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Research Article

Is Enhanced Recovery After Surgery Pathway (ERAS) Influential in Reducing Length of Patients Stay in Colorectal Surgery: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Background: A systematic review and meta-analysis was conducted after identifying from the literature that enhanced recovery after surgery (ERAS) pathway reduces length of stay (LOS) and control health expenses after colorectal surgery. This review paper follows PRISMA guidelines and retrieved randomized controlled trials (RCTs) to assess the efficacy of ERAS pathway in reducing LOS after colorectal surgical discharge. In addition, this review paper aims to evaluate other post-operative complications such as mortality rates, costs, and readmission rates with the implementation of ERAS pathway.

Methods: Eligible RCTs (n = 17) were included in this review paper from PubMed, CINAHL Plus, EMBASE, and MEDLINE from January 1st 2011 and March 31st 2020. Each trial was cross-checked in terms of its publication bias and quality rigor. Restrictions were set for English publications only.

Results: A total of 7500 patients were included in 17 RCTs. The ERAS pathway was associated to shorter mean LOS [MD = -1.07 days, (-1.99, -0.15), p for effect < 0.001, p for heterogeneity < 0.0001, I^2 = 98%] without increasing readmission rates and cost associated to colorectal surgery. Mortality rates were also controlled with the implementation of ERAS pathway as compared to standard care.

Conclusion: There was significant evidence in reduction in mean LOS after colorectal surgery with the implementation of ERAS pathways. The appropriate ERAS pathway implementation results in controlling other secondary complications.

Keywords: Colorectal Surgery; ERAS; Length of Stay; Randomized Controlled Trials

Introduction

The association between mean postoperative inpatient stays of up to 11 days and complication rate of approximately 20% with colorectal surgery has been widely studied [1-3]. The enhanced recovery after surgery (ERAS) principals have been predefined and optimized for facilitating discharge and perioperative care [4,5]. ERAS emphasized; as an evidence-based multimodal perioperative protocol, on the betterment of recovery and stress reduction [6]. It essentially shifts the conventional patient care in surgical departments to one that exercises in based on the extant evidence [7].

After major elective open colorectal surgery and with conventional perioperative care, factors such as postoperative ileus, stress, pain, and immobilization led to increased complication rates and length of stay (LOS) [8,9]. ERAS protocols are a preliminary deter-

minant of long-term survival, if an impediment occurs [10]. It has been observed that median patient survival over the following 10 years is reduced with the prevalence of any complication by approximately 65% [10]. Caring is also expensive for patients with impediments, aggregating a cost of $10,000 of a surgical impediment [11].

Existing evidence has shown that ERAS protocols are used in reducing postoperative complications and LOS regardless of increasing readmission and mortality rates [12-16]. On the contrary, evidence on LOS to ERAS protocols in colorectal surgery is limited. Previously, a significant reduction in hospital costing and complications were demonstrated in meta-analyses to ERAS protocols in liver surgery [14,15]. Similarly, Rawlinson., *et al*. [5] conducted a systematic review of ERAS protocols in colorectal surgery and found significant reduction in LOS. However, there lacks update evidence of ERAS protocols on LOS after colorectal surgery after 2011. Based on these reviews, the aim of this systematic review and meta-analysis was to present an updated evidence of ERAS protocols on LOS after colorectal surgery in both young and elderly populations.

Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were comprehensively followed in this review for both systematic review and meta-analysis [17]. The searching for articles was conducted in March 2020 on the following databases: (1) PubMed, (2) CINAHL Plus, (3) MEDLINE, and (4) EMBASE between 2011 and 2020 (March). Rawlinson., *et al*. [5] was set as a baseline as the review paper conducted systematic review on LOS after colorectal surgery. Therefore, to present updated evidence, this review paper searches publications from 2011 till date. English was the preferred language for the search criteria. This review has searched for randomized controlled trials (RCTs) for relevant studies and prepared a reference list. The search terms include: (1) perioperative care, (2) ERAS, (3) enhanced recovery, (4) reduction, (5) length of stay, (6) LOS, (7) colorectal surgery, (8) colon, and (9) rectal.

Inclusion/exclusion criteria

Articles were found eligible if they met the following inclusion criteria: (1) compared ERAS to traditional care, (2) studies of young and adult patients undergoing colorectal surgery, and (3) report LOS. Articles were excluded if: (1) not comparing ERAS to traditional care, (2) non-English and (3) transplant or non-elective patients.

Data extraction

The primary researcher has retrieved and extracted the eligible studies. A data extraction sheet was used to extract data, and was then validated by other researchers. Following data were extracted: author's names, type of surgery, sample size, follow-up period, outcomes measured, patient's characteristics, study design, and ERAS protocol items.

Outcomes of interest

LOS was the primary outcome for this systematic review. Hospital cost, compliance and mortality rates, readmission rates, and complication rate were considered as secondary outcomes.

Quality assessment

The Cochrane Collaboration's risk of bias tool was used to assess the quality of the eligible studies. The methodological quality of selected RCTs was assessed through the Modified Downs and Black checklist.

Statistical analysis

Review Manager (RevMan) version 5.3 was used to perform meta-analysis. All dichotomous variables were presented through relative risk; continuous variables through weight standardized mean and weight difference mean with 95% confidence interval (CI). A chi-squared test was used to assess statistical heterogeneity, with $p > 0.05$ as statistically significant level. The presence of publication bias was presented through funnel plots, whereas interquartile ranges and medians were used to present the study data.

Results

A total 299 studies were retrieved from all the four databases during the predefined period. Among these, seventeen articles [18-34] found eligible were published in peer-reviewed journals. All of the publications were in English. The focus of these publications was entirely on the randomized control trials. The qualitative synthesis was performed based on 6 articles while eleven published articles were selected in meta-analysis (Figure 1).

A total of 7500 patients underwent through either ERAS or conventional treatment in included 18 studies. Out of 7500 patients,

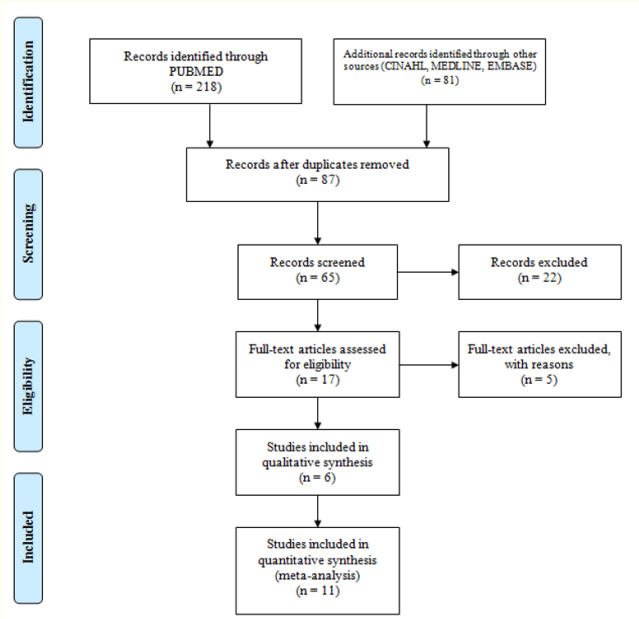

Figure 1: PRISMA Flowchart.

3017 patients underwent ERAS program whereas 4202 patients underwent conventional treatment for colorectal surgery. The methodological quality of the 17 articles is summarized in table below. Four studies were considered at high risk of bias.

Primary outcomes

Figure 2 illustrates the pooled estimates of LOS comparing ERAS program versus standard care. Mean LOS was 4.43 days in the ERAS group and 5.69 days in the standard care or conventional group [MD = -1.07 days, (-1.99, -0.15), p for effect <0.001, p for heterogeneity <0.0001, I^2 =98%].

Secondary outcomes

Cost

Evidence related to cost was merely found in the study of Miller., *et al*. [28]. According to the findings, there was a lower medical costs pattern identified in the ERAS group with statistically insignificant difference. On the contrary, cost data were typically skewed and need a major sample as compared to the available on in the Miller's study [28]. Thereby, Miller had used bootstrap analysis for observing the distribution of the differences in mean cost values

Trial	Multi-centric	Follow-up (days)	Procedure	Total patients	ERAS	Control
Aravani [18]	No		Colorectal	240	120	120
Aydin [19]	No	55	Colorectal	121	71	50
Chand [20]	No	55	Colorectal	140	91	49
Chiu [21]	Yes		Colorectal	255	129	126
Elsoud [22]	No		Colorectal	60	30	30
Forsmo [23]	No		Colorectal	307	154	153
Huebner [24]	Yes	30	Colorectal	346	78	268
Lee [25]	No		Colorectal	91	74	17
Li [26]	No	30	Colorectal	445	208	237
Melchor [27]	No	180	Colorectal	679	319	360
Miller [28]	No	30	Colorectal	241	142	99
Greco., *et al*. [29]	No	-	Colorectal	2376	1046	1053
Thanh., *et al*. [30]	No	30	Colorectal	1626	331	1295
Feng., *et al*. [31]	No	30	Colorectal	120	57	59
Wang., *et al*. [32]	No	30	Colorectal	117	57	60
Aarts., *et al*. [33]				336	110	226
Abraham and Al-bayati [34]	-	-	-	-	-	-

Table 1: Study characteristics.

Trial	Adequate sequence generation	Allocation Concealing	Blinding	Baseline characteristics similar	Overall risk of bias
Aravani [18]	Unclear	Unclear	No	Yes	Low
Aydin [19]	Yes	Yes	No	Yes	Low
Chand [20]	Yes	Unclear	No	Yes	Low
Chiu [21]	Unclear	Yes	No	Yes	Low
Moustafa [22]	Yes	Yes	No	Yes	Low
Forsmo [23]	Unclear	Yes	No	Yes	Low
Huebner [24]	Unclear	Unclear	No	Yes	Medium
Lee [25]	Unclear	Unclear	No	Yes	Medium
Li [26]	Yes	Yes	No	Yes	High
Melchor [27]	Yes	Yes	No	Yes	High
Miller [28]	Yes	Yes	No	Yes	High
Greco., *et al*. [29]	Unclear	Unclear	No	Yes	Medium
Thanh., *et al*. [30]	Unclear	Yes	No	Yes	Medium
Feng., *et al*. [31]	Unclear	Yes	No	Yes	Medium
Wang., *et al*. [32]	Unclear	Yes	No	Yes	Medium
Aarts., *et al*. [33]	Unclear	Yes	No	Yes	Medium
Abraham and Al-bayati [34]	Yes	Yes	No	Yes	High

Table 2: Risk of bias assessment.

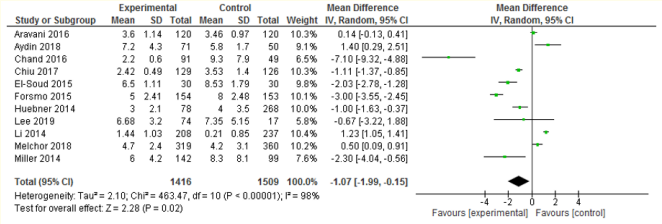

Figure 2: Pooled Estimates of Length of Stay comparing ERAS versus standard care. CI: confidence interval, RR: Risk ratio.

and revealed that the ERAS protocol would be anticipated for cost less than control in 82% and 85% of adjusted and unadjusted medical cost samples, respectively. This was majorly associated to the reduction in the length of stay in the ERAS group.

Mortality rates

The information related to mortality rates was found in total six articles [20,23,24,26-28]. Chand., *et al*. [20] reported 6.9% deaths in standard care group and 3.8% deaths in ERAS group. In addition, Forsmo., *et al*. [23] reported 0% deaths in standard care group and 1.9% deaths in ERAS group. Similarly Huebnar., *et al*. [24] have reported 0% deaths in ERAS group and 0.7% deaths in standard care. No deaths were reported by Li., *et al*. [26], whereas 2.5% and 4.7% of the deaths were reported in ERAS group and standard care group, respectively [27]. The findings indicated that there was 1% death in standard care group and 0% death in ERAS group [28].

Readmission

A total of seven out of 17 studies reported on readmission outcomes [20,22-24,26-28]. The highest readmission rate (20.2%) was reported by Miller., *et al*. [28] in standard care group while lowest readmission rate (0.7%) was reported by Moustafa., *et al* [22]. In the ERAS group, highest readmission rate (18.8%) was reported by Forsmo., *et al*. [23] and lowest readmission rate (0.7%) was reported by Moustafa., *et al* [22].

Risk of bias

A skewed or asymmetrical shape was not identified in visual inspection of funnel plot (Figure 3). There was no publication bias

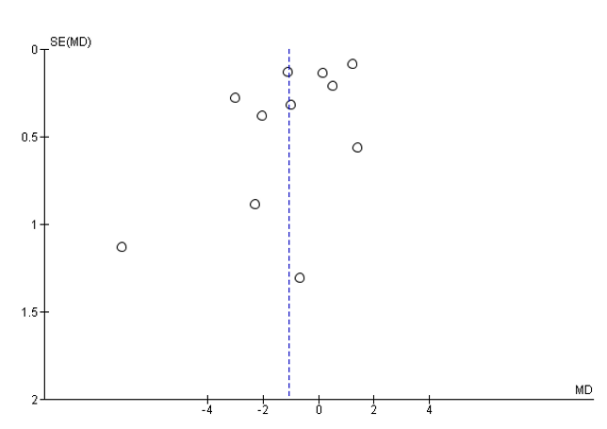

Figure 3: Funnel Plot presenting Risk of Bias.

reported in the quantitative assessment on the overall complication rate.

Discussion

It has been observed that the reduction in the hospital stay time, mortality, morbidity, and time taken for the patients' recovery was compiled within the recovery optimization. The core emphasis of ERAS is on the colorectal surgery concerning the fast-track surgery, which is applicable across different surgical patients.

Previously, Greco., *et al*. [29] have indicated that the ERAS reduced the 2.28 days of main LOS along with the complexities by 40% in patients undergoing colorectal surgery. ERAS has comprehensively encouraged the surgical patients to continue their normal lives and reduce caretaking burden regardless of compromising on the quality of life of such patients. It was also observed that approximately $2985 per patient was reserved in socially ERAS for achieving 100% cost-effectiveness. Similarly, Thanh., *et al*. [30] have identified the impacts of ERAS on the use of health facilities undertaking colorectal patients. These facilities include emergency department visit, LOS, readmissions, general physician, visit to specialist, and HSU). The study has used regression of multilevel negative binomial for a pre-and post-comparison of the groups of ERAS. The findings have shown that ERAS was significantly correlated with the reduction in LOS.

Feng., *et al*. [31] have utilized the ERAS protocols for the colorectal surgery undertaking 120 randomized surgical patients combined with conventional perioperative or laparoscopy care. The number of postoperative complications and LOS were significantly reduced by the ERAS as compared to the perioperative care team. In the ERAS group, there was a reduction of the medical expense for the hospitalization with cost-effective saving was one of the characteristics associated with ERAS for mitigating the use of drugs, specifically the antibiotics. Wang., *et al*. [32] have utilized the ERAS protocol by undertaking 57 colorectal patients. The study has noted and registered the clinical aspects of all the colorectal patients. The questionnaires were used to examine the quality of life. The study has indicated that the time duration and the therapy plan positively affected the quality of life of colorectal patients after the treatment.

Aarts., *et al*. [33] have indicated that there is a poor acceptance of ERAS protocol for colorectal surgery. The study has found a shortened hospital stay with the use of a laparoscopic technique. Furthermore, a reduced hospital stay was significantly correlated with ERAS protocol, which includes intraoperative fluid restriction, clear fluids of surgery, preoperative counseling, and early discontinuation of the Foley urinary catheter. Costs or materials were not included in any of these strategies. Therefore, ERAS guidelines should be implemented and promoted through local multidisciplinary strategies to obtain accurate documentation of the ERAS interventions for effective feedback and audit throughout the patient chart. Similarly, Abraham and Albayati [34] have witnessed that the integration of an ERAS protocol was related with a reduced length of hospital stay and faster recovery with no elevation in complications in readmission rates at the expense of a possible increase. In addition, no advantage was observed toward the use of laparoscopic technique as compared to the conventional open surgical approach.

In the surgical community, a common manifestation is that the LOS is reduced by ERAS pathway, but increase the hospital readmission rate. However, data from the randomized controlled trials, in this meta-analysis, reported reduction in LOS. An interesting finding was that there was no increase in the readmission rate in the ERAS group, which was similar to those of the control group (standard care). This finding was consistent with the findings of Greco., *et al*. [29] who reported similar results in his meta-analysis study conducted on colorectal surgery in 2014.

The mean LOS was 4.43, which was smaller than the mean LOS in control group. The importance of this finding can be claimed from the fact that mean LOS reported by Greco., *et al*. [29] was 5.8 days. The reason put forth by Greco., *et al*. [29] was the inadequate or incomplete implementation of ERAS pathway; however, the results seem quite satisfactory from the data reported in this meta-analysis. However, it should be of significant view that Greco., *et al*. [29] reported majorly all complications associated to ERAS program after colorectal surgery, but the focus of this review is entirely on the LOS reduction after colorectal surgery.

However, there was limited information on the secondary information. Out of 17 studies, only 7 studies had provided information related to readmission rates, six studies have provided information on mortality rates, and only one study had provided information on cost associated to ERAS implementation. Here, the assertion of Greco., *et al*. [29] might be true that studies fail to completely implement ERAS pathway.

Miller., *et al*. [28] have reported reduction in primary LOS, which in turn results in healthcare cost savings. According to Miller., *et al*. [28], every $1 invested in ERAS can bring $3.8 in return with respect to return on investment (ROI). Previously, Stowers, Lemanu, and Hill [35] have reported the similar findings claiming ERAS protocols to be cost-effective and clinically efficacious across different surgical specialties in the short-term. According to Lee., *et al*. [36], important economic evidence is provided by such findings for supporting a strategic to implement synchronous structured ERAS in order to expand multiple surgical sites and specialties across the health care institutes.

The findings have indicated that the rate of readmission ED visits and GP visits, and readmission LOS were reduced by ERAS within 30 days of surgical discharge. This finding was supported by Thanh., *et al*. [30] who reported statistically significant differences for these changes. Majority of the studies lacks in reporting statistical significant outcomes for secondary outcomes, even though compliance has increased up to 75% with the ERAS guideline. However, additional RCTs are required along with expert opinions for focusing on more optimum application of the guideline in improving the advantages of ERAS program. In fact, the increasing demand for the continuous enhancement of patient care usually has to experience the need for reducing health costs globally. A significant reduction of costs should be included in the short-term outcome benefits for patients underwent the ERAS pathway [37,38]. American and European surveys have emphasized the moderate application of ERAS pathways in spite of the improved quality of care (QoL) and reduced costs [39-41].

Strengths and Limitations

This systematic review and meta-analysis has presented a significant update from previous RCTs with respect to LOS reduction after colorectal surgery considering the implementation of ERAS pathways. A potential limitation of this review study was that four out of 17 studies were of low quality and underpowered. On the contrary, the influence of ERAS on postoperative outcome was confirmed when the investigation was limited to low-and medium-risk of bias trials or to the new studies. The current review recommends that the adoption of ERAS pathway is related with the shorter LOS and faster recovery with no upsurge in complication rates at the cost of a potential small increase in readmission rates. In addition, the laparoscopic technique does not believe to reveal any benefit over the standard open surgical approach with the adoption of such a program.

Conclusion

In conclusion, the length of hospital stay and readmission rates was reduced by the ERAS pathway, which in turn, was beneficial in controlling health care expenses. ERAS guidelines should be implemented and promoted by local multidisciplinary strategies. It will be important for a successful program to have appropriate documentation of the ERAS pathways undertaken throughout the patient chart for influential feedback and audit with the emergence of a local ERAS program. Thereby, new RCTs are not required for comparing the ERAS with the conventional care in colorectal surgery. Instead, it is clear that new policies have to be provoked to adopt ERAS pathway globally from current evidence.

Ethics Approval and Consent to Participate

N/A.

Consent for Publication

Not required.

Availability of Data and Materials

on request.

Competing Interests

None.

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