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Systematic Review

Is ERAS Protocol Necessary during Ileostomy Reversal in Patients after Anterior Rectal Resection—A Systematic Review and Meta-Analysis

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Abstract: Purpose: The aim of this study is to establish whether implement ation of the ERAS protocol has a beneficial effect postoperatively after ileostomy reversal. Introduction: Loop ileostomy is commonly performed during anterior rectal resection with total mesorectal excision to protect the newly created anastomosis. Ileostomy reversal is performed after rectal anastomoses are completely healed and can be associated with complications. The use of the ERAS protocol in elective colorectal surgery has been shown to significantly reduce the complication rate and length of hospital stay without an increased readmission rate. Methods: After PROSPERO registration (CRD42023449551), a systematic review of the following databases was carried out: MEDLINE/PubMed, EMBASE, Web of Science, and Scopus. This meta-analysis involved studies up to December 2023 without language restrictions. A random effects model meta-analysis was performed to assess complications, readmissions, and length of stay (LOS) in ileostomy reversal patients with and without ERAS protocol implementation. Results: Six articles were analyzed, and each study reported on the elements of the ERAS protocol. There was no significant difference between the ERAS and non-ERAS groups in terms of complications rate (OR = 0.98; 95%CI: 0.64–1.52; I^2 = 0%). Postoperative ileus was the most prevalent adverse event in both groups. The readmission rate did not differ significantly between the groups (OR = 1.77; 95%CI: 0.85–3.50, I^2 = 0%). In comparison to the control group, the LOS in the ERAS group was noticeably shorter (MD = −1.94; 95%CI: −3.38–−0.49; I^2 = 77%). Conclusions: Following the ERAS protocol can result in a shorter LOS and does not increase complications or readmission rates in patients undergoing ileostomy reversal. Thus, the ERAS protocol is recommended for clinical implementation.

Keywords: ERAS; loop ileostomy; anterior rectal resection; meta-analysis

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1. Introduction

A loop ileostomy is commonly performed during anterior rectal resection with total mesorectal excision to protect the newly created anastomoses [1,2]. The most dreadful complication of rectal cancer surgery is anastomosis leakage, which lowers oncological outcomes in terms of local recurrence and survival and raises morbidity and death rates [3]. The colon leakage score was established in order to estimate the possibility of an anastomotic leak after left-sided colorectal surgery, and it is an effective method for predicting the aforementioned complication [4]. Diverting fecal contents from an anastomosis is believed to reduce the rate of anastomotic leakage [5,6]. Nevertheless, some recent studies have reported that ileostomy presence does not reduce the leakage rate [7,8]. Moreover, ileostomy reversal performed after rectal anastomosis is healed can be associated with complication rates as high as 21% and even up to 45.9% in some studies [8,9]. Even 11% to 37% of ileostomies are becoming permanent and are never reversed after rectal surgery [1,10]. One of the factors that can have a significant influence on postoperative complications and has been widely explored is the interval from ileostomy creation to liquidation [11,12]. The other important aspect that could be responsible for perioperative complications is the perioperative care of patients undergoing ileostomy reversal. ERAS protocol use in elective colorectal surgery has been shown to significantly reduce the complication rate and LOS without an increase in readmission rates [13]. This fact has widely affected perioperative care worldwide, and many surgical centers have implemented the ERAS protocol for major colorectal surgeries such as hemicolectomy, sigmoid, or rectal resection in heterogeneous groups of patients [14–17]. No comparative meta-analysis regarding the influence of the ERAS protocol on patients undergoing ileostomy reversal has been available.

The aim of our study is to establish whether the implementation of the ERAS protocol has an effect on complication rates, LOS, and readmission rates in patients undergoing ileostomy reversal.

2. Materials and Methods

The authors followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, the PRISMA checklist (Supplementary File S1) is available as a supplement to this article [16]. Furthermore, our research was registered in the PROSPERO register under the following ID number: CRD42023449551.

2.1. Search Strategy

A thorough search of the following databases was conducted in July 2023: MEDLINE/PubMed, EMBASE, Web of Science, and Scopus. During the search, no filters were applied. Authors used the following phrases in the search: "ileostomy", "reversal", "ostomy", "ERAS", "recovery", " track", "protocol", and " perioperative care." The full search strategy is available as a supplement to this article.

After the articles were selected for this study, their reference lists were manually screened for further eligible publications.

2.2. Inclusion Process

The studies comparing ERAS protocol implementation and standard of care for ileostomy closure were included in the analysis following the inclusion and exclusion criteria.

Inclusion criteria:

1. Age 18 years or older.
2. Original clinical studies.
3. Outcomes, including LOS, complication rate, mortality, or rehospitalization rate.
4. End ileostomy or loop ileostomy closure.

Exclusion criterion:

1. Incorrect publication type, i.e., meta-analysis, case report.
2. Ileostomy reversal conducted as a part of a bigger procedure (e.g., liver resection due to metastases with concurrent ileostomy reversal).
3. Missing information about the inclusion of the fast track/ERAS protocol elements (e.g., pre-op counseling, avoiding fasting, opioid-sparing analgesia, early ambulation, early post-op diet, etc.) in the study.

First, the studies were screened independently by two researchers (JR and MZ). In case of any disagreement, a decision was made after discussion. Then, full texts of articles were read by two independent researchers, and the relevant studies were included. All disagreements were resolved by discussion and joint analysis of the datasets.

2.3. Extraction

Data were extracted from the included studies by two independent researchers (JR and MZ) with the use of a previously designed spreadsheet. In case of any disagreement, a consensus was reached after discussion. If required, an additional author was involved to reach a consensus (TS). Full texts were double-checked by the main author (MK) to confirm the presence of the necessary ERAS protocol data, with consequent eligibility for further data meta-analysis. For dichotomous variables, the number of events was collected. For continuous data (LOS), mean and standard deviation (SD) were necessary for the analysis. However, in three studies (Slieker 2018, Raue 2008, Shen 2023), medians, along with the first and third quartiles, were reported. Therefore, an appropriate estimation method was used to establish the mean and SD [18,19]. In case of missing identification data, the corresponding authors of the included articles were contacted.

2.4. Quality Assessment

After inclusion, the quality of each was assessed. For one randomized study, the Cochrane Risk of Bias Tool (RoB) was used, while other studies were evaluated by the Newcastle-Ottawa Quality Assessment for Cohort Studies (NOS) and its appropriate modification was used for case-control study evaluation. Quality assessment was performed by the review authors (JR, MZ, and TS). Any disagreement was resolved by involving senior researchers (TW and WMW). None of the articles were excluded due to poor quality.

2.5. Outcomes

The following data were extracted: name of the primary author, year of publication, study design (case-control, cohort, cross-sectional, RCT), population description (number of participants, country, age), ERAS protocol components, and characteristics of ileostomy procedures (number of complications, number of readmissions, mortality rate, and LOS).

2.6. Statistical Analysis

Meta-analyses were conducted for the following three major outcomes: complications, readmissions, and LOS. The analysis was conducted using the Revman 5 tool (Cochrane). All of the outcomes were analyzed by inverse-variance statistical methods. A random effects model was implemented while analyzing all of the outcomes. The effect measure for continuous data was the mean difference (MD), while for dichotomous data, the odds ratio (OR) was used. Both Chi^2 tests and I^2 tests were used to assess heterogeneity. I^2 results were interpreted as follows: 0–40% may not be important, 30–60% may indicate moderate heterogeneity, 50–60% may show substantial heterogeneity, and 75–100% may represent considerable heterogeneity. $p < 0.10$ was considered significant in the case of Chi^2 interpretation. All outcomes are presented as forest plots.

3. Results

At first, 882 studies were identified from the database search, and none of the references used were acquired from other sources. After automatic duplicate removal, the remaining 535 abstracts were screened, and afterward, 17 references were included for further full-text assessment. Finally, after eligibility evaluation, six studies (19–24) were included. A PRISMA flowchart of the inclusion process is shown in Figure 1.

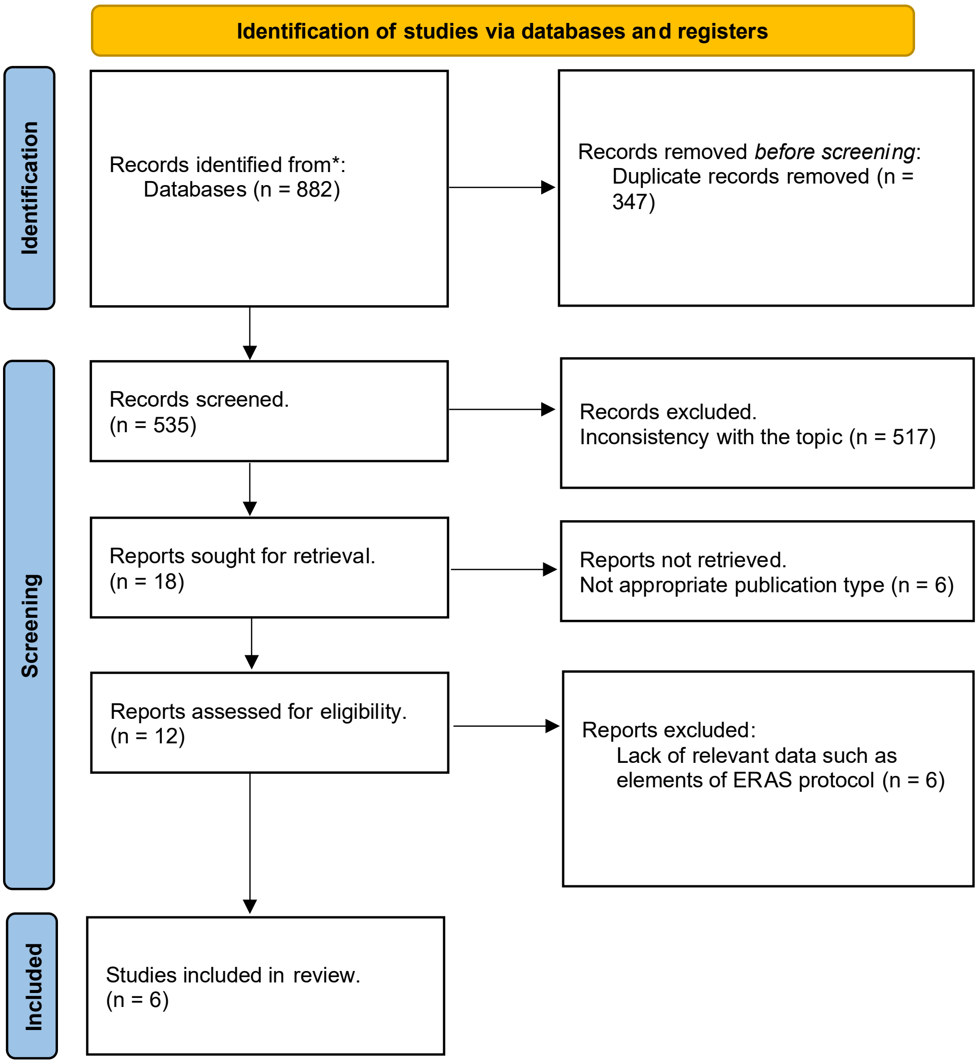

Figure 1. PRISMA flowchart of the inclusion process. * Type of source that data was identified.

3.1. Included Studies

Our meta-analysis consists of data from a total of 919 patients. The included studies were published between 2008 and 2023 and were conducted in the United Kingdom (145 patients), Switzerland (117 patients), USA (208 patients), Pakistan (60 patients), Germany (40 patients), and China (349 patients).

All studies reported the complication rate and LOS. However, not every study was included in the LOS analysis. Firstly, in Ottaviano 2020, only medians with interquartile ranges were reported, which made an estimation impossible. Secondly, in Yu Shen 2023, detailed information about LOS in the ERAS group was not presented.

Three studies reported the readmission rate (Table 1).

Table 1. Characteristics of the included studies [20–25].

First Author	Year	Country	Study Design	Mean Age (SD) in ERAS Group	Number of ERAS Patients	Mean Age (SD) in Control Group	Number of Control Patients
Bracey E	2015	UK	Cohort study	63.6 (12.84)	37	69.66 (12.04)	108
Slieker J	2018	Switzerland	Case-control study	Median (Q1–Q3): 59 (48.5–68.5)	69	Median (Q1–Q3): 64 (52.5–70.8)	48
Ottaviano K	2020	USA	Case-control study	54.2 (15.7)	59	51.1 (17.1)	149
Pirzada MT	2017	Pakistan	Randomized controlled trial	23.87 (4.56)	30	27.80 (9.99)	30
Raue W	2008	Germany	Non-randomized controlled trial	Median (Q1–Q3): 64.2 (29–75)	20	Median (Q1–Q3): 58.8 (25–73)	20
Shen Y	2023	China	Case-control study	Median (Q1–Q3): 55 (15–65)	213	Median (Q1–Q3): 62 (35–83)	136

3.2. ERAS Protocol

In their perioperative care sections, all of the included studies reported the characteristic components of the ERAS protocol. In every study, preoperative counseling was provided while carbohydrate loading was administered in almost all of the studies. Short-acting anesthetic drugs were used with opioids, limiting postoperative analgesia regimens in all the studies. The use of antithrombotic prophylaxis was not reported, and half of the studies reported the use of antibiotics and postoperative nausea and vomiting prophylaxis. Only two studies focused on nasogastric tube and drain usage postoperatively. Early postoperative diet and mobilization were mentioned in all the studies. Detailed information regarding the ERAS protocol components can be found in Table 2.

Table 2. ERAS protocol elements [20–25].

Study	Preoperative Counseling	Preoperative Carbohydrate Loading	Antithrombotic Prophylaxis	Antibiotic Prophylaxis	Laparoscopic Surgery	Balanced Intravenous Fluid Therapy	No Nasogastric Tubes Left Postoperatively
Bracey E 2015	Yes	No	No	No	No	Yes	No
Slieker J 2018	Yes	Yes	No	No	Yes	Yes	No
Ottaviano K 2020	Yes	Yes	No	No	Yes	No	No
Pirzada MT 2017	Yes	Yes	No	Yes	Yes	Yes	Yes
Raue W 2008	Yes	Yes	No	Yes	Yes	Yes	Yes
Shen Y 2023	Yes	No	No	Yes	Yes	No	No

3.3. Complications

Overall, all studies (a total of 919 patients) reported complication rates: 63 patients experienced complications in the ERAS group and 95 patients in the standard protocol group. There was no significant difference between the groups regarding the complication rate (OR = 0.98; 95%CI: 0.64–1.52), and there was no heterogeneity among the studies (I^2 =

0%) (Figure 2). Postoperative ileus was the most prevalent complication in both groups, as it appeared in 25 patients in the ERAS group and in 43 patients in the control group.

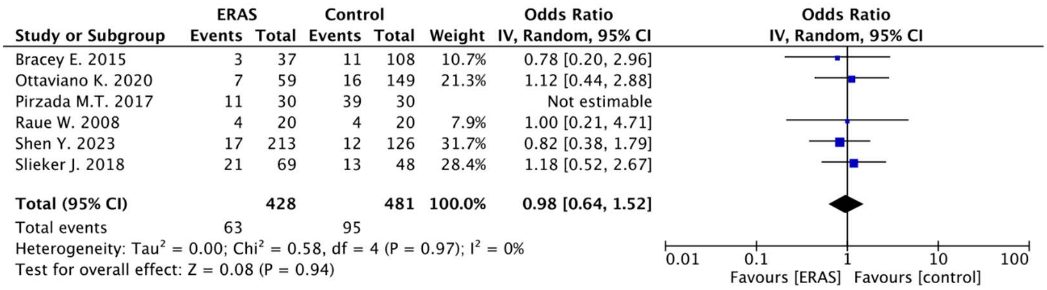

Figure 2. Meta-analysis comparing the complications rate between the groups [20–25].

3.4. Readmissions

Readmissions were reported by three studies, which totaled 702 patients; 21 patients were readmitted to the hospital in the ERAS group and 19 patients in the control group. We did not find a significant difference in readmission rate between the groups (OR = 1.77; 95%CI: 0.85–3.50), and there was no heterogeneity among the studies (I^2 = 0%) (Figure 3).

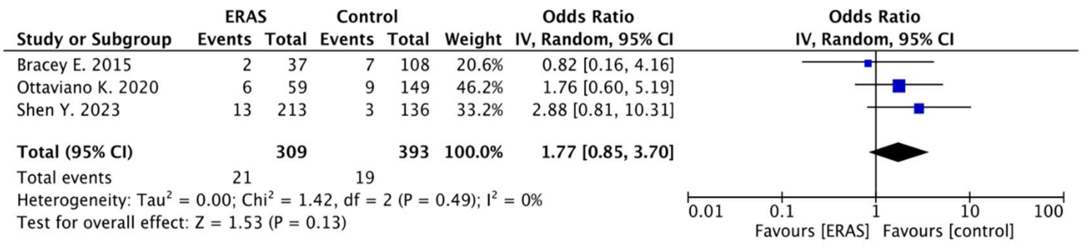

Figure 3. Meta-analysis comparing the readmission rate between the groups [22–24].

3.5. Length of Stay

Although all of the studies reported LOS, only four were included in the analysis (for a total of 332 patients); Ottaviano et al. reported only a median with IQR, and SD estimation is irrelevant on the basis of this data; Shen et al. did not report LOS for the ERAS group, providing information that it was shorter than 24 h [1,2]. LOS in the ERAS group is significantly shorter than that in the control group (MD = −1.94; 95%CI: −3.38–0.49). However, heterogeneity among the studies may be considerable (I^2 = 77%) (Figure 4).

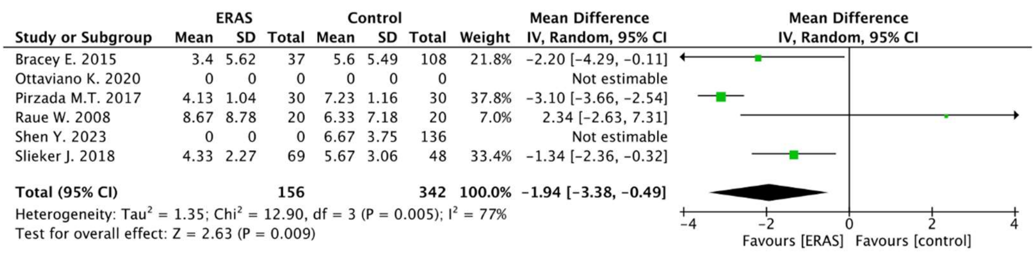

Figure 4. Meta-analysis comparing the length of stay between the groups [20–25].

4. Discussion

Implementation of the ERAS protocol in elective major colorectal surgery is known for its beneficial effect on the rate of perioperative complications and for LOS reduction with no additional increase in readmissions. The updated ERAS guidelines were published in 2018 [25]. The first attempts to use some elements of today's ERAS protocol in patients undergoing stoma reversal surgery were in 2008 [25]. It is known that the level of implementation of the ERAS protocol elements can be predictive of postoperative complications; the more elements of the ERAS protocol are incorporated into patient care, the smaller the risk of postoperative complications [26]. Classically, the number of complications in major elective colorectal procedures was lower when the ERAS protocol was used compared to patients treated conventionally. This could be due to significant perioperative stress reduction. Results from our meta-analysis have shown that despite the use of the ERAS protocol, the number of complications did not decrease in patients undergoing ileostomy reversal. This could be due to the smaller perioperative stress and, hence, smaller stress reduction in patients [27]. Moreover, data about the timing of stoma reversal were not present, and this could be a prognostic factor for perioperative complications, with some researchers suggesting that early ileostomy reversal should be a part of the ERAS protocol due to the lower perioperative complication risk [28,29].

Patients undergoing major colorectal laparoscopic resection benefit from a minimally invasive approach and have a much smaller inflammatory response [30]. Despite that, Sujatha-Bhaskar et al. presented that laparoscopic ileostomy reversal is feasible and is associated with shorter LOS and no increase in direct costs and that the majority of ileostomies reversed all around the world are performed by open surgery through the ileostomy site [31].

Another important element of the ERAS protocol is the preoperative carbohydrate load, which decreases insulin resistance perioperatively. As was shown in another study, this effect could be unnoticeable in cases of smaller procedures, like laparoscopic cholecystectomy. Similarly, this could be true for ileostomy reversal since our meta-analysis did not show any significant increases in the complication rate in the non-ERAS group [32]. Antithrombotic prophylaxis and antibiotic prophylaxis are widely used nowadays in every elective surgery in developed countries, showing an implementation rate of up to 99% in many studies [33–35]. In some of the analyzed studies, there was missing information about the level of antithrombotic and antibiotic prophylaxis, perhaps because their use was widely incorporated in perioperative care with or without implementation of the ERAS protocol. Despite this, the number of complications was similar between the ERAS and non-ERAS groups. Preoperative counseling, with the recommendation of smoking cessation prior to surgery, has proven to be crucial in the reduction of postoperative complications, especially wound infections that are very frequent after ileostomy reversal [36–38]. Preoperative counseling was mentioned in all of the studies. As the number of postoperative complications did not differ significantly, one can assume that counseling does not have a visible effect in cases of ileostomy reversal surgery. However, we recommend interpreting the findings carefully due to the presence of non-randomized case-control studies in the analyzed material and the risk of underreported minimal complications, like wound infections.

The length of hospital stay was significantly shorter in the ERAS group, but due to the heterogeneity of the included studies, we interpreted our findings solicitously. There are available case series concerning short (<24 h) stoma reversal hospitalizations with good results and high patient satisfaction [39]. In our opinion, these findings should not be extrapolated on a wider scale; this scenario could be possible only in countries with very developed outpatient monitoring of discharged patients, including various telemedicine instruments, medical assistants, or nurses available in outpatient settings for regular check-ups, in addition to outpatient control led by surgeons. Considering that even in many European countries, there is a constant shortage of medical professionals, a 24 h discharge policy should be considered only in selected, highly developed colorectal units with vast outpatient support [40,41]. Moreover, we should keep in mind that a lot of patients after ileostomy reversal are elderly, sometimes from rural areas, and commonly have no immediate access to hospital facilities in cases of post-discharge complications. Our meta-analysis did not find statistically significant differences in readmission rates between the two groups, which is one of the typically observed findings when the ERAS protocol is used [42]. According to Archer et al., faster patient discharge after ileostomy reversal was not associated with higher readmission rates; thus, it is beneficial for patients whose perioperative care was based on the enhanced recovery protocol. This may also be more cost-effective for health institutions. Faster discharge with no increase in readmissions can increase the number of hospital beds available and create additional patient volumes in hospitals incorporating this approach.

Among the limitations of our study is the presence of different study designs—randomized and non-randomized control studies, cohort studies, and case-control studies. Another limitation could be the variations in the early ERAS protocols introduced across surgical departments at the beginning of the ERAS protocol establishment. Perioperative care, involvement of minimally invasive techniques, and discharge policies could differ between the included studies, especially those containing data from 2005 to 2013 when the ERAS guidelines were published for the first time.

5. Conclusions

Patients undergoing ileostomy reversal do not fully benefit from all the positive aspects of the ERAS protocol. The ERAS protocol did not reduce the perioperative complication risk in patients undergoing ileostomy reversal. Nonetheless, ERAS allows for shorter LOS and does not increase the readmission rate, meaning that the ERAS protocol provides some benefits to patients undergoing ileostomy reversal and can be recommended with a more liberal approach (e.g., no need for laparoscopic technique use).

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/gastroent15030051/s1, Supplementary File S1: PRISMACheck-list.ERAS. Supplementary File S2: supplementary.eras.search.strategy.

Author Contributions: Conceptualization and study design: M.K. and W.M.W.; data collection: M.K., J.R., M.Z. and T.S.; statistical analysis: M.K., J.R., M.Z., T.S., M.P.-A. and W.M.W.; data interpretation: M.K., J.R., M.Z., T.S., M. P-A., T.W. and W.M.W.; manuscript preparation: M.K., J.R., M.Z., T.S., M.P.-A., K.R. and W.M.W.; literature search: M.K., J.R., M.Z. and T.S. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Ethical approval and the informed consent of the participants are not required in systematic reviews with meta-analysis.

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