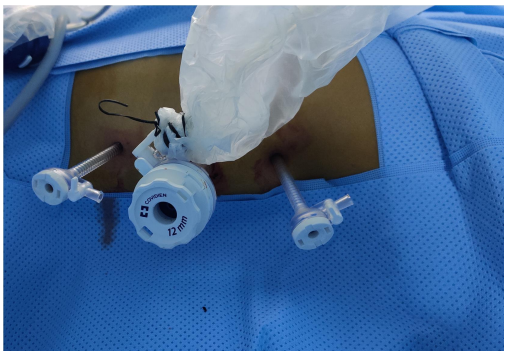


Figure 2: Port position in thoracoscopic phase.

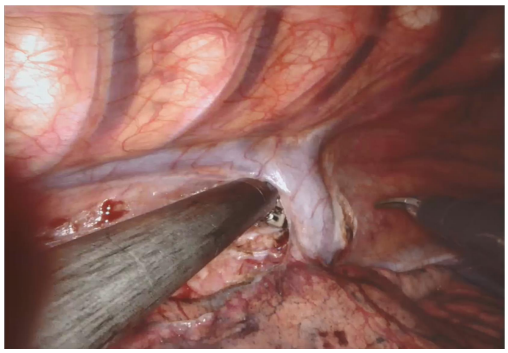


Figure 3: Dissection of arch of azygos vein

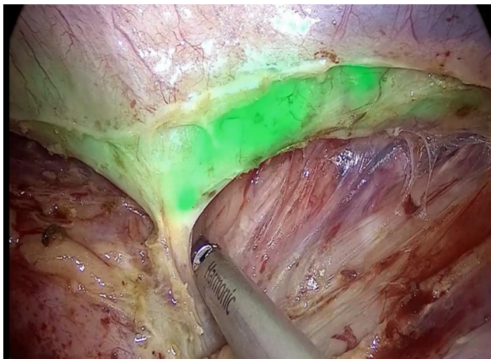


Figure 4: Thoracic duct visualization with Indocyanine green near infra-red spectroscopy (ICG: NIRS)

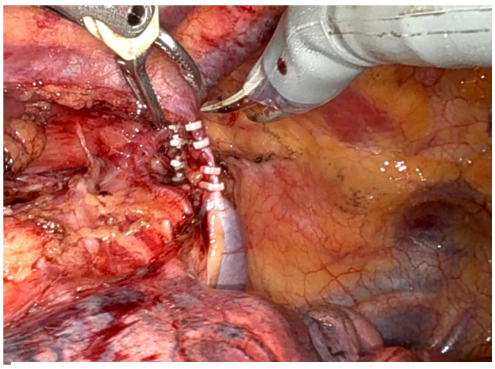


Figure 5: Clipping and dividing Azygos vein

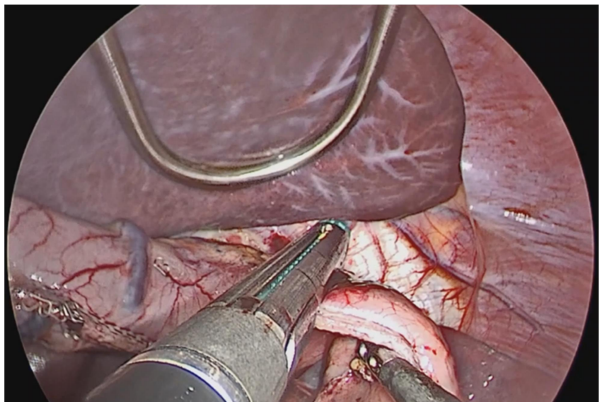


Figure 6: Laparoscopic creation of gastric conduit

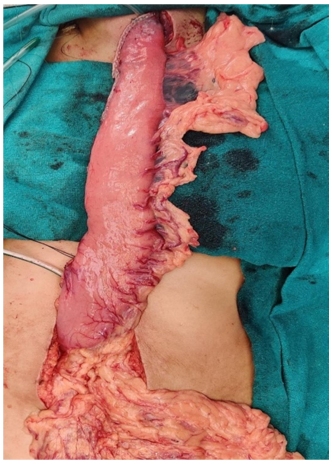


Figure 7: Gastric conduit

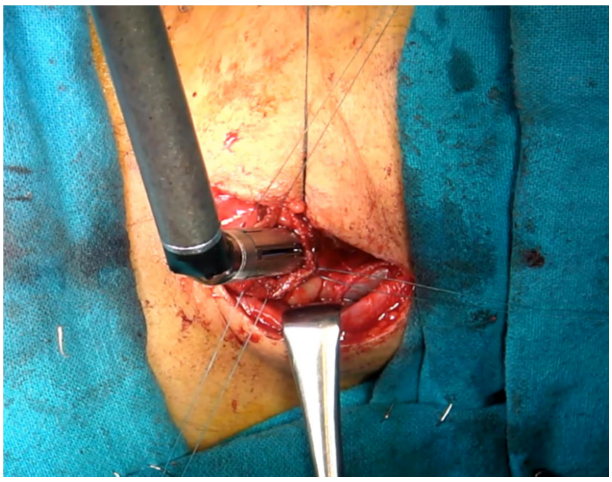


Figure 8: Semi–mechanical CEGA

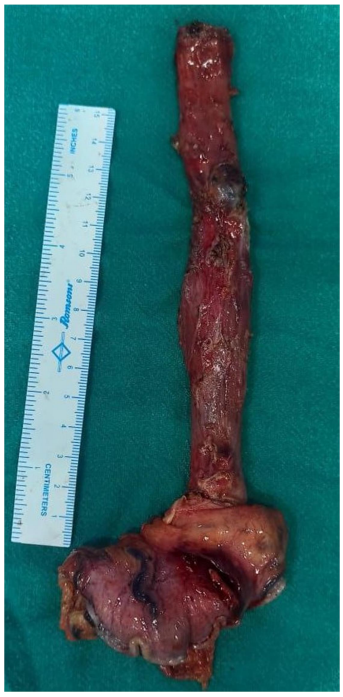


Figure 9: Esophagectomy specimen

RESULTS

Thirty–five patients with carcinoma of the esophagus were screened for the study during the study period from January 2021 to August 2022. Out of the 35, 7 patients were excluded from the study as NGT was inserted in these patients due to the surgeon's preference. Further, 5 patients were excluded as they underwent Ivor–Lewis esophagectomy, 1 patient had conduit necrosis, and 2 patients died in the immediate postoperative period due to intraoperative cardiac event (Figure 11).

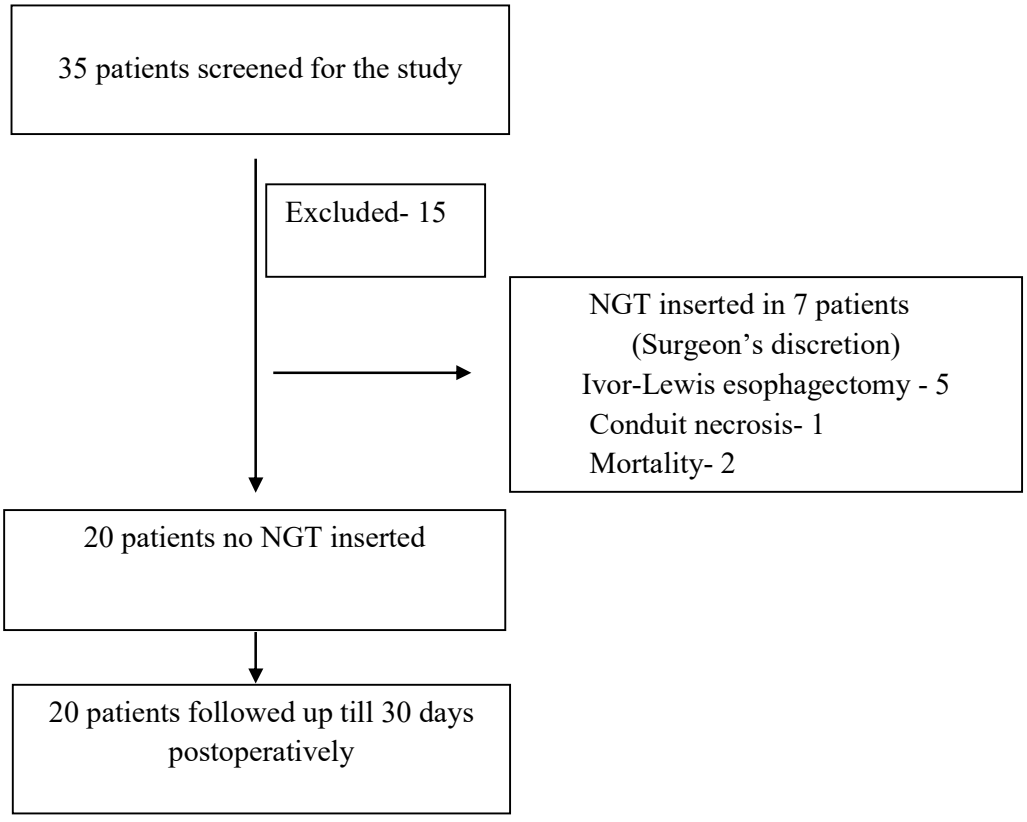


Figure 10: Study flow diagram

Baseline characteristics (Table 3):

Out of 20 patients studied, 11 (55%) were males. The median age (IQR) of the study population was 48.5 (40–60.5) years. All patients presented with dysphagia with

loss of weight (n=16, 80%) and loss of appetite (n=12, 60%). All 20 patients had squamous cell carcinoma of the esophagus, with 50% of tumors in the mid and distal thoracic esophagus, respectively. The majority of the patients had a performance status of ECOG grade 1 (n=19, 95%), and the median (IQR) body mass index (BMI) of the population was 21.5 (18.4–21.6) kg/m^2. The median (IQR) preoperative albumin level was 2.6 (2.3–2.9) mg/dl, and preoperative nutritional intervention through NG tube or FJ was done in 15% (n=3) of patients. All 20 (100%) patients received neoadjuvant therapy, 55% (n=11) received neoadjuvant chemoradiotherapy, and 45% (n=9) received neoadjuvant chemotherapy. Final pathological staging was stage I in 60% (n=12), stage II in 25% (n=5) and stage III in 15 %(n=3) of patients.

Table 3 : Baseline characteristics

Characteristics	n=20
Age [years, median(IQR)]	48.5 (40–60.5)
Gender	
Male, n (%)	11(55)
Female, n (%)	9 (45)
Presenting symptoms	
Dysphagia, n (%)	20 (100)
Loss of weight, n (%)	17 (85)
Loss of appetite, n (%)	13(65)
Addictions, n (%)	
Alcohol	4(20)
Smoking	5(25)
Tobacco chewing	8(40)
Comorbidity, n (%)	
Hypertension	4(20)
Diabetes mellitus	2 (10)
Coronary Artery Disease (CAD)	1(5)

Chronic obstructive pulmonary disease (COPD)	1(5)
Pulmonary Tuberculosis	1(5)
Histology	
SCC, n (%)	20 (100)
Tumor location	
Mid thoracic, n (%)	10 (50)
Lower thoracic, n (%)	10 (50)
ECOG score	
1	19 (95)
II	1 (5)
Grade of dysphagia, n (%)	
I	1 (5)
II	11(55)
III	4(20)
IV	2(10)
V	2 (10)
BMI [Kg/m2, median (IQR)]	21.5 (18.4, 21.6)
Preoperative albumin level [g/dl, median (IQR)]	2.6 (2.3–2.9)
Preoperative tube feeding, n (%)	3 (15)
Neoadjuvant therapy, n (%)	20 (100)
NACT, n (%)	9 (45)
NACRT, n (%)	11 (55)
Interval between neoadjuvant therapy and surgery [days, median (IQR)]	35 (29.25–51.75)
TNM (pathological stage)	
I	12 (60)
II	5 (25)
III	3 (15)

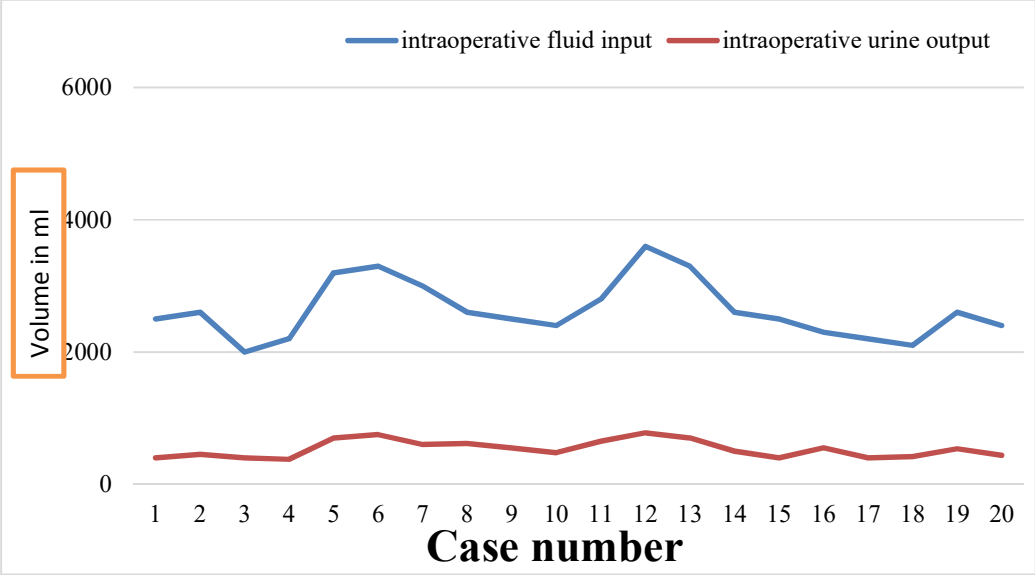
Intra–operative characteristics (Table 4):

The most common type of surgery performed was thoracoscopic assisted (n= 15, 75%), and 5 patients were operated by robotic–assisted. The median (IQR) duration of

surgery was 420 (360–480) minutes. Median (IQR) blood loss was 200 (175–300) ml, and median (IQR) amount of intraoperative fluid infused and urine output were 2550 (2350–2900) ml and 520 (410–635) ml, respectively (table 4, graph 1). Inotropes were used intraoperatively in half of the cases. The semi–mechanical cervical esophagogastric anastomosis was done in all 20 patients. Ninety per cent (n=18) of patients could be extubated immediately.

Table 4: Intra–operative characteristics

Characteristics	n=20
Type of surgery	
Thoracoscopic (%)	15(75)
Robotic n (%)	5 (25)
Type of cervical anastomosis	
Semi–mechanical, n (%)	20 (100)
Intraoperative blood loss [ml, median (IQR)]	200 (175, 300)
Duration of surgery [minutes, median (IQR)]	420 (360–480)
Intraoperative fluid transfusion [ml, median (IQR)]	2550 (2350–2900)
Intraoperative urine output [ml, median (IQR)]	520 (410–635)
Intraoperative inotrope usage, n (%)	10 (50)
Immediate extubation, n (%)	18 (90)



Graph 1: Graphical representation of intra–operative input–output

Outcomes

Primary and secondary outcomes (Table 5)

Anastomotic leak was present in 10% (n=2) cases, both had grade I anastomotic leak, and could be managed conservatively. Median (IQR) postoperative hospital stay was 6 (5.0–7.0) (table 5). One (5%) patient had to be readmitted within 30 days of discharge owing to poor intake due to an anastomotic leak. There was no mortality during the study period. Overall morbidity was seen in 40% (n=8), with major morbidity (Clavien–Dindo ≥3) in 5% (n=1). One patient developed postoperative pneumonia with pleural effusion, requiring oxygen support and chest tube insertion. One patient (5%) had conduit dilation for which NGT was reinserted. None of the patients developed chylothorax.

Table 5: Primary and secondary outcomes

Outcomes	n=20 (%)
Anastomotic leak (CEGA)– ECCG	2 (10)
1. Grade I	2 (10)
2. Grade II	0
3. Grade III	0
Pulmonary complications	5 (25)
30–day mortality, n (%)	0
Length of hospital stay(days), Median (IQR)	6 (5–7)
NGT reinsertion	1 (5)
30–day readmission rate	1 (5)
Chylothorax	0
Clavien–Dindo grade of complications	
1	1(5)
2	6(10)
≥ 3A	1(5)

Other outcomes (Table 6)

The median (IQR) days of ICU stay was 1 (0.0, 1.0) day, and ICU stay could be avoided in 80% (n=16) of cases. The median (IQR) POD for initiation of mobilization, enteral feeding, and chest physiotherapy was 1 (1.0, 1.0), and the urinary catheter was removed on a median (IQR) POD of 2 (2.0–3.0). ICD was removed on median (IQR) POD of 4 (3.0–4.0). Oral feeds were started on a median (IQR) POD of 4 (4.0, 5.0) after the oral contrast study with non–ionic contrast (iohexol), and 6 patients had mild aspiration. Oral soft diet were started directly in patients with aspiration with no evidence of anastomotic leak.

Table 6: Other outcomes

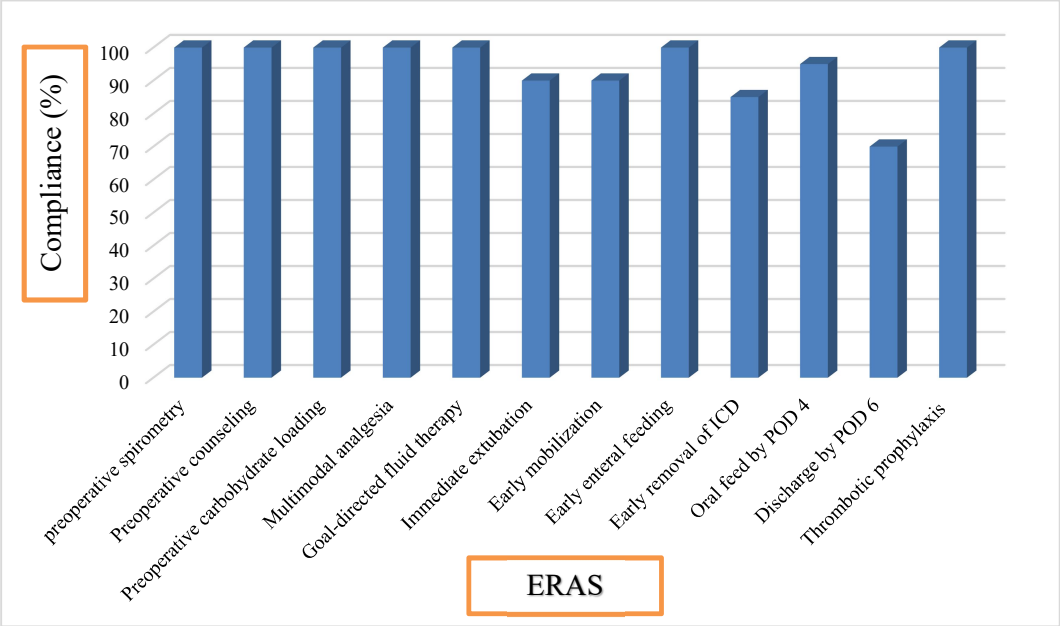
Outcomes	n=20
Patients requiring postoperative ICU stay, n (%)	4 (20)
Duration of ICU stay [days, median (IQR)]	1(0–1)
Day of initiation of chest physiotherapy [POD, median (IQR)]	1 (1–1)
Day of initiation of mobilization [POD, median (IQR)]	1 (1–1)
Day of initiation of enteral feed [POD, median (IQR)]	1 (1–1)
Day of urinary catheter removal [POD, median (IQR)]	2 (2–3)
Oral contrast study [POD, median (IQR)]	4 (4–5)
Day of initiation of oral feed [POD, median (IQR)]	4 (4–5)
Day of ICD removal [POD, median (IQR)]	4 (3–4)

Compliance with ERAS protocol (Table 7)

Compliance with each arm of the protocol ranged from 70% to 100% (table 7, graph 2). Preoperative counselling, carbohydrate loading, thromboprophylaxis, and incentive spirometry were followed in all patients (100%). Goal–directed fluid therapy was followed in all patients, and immediate extubation was possible in 90% of cases. Initiation of oral feed by POD 4 was possible in 95% of cases. 70% of patients were discharged by POD 6. More than 75% of the protocol could be followed in 90% (n=18) of the study population.

Table 7: Compliance with ERAS protocol

Components [n (%)]	Followed
Preoperative spirometry, n (%)	20(100)
Preoperative counseling, n (%)	20 (100)
Preoperative carbohydrate loading, n (%)	20 (100)
Multimodal analgesia, n (%)	20 (100)
Goal–directed fluid therapy, n (%)	20 (100)
Immediate extubation	18 (90)
Early mobilization, n (%)	18 (90)
Early enteral feeding, n (%)	20(100)
Early removal of ICD, n (%)	17 (85)
Oral feed by POD 4, n (%)	19 (95)
Discharge by POD 6, n (%)	14 (70)
Thrombotic prophylaxis, n (%)	20 (100)



Graph 2: Compliance with ERAS protocol

DISCUSSION

Fast–track recovery protocols, like ERAS, are now well established to improve outcomes after esophagectomy compared to the traditional standard of care. Since the inception of the fast–track protocol by Cerfolio et al.(8) in esophagectomy, there have been many modifications to improve the outcomes without increasing complications. Recently, ERAS guidelines for esophagectomy in 2018 advised the routine placement of NGT in the period with early removal by POD 3.(20)

However, a retrospective study by Nguyen et al.(15) comparing the NGT group with no NGT found that the anastomotic leak rate was insignificant between the two groups (7.7% vs. 9.2 %) among patients who underwent open Mckeown's esophagectomy. Further, an RCT by Daryaei et al.(16) comparing the NGT group versus no NGT with the Metoclopramide group found that anastomotic leak was more in the NGT group (6 vs. 0 cases, $p<0.02$). Another RCT by Mistry et al.(17) comparing the conventional group (POD 6–10) with the early removal group (POD 2) of NGT found no difference in the anastomotic leak. Single center RCT by Hayashi et al.(19) comparing the conventional group (POD 7) with the early removal group (POD 1) of NGT found no difference in the anastomotic leak (2.7% vs 8.8, $p=0.34$).

Our study prospectively analyzed the impact of NGT exclusion following MIE (McKeown's) on anastomotic leak (CEGA) and pulmonary complications keeping all other parameters of the ERAS pathway constant. In our analysis, the anastomotic leak rate was 10%, which is consistent with the literature.(3) Hence, routine use of nasogastric decompression seems to increase patient discomfort, and avoiding NGT does not increase anastomotic complications. Comparison of various studies on outcomes of NGT decompression is shown in table 8.

A meta–analysis of 7 studies on nasogastric decompression following esophagectomy found no significant difference in the anastomotic leak rate.(36) The study included four RCTs and three comparative cohort studies comparing the conventional group of NGT with the no NGT group. However, the numbers were small and studies included were heterogenous in surgical procedures and peri–operative measures, and ERAS protocol was not followed in all studies. The advantage of our study is that the population analyzed was homogenous, with all patients undergoing MIE, and ERAS protocol followed uniformly, increasing the authenticity of the results.

Although anastomotic leak rates are similar in both hand–sewn and stapled anastomotic techniques after CEGA, patients having anastomotic leak develop more often anastomotic stricture after hand–sewn anastomosis compared to the stapled anastomosis.(78) The meta–analysis of 13 RCTs comparing hand–sewn versus stapled CEGA have shown no significant difference in the anastomotic leak rate.(78) The peculiarity of our study is that all patients underwent the same semi–mechanical anastomosis with pyloric ring fracturing.

Table 8: Outcomes of NGT decompression on complications in various studies

Study	NGT removal Mean days $\pm SD$	NGT reinserted	Anastomotic location	Anastomotic type	Anastomotic leak	Pulmonary complications	Length of stay (mean $\pm SD$) or median (IQR) days
Daryaei 2009(16) (n=40)	I:4.2$\pm$1.3 / II :0	I:0 / II: 1	Cervical	Hand–sewn	I : 27% / II: 0 p=0.01	I: 0 / II : 11%	I: 10 ($\pm$3.5) / II: 13 ($\pm$8.2)
Mistry 2012(17) (n–150)	I :6–10 / II : 2	I: 7 / II: 23	Cervical	Hand–sewn, stapled	I:11% / II: 8% p= 0.81	I: 33% / II: 24%	I:25 ($\pm$ 18) / II: 27 ($\pm$ 12)
Hayashi 2019(19) (n–75)	I :7 / II: 1	I:1 / II: 1	Cervical	Hand–sewn	I: 2.7 % / II: 8.8% p= 0.26	I: 21% / II: 22%	I: 12 (10–17)/ II: 12 (9–17)
Our study (n–20)	**II: 0**	**II: 1**	**Cervical**	**stapled**	**II: 10%**	**II: 25%**	**II: 6 (5–7)**
I: NGT group ; II: No NGT group							

Pulmonary complications are the most common complication reported after esophagectomy and are the leading cause of mortality.(8,13) The implementation of the ERAS protocol by Shewale et al.(5) found significantly less acute respiratory distress syndrome, re–intubation, atrial arrhythmia requiring treatment, and overall pulmonary complications. Munitiz et al.(27) observed significantly fewer pulmonary complications in the ERAS protocol group than in the conventional group (14% vs 23 %, p=0.02). The use of NGT following upper gastrointestinal surgeries has been found to cause a higher incidence of pulmonary complications because they decrease the adequate clearance of pulmonary secretions and increase the risk of aspiration.(79) However, a meta–analysis by Weijs et al.(36) found that early removal or no NGT insertion had no impact on pulmonary complications compared to standard NGT removal on POD 6–10. In our study, we observed pulmonary complications in 25% of the patients despite following the ERAS protocol, which was slightly high as compared to the literature. Six patients had aspiration on oral contrast study due to transient vocal cord palsy. However, only four patients developed pneumonia requiring minimal oxygen support with the upgradation of intravenous (IV) antibiotics and aggressive chest physiotherapy. One patient developed pneumonia with massive pleural effusion requiring chest tube insertion. All five patients were managed conservatively, and 3 patients had prolonged LOS. Since all our patients were operated on during the COVID–19 pandemic, whether it had a causal link with pulmonary complications is debatable, as patients were also chronic smokers with pre–existing COPD, which may have led to additional pulmonary issues. Further, the increased pulmonary complications is linked to the omission of NGT may require further evaluation by a large sample size.

The median (IQR) hospital stay in our study was 6 (6.0 – 7.0) days. In the available literature, the average LOS after MIE was eight days.(80) In our study, avoiding NGT in the postoperative period reduced patient discomfort with improved compliance to ERAS protocol

allowing for early ambulation, early removal of chest tubes & urinary catheters, and early oral intake with better pulmonary toileting, thereby reducing the complications which might have lead to reduced length of hospital stay. A meta–analysis by Weijs et al.(36) of 4 RCTs and 3 retrospective studies found that hospital stay was significantly shorter with preoperative or early removal of NGT when all trials were included but not when limited to RCTs. However, a recent meta–analysis by Kaaki et al.(37) of six RCTs found that early removal of NGT has no impact on LOS, whereas early oral intake found shorter LOS. A meta–analysis of 13 studies on ERAS protocol in esophagectomy found a significant reduction in LOS with a mean difference of –3.55 (95% CI –4.41 to –2.69) days.(35) The positive impact on LOS in ERAS protocol was found only in patients without any peri–operative complications or with only minor complications. In addition, a fast–track protocol could decrease hospital expenditure associated with both primary and readmission within 90 days of surgery.(5)

In our study, the only significant factor associated with prolonged LOS was major complications, which were not influenced by neoadjuvant therapy. Three patients in our study had prolonged hospital stays, one required 22 days, and the other two required 13 and 11 days, respectively. Overall morbidity in our study was 40%, with a major morbidity rate of 5%. In literature, overall morbidity after esophagectomy ranges between 26–71%.(4,8,12,22,28,30) One of the recent meta–analyses found a similar complication rate between ERAS and traditional treatment protocol following esophagectomy; however, patients in the ERAS group had lesser nonsurgical and pulmonary complications.(35) This difference in finding about complication rate in literature may be because postoperative complications occur due to a variety of reasons and all of which are not addressed by ERAS pathways.

The most common complications reported are pneumonia and arrhythmia.(3) Chylothorax though rare, is a dreaded complication after esophagectomy. Its incidence ranges between 0.5% to 4%, and factors like an incomplete response to neoadjuvant therapy, difficult mediastinal dissection, and tumour location were associated with the risk of postoperative chylothorax.(3,81) In our study, none of our patients had developed chylothorax and cardiac complications. We have previously published our experience regarding the utility of the ICG–NIRS system in preventing chylothorax.(82) No chyle leak in our study is attributed to the routine use of ICG–NIRS system for identification of the thoracic duct by intranodal injection of ICG during the thoracic phase, thereby preventing its injury.

The readmission rate after esophagectomy is higher than most other oncological surgeries, varying between 2.5% to 25%, and is similar between ERAS and conventional care groups.(12,22,23,31) Thrity–day readmission rate has been considered an important outcome indicator after esophagectomy.(83) Park et al.(84) found that anastomotic leaks were associated with increased readmission rate, but vocal cord palsy, neoadjuvant therapy, age, and pathological stage were not. One (5%) of our patients had to be readmitted on POD–14 within 30 days of discharge due to an anastomotic leak with poor intake despite the oral contrst study was normal on POD 4. The patient was managed conservatively with NPO and enteral nutrition via FJ following which he was discharged with an uneventful course.

Gastroparesis is not uncommon after esophagectomy and can lead to gastric conduit dilatation. Delayed gastric emptying (DGE) is a major complication following esophagectomy in 15–39% of patients.(85–87) Post esophagectomy DGE is multifactorial with a combination of anatomical and physiological changes, which includes unfavorable pressure gradient (negative intrathoracic pressure, positive abdominal pressure),

dysfunctional peristalsis (complete vagotomy), dysfunctional relaxation of the pylorus and redundant gastric conduit. Among the interventions, pyloromyotomy and pyloroplasty are the most commonly performed procedures to reduce DGE. In a study by Deng et al. pyloric finger fracture could effectively decrease the risk of DGE without long–term complications like dumping syndrome and bile reflux.(88) A systematic review including all different pyloric interventions has shown a non–significant trend toward a lower risk of DGE.(89) However, in the study, significant heterogeneity existed among the different pyloric interventions.

Gravity is the key factor driving gastric emptying in the early period, as the gastric contraction and viscous force are negligible. Hence, DGE decreases as the diameter of the gastric conduit decreases. In the retrospective study by Nguyen et al.,(15) and RCT by Daryaei et al.,(16) one patient in no NGT group required NGT reinsertion for gastric conduit dilatation. In an RCT by Mistry et al.(17) comparing early removal of NGT (POD 2) with late removal of NGT (POD 7), 23 (30%) patients out of 75 required NGT reinsertion. In the late removal group, 7 (9.3%) patients out of 75 required NGT reinsertion. In their study, NGT reinsertion was most commonly required for gastric conduit dilatation (12%), repeated vomiting (10%), anastomotic leak (5.3%), and postoperative ileus (2.7%). In an RCT by Hayashi et al.(19) comparing early removal of NGT (POD 1) with delayed removal (POD 7), 1 patient in both NGT and no NGT group required reinsertion. In our study, 1 (5%) of 20 patients required NGT reinsertion for conduit dilatation, resolved with conservative management. Further, pyloric finger fracture was done in all patients, and the conduit diameter was ~4 cm. The decreased conduit diameter and intraoperative pyloric dilatation by the pyloric finger fracture technique may explain the low DGE in our patients. However, RCT is required to evaluate the efficacy of pyloric finger fracture in reducing DGE.

Retention of NGT in the postoperative period prevents effective coughing and expectoration, compromising pulmonary hygiene and increasing the patient's discomfort. A Cochrane review of 37 randomized controlled trials of nasogastric decompression after abdominal surgery strongly indicated that its routine placement of NGT was associated with inherent risk like throat pain, nasal mucosal damage, sinusitis, and epistaxis without any added benefit.(10) A RCT by Mistry et al. (17) found that following esophagectomy NGT early removal had less patient discomfort. They assessed the patient discomfort by a simple patient–reported score on the day of NGT removal. As the patients are not uncomfortable in the postoperative period, it allows for early ambulation and oral intake. In a meta–analysis by Hester et al.(90) of nasogastric intubation after abdominal surgery, discomfort due to NGT was reported in 60% of the pateints. In their study, patients in no NGT group had short LOS. In our study, as NGT was not inserted postoperatively, assessing the patient discomfort using the questionnaire was not feasible. In our study, avoiding the NGT postoperatively reduced the patient discomfort with better compliance to ERAS protocol which could have contributed to reduced length of hospital stay.

Early enteral nutrition via FJ or nasojejunal (NJ) tube is essential to reduce malnutrition–related complications.(21) Early enteral feeding was associated with lesser time to pass the first flatus.(13) We started enteral feed via FJ on POD 1 itself and gradually increased the feed to meet the caloric requirement by POD 3. Further, several reviews and meta–analyses have shown that early oral feeding (EOF) is also a safe practice without any significant increase in complications in a patient undergoing colonic and gastric surgery.(91) However, many surgeons are reluctant to practice EOF following esophagectomy due to the risk of anastomotic leak and aspiration pneumonia. EOF benefits patients by improving the recovery of gut function, protecting the gut mucosal barrier, and strengthening the immune response. In a randomized controlled non–inferiority trial, patients in EOF (POD 1) following

Mckeown's esophagectomy had similar complications to the late oral feeding (LOF) group (POD 7).(70) Patients in the EOF group had a significantly shorter time to pass flatus and bowel movements compared to LOF. The length of postoperative hospital stay was significantly less in the EOF group compared to the LOF group. A meta–analysis of 2 RCTs by Kaaki et al.(37) has shown that EOF does not increase the risk of anastomotic leak and aspiration pneumonia. In our study, orals were initiated on POD 4 after the oral contrast study confirmed no CEGA leak. As our study is the first in our population to completely eliminate NGT in the perioperative protocol, we were cautious about initiating EOF. However, after the positive results that NGT exclusion did not affect the anastomotic leak and major Clavien–Dindo complications, it might be safe to start EOF from POD 1.

The success of fast–track protocol is multifactorial and postoperative complications deviate from the adherence to the planned protocol. A retrospective study by Cerfolio et al.(8) found that ERAS could be followed in more than 75% of the study population. Similar findings were also found in an RCT by Zhao et al.(12) The compliance with ERAS protocol in esophagectomy varies between 72% to 88%. Compliance with more than 75% of ERAS protocol was possible in 90% of our patients. In our study, the only factor associated with failure of compliance with ERAS protocol was the occurrence of a major complication. Postoperative complications were the main factor contributing to non–compliance with ERAS protocol.

The multimodal ERAS pathway management helps organise perioperative care for patients. Pre–operative counselling could play an essential role in reducing patient's and relatives anxiety and increasing their participation in postoperative care. The prevalence of malnutrition is high in esophageal malignancy, and it predisposes to increased complications and hospital stays. Pre–operative dietician referral was obtained in all our patients, and tube

feeding, either by NG or FJ, was needed in 15% of our patients. Carbohydrate loading before surgery, early enteral nutrition, and epidural analgesia could decrease the inflammatory response to surgery and may provide immunologic protection.(33) In our protocol, we administered 800 ml of 10% dextrose at 12 hours and 400 ml at 2–3 hours before surgery. In our study, Pharmacological prophylaxis with LMWH was started 12 hours before surgery and continued till POD 5 in all 20 patients. None of our patients had developed pulmonary thromboembolism in the postoperative period. ERAS guidelines recommend antithrombotic prophylaxis with LMWH 2–12 hours before surgery combined with mechanical prophylaxis and continued up to 4 weeks after the operation.(74,76)

The ICU stay after surgery could be reduced from 26% to 0% with the introduction of a fast–track pathways in patients undergoing esophagectomy. In our study, ICU stay could be avoided in 80% of cases, and the median ICU stay was one day. Liberal peri–operative fluid administration has been shown to increase pulmonary complications in esophagectomy.(63,64) Intra–operative goal–directed fluid therapy and prevention of hypothermia are associated with fewer complications and reduced length of hospital stay.(20) The structured pattern of postoperative mobilization, incentive spirometry and chest physiotherapy in the incremental pattern is an effective implementation strategy to reduce pulmonary complications, and ICU stay.(53,54) Early chest tube removal and urinary catheter removal improve patient mobility and promote early discharge. In our study, neck and abdominal drains were not placed routinely, as recommended by ERAS guidelines, and it did not have a negative impact on postoperative outcomes.(21)

Further, we have compared our results with the existing literature regarding outcomes of various studies for esophagectomy with ERAS protocol (Table 9) and components of ERAS protocol followed across different studies (Table 10).

Table 9: Outcomes of various studies on ERAS protocol in esophagectomy

Study	Cerfolio et al (8)	Low et al (25)	Jiang et al (22)	Munitiz et al (27)	Blom et al (28)	Cao et al (14)	Ford et al (31)	Pan et al (13)	Shewale et al (5)	Chen et al (33)	Giacopuzzi et al (4)	Our study
Study design	Retrospective	Retrospective	Retrospective observational	Retrospective case–control	Retrospective case control	Retrospective case–control	Prospective	Retrospective case–control	Retrospective case–control	RCT	Prospective–retrospective case control	Prospective cohort
Year	2004	2007	2009	2010	2013	2013	2014	2014	2015	2016	2017	2022
No. of patients												
Conventional	–	–	–	74	103	57	121	40	322	132	22	–
ERAS	90	340	114	74	78	55	70	40	386	128	17	20
Type of surgery	Open	Open	Open	Open	Open	Mixed	Mixed	MIE	Mixed	Mixed	Mixed	MIE
LOH (POD)												
Conventional	–	–	–	13	15	14.8	13	12	12	12.5	10	–
ERAS	7	7	7	9	14	7.7	10	7	8	7.6	9	6
Complications(%)												
Conventional	–	–	–	38	68	47.4	52	40	27	12	44	–
ERAS	26	45	64	31	71	29	64	29	20	8.6	27	40
Readmission rate (%)												
Conventional	–	–	–	–	10.3	5.3	11	5	12	2.3	–	–
ERAS	4.4	4	4	0	9.7	3.6	13	7.5	15	2.3	–	5
Mortality rate (%)												
Conventional	–	–	–	5	1	5.3	0	0	3	1.5	0	–
ERAS	4	0.3	2.6	1	4	1.8	0	0	2	1.6	0	0

[RCT: Randomized controlled trial; LOH: Length of hospital stay; ERAS: enhanced recovery after surgery]

Table 10: Components of ERAS protocol in various studies

Components	Chen et al(33)	Shewale et al(5)	Pan et al(13)	Ford et al(31)	Cao et al(14)	Blom et al(28)	Munitiz et al(27)	Jiang et al(22)	Low et al(25)	Cerfolio et al(8)	Our study
ERAS followed (%)	–	–	–	–	73	42–93	59	88	88	76	90
ICU stay day (POD)	N	1.2	N	1	N	1	3	–	1	1	1
NGT removal (POD)	N	5	N	5	N	2	5	3	5–6	3	–
ICD removal (POD)	6	5	3	5–6	3	2	4	4	3–5	3	4
Initiation of oral feed (POD)	7	10	2	6	4	5	5	5	5–6	5	4
Initiation of enteral feed [POD]	1	3	0	1	1	0	5	2	3	1	1
Initiation of mobilization [POD]	1	1	2	1	1	–	2	2	1	1	1
Initiation of chest physiotherapy [POD]	1	1	1	1	2	1	–	2	1	1	1
Neck drain removal [POD]	N	N	N	N	N	N	N	N	N	N	–
Abdominal drain removal [POD]	N	N	N	3	N	N	N	N	N	N	–
Urinary catheter removal [POD]	2	3	3	3	1	–	4	2	–	3	2
Thrombotic prophylaxis	N	N	N	N	N	N	Y	–	–	–	Y

[POD: Postoperative day; ICD: Intercostal drain; ICU: Intensive care unit; N: No; Y: yes]

STRENGTHS AND LIMITATIONS

Strengths of the study:

1. Homogenous population of minimally invasive esophagectomy operated by the same surgical team
2. Standardized protocol throughout the study period
3. Good compliance with the protocol
4. First prospective study in the Indian population to evaluate the impact of NGT exclusion on postoperative outcomes.

Limitations of the study:

1. Small number of study population
2. Lack of control population
3. Early oral feeding was not initiated despite NGT was not used routinely
4. Patient satisfaction not measured

CONCLUSION

The exclusion of NGT with ERAS protocol for minimally invasive Mckeown's esophagectomy with CEGA did not impact the anastomotic leak rate and other major Clavien–Dindo complications. However, a randomized trial is required to incorporate exclusion of NGT into the ERAS guidelines.

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Annexure – 1

Ethical clearance

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

No. AIIMS/IEC/2021/3472 Date: 12/03/2021

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3307**

Project title: **"Impact of nasogastric tube exclusion after minimally invasive esophagectomy for esophageal cancer-a prospective observational study"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**M.Ch. Dissertation**
Student Name:	**Dr. Vignesh N**
Guide:	**Dr. Vaibhav Kumar Varshney**
Co-Guide:	**Dr. Subhash Chandra Soni & 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

Annexure – 2

PARTICIPANT INFORMED CONSENT FORM (PICF)

Participant identification number for this trial: _____

Title of project: **IMPACT OF NASOGASTRIC TUBE EXCLUSION AFTER MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER– A PROSPECTIVE OBSERVATIONAL STUDY**

Name of Principal Investigator: Dr Vignesh N Tel.No(s). 9486025665

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 permit 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	2) Witness – 2
Signature	Signature
Name:	Name:
Address:	Address:

सहभागी सुचित सहमति प्रपत्र

इस जाचं के लिए सहभागी पहचान नमबर_____

अनुसन्धान शीर्षक: **IMPACT OF NASOGASTRIC TUBE EXCLUSION AFTER MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER– A PROSPECTIVE OBSERVATIONAL STUDY**

मुख्य अन्वेषक का नाम : Dr Vignesh N फोन नंबर:9486025665

मैंने दिनांक_____ के सूचना पत्र में दिये गए सभी तथ्यो को पड़ लिया हैं। मुझे समझ आने वालीं भाषा मैं विस्तारपूर्वक बत्ता दिया है और मैनें तथ्यो को भली भांति 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 चिकित्सीय नोटों 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 प्रदान करता /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
नाम
पता

२) गवाह के हस्ताक्षर
नाम
पता

Annexure – 4

INFORMATION TO PARTICIPANTS

Title: **IMPACT OF NASOGASTRIC TUBE EXCLUSION AFTER MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER– A PROSPECTIVE OBSERVATIONAL 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 the research?

This study looks into the short term outcomes of protocol–based perioperative care with complete nasogastric tube exclusion in patients undergoing esophagectomy for carcinoma of esophagus. Enhanced recovery protocols are the standard of perioperative care in many surgeries. If you enroll in it you will be benefitted from better perioperative outcomes and early discharge. We have obtained permission from the Institutional Ethics Committee for conducting this study.

The study design

The study will be a single–center retrospective–prospective observational study and patients will be recruited from the department of Surgical gastroenterology.

Study Procedures

The study involves the evaluation of short–term outcomes of enhanced recovery protocol with nasogastric tube exclusion from the immediate postoperative period in patients undergoing esophagectomy for carcinoma of esophagus. You will be counseled about the entire perioperative care before surgery. You will be advised to follow regular respiratory exercise, early mobilization after surgery and the ICD drain will be removed as soon as possible. All the events will 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

Complete nasogastric tube exclusion from the immediate postoperative period prevents patient discomfort and throat irritation and protocol–based perioperative care is found to fasten the recovery of the gastrointestinal tract after surgery. This also decreases the length of hospital stay

Compensation

Nil

Possible benefits to other people

The results of the research may provide benefits to society in terms of the 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?

Participation in this research is purely voluntary and you have the right to withdraw from this study at any time during 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 the 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. Vignesh N
Senior resident
Dept. of Surgical Gastroenterology
Ph: 9486025665
email: vikinatesan@gmail.com

Principal guide and Co–Investigator
Dr. Vaibhav Kumar Varshney
Associate professor
Dept. of Surgical Gastroenterology
Ph: 9968223072
email: drvarshney09@gmail.com

Annexure – 5

भागीदारों के लिए सूचना

शीर्षक: IMPACT OF NASOGASTRIC TUBE EXCLUSION AFTER MINIMALLY INVASIVE ESOPHAGECTOMY FOR ESOPHAGEAL CANCER– A PROSPECTIVE OBSERVATIONAL STUDY

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 में आपकी सहायता करने के लिए है कि भाग लेना है या नहीं। कृपया पूछें कि क्या आपके पास कोई प्रश्न या चिंता है या नहीं।

आपको एम्स, जोधपुर में आयोजित इस अध्ययन में भाग लेने के लिए कहा जा रहा है क्योंकि आप हमारे योग्यता मानदंडों को पूरा करते हैं।

शोध का उद्देश्य क्या है?

यह अध्ययन कैंसरोमा एसोफैगस के लिए एसोफेजक्टोमी से गुजर रहे मरीजों में प्रोटोकॉल आधारित पेरीओपरेटिव देखभाल के अल्पकालिक परिणामों को देखता है। उन्नत सर्किट प्रोटोकॉल कई सर्जरी में पेरीओपरेटिव देखभाल का मानक हैं। यदि आप इसमें नामांकन करते हैं तो आपको बेहतर पेरीओपरेटिव परिणामों से फायदा होगा ... ... हमने इस अध्ययन के संचालन के लिए संस्थागत नैतिकता समिति से अनुमति प्राप्त की है.

अध्ययन डिजाइन

अध्ययन एक एकल–केंद्र पूर्वव्यापी–भावी अवलोकन अध्ययन होगा और रोगियों को सर्जिकल गैस्ट्रोएंटरोलॉजी विभाग से भर्ती किया जाएगा।

अध्ययन प्रक्रियाएं

अध्ययन में घुटकी के कार्सिनोमा के लिए घुटकी से गुजरने वाले रोगियों में तत्काल पश्चात की अवधि से नासोगैस्ट्रिक ट्यूब अपवर्जन के साथ संवर्धित रिकवरी प्रोटोकॉल के अल्पकालिक परिणामों का मूल्यांकन शामिल है। सर्जरी से पहले आपको पूरी देखभाल के बारे में परामर्श दिया जाएगा। आपको नियमित श्वसन व्यायाम, सर्जरी के बाद जल्दी जुटने और आईसीडी नाली को जल्द से जल्द हटाने की सलाह दी जाएगी। सभी घटनाओं को दर्ज किया जाएगा।

आपके लिए संभावित जोखिम

शल्य चिकित्सा और बीमारी के कारण जोखिम के अलावा कोई अतिरिक्त जोखिम नहीं है।

आपके लिए संभावित लाभ

तत्काल पश्चात की अवधि से पूरा नासोगैस्ट्रिक ट्यूब बहिष्करण रोगी की परेशानी और गले में जलन को रोकता है और सर्जरी के बाद गैस्ट्रोइंटेस्टाइनल ट्रैक्ट की वसूली को तेज करने के लिए प्रोटोकॉल आधारित पेरिऑपरेटिव देखभाल पाई जाती है। इससे अस्पताल में रहने की लंबाई भी घट जाती है

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 देखभाल / उपचार प्रदान किया जाएगा।

आप से 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 जांचकर्ताओं, 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 देखभाल या जांचकर्ता या संस्थान के साथ आपके संबंध प्रभावित नहीं होंगे। आपका डॉक्टर अभी भी आपकी देखभाल करेगा और आप किसी भी लाभ को खो देंगे नहीं जिसके 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 जांचकर्ता 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:

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Annexure – 6

PROFORMA

Patient ID:

BASIC INFORMATION OF PATIENT

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

CHIEF COMPLAINTS

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

Dysphagia grade at admission (Modified Takita grading):

ADDICTION

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

Patient ID:

CO MORBIDITIES

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

Ht..... Wt.....BMI……. ECOG…….

UPPER GI SCOPY

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

Pre op CECT (STAGE):

PREOPERATIVE PERIOD

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

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

ESOPHAGECTOMY AND GASTRIC PULL THROUGH

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

Patient ID:

OPERATIVE DETAILS

PARAMETERS	
Thoracoscopy assisted(TA)/ Thoracolaparoscopy(TL)/Robotic(RA)	
Thoracotomy Conversion (Yes/No) and Reason	
Type of esophagogastric anastomosis (St/HS)	
Intraoperative blood loss (ml)	
Input/Output (ml)	
Restrictive fluid strategy	
Intraoperative blood transfusion (units)	
Duration of surgery(hours)	
Inotropes (Yes/No)	
Extubated (Yes/No)	

St– Stapled; HS– Hand Sewn

POSTOPERATIVE PERIOD

	NO. OF POSTOPERATIVE DAYS
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	
VTE prophylaxis	

Patient ID:

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

POSTOPERATIVE COMPLICATIONS

	CLAVIEN DINDO SCORING (IN GRADES)
Haemorrhage	
Cervical anastomotic leak	
Change in voice	
Pulmonary complication	
Cardiac complication	
Chylothorax	
Other complications	

	YES	**NO**	**POD**
Re admission			
Mortality			

Final Biopsy:

Annexure –7

PLAGIARISM

thesis

ORIGINALITY REPORT

14%
SIMILARITY INDEX

PRIMARY SOURCES

1	zenodo.org Internet	123 words — 1%
2	jamanetwork.com Internet	99 words — 1%
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5	Sunita Suman, Vaibhav K Varshney, Subhash Soni, Sanjeev Sachdeva, Sabir Hussain, Narendra Bhargava. "Comparative Analysis of Heller Myotomy With Dor Versus Toupet Fundoplication for Achalasia Cardia", Cureus, 2022 Crossref	71 words — < 1%
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7	"Abstract : Abstract", Diseases of the Esophagus, 2014. Crossref	58 words — < 1%
8	"2016 Scientific Session of the Society of American Gastrointestinal and Endoscopic	51 words — < 1%

ANNEXURE –8

KEY TO MASTER CHART

A	SI no.	
B	Age	
C	Sex	0–Male, 1–Female
D	Dysphagia duration	
E	Grade of dysphagia	
F	Preoperative nutritional intervention	0–Yes, 1– No
G	Cough	0–Yes, 1– No
H	Loss of weight	0–Yes, 1– No
I	Loss of appetite	0–Yes, 1– No
J	Alcohol abuse	0–Yes, 1– No
K	Smoking	0–Yes, 1– No
L	Tobacco chewing	0–Yes, 1– No
M	Hypertension	0–Yes, 1– No
N	Diabetes Mellitus	0–Yes, 1– No
O	Coronary artery disease	0–Yes, 1– No
P	Chronic obstructive pulmonary disease	0–Yes, 1– No
Q	Pulmonary Tuberculosis	0–Yes, 1– No
R	Body mass index	
S	ECOG performance status	
T	Upper margin of growth	
U	Location of tumor in thorax	0–upper, 1– middle, 2–lower
V	Scope negotiable beyond tumor	0–Yes, 1–No
W	Differentiation	0–Well, 1– Moderately,2– Poorly
X	Clinical stage	
Y	Neoadjuvant treatment	0–NACT,1–NACRT
Z	Hospital stay	0–No, 1– Yes
AA	Thoracic phase	1–Thoracoscopic, 2–Robotic

AB	Conversion	0–Yes, 1–No
AC	Anastomotic technique	0–Stapled, 1– Handsewn
AG	Intraop blood transfusion	0–Yes, 1–No
AI	Intraop Inotropes	0–Yes, 1–No
AJ	Immediate extubation	0–Yes, 1–No
AK	ICU stay	
AL	Early mobilization	
AM	POD of Urinary catheter removal	
AN	POD of Epidural removal	
AO	POD of ICD removal	
AP	Oral initiation day	
AQ	VTE prophylaxis last dose	
AR	Pulmonary complications	0–Yes, 1–No
AS	Cardiac complications	0–Yes, 1–No
AT	Chylothorax	0–Yes, 1–No
AU	NG reinsertion	0–No, 1–Yes
AV	Anastomotic leak	0–Yes, 1–No
AW	Clavien dondo grade	
AX	Readmission	0–Yes, 1–No
AY	Mortality	0–Yes, 1–No
AZ	75% ERAS	0–No, 1–Yes