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RESEARCH ARTICLE

ASSESSMENT OF ENHANCED RECOVERY AFTER SURGERY (ERAS®) PROTOCOL IN COLORECTAL CANCER SURGERY

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Abstract

Introduction: Colorectal cancer is the third most common type of cancer among men and is second in women. Enhanced Recovery After Surgery (ERAS) is used to improve the patient who underwent colorectal cancer surgery. Therefore, this study analyzed the clinical data of patients with colorectal cancer surgery who were treated according to the ERAS protocol.

Method: Patients scheduled for elective colorectal surgery between January 2017 and August 2022 were recruited in the current study. On the day of admission, patients were informed of the ERAS protocol and written informed consent form was taken from each patient. The ERAS team closely monitored and documented each ERAS protocol. The study outcome includes post-operative complications, re-admission and re-operation rate within 30 days, and length of hospital stay. The intention-to-treat statistical model was used for the current study. The data were analyzed using SPSS v25 and Jamovi®.

Results: The mean age of the study participants was 61.85 ± 8.45 years. Most of the participants were male (64.2%), and the most common co-morbidities were hypertension (27.6%) and diabetes (26.8%). The patients in the high adherence group showed a significant reduction in the post-operative complications($p<0.001$) based on Clavien–Dindograding. Surgical wound infection was most reported surgical complication (30.1%). Additionally, paralytic ileus (17.9%) and abdominal abscess (16.3%) were also common. Overall, the post-operative surgical complications were significantly reduced in the high adherence group. More than half of the study participants were re-admitted within 30 days (54.5%), and most prevalent in the low and mild adhered groups.

Conclusion: The present research found that when adherence to the ERAS protocol increased, surgical complications, re-admission, re-operation, and duration of stay in the hospital decreased significantly.

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Introduction:-

Colorectal cancer is the third most common type of cancer among men and is second in women(Hussain, Majeed et al. 2021). In 2020, the International Agency for Research on Cancer (IARC) reported 1.9 million new cases and 0.8 million deaths from colorectal cancer. The American Cancer Society (ACS) estimates that there will be 0.14 million cases of colorectal cancer in 2022. In South Asia, 0.18 million people were diagnosed with colorectal cancer, and 0.11 million died from this disease. Colorectal cancer is sixth among all types of cancer in Pakistan(Petimar, Smith-Warner et al. 2019, ACS 2022).

Most colorectal malignancies are adenocarcinomas. Some subtypes of adenocarcinoma, such as signet ring and mucinous, may have a worse prognosis than others. The other less common type of colorectal cancer includes carcinoid tumors, gastrointestinal stromal tumors (GISTs), lymphomas, and Sarcomas(Mäkinen 2007, Mattiuzzi, Sanchis-Gomar et al. 2019). These malignancies usually start in the mucus secreting cell and then spread either through direct invasion, hematogenous, lymphatic routes(Pretzsch, Bösch et al. 2019).

Surgery is usually the primary therapeutic option for colorectal cancer. The type of surgery performed is determined by location, stage of the tumor, and the intended outcome of the procedure(Matsuda, Yamashita et al. 2018).Colorectal cancer can be operated with colonoscopy, polypectomy, or local excision at early stages. Moreover, colectomy, anterior resection, and abdominal perianal resection (APR) are the various surgical options for colorectal cancer, depending on the tumor's location(Matsuda, Yamashita et al. 2018, Vassos and Piso 2018).

Enhanced Recovery After Surgery (ERAS) is a set of improvement metrics based on evidence-based medicine theory that is used to guide the optimization of the patient in the pre, peri, and post-operative periods. The development of an ERAS team has achieved good clinical outcomes. Previous studies showed a lower incidence of post-operative complications and shorter post-operative hospital stays by following ERAS protocol. Thus, these findings support the cost-effectiveness of ERAS (Kehlet and Dahl 2003, Pedziwiatr, Kisialeuski et al. 2015). ERAS protocol is most commonly used in the colorectal cancer surgery. Several clinical studies have found that compliance rates with the ERAS protocol are highly associated with good prognoses in patients with colorectal cancer. However, the data is still insufficient owing to the small number of elements in previous Eras studies(Gustafsson, Hausel et al. 2011, Geltzeiler, Rotramel et al. 2014, Pedziwiatr, Kisialeuski et al. 2015, Gustafsson, Oppelstrup et al. 2016).In this prospective study, we analyzed the clinical data of patients with colorectal cancer surgery who were treated according to the ERAS protocol.

Method:-

Patients scheduled for elective colorectal surgery between January 2017 and August 2022 were recruited. On the day of admission, patients were informed of the ERAS protocol and written informed consent was taken from each patient. Patients that were being above the age of 18 and having elective open or laparoscopic colorectal surgery were included in the current study. The exclusion criteria were patients with cognitive impairment, multiple organ resection, inability to get informed permission. The patient selection procedure can be seen in Fig. 1.

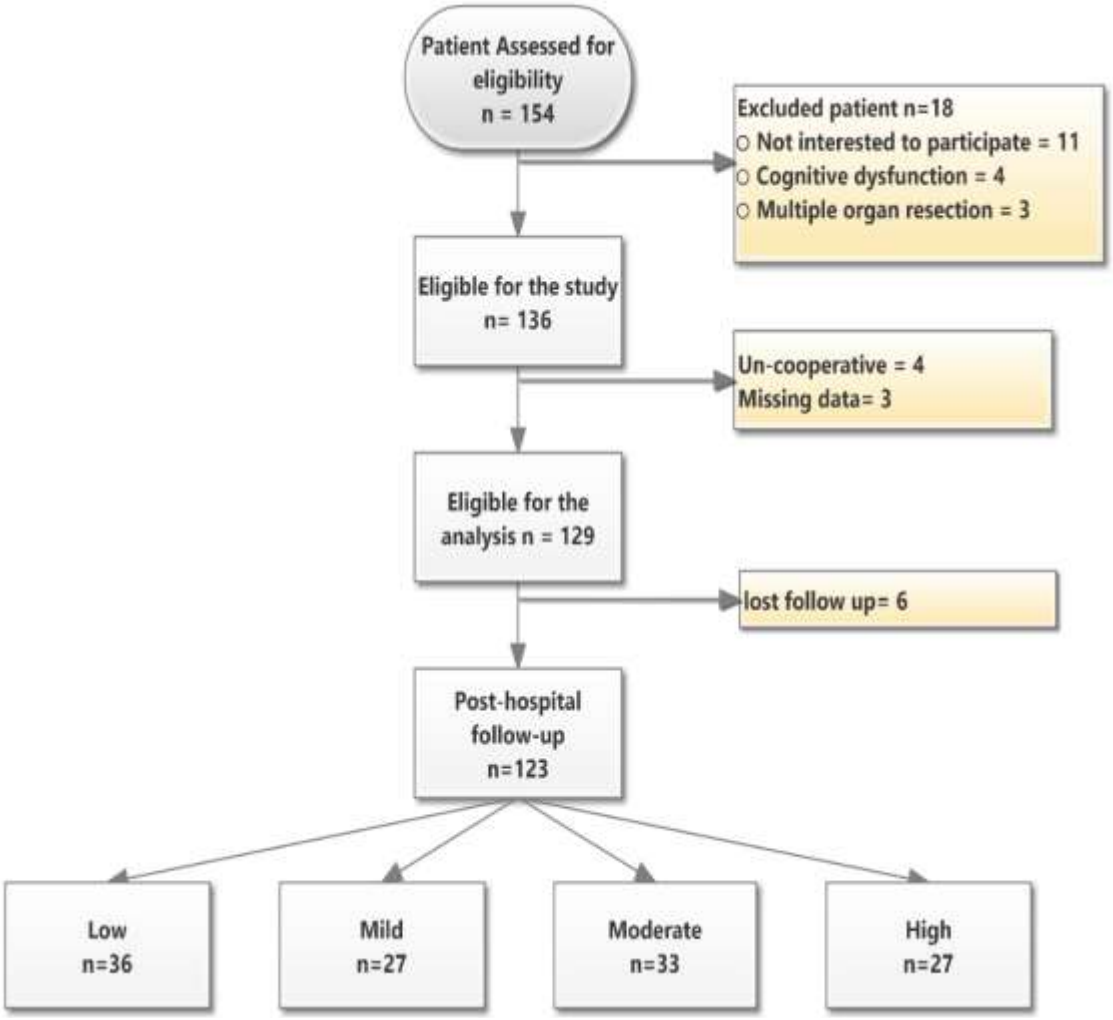

Figure 1:- Patient selection procedure.

The ERAS team was constituted by colorectal surgeons, anesthesiologist, physiotherapist, nutritionist, and nurses to efficiently apply the ERAS protocol. At weekly meetings, everyone on the team reported their work and talked with one another to verify that the procedure was working well(Kahokehr, Sammour et al. 2009, Gillissen, Ament et al. 2015). The ERAS protocol consisted of twenty-six items divided into preoperative, intraoperative, and post-operative interventions, as shown in supplementary table S1. Each patient's application of each item was documented. The number of perioperative interventions completed from the twenty-six items ERAS protocol was used to compute the compliance rate. Patients were separated into four groups based on their adherence to the ERAS protocol, including poor adherence (0-60%), mild adherence (60-70%), moderate adherence (70-80%), and high adherence (80-100%) as shown in Fig. 1.

Outcome variable

The post-operative complicationsweregraded based on Clavien–Dindo classification (CDC)(Dindo 2014). The post-operative complications were divided into five grades ranging from Grade I to Grad V, as shown in supplementary tableS2. Moreover, the main outcomes of the current study were surgical complications, re-admission rate at 30-day, re-operation for any indication within 30 days, and length of stay in the hospital.

Statistical analysis

The statistical analysis was performed using the statistical package for social sciences (SPSS v25) andJamovi®. The statistical model for the current study was the intention-to-treat model. Descriptive statistics was implied to assess the summary of the demographic data. Inferential statistics were used to assess the association betweendifferent strata of the ERAS protocol with study outcomes. The p-value was considered significant at 0.05 for all analyses.

Results:-

In the current study, the mean age of the study participants was 61.85 ± 8.45 years. Most of the participants were male (64.2%), and the most common co-morbidities were hypertension (27.6%) and diabetes (26.8%). General anesthesia and combined TAP block were used in almost equal proportions. The mean BMI of the study participants was 24.98 ± 2.18. The detail of the patient profile can be found in table 1.

Table 1:- Patient demographic characteristics.

		Overall N (%)	ERAS adherence level							
			Low		Mild		Moderate		High	
			N	%	N	%	N	%	N	%
Age (Mean±SD)		61.85 ± 8.45	65.25 ± 10.73		61.67 ±8.76		61.70 ±5.83		57.67±5.26	
Gender	Male	79(64.2)	21	26.6%	14	17.7%	21	26.6%	23	29.1%
	Female	44(35.8)	15	34.1%	13	29.5%	12	27.3%	4	9.1%
Co-morbidities	Hypertension	34(27.6)	15	44.1%	7	20.6%	6	17.6%	6	17.6%
	Diabetes mellites	33(26.8)	9	27.3%	5	15.2%	15	45.5%	4	12.1%
	CHD	18(14.6)	3	16.7%	6	33.3%	3	16.7%	6	33.3%
	COPD	23(18.7)	3	13.0%	7	30.4%	7	30.4%	6	26.1%
	Other	15(12.2)	6	40.0%	2	13.3%	2	13.3%	5	33.3%
Anesthesia	General anesthesia	64(52.0)	30	46.9%	11	17.2%	2	3.1%	21	32.8%
	combined TAP block	59(48.0)	6	10.2%	16	27.1%	31	52.5%	6	10.2%
Site	rectal	55(44.7)	18	32.7%	18	32.7%	10	18.2%	9	16.4%
	Colon	68(55.3)	18	26.5%	9	13.2%	23	33.8%	18	26.5%
BMI (Mean±SD)		24.98 ± 2.18	26.33 ±2.39		24.67±1.49		24.21±1.96		24.41±1.99	
Length of operation (Mean±SD)		13.07 ± 2.30	13.17±2.22		14.63±1.96		12.21±2.47		12.44±1.72	

The overall grading of the post-operative complication ranged from grade III to grade I. The patients in the high adherence group showed a significant reduction in the post-operative complications($p<0.001$). The CDC classification can be seen in Table 2.

Table 2:- CDC post-operative complication grading.

		Overall N (%)	ERAS adherence level								P-value
			Low		Mild		Moderate		High		
			N	%	N	%	N	%	N	%	
CDC	**Grade I**	32(26.0)	1	3.1%	4	12.5%	9	28.1%	18	56.3%	<0.001
	Grade II	21(17.1)	3	14.3%	5	23.8%	9	42.9%	4	19.0%	
	Grade III	34(27.6)	14	41.2%	9	26.5%	9	26.5%	2	5.9%	
	Grade IV	22(17.9)	9	40.9%	7	31.8%	4	18.2%	2	9.1%	
	Grade V	14(11.4)	9	64.3%	2	14.3%	2	14.3%	1	7.1%	

CDC - Clavien–Dindo classification

Surgical wound infection was the most reported surgical complication (30.1%). Additionally, paralytic ileus (17.9%) and abdominal abscess (16.3%) were also common. Overall, the post-operative surgical complications were significantly reduced in the high adherence group. More than half of the study participants were re-admitted within 30 days (54.5%) and were most prevalent in the low and mild adhered groups. Moreover, 17.9% of the study participants were re-operated within 30 days, low and mild adhered groups were the main contributors. The detail can be seen in Table 3.

Table 3:- Assessment of outcome variable of the study.

			Overall N (%)	ERAS adherence level								P-value
				Low		Mild		Moderate		High		
				N	%	N	%	N	%	N	%	
Surgical complication	Paralytic ileus		22(17.9)	8	36.4%	6	27.3%	6	27.3%	2	9.1%	0.193
	Surgical wound infection		37(30.1)	6	16.2%	4	10.8%	11	29.7%	16	43.2%	
	Abdominal abscess		20(16.3)	6	30.0%	5	25.0%	5	25.0%	4	20.0%	
	Intestinal fistula		18(14.6)	6	33.3%	6	33.3%	4	22.2%	2	11.1%	
	Anastomotic dehiscence		16(13.0)	6	37.5%	3	18.8%	5	31.3%	2	12.5%	
	Mortality		10(8.1)	4	40.0%	3	30.0%	2	20.0%	1	10.0%	
Re-admission rate at 30 day all cause		Yes	67(54.5)	24	35.8%	18	26.9%	16	23.9%	9	13.4%	0.028
		No	56(45.5)	12	21.4%	9	16.1%	17	30.4%	18	32.1%	
Re-operation for any indication within 30 days		Yes	22 (17.9)	9	40.9%	7	31.8%	4	18.2%	2	9.1%	0.158
		No	101(82.1)	27	26.7%	20	19.8%	29	28.7%	25	24.8%	
LOS (mean±SD)			11.91 ± 2.75	14.06±2.12		12.93±2.40		10.70±1.79		9.52±2.12		<0.001

Discussion:-

The current study explored a significant positive effect of the ERAS protocol on the post-operative complications in patients who underwent colorectal cancer surgery. Based on CDC grading, the post-operative complications were significantly reduced from severe to mild complications by high adherence to the ERAS protocol. It has been seen in the current study that surgical complications, re-admission, re-operation, and length of stay in the hospital was greatly reduced as adherence to the ERAS protocol increased.

The ERAS idea has been adopted and implemented at our institution, and the multidisciplinary team members (MDT) have obtained complete coordination and collaborated more closely. However, to guarantee patient safety, we respected the patients' autonomy. This may attribute to variability among the study group regarding compliance rate(Li, Jin et al. 2017). In the lowest compliance group, carbohydrate drinks, anesthetic protocols, perioperative fluid management, multimodal analgesic treatments, early oral intake, early mobility, early drainage tube removal, and early urine catheter removal had reduced implementation rates. Due to established ideology, these therapies are administered seldom or rarely at all during standard perioperative care, which may result in a poor prognosis for patients following colorectal surgery, as reported previously (Urbach, Kennedy et al. 1999, Lovely, Maxson et al. 2012, Smith, McCall et al. 2014, Miller, Roche et al. 2015).

We did not employ the grouping approach based on the ERAS protocol's implementation phase(Pędziwiatr, Kisialeuski et al. 2015). To increase the accuracy of the conclusion and control for characteristics that may vary over time, patients were immediately categorized according to the range of compliance rates. In the current study, post-surgical complications were decreased as the ERAS adherence increased, except for surgical wound infections. In addition, the rate of re-admission and re-operation was gradually reduced with an increase in ERAS adherence. The hospital stay was significantly reduced in patients with greater ERAS adherence. Overall, the ERAS was significantly cost-effective in patients who underwent colorectal cancer surgery. These findings were consistent with the previously reported study (Li, Jin et al. 2017).

Several limitations of the current study must be noted. First, the rate of implementation of some aspects of the ERAS protocol, such as no prior bowel preparation and early urine catheter removal, was typically insufficient. To enhance the execution of ERAS protocols, close interdisciplinary collaboration is required. Secondly, this was a single-center observational analysis; certainly, multicenter, and large-scale studies are necessary to confirm the present findings. The relationship between enhanced adherence to the ERAS procedure and improved long-term outcomes after colorectal surgery needs additional exploration in the future. In addition, a particular ERAS protocol should be designed for colorectal cancer surgery to offer patients with tailored perioperative care.

Conclusion:-

The current study looked at whether the ERAS protocol substantially decreased post-operative complications in patients who underwent colorectal cancer surgery. Based on CDC grading by strictly adhering to the ERAS protocol, post-operative complications decreased from severe to moderate. The present research found that when adherence to the ERAS protocol increased, surgical complications, re-admission, re-operation, and duration of stay in the hospital decreased significantly.

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Supplementary Table S1. ERAS protocol applied in the study

1	Preoperative counseling, patient education
2	Nutritional assessment and enteral nutrition support
3	Cardiopulmonary function evaluation and optimization
4	No preoperative bowel preparation
5	Preoperative fasting time: 6-8 hours for solid food, 2 hours for clear liquids
6	Oral intake of 400 ml carbohydrate drink: up to 2-3 hours before the induction of anesthesia
7	Intravenous antibiotics 30 minutes before incision
8	No preanesthetic medication
9	General anesthesia with rapid short-acting agents combined with TAP block
10	Laparoscopic surgery
11	Anesthesia depth monitoring with bispectrality index or narcotrend index
12	Intraoperative lung-protective ventilatory strategy
13	Intraoperative neuromuscular monitoring
14	Prevention of intraoperative hypothermia
15	Intraoperative goal-directed fluid therapy and post-operative restrictive fluid administration
16	Perioperative blood glucose control
17	Multimodal prevention of PONV
18	Multimodal prevention of DVT (physical prophylaxis combined with low molecular weight heparin administration)
19	No nasogastric tube postoperatively
20	Prevention of stress ulcer (perioperative administration of proton pump inhibitor)
21	Multimodal management of post-operative pain (PCIA, TAP, NSAIDs, COX-2 inhibitor)
22	Avoiding incision infection
23	Early oral intake (drink water 2 hours after surgery, oral nutritional supplements on the first day after surgery, semi-solid diet on the second day after surgery)
24	Early mobilization (out-of-bed activity for 2 hours on the first post-operative day and 4-6 hours from the second post-operative day to discharge)
25	Removal of drainage tubes within three days after surgery

26	Removal of urinary catheter as soon as possible (within 24 hours for colon surgery patients; within 48 hours for rectal surgery patients)

Supplementary Table S2. Clavien–Dindo classification of post-surgical complications

Grades	Definition
I	Any deviation from the normal post-operative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside
II	Requiring pharmacological treatment with drugs other than such allowed for Grade I complications. Blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic, or radiological intervention
IV	Life-threatening complication requiring ICU (intensive care unit) management
V	Death

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