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Compliance and outcome of enhanced recovery after surgery(eras) protocol in esophageal cancer patients undergoing esophagectomy

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Abstract

Background: ERAS programs have been developed to provide multidisciplinary care in the perioperative period and have been shown to predictably improve short term surgical outcomes. Esophagectomy has traditionally been associated with high morbidity and mortality and ERAS principles specifically designed for this purpose will improve outcomes considerably. The latest ERAS guidelines for esophagectomy, published in February 2019, has concepts validated by previous studies and also new recommendations to cover areas unique to this procedure.

Aims and Objectives

1. To assess the compliance of ERAS protocol in esophageal cancer patients undergoing esophagectomy.
2. To assess the postoperative length of hospital stay and postoperative complications following esophagectomy for esophageal cancer.

Methodology: A prospective observational study was conducted on 19 patients operated in the Department of Surgical Gastroenterology and Surgical Oncology, JIPMER, Puducherry between May 2019 and August 2021. Patient demographic details, ASA score and BMI were documented. All patients underwent ERAS

protocol as recommended by ERAS society and compliance to each component was noted.

Results: The mean age was 56.16 in the study group, included 8 men and 11 women. Most of patients were nutritionally poor- mean BMI-18.18. Our patients were compliant to preoperative nutritional assessment, MDT, cessation of alcohol and smoking, preoperative carbohydrate loading, balanced fluid therapy, minimally invasive approach, no drains, early enteral nutrition, early removal of urinary catheter, use of epidural and opioid sparing analgesia and early mobilization and partially compliant to removal of intercostal drain tube on POD3 [47.4%] and early removal of NG tube on POD4 [36.8%]. They were not compliant to early shift from ICU on POD3 [most of our patients had ICU stay > 4 days (63.15%)], early oral feeds on POD4 and discharge on POD4. Our median post op hospital stay was 13 days (range 10 - 26 days). The most common post-op complications were LRTI (42.10%), vocal cord palsy (31.58%), SSI (31.58%) and anastomotic leak (26.31%). Grade 1 and 2 Clavien-Dindo complications were seen in 47.36% and Grade III complications were seen in 42.11% of patients. Correlation coefficient of descriptive parameters to non-compliant variables revealed a statistically significant correlation of prolonged duration of surgery with longer ICU stay (p= 0.028) and non-removal of intercostal drain tube on POD3(p= 0.021).

Conclusion: This study shows the safety and feasibility of ERAS protocol for esophageal surgery in a tertiary center though there may be partial or non-compliance to few components which may be modified in future guidelines. Studies with larger sample size and RCTs are the need of the hour for further validation.

Keywords: Compliance, esophageal, cancer, esophagecto my, enhanced, recovery

Introduction

Esophageal cancer is 9th most common malignancy and 6th most common cause of malignancy-related deaths worldwide.[1]Surgical management is the only means of cure for esophageal cancer[2–5] but esophagectomy with radical lymphadenectomy is associated with high morbidity and mortality. [6,7]The ERAS program is surgeon-led program centered around patients and combining various disciplines like anesthesia, nursing, nutrition and science that was pioneered by Henrik Kehlet in the Nineties.[8,9] Its main objective is to reduce surgical stress, scale back surgical complications, and enhance surgical recovery within the perioperative period. The ERAS program has been successful in numerous surgical disorders.[10–12]It developed comparatively late in esophagectomy in view of complexity of the procedure and high morbidity. Recently, with the popularity of thoraco-laparoscopic approaches, better anesthesia and perioperative care, ERAS has been introduced successfully for esophagectomy.[13–16]Few systematic reviews with meta-analysis delineate the practicability and safety of ERAS compared to standard care.[17,18]Pisarska et al.[17] reported that there have been important variations in nonsurgical and respiratory organ complications between ERAS and standard care. However, Marker et al[18]suggested results contrary to those of the former in these aspects. It's still unclear as to the feasibility of ERAS principles for esophagectomy. Results from meta-analysis published in 2007 revealed reductions in perioperative and respiratory complications and shorter length of hospital stay among ERAS patients. [11] However, conclusions from this review were criticized because of lack of RCTs.

Aim and objectives

1. To assess the compliance of ERAS protocol in esophageal cancer patients undergoing esophagecto my.
2. To assess the postoperative length of hospital stay, postoperative complications and readmission rate within 30 days after surgery

Methodology

This prospective observational study was done in the Department of Surgical Gastroenterology, JIPMER, Puducherry. We studied 19 patients operated in the JIPMER Hospital between May 2019 and August 2021. ERAS protocol as per latest guidelines published in February 2019 was followed[4]. After obtaining informed consent all consecutive patients with esophageal cancer fulfilling inclusion criteria were included in the study [Table A]. Patient demographic details, ASA score and BMI were documented. All patients underwent Robot assisted or thoracolaparoscopic esophagectomy, total 2 field lymphadenectomy, cervical esophagogastric anastomosis, 4 to 6 weeks after neoadjuvant therapy as per CROSS protocol.

ERAS protocol includes pre operative, intra operative and postoperative elements which were implemented as described below [Table B-D]. Data was collected prospectively regarding compliance, postoperative complications and recorded in excel sheet.

Statistical analysis

The statistical analysis was done using IBM SPSS statistics version 22. Both descriptive and inferential statistics were used to analyse the data. Baseline characteristics of the patients were presented by descriptive statistics. Categorical data was described using percentages and frequencies and compared by using Fischer exact test or Chi square test. The normality of continuous data was assessed by Kolmogorov-Smirnov test. The normally distributed data was described by mean ± standard deviation and median and interquartile range was used for non-Gaussian data. Comparison of the continuous data between the two groups was done by independent Student's t-test for parametric data and Mann–Whitney U-test for nonparametric data. 95% confidence interval was calculated and reported for the outcome measures and statistical analysis was carried out at 5% level of significance and $p<0.05$ was considered as statistically significant.

Results

We studied 19 patients operated in the JIPMER Hospital between May 2019 and August 2021.

The mean age was 56.16 in the study group, included 8 men and 11 women. Most of patients were poor nutritionally- mean BMI-18.18. [Table 1]. Most of them (73%) had no co-morbidities. Our patients were compliant to preoperative nutritional assessment and treatment , Multidisciplinary tumour board (MDT) evaluation, adequate medical optimisation of the patient preoperatively, cessation of alcohol and smoking at least 4 weeks ahead of surgery, preoperative carbohydrate loading , surgery after 4-6 weeks following the last day of chemoradiotherapy, intraoperative balanced fluid therapy, minimally invasive approach, tubularized gastric conduit, total two field lymphadenectomy, non-placement of cervical or abdominal drains, early enteral nutrition through FJ on postoperative day 1(POD1) [84.2%], early removal of urinary catheter on POD2, use of epidural analgesia and opioid sparing analgesia in the postoperative period, early mobilization on POD1 [89.5%] and partially compliant to removal of intercostal drain tube on POD3 [47.4%] and early removal of NG tube on POD4 [36.8%]. [Table 2]

They were not compliant to early shift from ICU on POD3 [most of our patients had ICU stay > 4 days (63.15%)], early oral feeds on POD4 and discharge on POD7.[Fig 1]

Our median post op hospital stay was 13 days (range:10 - 26 days). The most common post-op complications were LRTI (42.10%), vocal cord palsy (31.58%), SSI (31.58%) and anastomotic leak (26.31%). [Table 3] [Fig 2]. Grade 1 and 2 Clavien-Dindo complications were seen in 47.36% and Grade III complications were seen in 42.11% of patients. [Table 4]

Correlation coefficient of descriptive parameters to non-compliant variables revealed a statistically significant correlation of prolonged duration of surgery with longer ICU stay (p= 0.028) and non-removal of intercostal drain tube on POD3(p= 0.021).

Discussion

The Enhanced recovery after surgery (ERAS) protocol for esophagectomy was published in February 2019[4]. Esophagectomy has traditionally been associated with high degree of complexity with significant perioperative morbidity and ERAS principles specifically designed for this purpose will improve outcomes considerably. ERAS has not been uniformly employed at all centers and gained greater acceptance only recently, however, the feasibility and compliance of ERAS recommendations has not been prospectively evaluated which was the main objective of present study.

The mean age was 56.16 in the study group, included 8 men and 11 women. Most of patients were poor nutritionally- mean BMI-18.18.

Our patients were compliant to preoperative nutritional assessment and treatment , Multidisciplinary tumour board (MDT) evaluation, adequate medical optimisation of the patient preoperatively, like cessation of alcohol and smoking at least 4 weeks ahead of surgery, preoperative carbohydrate loading , surgery after 4-6 weeks following the last day of chemoradiotherapy, intraoperative balanced fluid therapy, minimally invasive approach using thoraco-laparoscopic or robot assisted minimally invasive esophagectomy, tubularized gastric conduit , total two field lymphadenectomy, non-placement of cervical or abdominal drains , early enteral nutrition through FJ on postoperative day 1(POD1) [84.2%], early removal of urinary catheter on POD2, use of epidural analgesia and opioid sparing analgesia in the postoperative period, early mobilization on POD1[89.5%] and partially compliant to removal of intercostal drain tube on POD3[47.4%] and early removal of NG tube on POD4 [36.8%].

They were not compliant to early shift from ICU on POD3 [most of our patients had ICU stay > 4 days (63.15%)]. We do not start early oral feeds on POD4 in view of the fact that we routinely perform FJ for all patients with initiation of FJ feeds on POD1 thereby providing adequate enteral nutrition. Our patients also had poor compliance to discharge on POD7 in view of longer ICU stay, delayed removal of NG tube and delay in initiation of oral feeds. Our study is perhaps among very few studies which have tried to determine the compliance of our patients to various components of ERAS so that future guidelines can incorporate or modify them.

Our median post op hospital stay was 13 days (range 10-26 days) which was slightly more than previous studies like that reported by Shewale et al [19](median of 8 days) probably due to our small sample size. In a recent meta-analysis,[20] the mean length of hospital stay following ERAS was 9.9±2.8 which is less than our mean hospital stay of 13.6 days. Our pulmonary complication rate was

also higher than other studies (42% vs 27%) probably again due to small sample size. The disparity could also be due to fact that all our patients received neoadjuvant therapy as per CROSS protocol compared to 85% patients in previously mentioned study resulting in technically more difficult surgery with more prolonged operative times and more pulmonary complications and higher vocal cord paresis rate (31.58%). Our vocal cord paresis rate is high in view of the fact that we routinely perform total 2 field lymphadenectomy and all our patients recovered completely between 4 weeks to 3 months. The other common post-op complications were SSI (31.58%) and anastomotic leak (26.31%).

The results showed reduced surgical morbidity (none or Clavien-Dindo grade I complications seen in 31.57%, grade III complications seen in 42%) which is comparable to other studies which showed reduction of LOS and complication rates.[21-23]Esophageal resections are technically complex involving abdominal, thoracic and cervical resections. Therefore, the morbidity related to this procedure is comparatively high, which was additionally confirmed in this study.

Presently, it's emphasized that a full practical recovery, instead of the postoperative hospital stay alone should be taken into account as a measure of perioperative careto evaluate the efficacy of ERAS protocol in esophageal surgery because shorter LOS with higher readmission rates also impede the overall recovery of patients.[24]

Though the current study adds substantial proof for the utilization of ERAS protocol in esophageal surgery, RCTs with larger sample size is required to assess its feasibility and compliance.

The strength of this study

Prospective study

Standardized neoadjuvant therapy and surgical procedure

Standardized lymphadenectomy

Compliance to various components of latest ERAS guidelines (2019) studied

The Limitations of the study

Small sample size (partially due to COVID 19 epidemic)

Single center study

Conclusion

This study shows the safety and feasibility of ERAS protocol for esophageal surgery in a tertiary center though there may be partial or non-compliance to few components which may be modified in future guidelines. Studies with larger sample size and RCTs are the need of the hour for further validation.

Tables

Table 1: Inclusion and exclusion criteria

Inclusion criteria
Patients with esophageal cancer (squamous or adenocarcinoma) planned for esophagectomy with
Age >18 and < 75 years
Adequate haematological, renal, hepatic and pulmonary functions
An ECOG performance status < 2
Exclusion criteria
Active or uncontrolled infection
Uncontrolled psychiatric or neurologic problems
Uncontrolled cardiopulmonary disease
Metastatic disease

Table 2: Enhanced recovery after surgery (ERAS) program protocol

Preoperative period	**Method**
Patient education	Illustrated charts prepared by the department
Preoperative nutrition	Carbohydrate loading 100 gm the day before surgery and 50gm, 3hours before surgery
Postoperative Day	**Targets for postoperative management**
POD 0	Postoperative analgesia: epidural Injection Ketorolac on demand Mobilization to sit
POD 1	Postoperative analgesia: oral acetaminophen (1gram Q8 hourly), Injection Ketorolac on demand Urinary catheter will be removed if the urine output is adequate over the last 24 hours (1ml/kg/hr) Mobilization to sit for 1 hour FJ trial feeds
POD 2	FJ half strength feeds Mobilization: sit for 2 hour Removal of ICD
POD 3	Postoperative analgesia: stop epidural Balanced fluid therapy Transfer to ward if criteria is met Mobilization: Sit for 2-hour, short walk around bed Nutrition: Full strength FJ feeds
POD 4	Mobilization: walking for 20 mins Nutrition: Full strength FJ feeds NGT removal (if clinically appropriate)
	Oral fluids (if clinically appropriate)
POD 5	Nutrition: Full strength FJ feeds
POD6	Oral semisolids (if clinically appropriate) Nutrition: Supplementary FJ feeds
POD7	Discharge from Hospital (If discharge criteria met)

Table 3: Criteria for postoperative management target in ERAS protocol.

ICU discharge	**Respiratory** Respiratory rate >10 and < 20 breaths/min on 40% O2 SpO2 >95% Good cough reflex **Cardiovascular** Able to mobilize out of bed without inotropic supports **Renal** Stable renal function, passing urine 1ml/kg/hour Urea and creatinine - normal **Neurological** Patient alert and obeying commands **Analgesia** Pain is well controlled **Blood tests** Stable or improving **General** Able to mobilize out of bed
Hospital discharge	**Patient must achieve the following criteria** Adequate pain control on oral analgesia Independent mobility (can mobilize independently to toilet) Return of blood tests to normal

Table 4: Clavien-Dindo classification of surgical complication

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs such as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than those allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IV	Life-threatening complication (including CNS complications) requiring IC/ICU management
Grade V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of discharge (see examples in Table 2), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for follow-up to fully evaluate the complication.

Table 5: Patient characteristics

Variables	N	Mean	Median
Age	19	56.16	57
BMI	19	18.18	17.6
Duration of sympto (days)	19	115.47	90
Baseline pulse	19	81.37	82
Baseline HB	19	10.95	11.2
Duration of surgery (Hours)	19	8.11	8.5
Blood loss(ml)	19	242.11	200
Post op stay	19	13.6	13

Table 6: Patient characteristics -Frequency distribution

		No. of patients (Percentage)
Sex	F	11 (57.9)
	M	08 (42.1)
	Total	19 (100)
ASI grade II	Yes	19 (100)
Co-morbidity	None	14 (73.68)
	COPD	01 (05.26)
	HTN	03 (15.78)
	CAD,CKD	01 (05.26)
	Total	19(100)
Extra analgesics	Yes	03 (15.78)
	No	16 (84.2)
	Total	19 (100)
MDT		19 (100)
Pre-op carbohydrate loading	Yes	19 (100)
Balanced fluid therapy	Yes	19 (100)
Minimally invasive	Yes	19 (100)
gastric conduit	Yes	19 (100)
2 field lympha denectomies	Yes	19 (100)
No cervical or abdominal drains	Yes	19 (100)
FJ feeds-POD1	Yes	16 (84.2)
	No	03 (15.78)

	Total	19 (100)
Urinary catheter- POD2	Yes	19 (100)
ICD- POD3	Yes	09 (47.4)
	No	10 (52.6)
	Total	19 (100)
Epidural analgesia	Yes	18 (94.7)
Opioid sparing analgesia	Yes	19 (100)
Early mobilization on POD1	Yes	17 (89.5)
	No	02 (10.5)
	Total	19 (100)
Intra-op opioids	Yes	02 (10.5)
	No	17 (89.5)
	Total	19 (100)
NG tube- POD4	Yes	07 (36.8)
	No	12 (63.2)
	Total	19 (100)
Prolonged ileus		02 (10.5)
ICU stay > 4 days		12 (63.2)

Table 7: Post-op complications

	No. of patients (Percentage)
Hyponatremia (grade I)	4 (21.05)
LRTI (grade II)	8 (42.10)
Anastomotic leak (grade I)	5 (26.31)
Hypokalemia (grade- I)	5 (26.31)
Pneumothorax (grade- IIIa)	1 (5.26)
Pleural effusion (grade II)	3 (15.79)
Vocal cord palsy	6 (31.58) {grade I -3, grade IIIb-2}
SSI (grade I)	6 (31.58)
Atrial fibrillation (grade II)	1 (5.26)
Wound dehiscence (grade IIIa)	1 (5.26)
Conduit dilatation	2 (10.5)
Gastroparesis	2 (10.5)
Grade I gastric conduit ischemia (grade IIIa)	1 (5.26)
Hypoalbuminemia	2 (10.5)
Mediastinitis (grade II)	1 (5.26)

Table 8: Post-op complication s – Clavien - Dindo classification

	No. of patients (Percentage)
None	2 (10.52)
Grade I	4 (21.05)
Grade II	5 (26.31)
Grade III	8 (42.11)
Total	19 (100)

Figures

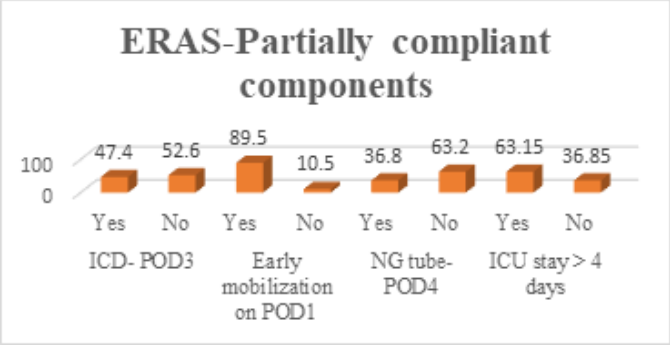

Fig 1

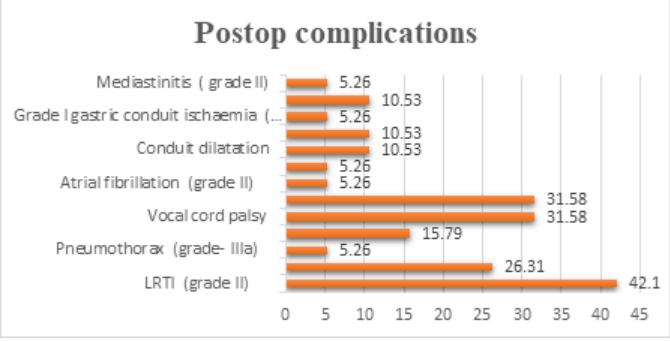

Fig 2

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