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Enhanced Recovery after Colo-Rectal Surgeries (ERAS) V.S Conventional Care A systematic review and meta-analysis

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Abstract: Background: ERAS programs are not only used in abdominal surgeries, they are also used in cardiothoracic, gynecology, urology, orthopedic, and neurosurgery. Many authors and surgeons worldwide have been adapting this program, also trying to modify it due to its promising outcomes and it's low damage toit's continence. **Objective:** To present an updated assessment of perioperative care in colorectal surgery from the available evidence and Enhanced Recovery After Surgery (ERAS) group recommendations. **Patients and Methods:** We performed this systematic review and meta-analysis in accordance to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) statement. PRISMA and MOOSE are reporting checklists for Authors, Editors, and Reviewers of Meta-analyses of interventional and observational studies. According to International committee of medical journal association (ICJME), reviewers must report their findings according to each of the items listed in those checklists. An electronic search was conducted from the inception till March 2019 in the following bibliographic databases: Medline via PubMed, SCOPUS, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and Google Scholar to identify relevant articles. We used different combinations of the following queries: ("Colorectal Surgery"[Mesh]) AND ("Enhanced recovery" OR "conventional care"). The search have been done with no limit regarding the year publication or language. **Results:** In the present study, we searched Medline via PubMed, SCOPUS, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar from their inception till March 2019. The search retrieved 2861 unique records. We then retained 41 potentially eligible records for full-texts screening. Finally, 28 reports of 25 RCTs were included in the present systematic review and meta-analysis. **Conclusion:** ERAS was proven to be feasible, minimally invasive, cheap, relatively easy, which is safe and effective at the same time. This program can be ideal for patients undergoing elective colo-rectal surgery, yet more studies should be conducted in Egypt to compare results regarding different approaches of this program with longer follow up and randomization of patients.
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1. Introduction

Enhanced recovery after surgery (ERAS) programmes have been shown to improve outcomes after colonic surgery. However, there is less evidence supporting ERAS in rectal surgery. The aim of this study was to compare outcomes of conventional perioperative care with those of an ERAS pathway including both colonic and rectal surgery patients.

Colorectal surgery is associated with significant complication rates (10% to 20%), and average post‐operative hospital stays of 6–10 days. [1-5] Fast‐track or enhanced recovery after surgery (ERAS) programmes have been introduced to optimize perioperative care and to minimize the physiological stress response encountered when undergoing surgery, thereby reducing complication rates and accelerating recovery. [2-3] Enhanced recovery programmes are multidisciplinary and include a variety of pre‐, intra‐ and post‐operative components. [2-3-4-5] Preoperative elements include extensive preoperative education, avoidance of mechanical bowel preparation and excessive fasting, use of prebiotics and carbohydrate loading. Intra‐operative elements include maintenance of normothermia, strict fluid balance to avoid fluid overload and transverse incisions. Epidural anaesthesia or intrathecal analgesia may also be included in ERAS pathways. Post‐operative elements include multimodal analgesia with minimal opiate use, early mobilization and enteral feeding,

avoidance of routine nasogastric tube placement, avoidance of peritoneal drains and early removal of urinary catheters.

Dr. Kehlet, served as the Chief of Surgery and Professor of Surgery, Copenhagen University at Hvidovre University Hospital from 1989 to 2004, first developed a multimodal enhanced recovery programme for elective colorectal surgery. [6-7] Recommendations were classified separately as pre, intra and postoperative interventions, with the intention to reduce hospital stay to a mean of four days. Subsequently, several protocols have been established by different groups consisting of different perioperative recommendations as mentioned before.

Review of the published data reveals that the ERAS protocols have a role in reducing postoperative morbidity and result in an accelerated recovery following colorectal surgery. Similarly, both primary and overall hospital stays are reduced significantly. However, the available evidence suggests that ERAS protocols do not reduce hospital readmissions or mortality. Laparoscopically assisted surgery demonstrates improvements in outcome measures, including length of primary hospital stay and morbidity. [8] Laparoscopic resectional surgery is currently considered to be the key interventional change in traditional care that has led to improvements in recovery rates and reductions in morbidity following colorectal surgery. RCTs have demonstrated a reduction in primary length of hospital stay in association with laparoscopic colorectal surgery. [9-10] The combination of ERAS protocols and laparoscopically assisted colonic resections has been evaluated in three separate trials [11–12] that, unfortunately, have not yielded a pervasive message. These trials failed to elicit significant differences in outcome between groups that had undergone open as compared with laparoscopic colorectal resection within the context of an ERAS protocol.

A case-matched study has demonstrated the feasibility and effectiveness of ERAS programme in the setting of emergency colorectal surgery. Compared with those having a conventional care pathway, patients within an ERAS programme had a shorter length of hospital stay, faster bowel recovery and shorter time to start adjuvant therapy. The reduction in hospital stay did not lead to an increase in 30-d readmission, or a higher rate of postoperative complication. In fact, the incidence of postoperative complication tended to be reduced in the ERAS group. The magnitude of reduction in hospital stay is fairly comparable to those reported from the ERAS pathway for elective colorectal surgery. [13-14]

The reduction of postoperative complication in ERAS programme for patient undergoing emergency resection for obstructing colorectal cancer is likely to result from a combination of multimodal perioperative interventions, rather than single maneuver alone, aiming to attenuate metabolic response to surgery, to support the recovery of organ function, and to preserve postoperative immune system. [15-16-17]

Interestingly, a recent systematic review and meta-analysis has demonstrated that colorectal cancer patients with shorter convalescence between surgery and chemotherapy had a better overall survival and disease-free survival. [18]

Following an extensive review of the literature, the available evidence supports the contention that ERAS protocols reduce healthcare costs [19-20] and, importantly, that there is a significant reduction in patient morbidity with an acceleration of postoperative recovery. These findings help to confirm that ERAS protocols should now be implemented as the standard approach to perioperative care in colorectal surgery. To develop the evidence base further, future RCTs of ERAS protocols with strict pathway compliance will be required. It is suggested that these results are the effect of a combination of the ERAS protocol with laparoscopic colectomy.

Aim of the Work

The aim of this systematic review is to present an updated assessment of perioperative care in colorectal surgery from the available evidence and Enhanced Recovery After Surgery (ERAS) group recommendations.

2. Materials and Method

We performed this systematic review and meta-analysis in accordance to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) statement. PRISMA and MOOSE are reporting checklists for Authors, Editors, and Reviewers of Meta-analyses of interventional and observational studies. According to International committee of medical journal association (ICJME), reviewers must report their findings according to each of the items listed in those checklists ***(Moher D, Liberati A, 2009).***

Study Selection and Eligibility Criteria:

The present review included studies that fulfilled the following criteria:

(1) Studies that included adults' patients undergoing elective colorectal surgery;

(2) Studies that assessed the effectiveness of enhanced-recovery after surgery (ERAS) protocol that consist of a protocol of preadmission, preoperative, intraoperative, and/or postoperative components;

(3) Studies that compared the ERAS with none or usual care protocol;

(4) Studies that reported any of the following outcomes: health-related outcomes (eg, length of stay, overall morbidity, mortality, readmission rate, ileus, clinically important difference in pain scores, and clinically meaningful changes in quality of life), intermediate outcomes (eg, return of bowel function, intravenous fluid administration, early patient mobilization, and pain scale scores), and harms (eg, surgical site infection, anastomotic leakage cardiovascular or respiratory complications, urinary tract infection, need for reoperation, bleeding, and Foley catheter reinsertion and complications).

(5) Studies that were randomized controlled trials (RCTs), comparative studies, prospective cohort, or retrospective charts studies.

We excluded review articles, non-English studies, theses, dissertations and conference abstracts, and trials with unreliable date for extraction.

Search Strategy and Screening

An electronic search was conducted from the inception till March 2019 in the following bibliographic databases: Medline via PubMed, SCOPUS, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and Google Scholar to identify relevant articles. We used different combinations of the following queries: ("Colorectal Surgery"[Mesh]) AND ("Enhanced recovery" OR "conventional care"). The search have been done with no limit regarding the year publication or language. The results of the electronic search are indicated in **Table 1.**

Table (1): Electronic search

Database	Data of search	Results
PubMed	15th December 2018	162
SCOPUS	15th December 2018	828
Web of Science	15th December 2018	623
CENTRAL	15th December 2018	171
Google Scholar	15th December 2018	876

Screening:

Retrieved citations were imported into EndNote X7 for duplicates removal. Subsequently, unique citations were imported into an Excel sheet and screened by two independent reviewers; the screening was conducted in two steps: title and abstract screening, followed by a full-texts screening of potentially eligible records.

Data Extraction:

Data entry and processing were carried out using a standardized Excel sheet and reviewers extracted the data from the included studies. The extracted data included the following domains: (1) Summary characteristics of the included studies; (2) Baseline characteristics of studied populations; and (3) Study outcomes. All reviewers' independently extracted data from the included articles and any discrepancies were solved by discussion.

Dealing with Missing Data:

Missing standard deviation (SD) of mean change from baseline was calculated from standard error or 95% confidence interval (CI) according to Altman (**Altman and Bland**, **2005**).

Data Synthesis:

Continuous outcomes were pooled as mean difference (MD) or standardized mean difference (SMD) using inverse variance method, and dichotomous outcomes will be pooled as relative risk (RR) using Mantel-Haenszel method. The random-effects method was used under the assumption of existing significant clinical and methodological heterogeneity. We performed all statistical analyses using Review Manager (RevMan) 5.3 or Open Meta-analyst for windows.

Assessment of Heterogeneity:

We assessed heterogeneity by visual inspection of the forest plots, chi-square, and I-square tests. According to the recommendations of Cochrane Handbook of Systematic Reviews and meta-analysis, chi-square p-value less than 0.1 denote significant heterogeneity while I-square values show no important heterogeneity between 0% and 40%, moderate heterogeneity from 30% to 60%, substantial heterogeneity from 50% to 100%. If any trials were judged to affect the homogeneity of the pooled estimates, we planned to perform a sensitivity analysis to assess outcomes with and without the trials that were affecting the homogeneity of the effect estimates.

Assessment of publication biases:

We intended to test for publication bias using funnel plots if any of the pooled analysis included more than 10 studies in the review ***(Higgins 2011).***

Results and Discussion

I. Characteristics of the included studies

In the present study, we searched Medline via PubMed, SCOPUS, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar from their inception till March 2019. The search retrieved 2861 unique records. We

then retained 41 potentially eligible records for full-texts screening. Finally, 28 reports of 25 RCTs were included in the present systematic review and meta-analysis (**Figure 1**).

II. Characteristics of The included studies

Among the 25 trials, 13 RCTs of open surgery compared an enhanced recovery protocol with a usual care protocol, 6 RCTs and 2 comparative studies compared protocols in patients undergoing laparoscopic surgery; while 3 (2 RCTs and 2 comparative studies) studies included 4 groups of patients providing comparisons of enhanced recovery and usual care for both open and laparoscopic surgery. One additional RCT included both open and laparoscopic surgery with the surgeon deciding the surgical approach. There were 10 trials from China, 10 from Europe, 3 from the United Kingdom, 1 from Japan, and 1 from India. There were 12 trials of patients with colorectal cancer, 7 trials of patients with either colorectal cancer or benign conditions, 3 trials of patients with rectal cancer, and 3 trials of patients with noncancerous colorectal conditions. The mean age of the included patients ranged from 36-75 years old. In addition, the majority of patients were males. **Table 1** shows the summary characteristics of the included studies.

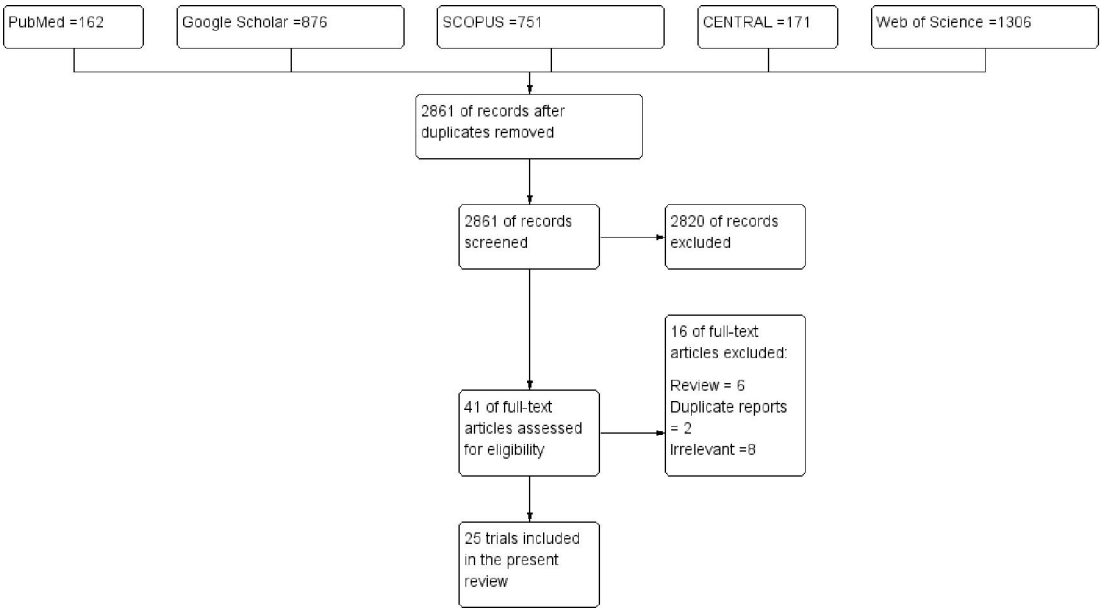

Figure 1: PRISMA flow-chart.

Table (2): Summary Characteristics of the included studies.

Author, year	Country	Study Design	Inclusion	Intervention (n), Control (n), Follow-up	Demographics
Open Surgery Studies					
Feng 2016	China	RCTs	Inclusion: age 18-70 years; histological diagnosis of colorectal cancer; no radiotherapy or chemotherapy treatment; no severe diarrhea, liver and kidney function failure, or cardiopulmonary insufficiency; ASA I-III; BMI 18.5-30; abdominal CT with no obvious lymph node or distant metastasis	Intervention: fast track surgery (n=121) Control: traditional care (n=120) Follow-up: 30 days	N=241 (data for 230) Colorectal conditions (%): 44 colon, 56 rectum Procedures (%): NR Age (mean): 58 Gender (% male): 56 BMI: 24 Comorbidity status: ASA I (27), ASA II (50), ASA III (23)
Pappalardo 2016	Italy	RCTs	Inclusion: extraperitoneal tumor location (within 12 cm above anal verge); cT2-T4 tumors with or without positive lymph nodes, elective procedure; neoadjuvant therapy where indicated	Intervention: fast track protocol (n=25) Control: traditional care (n=25) Follow-up: 30 days	N=50 Colorectal conditions (%): 100% rectal cancer Procedures (%): anterior resection (62), ultra-low anterior resection (36) Castrini technique (4) Age (mean): 67 Gender (% male): 52

Author, year	Country	Study Design	Inclusion	Intervention (n), Control (n), Follow-up	Demographics
					BMI: 38% <25; 20% >30 Comorbidity status: ASA I (10), ASA II (42), ASA III (48)
Jia 2014	China	RCTs	Inclusion: elderly patients with colorectal carcinoma admitted for open curative resection	Intervention: fast track surgery (n=120) Control: traditional care (n=120) Follow-up: NR, perioperative period	N=240 (all elderly, ages 70-88) (data for 233) Colorectal conditions (%): colon cancer (49); rectal cancer (51) Procedures (%): colectomy (45); Dixon (32), Miles (23) Age (mean): 75 Gender (% male): 63 BMI: NR Comorbidity status: NR
Nanavati 2014	India	RCTs	Inclusion: age 16-66 years, undergoing anastomosis anywhere distal to the ileum	Intervention: fast track peri-operative care (n=30) Control: traditional perioperative care (n=30) Follow-up: 30 days	N=60 Colorectal conditions (%): ileostomy closure 42 colostomy closure 28 abdominal pain 13 ileocolostomy closure 8 other 9 Age (mean): 34 Gender (% male): 53 BMI: NR Comorbidity status: NR
Gouvas 2012 CCT	Greece	CCT	Inclusion: diagnosed with adenocarcinoma of lower 2/3 of rectum	Intervention: open surgery combined with fast track (n=36) Control: open surgery usual care (n=45) Follow-up: 30 days	N=81 Colorectal conditions (%): rectal cancer (100) Age (mean): 64 Gender (% male): 67 (fast track 53% vs 78% usual care, P=.001 across groups) BMI: 28 Comorbidity status (%): ASA I (42); ASA II (46), ASA III (12)
Ren 2011	China	RCT	Inclusion: age 20-80 years, single colorectal lesion, medically eligible for radical colorectal surgery	Intervention: ERAS group (n=299) Control: usual care (n=298) Follow-up: 30 days	N= 676 (Data for 597) Procedures (%): right hemicolectomy (28), left hemicolectomy (6), low anterior resection (44), abdominoperineal resection (13), other (9) Age (median): 59 (ERAS), 61 (control) Gender (% male): 62 BMI (median): 22.5 Comorbidity status: ASA (mean) Control 1.4 (0.4) ERAS 1.4 (0.3)
Wang 2012	China	RCT	Inclusion: no disease of immune system, no pre-operative radiotherapy or chemotherapy, no history of operation on abdominal and distant metastases, ASA score I–III, and self-care function prior to hospitalization	Intervention: open surgery combined with fast track (n=42) Control: open surgery usual care (n=44) Follow-up: 30 days	N=86 (data for 83) Colorectal conditions (%): colon cancer 100 Age (median): 55 (fast track), 57 (usual care) Gender (% male): 59 BMI: 22.5 Comorbidity status (%): ASA I (40), ASA II (46), ASA III (14)
Yang 2012	China	RCT	Inclusion: age 18-80, diagnosed with colorectal carcinoma, no preoperative chemotherapy or radiotherapy, ASA score I-II, BMI 17.5-27.5, preoperative serum albumin ≥30g/L, elective open	Intervention: fast-track group (n=35)	N= 70 (data for 62) Procedures (%): right hemicolectomy (21),

Author, year	Country	Study Design	Inclusion	Intervention (n), Control (n), Follow-up	Demographics
			colorectal resection with tracheal intubation and general anesthesia	Control: conventional care (n=35) Follow-up: 30 days	left hemicolectomy (8); sigmoidectomy (21), Dixon operation (50) Age (median): 57 (fast track), 60 (usual care) Gender (% male): 68 BMI (median): 22 Comorbidity status: NR
Vlug 2011 *LAFA-study*	Netherlands	RCT	Inclusion: ages 40-80 years; ASA I, II, or III; elective segmental colectomy for histologically confirmed adenocarcinoma or adenoma; without evidence of metastatic disease	Intervention: open surgery combined with fast track (n=103) Control: open surgery usual care (n=108) Follow-up: 30 days	N=211 (data for 191) Colorectal conditions (%): colon cancer and benign disease 100 Procedures (%): right colectomy (45), left colectomy (55) Age (mean): 66 Gender (% male): 59 BMI: 26 Comorbidity status (%): ASA I or II (79), III (21)
Wang 2011	China	RCT	Inclusion: NR	Intervention: fast track rehabilitation (n=106) Control: conventional care (n=104) Follow-up: 30 days	N=230 (data for 210) Colorectal condition (s) (%): colon (65), rectum (35) Procedures (%): right hemicolectomy (26), left hemicolectomy (20), sigmoid colectomy (29), anterior resection (25) Age (median): 57 (fast track), 55 (conventional care) Gender (% male): 60 BMI: NR Comorbidity status (%): ASA I (28), ASA II (55), ASA III (17)
Ionescu 2009	Romania	RCT	Inclusion: ASA score I-III, admitted to hospital for elective open colorectal surgery for neoplasm	Intervention: fast track protocol (n=48) Control: conventional care program (n=48) Follow-up: NR (\	N=96 (Data for N=96) Colorectal conditions (%): rectosigmoid (58); colon (42) Procedures: right hemicolectomy (29). left hemicolectomy (11), segmental colonic resection (1), rectosigmoidian resection (58) Age (mean): 62 Gender (% male): 64 BMI: NR Comorbidity status (%): ASA I (52), ASA II (45), ASA III (3) Subgroups noted [a]: None
Muller 2009	Switzerland	RCT	Inclusion: age >18, elective open colonic resection with a primary anastomosis	Intervention: fast track program (n=76) Control: standard care (n=75) Follow-up: 30 days	N= 156 (data for 151) Procedures (%): sigmoid resection or left hemicolectomy (67), resection of transverse colon (1), right hemicolectomy (32) Age (median): 62 (fast track), 59 (standard care) (P=.04) Gender (% male): 51 BMI (median): 24 (fast track), 26 (standard care) Comorbidity status (%): ASA I (3), ASA II (69); ASA III (28)
Šerclová 2009	Czech Republic	RCT	Inclusion: age 18-70 years, ASA score between I or II, open intestinal resection	Intervention: fast-track group (n=53)	N= 105 (data for 103) Colorectal conditions (%): Crohns disease

Author, year	Country	Study Design	Inclusion	Intervention (n), Control (n), Follow-up	Demographics
			Exclusion: pelvic radiation, multi-organ resections, cancer, pregnant women	Control: conventional care (n=52) Follow-up: 30 days	(78), ulcerative colitis (9), familial adenomatous polyposis (5), carcinoma (7), other (2) Procedures (%): simple bowel resection (54), multiple (25), resection and stomy (20) Age (mean): 36 Gender (% male): 50 BMI (median): NR Comorbidity status (%): NR
Khoo 2007	UK	RCT	Inclusion: elective surgery for colorectal cancer.	Intervention: multimodal package (n=35) Control: usual care (n=35) Follow-up: 10-14 days	N=81 (data for 70) Colorectal conditions (%): colon cancer (67), rectal cancer (33) Age (median): 69 (multimodal), 73 (usual care) Gender (% male): 39 BMI: NR Comorbidity status (%): ASA I (11), ASA II (74), ASA III (14)
Gatt 2005	UK	RCT	Inclusion: requiring elective colorectal surgery, living independently at home	Intervention: multimodal optimization (n=19) Control: usual care (n=20) Follow-up: 30 days	N=39 Colorectal conditions (%): malignant disease (69) Procedures (%): right hemicolectomy (28), left hemicolectomy (5), anterior resection (38), sigmoid colectomy (5), subtotal colectomy (8), abdominoperineal resection (5), other (11) Age (median): 67 (both groups) Gender (% male): 59 BMI: medians 24 (multimodal), 27 (usual care) Comorbidity status: POSSUM score (medians) 28 (multimodal), 32 (usual care); ASA (median)=2 (both groups)
Anderson 2003	UK	RCT	Inclusion: lived independently at home and required left or right hemicolectomy.	Intervention: multimodal optimization (n=14) Control: usual care (n=11) Follow-up: 30 days	N=25 Colorectal conditions (%): malignant disease 72% Age (medians): 64 (multimodal), 67 (usual care) Gender (% male): 44 BMI: medians 24 (multimodal), 26 (usual care) Comorbidity status: POSSUM score (median) 26 (both groups); ASA I/II 92%, III 8%
Laparoscopic Studies					
Ota 2017	Japan	CCT	Inclusion: ASA grade I or II, elective surgery for colonic or rectosigmoid cancer in 1 of 6 hospitals, white blood cell count ≥3000/μL, platelet count ≥100,000/μL, serum aspartate aminotransferase or alamine aminotransferase level ≤100IU/μL, total bilirubin ≤2mg/dl, serum creatinine ≤1.5 mg/dl	Intervention: enhanced recovery after surgery (n=159) Control: conventional perioperative care (n=161) Follow-up: 30 days	N=320 Colorectal locations (%): cecum (16), ascending (29), transverse (12), descending (7), sigmoid (29), rectosigmoid (14) Age (medians): 69 (ERAS), 68 (conventional care) Gender (% male): 50 BMI: NR Comorbidity status (%): ASA I (37), ASA II (63)
Scioscia 2017	Italy	RCT	Inclusion: age >18 years, preoperative evidence of bowel endometriosis (imaging or other), primary laparoscopic approach	Intervention: fast track care (n=62)	N=227 Colorectal conditions (%): bowel

Author, year	Country	Study Design	Inclusion	Intervention (n), Control (n), Follow-up	Demographics
				Control: conventionall care (n=165) NOTE: 1:3 ratio for randomization Follow-up: 30 days	endometriosis (100) Procedure (%): bowel segmental resection (86) Age (mean): 35 Gender (% male): 0 BMI: 22 Comorbidity status: Barthel index (median) 100 for both groups (complete independence)
Mari 2016	Italy	RCT	Inclusion: indication for major colorectal surgery, age 18-80 years, ASA I to III, autonomous for mobilization and walking, eligible for laparoscopic technique	Intervention: ERAS (n=70) Control: standard care (n=70) Follow-up: 5 days	N=140 Colorectal conditions (%): diverticulitis (25), adenocarcinoma (75) (left 43%, right 31%, rectal 26%) Age (mean): 66 Gender (% male): 53 BMI: 27 Comorbidity status (%): ASA I (23), ASA II (64), ASA III (14)
Wang 2015	China	CCT	Inclusion: underwent colonic surgery (radical resection of colonic cancer) by one surgical group (July 2012-Oct 2013)	Intervention: ERAS program (n=57) Control: usual care (n=60) Follow-up: 28 days	N=117 Colorectal conditions (%): cancer 100 (right side 79%, left side 21%) Age (mean): 59 Gender (% male): 47 BMI: 24 Comorbidity status: ASA score=1 72%, ASA score=2 28%
Feng 2014	China	RCT	Inclusion: age 18-75 years; diagnosed with rectal cancer based on clinical symptoms, imaging, and pathological evidence, with no findings of tumor invasion to adjacent organs, local, or distal metastasis; no preoperative radiotherapy or chemotherapy; ASA physical status I or II	Intervention: fast track surgery (n=60) Control: usual care (n=60) Follow-up: 4 weeks	N=120 (data for n=116) Colorectal condition (s): rectal cancer Procedure: radial anterior resection with TME Age (mean): 55 Gender (% male): 66 BMI: 22 Comorbidity status (%): ASA I (4), ASA II (96)
Mari 2014	Italy	RCT	Inclusion: age 18-85 years, total laparoscopic high anterior resection, ASA score I-III, BMI<30, no intestinal diversion.	Intervention: fast track program (n=26) Control: usual care (n=26) Follow-up: 30 days	N=52 (data for 50) Colorectal condition (s) (%): colon cancer (69), diverticular disease (31) Age (median): 66 (29-83) Gender (% male): 48 BMI: 25 Comorbidity status (%): ASA, I (67), ASA II (29), ASA III (2)
Gouvas 2012	Greece	CCT	Inclusion: diagnosed with adenocarcinoma of lower 2/3 of rectum	Intervention: laparoscopy combined with fast track (n=42) Control: laparoscopy usual care (n=33) Follow-up: 30 days	N=75 Colorectal conditions (%): rectal cancer (100) Age (mean): 66 Gender (% male): 44 (fast track 52% vs 33% usual care, P=.001 across groups) BMI: 28 Comorbidity status (%): ASA I (52), ASA II (36), ASA III (12)
Wang 2012	China	RCT	Inclusion: no disease of immune system, no pre-operative radiotherapy or chemotherapy, no history of operation on	Intervention: laparoscopy combined	N=84, data for 80

Author, year	Country	Study Design	Inclusion	Intervention (n), Control (n), Follow-up	Demographics
			abdominal and distant metastases; ASA score I–III, and self-care function prior to hospitalization	with fast track (n=42) Control: laparoscopy usual care (n=42) Follow-up: 30 days	Colorectal conditions (%): colon cancer 100 Procedures (%): right hemicolectomy (39), left hemicolectomy (34), sigmoid colectomy (28) Age (median): 56 (both groups) Gender (% male): 66 BMI: 22 Comorbidity status (%): ASA I (39), ASA II (48), ASA3 (14)
Wang 2012	China	RCT	Inclusion: no previous abdominal surgery, no preoperative chemotherapy or radiotherapy, absence of distant metastases, ASA physical status I=III	Intervention: fast track rehabilitation (n=54) Control: usual care (n=54) Follow-up: 30 days	N=107 (data for 99) Colorectal condition (s): adenocarcinoma of colon Procedures (%):right hemicolectomy (34), left hemicolectomy (26), sigmoid colectomy (39) Age (median): 54 (fast track), 53 (usual care) Gender (% male): 60 BMI: median 22 (both groups) Comorbidity status (%): ASA I (28), ASA II (52), ASA III (20)
Wang 2012	China	RCT	Inclusion: age > 65 years, diagnoses of colorectal cancer, undergoing laparoscopic colorectal resection	Intervention: fast track rehabilitation (n=40) Control: usual care (n=38) Follow-up: 3-44 months	N=78 Colorectal conditions (%): colon cancer (68), rectal cancer (32) Procedures (%): right hemicolectomy (17), left hemicolectomy (4), sigmoid colectomy (29), anterior resection (25) Age (median): 71 (fast track), 72 (usual care) Gender (% male): 54 BMI: NR Comorbidity status (%): ASA I (28), ASA II (55), ASA III (17)
Vlug 2011 *LAFA-study*	Netherlands	RCT	Inclusion: ages 40-80 years; ASA I, II, or III; elective segmental colectomy for histologically confirmed adenocarcinoma or adenoma; without evidence of metastatic disease	Intervention: laparoscopy combined with fast track (n=106) Control: laparoscopy usual care (n=110) Follow-up: 30 days	N=216 (data for 209) Colorectal conditions (%): colon cancer and benign disease 100 Procedures (%): right colectomy (47), left colectomy (53) Age (mean): 67 Gender (% male): 58 BMI: 26 Comorbidity status (%) ASA I/II (81), III (19)Comorbidity (%): 69
Mixed Open and Laparoscopic Surgery Studies					
Forsmo 2016	Norway	RCT	Inclusion: age >18 years, scheduled for elective open or laparoscopic colorectal surgery for malignant or benign disease; also included rectal cancer patients who had pelvic radiation	Intervention: enhanced recovery after surgery (n=162) Control: standard care (n=162) Follow-up: 30 days	N=324 (data for 307) Colorectal conditions (%): colon (46), rectal (54) (overall 79% malignant) Procedures (%): right (25), left or sigmoid (21), low anterior resection (30), abdominoperineal (20), proctocolectomy (5) Age (median): 65 (ERAS), 66 (usual care) Gender (% male): 54 BMI: NR Comorbidity status (%): ASA I (21), ASA II (63), ASA III (15)

Table 2 shows the enhanced recovery protocol components specified for the enhanced recovery group and for the usual care group. No study included preadmission components. The most common preoperative components in the enhanced recovery protocols were carbohydrate treatment, no routine use of bowel preparation, and preoperative fasting. The most common intraoperative components were early removal of nasogastric tubes, standardized anesthesia protocols, and restrictive use of surgical site drains. Postoperatively, the most common components were early mobilization, early intake of oral fluids and solids, and a multimodal approach to opioid-sparing pain control. In the standard care protocols, the most commonly included enhanced recovery components were standardized anesthesia protocols, infection prophylaxis, and multimodal approach to pain control. Authors rarely described specific component implementation or what defined successful adherence to a specific component.

Table 1: ERAS protocol component of the included studies.

Phases	Eras Components	Eras Protocol	Standard Care Protocol
Preadmission	Smoking/alcohol cessation	0	0
	Nutritional screening/support	0	0
	Medical optimization of chronic disease	0	0
Preoperative	Structured information/patient and caretaker engagement	12	0
	Bowel preparation (no routine use of mechanical bowel prep)	16	2
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	16	3
	Carbohydrate treatment	18	0
	Thrombosis prophylaxis	4	2
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	11	8
	Nausea and vomiting prophylaxis	5	2
	Pre-anesthetic sedative medication (no routine use)	3	0
Intraoperative	Minimal invasive surgical techniques	2+10 Lap	0+10 Lap
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	16	9
	Maintain fluid balance; vasopressors for blood pressure control	14	3
	Restrictive use of surgical site drains	15	5
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	21	5
	Control of body temperature	9	4
Postoperative	Early mobilization	22	4
	Early intake of oral fluids and solids	23	1
	Early removal of urinary catheters and intravenous fluids	18	2
	Chewing gum, laxatives, peripheral opioid-blocking agents	7	1
	Protein and energy-rich nutritional supplements	11	0
	Glucose control	1	0
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	21	6
	Multimodal approach to control of nausea and vomiting	0	0
	Prepare for early discharge	2	1

Conclusion

ERAS was proven to be feasible, minimally invasive, cheap, relatively easy, which is safe and effective at the same time. This program can be ideal for patients undergoing elective colo-rectal surgery, yet more studies should be conducted in Egypt to compare results regarding different approaches of this program with longer follow up and randomization of patients.

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