AUDIT ARTICLE

Compliance of enhanced recovery after surgery (ERAS) protocol in emergency and elective colorectal cancer surgery with a perspective from a developing country

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Abstract

Objective: To evaluate compliance with enhanced recovery after surgery protocol of patients undergoing colorectal carcinoma surgery, and to compare its effect on outcomes.

Method: The retrospective study was conducted at the Maroof International Hospital, Islamabad, Pakistan, and comprised data from July 15, 2016, to March 20, 2022, of patients of either gender undergoing elective or emergency colorectal carcinoma surgery. Data included age, gender, tumour site, type of surgery, surgical approach, compliance with each of the 25 components of the enhanced recovery after surgery protocol, length of hospital stay, surgery duration, 30-day readmission rate and perioperative mortality. Data was analysed using SPSS 23.

Results: Of the 96 patients with mean age 50.03±14.86 years (range: 20-79 years), 65(67.7%) were males, 70(72.91%) were aged at least 40 years, and 75(78.12%) underwent elective surgery. Most common tumour site was rectum and sigmoid 49(51%). Laparoscopic surgery was performed in 17(17.7%) patients. No compliance was seen with carbohydrate loading of patients or limiting use of opioids in standard anaesthesia protocol. No nutritional supplementation was started from postoperative day 1. Mean compliance with all the protocol components was 74.9%±37.652 for both elective and emergency cases. Mean duration of surgery was 192.50±75.33 minutes, while mean length of hospital stay was 5.52±1.57 days. Re-admission within 30 days was needed in 2(2.1%) cases. There was no perioperative mortality.

Conclusions: Better compliance with enhanced recovery after surgery protocol resulted in better perioperative outcomes.

Key Words: Colorectal, ERAS, Compliance, Length of stay, Morbidity.

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Introduction

Colorectal carcinoma (CRC) is the third most common cancer worldwide.[1,2] The management of CRC involves a multidisciplinary approach that includes surgery, chemotherapy, radiotherapy and targetted drug therapy.[3] In the recent past, there have been improvement in long-term outcomes of patients suffering from CRC that are attributed to early detection and advancement in treatment options.[2] The early outcomes have also improved with the introduction of minimally invasive techniques and adherence to enhanced recovery after surgery (ERAS) protocol. The main obstacles in the transformation to minimally invasive techniques in developing countries are lack of expertise and resources. In developing countries, particularly Pakistan, adherence to ERAS protocol4 has not been attempted seriously in a systematic manner as evidenced by limited data published from this part of the world. The ERAS protocol is an evidence-based patient-focussed perioperative care pathway to accelerate postoperative recovery of CRC patients.[4] ERAS guidelines for CRC surgery are well-established and are now practised worldwide. The latest revision was published in 2018 that included 25 elements for CRC surgery with 4 major subdivisions; preadmission, preoperative, intraoperative and postoperative.[4] Compliance with complete ERAS protocol is difficult to achieve, therefore variation in compliance is seen even in specialised CRC centres.[5,6] While it is understandable that 100% compliance with the ERAS protocol cannot be achieved, studies have shown that adherence to the protocol improves outcomes in terms of decreased perioperative morbidity and mortality alongside decrease in length of hospital stay (LOS).[6,7]

While the concept of ERAS is still evolving, in developing countries like Pakistan resources are limited even in tertiary care setups and adherence to ERAS becomes

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challenging. Additionally, lack of proper screening guidelines for CRC patients results in patients presenting at an advanced stage. The current study was planned to evaluate compliance with ERAS protocol of patients undergoing CRC, and to compare its effect on outcomes.

Patients and Methods

The retrospective study was conducted at the Surgical Oncology section of the Department of Surgery, Maroof International Hospital, Islamabad, Pakistan, and comprised data from July 15, 2016, to March 20, 2022. Inclusion criteria were adult patients of either gender diagnosed with primary or metastatic CRC and underwent elective or emergency surgery. Exclusion criteria included those patients who were converted to open surgery after laparoscopic surgery, pregnancy, severe mental illness and preoperative intensive care unit stay. After approval from the institutional ethics review board, the sample size was calculated in the light of an earlier study.[8]

All CRC surgery cases meeting the inclusion criteria were discussed in multidisciplinary team (MDT) meetings comprising surgical oncologists, radiologists, pathologists, medical oncologists, urologists, gynaecologists and general surgeons. Those with limited metastatic CRC disease to liver underwent oncological resection, while those with intestinal obstruction or perforation secondary to CRC in addition to metastatic disease underwent surgical resection after MDT discussion. All the surgeries were performed by the same team, led by a surgical oncologist. The 25–item ERAS protocol[4] was in place (Table 1).

Data was collected from prospectively maintained computerised hospital database and medical record files of the patients. Data included age, gender, compliance with each ERAS component, LOS, duration of surgery, type of presentation either elective or emergency, need for blood transfusion, tumour site, surgical approach either open or laparoscopic, 30-day readmission rate and perioperative mortality.

Ceftriaxone 1g and metronidazole 500mg or tazobactam + piperacillin 4.5g and metronidazole 500mg were used for antimicrobial prophylaxis. The latter was used mostly in emergency cases, especially those presenting with perforation and peritonitis. Bowel preparation, when required, consisted of a combination of strict liquid-only diet 24 hours prior to surgery, oral laxatives (bisacodyl 4 tablets 48 hours and 4 tablets 24 hours prior to surgery) and enema (12 hours and 4 hours prior to surgery). Bowel preparation was performed in patients with rectal cancers who had planned elective surgeries, while no bowel preparation was performed in patients undergoing emergency surgery or colon cancer surgery. Intraoperatively, warm intravenous (IV) fluids and air-warmers were used to avoid hypothermia.

Data was analysed using SPSS 23. Univariate general linear model analysis and one-way analysis of variance (ANOVA) tests were used as appropriate. $P<0.05$ was considered statistically significant.

Results

Of the 96 patients with mean age 50.03±14.86 years (range: 20-79 years), 65(67.7%) were males, 70(72.91%) were aged at least 40 years, and 75(78.12%) underwent

Table-1: Working definition of enhanced recovery after surgery (ERAS) protocol components

Sr.	Element	Compliance considered valid when followed where applicable
1	Preadmission information, counselling and education	Detailed procedure specific, patient centred information sessions with patient and attendant's involvement of multidisciplinary team prior to surgical intervention
2	Preoperative optimisation	Optimisation of systemic diseases with cardiologist, pulmonologist, medical specialist, nephrologist, anaesthetist, etc.Smoking and alcohol cessation for minimum of two weeks prior to surgical intervention except in emergency surgeries
3	Prehabilitation	Daily walk & incentive spirometry exercises to improve physiological reserve minimum of two weeks prior to surgical intervention except in emergency surgeries
4	Preoperative nutritional care	Oral or parenteral supplementation using serum albumin as marker or malnutrition universal screening tool
5	Management of Anaemia	Anaemia target of 10mg/dl kept during perioperative time and corrected by intravenous iron and blood transfusion
6	Prevention of Nausea and Vomiting	Multimodal antiemetic prophylaxis using one or more of the following. Ondansetron, metoclopramide, dexamethasone (selectively in patients with poor diabetes control) and intravenous paracetamol
7	Pre-anaesthesia medications	Preoperative patient education by anaesthetist and use of paracetamol and non-steroidal anti-inflammatory drugs in anaesthesia

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9	Bowel preparation	Use of oral bisacodyl, kleen enema or both for bowel preparation in rectal surgery and avoidance in colonic and emergency surgeries
10	Preoperative fluid and electrolyte therapy	Intravenous fluids to maintain euvolaemic state as much as possible especially in cases of bowel preparation
11	Preoperative fasting and carbohydrate loading	6 hours of fasting for solids2 hours of fasting for clear liquids or carbohydrate drinks
12	Standard anaesthesia protocol	Opioid sparing Propofol and short acting opioids Maintaining muscle relaxation Reversal of neuromuscular blockade Low pressure 10-12mmHg for laparoscopy
13	Intraoperative fluid and electrolyte therapy	Goal directed fluid therapy with intention to keep near – zero perioperative fluid balance
14	Prevention of intraoperative hypothermia	Use of warm intravenous and lavage fluids Use of blanket and air warmerMinimum temperature of 22 ^{0}C
15	Surgical access (open versus minimally invasive)	Laparoscopic approach preferred over open surgery
16	Drains placement	No drain placement
17	Nasogastric intubation	Placement of nasogastric tube (NG) during peri-operative time only in emergency cases
18	Postoperative analgesia	Multimodal injectable analgesia including paracetamol and NSAIDs avoiding opioids and use of epidural analgesia or abdominal wall blocks
19	Thromboprophylaxis	Mechanical Low molecular weight Heparin
20	Postoperative fluid and electrolyte therapy	Near zero fluid and electrolyte balance
21	Urinary drainage	Catheter removal within 3 days
22	Prevention of postoperative ileus	Limiting use of opioid analgesics Use of minimally invasive surgery Avoiding routine nasogastric tube Goal directed fluid therapy Multimodal analgesia
23	Postoperative glycaemic control	Avoiding hyperglycaemiaUse of insulin for maintaining glucose levels
24	Postoperative nutritional care	Early resumption of oral intake (6 hours after surgery)Oral nutritional supplementation from day 1
25	Early mobilisation	Within 12 hours of surgery

Table-2: Demographic data.

Presentation	Gender	Count (Percentage)	Age Mean	Age Median	Age Standard deviation
Emergency	male	15 (15.62%)	58.40	60.00	15.94
	female	6 (6.25%)	53.00	49.50	10.26
Elective	male	50 (52.08%)	49.10	49.50	14.73
	female	25 (26.04%)	46.16	47.00	14.10
P Value		***0.684***		***0.016***	

Table-3: Tumour site distribution with respect to gender and type of surgical intervention.

Parameter	Ascending colon N (%)	Transverse colon N (%)	Descending colon N (%)	Sigmoid & Rectosigmoid N (%)	Rectum N (%)	Metastatic N (%)	Total n (%)
Male	15 (23.1%)	1 (1.5)	8 (12.3)	14 (21.5)	24 (36.9)	3 (4.6)	65 (100%)
Female	10 (32.3%)	1 (3.2)	1 (3.2)	8 (25.8)	3 (9.7)	8 (25.8)	31 (100%)
Emergency	2 (9.5%)	2 (9.5%)	3 (14.28%)	8 (38%)	4 (19%)	2 (9.5%)	21 (100%)
Elective	23 (30.66%)	-	6 (8%)	14 (18.66%)	23 (30.66%)	9 (12%)	75 (100%)
Total	25 (26%)	2 (1.9%)	9 (9.3%)	22 (22.9%)	27 (28.1%)	11 (11.45%)	96 (100%)

elective surgery (Table 2).

Most common tumour site was rectum and sigmoid 49(51%) Prevalence of CRC site in relation to gender and mode of presentation was noted (Table 3).

Laparoscopic surgery was performed in 17(17.7%) patients, 36(37.5%) patients had received neoadjuvant chemotherapy prior to surgery, and 4(4.1%) had received chemotherapy as well as radiotherapy prior to surgery (Table 4).

In order to achieve target haemoglobin (Hb) levels as per ERAS protocol, 28(29.16%) patients required blood transfusion, 2(2.08%) required IV iron supplementation, and

Table-4: Presentation and surgical approach versus upfront surgery or neoadjuvant chemo-radiotherapy.

Presentation	Open Surgery No = 79	Laparoscopic Approach No = 17	Upfront Surgery n=96	Neoadjuvant chemotherapy	Post chemo-radiation therapy
Emergency (N=21)	18 (22.78%)	3 (17.64%)	17 (17.7%)	3 (3.12%)	1 (1%)
Elective (N=75)	61 (77.21%)	14 (82.35%)	39 (40.62%)	33 (34.37%)	3 (3.1%)
P Value	***0.646***		***0.017***	***0.013***	***0.879***

Table-6: Outcome variables.

Outcome parameter	Analysis	Emergency	Elective	Total	P Value
Duration of surgery in minutes	Median	150	205	190	0.000
	Mean ± SD	133.10 ± 60.176	209.13 ± 70.894	192.50 ± 75.338	
Length of hospital stay	Median (Minimum-Maximum)	5 (2-10)	6 (2-9)	6 (2-10)	0.042
	Mean ± SD	4.90 ± 1.868	5.69 ± 1.452	5.52 ± 1.576	
30 days readmission	Median	2	2	2	0.336
	Mean ± SD	1.95 ± 0.218	1.99 ± 0.115	1.98 ± 0.144	
Mortality	Nil	Nil	Nil	Nil	-

SD: Standard deviation.

7(7.2%) patients with right hemicolectomy received bowel preparation where resection anastomosis was planned prior to surgery. Carbohydrate loading was not done in any surgery, 33(44%) had nasogastric (NG) tube placed perioperatively in the elective group, 42(56%) showed compliance with ERAS protocol in the elective group. Besides, 12(57.14%) in the emergency group required the passage of NG tube against ERAS recommendations, with 9(42.85%) showing compliance in the emergency group. Further, 46(47.91%) patients required opioid analgesia postoperatively in addition to multimodal analgesia. As a part of multimodal analgesia, 26(27.08%) patients were given abdominal blocks and 43(44.79%) patients received epidural analgesia. Postoperatively, no nutritional supplementation was started on day 1, and nil per oral (NPO) time duration was invariably >6 hours. Mean compliance with all the protocol components was 74.9%±37.652 for both elective and emergency cases (Table 5).

Mean duration of surgery was 192.50±75.33 minutes, while mean LOS was 5.52±1.57 days (range: 2-10 days). Re-admission within 30 days was needed in 2(2.1%) cases (Table 6). There was no perioperative mortality.

Discussion

The median age of patients in the current study was 49.50 years with Interquartile Range (IQR) of 24 with male predominance. The findings were comparable with those of local and international studies.[8-10] Besides, age distribution was statistically significant ($p<0.05$) and showed that patients who underwent emergency surgery had mean age 56.86±4.503 years.

The debate between open and laparoscopic approach in CRC surgery still persists, especially with regard to complete mesocolic excision.[11] Studies showed non-inferiority of laparoscopic surgery with respect to oncological principles of surgery and longer operative time.[12,13] A study in Japan found similar oncological outcomes in both approaches, suggesting that laparoscopy was safe and could be the preferred approach.[14] A meta-analysis dne in the United Kingdom showed no short-term difference in morbidity and mortality between the two approaches.[12] Additionally, less bleeding and shorter duration were seen with the laparoscopic approach.[12] Overall, the ERAS guidelines are associated with improved outcomes regardless of open or laparoscopic surgery.[15] The current study showed no difference of compliance between open or laparoscopic approach between elective and emergency surgeries ($p=0.646$). The most common tumour site was rectum and sigmoid colon in emergency (57%) and elective (41.66%) cases, which was in line with a Turkish study.[16] Preadmission information, counselling, education, optimisation and prehabilitation is a routine that is followed in each patient at the institutional level, and was done in all patients except where it was not possible because of emergency surgery. The reason for 100% compliance in this regard was the detailed session done by the lead surgeon and team with the patients and attendants weeks before the actual surgery or before the emergency procedure. This enabled the identification and management of patient's risk factors, fears regarding the procedure and understanding of the disease and management. Hence, improved patient's confidence towards the treating surgeon as well as compliance to ERAS components was possible. High compliance in these components has also been documented internationally.[17] No significant difference ($p=0.285$) was observed between elective and emergency cases in terms of nutritional care compliance as per the ERAS guidelines4. Although elective, only 4.1% patients received preoperative nutritional care supplementation prior to surgery, which was a parameter that could be improved in the future. The documented compliance to nutritional component was poor in the current and in an earlier study as well.[17] A few studies have reported

preoperative nutritional care elements in their ERAS programmes.[18] However, improving nutritional care for 7-14 days prior to surgery improved outcomes.[19]

Optimisation of Hb levels where required, prevention of nausea and vomiting, pre-anaesthesia medications and antimicrobial prophylaxis are routinely done at the institutional level, thus there was 100% compliance in these elements in the current study comparable to earlier studies.[20,21] In elective CRC surgeries, the institutional practice is to use a combination of ceftriaxone and metronidazole for antimicrobial prophylaxis, whereas in emergency cases, tazobactam + piperacillin is used owing to increased risk of infective process due to perforation, obstruction or peritonitis.

In the current study, no bowel preparation in emergency cases was done, which was in accordance with ERAS guidelines[4]. In elective cases, bowel preparation was done in rectal surgeries and in those elective surgeries where resection-anastomosis was performed. Overall compliance was 92% whih was comparable to a study in Portugal.[21] Previously, bowel preparation prior to surgery was presumed to reduce stool mass, risk of surgical site infection (SSI) or risk of anastomotic leakage. However, with time, multiple studies have reported no difference in outcomes with or without bowel preparation.[22-24]

According to the ERAS guidelines, preoperative fasting of 6 hours for solids and 2 hours for clear liquids, including carbohydrate drinks, is highly recommended.[4] However in the current study, no carbohydrate loading in any patient was done, and NPO time was invariably >6 hours. This was also reported by a study in eastern India.[20]

Many of the patients were advised to come in fasting that started from the preceding night, and the patients were admitted early morning for surgery. Hence, the fasting time was variably >6 hours. Carbohydrate loading in patients with diabetes and delayed gastric emptying is still debatable, and is a routine that is still not very commonly followed even in -end healthcare systems.[25]

Opioid-sparing anaesthesia in ERAS pathway allows rapid awakening of the patient with minimal residual side effects, like bradycardia, respiratory depression, delayed mobilisation, postoperative nausea, vomiting and ileus.[4,26] In the current study, standard anaesthesia protocol with opioid-sparing was not the routine. The debate between complete opioid-sparing anaesthesia still persists as per the American Society of Colon and Rectal Surgeons and the Society of American Gastrointestinal and Endoscopic Surgeons. Thus a consensus remains on opioid-sparing anaesthesia rather than opioid eradication.[27] A study in India also reported a low compliance of 9% in this regard.[21] Hypothermia is the least-monitored complication during anaesthesia. Prevention of hypothermia intraoperatively is an important component, especially in open surgeries.[28] Temperature management intraoperatively causes decrease in SSIs and blood transfusion.[4,29] The current study had 100% compliance with the element of hypothermia, which was comparable to previous studies.[20,30] Combined compliance to minimally invasive surgery was 17.7% which was slightly lower than the finding of a study in Japan.[31] Compliance was low in the current study owing to lack of available resources, technicalities, costing and usually advance stage of CRC patients at the time of surgery. However, most of the laparoscopic surgeries were performed electively after the evaluation of comorbid conditions, size of tumour mass, patient's anaesthesia fitness, obesity, etc. Most of the emergency cases were addressed by open approach (80%). Emergency surgery was performed in 21.9% patients, which correlated with international data.[32] These patients presented with acute or subacute intestinal obstruction, localised perforation or full-blown peritonitis owing to tumour itself or due to closed loop phenomenon. Compliance with the placement of drains was seen more in emergency cases compared to elective cases (p=0.002). The current compliance rate was 13.54% which was comparable to 10% in an international study.[30] However, as per the ERAS guidelines[4], placement of drains confers no advantage on postoperative outcomes. Compliance with the placement of NG tubes in selective emergency cases and no elective cases was 53% in the current study, which was comparable to the 44% reported in an Indian study.[20] In contrast, a study in Portugal reported up to 80% compliance with ERAS guidelines for NG tubes placement.[21] The lack of compliance in the current study was secondary to conventional management pathways that are still being followed at the study institution. The difference of compliance between emergency and elective cases was non-significant (p=0.291).

Postoperative multimodal analgesia compliance was 48.8% in the current study, which included use of epidural and abdominal wall blocks for pain management. As a part of multimodal analgesia, 26 (27..08%) patients were given abdominal blocks and 43(44.79%) patients received epidural analgesia. Use of opioids was still required in many patients. Many of them were those who were not given epidural or abdominal wall adjuncts or those who could not be given non-steroidal anti-inflammatory drugs (NSAIDs) due to deranged renal function tests. There was no significant difference with respect to postoperative

opioid analgesia compliance between emergency and elective groups (p=0.344). Compliance with goal-directed fluid therapy, postoperative glycaemic control and thromboprophylaxis was 100% in the current study which was comparable to the findings of an international study.[33]

Compliance with the removal of urinary catheters in patients was 98.95% in the current study, which was similar to a study in Spain.[33] Since the current study could not limit postoperative opioid usage or perform laparoscopy in majority of the cases, and, additionally, the use of NG tubes could not be reduced, the compliance with the prevention of postoperative ileus was 62.92%.

Early mobilisation within 12 hours of surgery was achieved in 100% of the current patients in emergency as well as elective cases, which matched the finding of an Indian study.[20] Overall mean value of compliance with all the 25 ERAS components was 74.91% and that was comparable to a study in Switzerland.[34] Mean duration of surgery was 192.50 minutes, which was almost similar to a study in Japan.[31] Median LOS was 6 days, which was comparable to other studies.[32,35] Only 2(2.1%) patients required readmission within 30 days of surgery, which was in line with earlier studies.[23,31] No perioperative mortality was noted in the current study. ERAS guidelines have shown to decrease LOS and perioperative mortality.[36,37]

In the region where the current study was conducted, there is no proper screening programme for CRC patients. The fact that 70% of the current sample was aged at least 40 years advocates the need for proper local screening guidelines.

The current study has its limitations because of its retrospective design, and single–centre data. The study did not have a control group for comparison. Due to technical issues and cost limitations, laparoscopic surgery could not be offered to all patients, especially those who were in the earlier half of the study duration. Carbohydrate loading, although feasible, was not followed. The evolution of maximal drains and NG tubes usage to minimal or no placement is still in the process of acceptance at the institutional level. The study lacks comparison of compliance between non-ERAS and ERAS groups or among variable compliance subgroups within the ERAS group. No detailed effect of comorbid conditions, like diabetes, hypertension and chronic kidney disease, is taken into account.

Conclusion

There was no difference in compliance with ERAS elements in elective and emergency CRC surgeries. A favourable compliance of 74% reduced LOS, 30-day readmission rate and perioperative mortality. Compliance with ERAS protocols could improve further in parameters related to nutritional care, opioid sparing anaesthesia and analgesia, laparoscopic surgery, drains and NG tube placement.

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Authors' Contribution:
MU: Concept, data acquisition, analysis and agreement to be accountable for all aspects of the work.
MKK: Final approval.
AA: Data acquisition and interpretation.
MFM: Revision.
AS: Drafting.