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SCIENTIFIC ARTICLE

Enhanced recovery after surgery protocol versus conventional perioperative care in colorectal surgery. A single center cohort study



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KEYWORDS

Perioperative;
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Abstract

Background: Enhanced recovery after surgery (ERAS) protocols consist of a set of perioperative measures aimed at improving patient recovery and decreasing length of stay and postoperative complications. We assess the implementation and outcomes of an ERAS program for colorectal surgery.

Methods: Single center observational study. Data were collected from consecutive patients undergoing open or laparoscopic colorectal surgery during 2 time periods, 3 years before (Pre-ERAS) and 2 years after (Post-ERAS) the implementation of an ERAS protocol. Baseline characteristics of both groups were compared. The primary outcome was the number of patients with 180 days follow-up with moderate or severe complications; secondary outcomes were postoperative length of stay, and specific complications. Data were extracted from patient records.

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Results: There were 360 patients in the Pre-ERAS group and 319 patients in the Post-ERAS Group. 214 (59.8%) patients developed at least one complication in the pre ERAS group, versus 163 patients in the Post-ERAS group (51.10%). More patients in the Pre-ERAS group developed moderate or severe complications (31.9% vs. 22.26%, $p=0.009$); and severe complications (15.5% vs. 5.3%; $p<0.0001$). The median length of stay was 13 (17) days in Pre-ERAS Group and 11 (10) days in the Post-ERAS Group ($p=0.034$). No differences were found on mortality rates (4.7% vs. 2.5%; $p=0.154$), or readmission (6.39% vs. 4.39%; $p=0.31$). Overall ERAS protocol compliance in the Post-ERAS cohort was 88%.

Conclusions: The implementation of ERAS protocol for colorectal surgery was associated with a significantly reduction of postoperative complications and length of stay.

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PALAVRAS-CHAVE

Perioperatório;
Aceleração da
recuperação
pós-operatória;
Complicações
pós-operatórias

Aceleração da recuperação após protocolo cirúrgico versus cuidados perioperatórios convencionais em cirurgia colorretal. Um estudo de coorte em centro único

Resumo

Justificativa: O protocolo ERAS — do Inglês *Enhanced Recovery After Surgery* — consiste em um conjunto de medidas perioperatórias destinadas a melhorar a recuperação do paciente e diminuir o tempo de internação e as complicações pós-operatórias. Avaliamos a implementação e os resultados de um protocolo ERAS para cirurgia colorretal.

Métodos: Estudo observacional em centro único. Os dados foram coletados de pacientes consecutivos submetidos à cirurgia colorretal aberta ou laparoscópica durante dois períodos: três anos antes (pré-ERAS) e dois anos após (pós-ERAS) a implementação de um protocolo ERAS. As características basais de ambos os grupos foram comparadas. O desfecho primário foi o número de pacientes com 180 dias de acompanhamento com complicações moderadas ou graves. Os desfechos secundários foram tempo de internação pós-cirurgia e complicações específicas. Os dados foram extraídos de prontuários dos pacientes.

Resultados: O grupo pré-ERAS foi composto por 360 pacientes e o grupo pós-ERAS por 319. No grupo pré ERAS, 214 pacientes (59,8%) desenvolveram pelo menos uma complicação versus 163 pacientes (51,10%) no grupo pós-ERAS. Um número maior de pacientes do grupo pré-ERAS desenvolveu complicações moderadas ou graves (31,9% vs. 22,26%, $p=0,009$); e complicações graves (15,5% vs. 5,3%; $p<0,0001$). A mediana do tempo de internação foi de 13 (17) dias no grupo Pré-ERAS e de 11 (10) dias no grupo pós-ERAS ($p=0,034$). Não houve diferença nas taxas de mortalidade (4,7% vs. 2,5%; $p=0,1554$) ou de reinternação (6,39% vs. 4,39%; $p=0,31$). A conformidade geral do protocolo ERAS na coorte pós-ERAS foi de 88%.

Conclusões: A implantação do protocolo ERAS para cirurgia colorretal foi associada a uma redução significativa das complicações pós-operatórias e do tempo de internação.

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Introduction

Despite all advances in surgical and anesthetic care, morbidity after abdominal surgery it remains high. Colorectal surgery is associated with a high risk of morbidity and mortality in comparison to other general surgical procedures. Overall mortality rates after colorectal surgery range from 1% to 16.4%,¹⁻³ with morbidity rates as high as 35%.^{1,2,4} The aim of fast-track surgery, also called Enhanced Recovery After Surgery (ERAS) or multimodal surgery involves the use of several perioperative strategies to facilitate better surgical conditions and achieving faster recovery and early discharge from hospital. ERAS protocols have shown repeatedly by reducing the length of stay (LOS)⁵⁻⁷; without

influencing complication or readmission rates.^{7,8} Although individual components may vary, most of the ERAS programs include avoidance of fasting, preoperative nutritional optimization, preoperative carbohydrate loading, avoidance of bowel preparation, goal-directed hemodynamic therapy, multimodal analgesia without opiates, avoidance/early removal of tubes (nasogastric tube, Foley catheter, and drains), support of gastrointestinal function, and early convalescence.^{9,10}

The prediction of success or failure of ERAS has become a matter of interest.¹¹ There are evidences to suggest that increasing overall compliance with the individual elements of an ERAS program improves clinical outcomes.^{12,13}

This prospective study assessed how implementation of an ERAS program affects postoperative complications in patients undergoing elective colorectal surgery.

Materials and methods

This study is reported according to the STROBE guidelines for the conducting and reporting of observational cohort studies.¹⁴

Study design

As part of a quality improvement initiative, the working group was established in 2013 to implement the ERAS protocol for colorectal procedures. The multidisciplinary ERAS group included surgeons, anesthesiologists, nutritionists and a medical librarian to help with literature searches. The group worked with clinical experts, reviewed the literature for best practices in perioperative care and reached consensus on each step of patient care. Drafts were presented to surgeons and anesthesiologists at our institution for reviewing, and an iterative process of review was followed until consensus was reached. An anesthesiologist coordinator managed the project. The main goals of ERAS program were to improve recovery and to decrease postoperative complications through intraoperative Goal Directed Hemodynamic Therapy (GDHT), early nutrition and ambulation, avoidance or prompt removal of drains and tubes. The clinical pathway was based on the ERAS society guidelines.^{15,16} The ERAS protocol was implemented in March 2013 after staff training. A 3-month period of implementation allowed all staff to become familiar with the ERAS protocol. The protocol was a hospital-wide, evidence-based quality improvement project and it was considered the standard practice.

After the approval of the Infanta Leonor University Hospital Ethics and Research Committee (approved 2/12/2015), we compared data from consecutive adult patients undergoing elective open or laparoscopic colorectal surgery within the ERAS protocol, with a previous cohort of patients before introduction of the ERAS protocol. Excluding those patients who were operated during the training period, all patients who had an elective colon or rectal resection were included in this analysis. Patients who received conventional perioperative care underwent surgery from November 2010 through January 2013 (Pre-ERAS group). Patients who received perioperative care according to the ERAS protocol underwent surgery from March 2013 through December 2015 (Post-ERAS group). Due to the ERAS program's implementation, was considered as part of the standard patient care, the written consent was not requested to the patients.

Pre-ERAS group management

Before the introduction of the ERAS pathway, there was little standardization of care. Patients were fasted from midnight on the day of the surgery, and all patients received bowel preparation. All other patient managements were at the discretion of the surgical and anesthesia providers. Cardiac

output, central venous pressure and invasive blood pressure monitoring were performed at the discretion of the anesthesia providers. Intraoperative fluid administration was usually based on changes in hemodynamic (arterial blood pressure and heart rate) and urine output. Early mobilization and feeding were not undertaken.

Post-ERAS group management

After the implementation of the ERAS pathway, the protocol was standardized using a pathway that was adapted from the evidence described in the ERAS consensus statement¹⁶ (Table 1) Patients in the ERAS group were educated in the preoperative surgical clinic about the ERAS pathway. Routine bowel preparation was not performed for colonic procedures, and patients were allowed to drink clear fluids until 2 h preoperatively. Patients also were given 400 mL oral preoperative carbohydrate drink (PreOP[®], Nutricia; Numico, Zoetermeer, the Netherlands), which they were told to drink 2 h preoperatively. Preoperative sedatives were not allowed. Epidural anesthesia was not performed in laparoscopic surgery, however, in planned open surgery an epidural catheter was placed at the T8–T10 level. In these patients, intraoperative analgesia was provided using a single epidural dose of bupivacaine at induction (25–30 mg), followed by an infusion of bupivacaine (2.5 mg.mL⁻¹ at mL.h⁻¹).

IV opioids (fentanyl) were given after induction of anesthesia in all patients undergoing laparoscopic surgery. An infusion of lactated Ringer's solution was started and maintained throughout the procedure using a dedicated infusion pump (set at 3 mL.kg⁻¹.h⁻¹ for laparoscopic colectomy, and 5 mL.kg⁻¹.h⁻¹ for open colectomy, based on lean body weight).

All patients received intraoperative Goal-Directed Hemodynamic Therapy (GDHT) with a minimally invasive Cardiac Output (CO) monitor. Oesophageal Doppler (EDMTM Deltex Medical, Inc., Irving, TX) or Vigileo/Flotrac (Edwards, Irvine, USA) were used according to the need for invasive monitoring of blood pressure, which was not protocolised, and was based on the preferences of the anesthesiologist. Bolus of IV colloid (hydroxyethyl starch 130/04, Voluven, Fresenius Kabi, Germany) was given to optimize stroke volume (SV) using a 10% algorithm (Fig. 1). Hypotension was preferably treated with a vasopressor agent (ephedrine 5 mg or phenylephrine 0.1 mg) instead of intravenous fluid bolus in order to maintain a neutral fluid balance. Ondansetron and dexamethasone were administered according individual Apfel score¹⁷ to prevent postoperative nausea and vomiting. Nasogastric tubes and surgical drains were not routinely used.

Postoperatively patient's urinary catheter was removed on the day after surgery. Postoperative analgesia was provided by using acetaminophen and no steroidal anti-inflammatory drugs. Opioid were avoided when possible. Patients were encouraged to drink liquids immediately after surgery. IV fluid administration was discontinued once adequate oral intake was achieved, usually on the first morning after surgery. Patients were encouraged to get up on a chair 6 h after surgery, and to walk after the first 12 postoperative hours.

Table 1 ERAS guidelines recommendations.

Item	ERAS recommendation
Preoperative information, education and counseling	Patients should routinely receive dedicated preoperative counseling
Preoperative optimization	Smoking and alcohol consumption (alcohol abusers) should be stopped four weeks before surgery
Preoperative bowel preparation	Mechanical bowel preparation should not be used routinely in colonic surgery
Preoperative fasting and carbohydrate treatment	Clear fluids should be allowed up to 2 h and solids up to 6 h prior to induction of anesthesia. Preoperative oral carbohydrate treatment should be used routinely
Preanesthetic medication	Patients should not routinely receive long- or short- acting sedative medication before surgery because it delays immediate postoperative recover
Prophylaxis against thromboembolism	Patients should wear well-fitting compression stockings, have intermittent pneumatic compression, and receive pharmacological prophylaxis
Antimicrobial prophylaxis and skin preparation	Routine prophylaxis using intravenous antibiotics should be given 30–60 min before initiating surgery. Additional doses should be given during prolonged operations according to half life of the drug used preparation with chlorhexidine-alcohol should be used
Standard anesthetic protocol	A standard anesthetic protocol allowing rapid awakening should be given the anesthetist should control fluid therapy, analgesia and hemodynamic changes to reduce the metabolic stress response
Postoperative nausea and vomiting (PONV)	A multimodal approach to PONV prophylaxis should be adopted in all patients with 2 or more risk factors undergoing major colorectal surgery
Laparoscopy and modifications of surgical access	Laparoscopic surgery for colonic resections is recommended if the expertise is available
Nasogastric intubation	Postoperative nasogastric tubes should not be used routinely. Nasogastric tubes inserted during surgery should be removed before reversal of anesthesia
Preventing intraoperative hypothermia	Intraoperative maintenance of normothermia with a suitable warming device and warmed intravenous fluids should be used routinely to keep body temperature
Perioperative fluid management	Patients should receive intraoperative fluids (colloids and crystalloids) guided by flow measurements to optimize cardiac output
Drainage of peritoneal cavity after colonic anastomosis	Routine drainage is discouraged because it is an unsupported intervention that is likely to impair mobilization.
Urinary drainage	Routine transurethral bladder drainage for 1–2 days is recommended
Prevention of postoperative ileus	Fluid overload and nasogastric decompression should be avoided
Postoperative analgesia	Open surgery: Thoracic epidural anesthesia (TEA) using low-dose local anesthetic and opioids Laparoscopic surgery: No TEA
Perioperative nutritional care	Patients should be screened for nutritional status and if at risk of under nutrition given active nutritional support postoperatively patients should be encouraged to take normal food as soon as lucid after surgery
Postoperative glucose control	Hyperglycaemia is a risk factor for complications and should therefore be avoided
Early mobilization	Prolonged immobilization increases the risk of pneumonia, insulin resistance and muscle weakness. Patients should therefore be mobilized

Interventions unchanged between groups

All patients underwent basic anesthetic monitoring with five-lead-electrocardiogram, pulse oximetry and blood pressure cuff; at least two peripheral intravenous lines were established. Antibiotic prophylaxis (cefazolin 2 g and metronidazole 500 mg intravenously) was given 30 min before surgery incision. All patients received general anesthesia with an oral endotracheal tube. All patients received balanced or total intravenous anesthesia, intravenous anesthetic induction, and neuromuscular relaxants; for pragmatic reasons, their administration was made at the

discretion of the anesthesiologist. Bispectral Index monitoring system (BIS, Medtronic, Dublin, Ireland) was used to monitor the depth of the anesthesia. Sevoflurane or propofol was used for anesthesia maintenance; with the target range of BIS values between 40–60. All patients received standard measures to maintain optimal oxygenation (oxygen saturation by pulse oximetry $\geq 94\%$), core temperature (37°C) and heart rate (<100 min). Ventilation with inspired oxygen fraction of 60% was mechanically controlled to maintain PaCO₂ between 35 and 45 mmHg, with a positive end-expiratory pressure of 4–6 mmHg and tidal volume of 6–8 mL.kg⁻¹. Normothermia was maintained using convective air warming

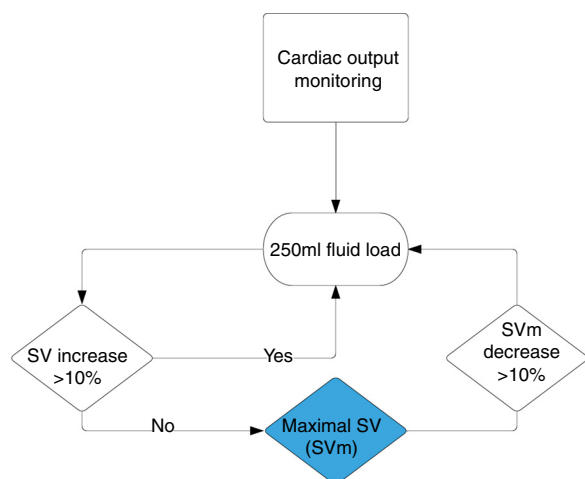


Figure 1 Goal Directed Fluid Therapy algorithm (SV, stroke volume; SVm, maximal stroke volume).

system (Bair Hugger; 3M-Switzerland, Rüschlikon, Switzerland) and Hotline[®] fluid warmer (Smith Medical International Ltd., Ashford, Kent, United Kingdom).

At the end of the intervention all patients were followed in intensive care for at least 24 h. Postoperative administration of fluids was not protocolized.

Outcomes

The aim of our study was the prospective evaluation of an ERAS protocol that includes the whole application of all ERAS principles in adult patients undergoing elective colorectal surgery. The primary endpoint was the percentage of patients who developed pre-defined moderate-severe postoperative complications within 180 days after surgery, including complications that occurred before or after hospital discharge and required ambulatory or in-hospital care.

Postoperative complications were defined according to standard definitions and using the outcome measures for clinical effectiveness research in perioperative medicine (EPCO).¹⁸ All complications were classified in mild, moderate and severe.

Secondary endpoints were: LOS (defined as the number of days spent in the hospital: from the day of surgery to hospital discharge or death), re-admission, all-cause mortality within 180 days after surgery, and ERAS protocol compliance (Table 2). Overall ERAS protocol compliance was calculated in the ERAS cohort as the average of all pre- and intraoperative ERAS elements, as specified in the ERAS Guidelines of Colon and Rectal surgery. Hospital readmission for any postoperative complication occurring within 180 days after discharge was also recorded.

Data collection

Three researchers who did not participate in the perioperative management of patients performed data collection. All data were retrieved from the patients' database and clinical records, which in our center is fully computerized. The following data were extracted: sex, age, comorbidity (diabetes

Table 2 ERAS protocol compliance in the ERAS group.

	%
Preoperative information and counseling	98.9
Preoperative optimization	98.9
Preoperative bowel preparation	92.4
Preoperative fasting and carbohydrate treatment	67.5
Pre anesthetic medication	96.2
Prophylaxis against thromboembolism	100
Antimicrobial prophylaxis	100
Standard anesthetic protocol	100
PONV	71.6
Laparoscopy	79.2
Nasogastric intubation	87.9
Preventing intraoperative hypothermia	99.6
Goal Directed Hemodynamic therapy	100
Drainage of peritoneal cavity	70.9
Urinary drainage	99.6
Fluid balance < 1500 mL/24 h	85.5
Postoperative analgesia	100
Perioperative nutritional care	68.5
Postoperative glucose control	100
Early mobilization	50.2
Overall compliance	88.4

PONV, postoperative nausea and vomiting.

mellitus, hypertension, ischemic heart disease, respiratory disease), American Society of Anesthesiologists.

Physical Status (ASA), surgical approach (open, laparoscopic), type of anesthetic procedure, operation time and complications.

Statistical analysis

Descriptive statistics of the pre-ERAS and post-ERAS groups were compared for all relevant patient characteristics, perioperative and postoperative data. The discrete variables were described as *n* (%) and the continuous variables as mean (standard deviation) and median (interquartile range). Statistical comparisons between pre-ERAS and post-ERAS groups were performed with the Mann-Whitney *U* tests, and Fisher's exact test as appropriate. The statistical significance level for all comparisons was set at a two-tailed $\alpha = 0.05$.

The data set was analyzed using the percentage of patients with postoperative complications. The influence of the following factors was assessed: sex, age, ASA status, surgical approach (open, laparoscopic), type of anesthetic procedure, duration of surgery, intraoperative fluid administration and first 24 h fluid balance; and ERAS protocol.

All analyses were performed using JMP version 12.1.0 (SAS Institute, Cary, Carolina del Norte, USA).

Results

There were 360 procedures on 360 individual patients in the Pre-ERAS group and 319 procedures on 319 individual patients in the Post-ERAS Group. There were no patients or procedures excluded or deleted from either cohort of

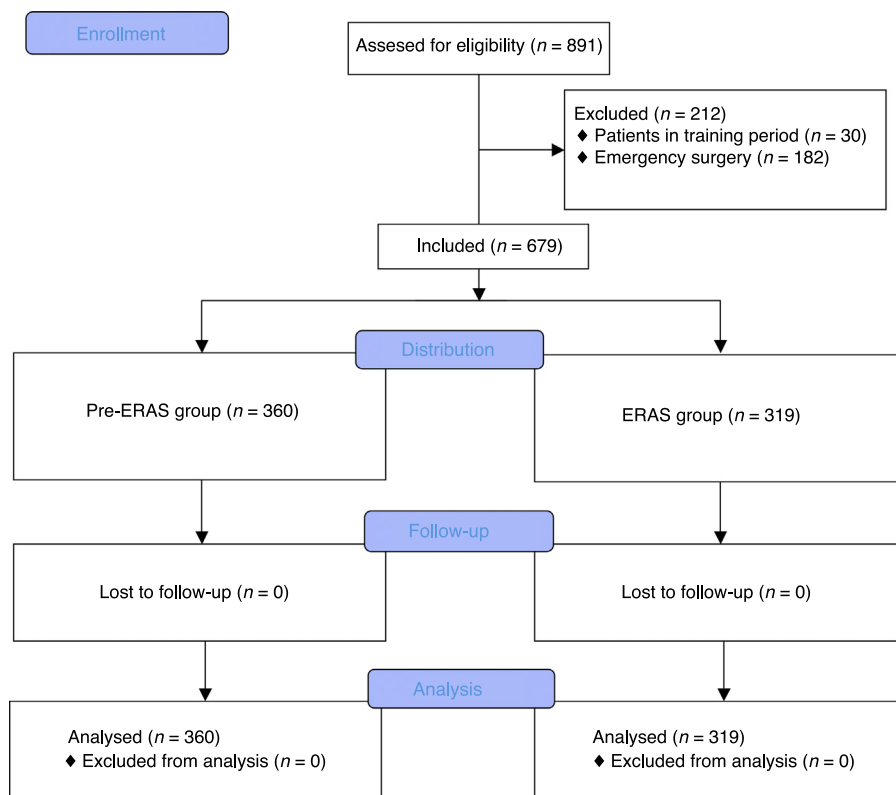


Figure 2 CONSORT flow chart.

consecutive cases enrolled in the analysis. There were no losses of follow up (Fig. 2).

Patient characteristics are reported in Table 1. There was no statistically significant difference in age, body mass index, or ASA rating. However, there were more women in the pre-ERAS group. Chronic health conditions such as diabetes and chronic cardiac conditions were equally represented in both groups. More patients in the Pre-ERAS group underwent surgery with open surgical approach, and more patients received combined anesthesia (general epidural). Significantly less intravenous fluid were administered during the day of surgery and in the first 24h after surgery in patients receiving ERAS perioperative care (Table 1).

A total of 214 (59.8%) patients developed at least one complication in the Pre-ERAS group, versus 163 patients in the ERAS group (51.1%). More patients in the Pre-ERAS group developed moderate or severe complications (31.9% vs. 22.2%, $p=0.009$); and severe complications (15.5% vs. 5.3%; $p<0.001$). No differences were found on mortality rates (4.7% vs. 2.5%; $p=0.154$) (Fig. 3) nor readmission (6.39% vs. 4.39%; $p=0.31$). The rate of specific complications is presented in Table 3. Postoperative ileus was the most frequent complications in both groups, however there were significant fewer patients in the Post-ERAS group (33.6% vs. 19.2%, $p<0.001$). There were also significant fewer patients with deep and organ-space surgical site infection in the Post-ERAS group. More patients developed anastomotic breakdown in the Pre-ERAS group (10% vs. 4.7%; $p=0.012$). No significant differences in other analyzed complications were observed. There was a significant difference in LOS between both groups. The median postoperative hospital stay was

13 (17) days for patients receiving conventional care and 11 (10) days for patients that had followed the ERAS protocol ($p=0.034$). Patient characteristics, operative factors, and ERAS component that influenced the development of complications are summarized in Table 4.

The average percentage of completion was 88.4% in the Post-ERAS patient cohort (Table 5). All patients complied with the items on antithrombotic and antimicrobial prophylaxis, anesthetic protocol, fluid therapy, postoperative analgesia and glycaemic control. The lowest compliance item was early mobilization (50.2%), followed by fasting and preoperative carbohydrate loading (67.5%), perioperative nutritional care (68.5%) and non-placement of surgical drains (70.9%).

Discussion

When implementing an ERAS protocol, it is imperative to examine the Pre- and Post-ERAS implementation data to ensure that any unintended consequences are appropriately detected, and the hypothesized improvements actually occurred in patient outcomes. The results of this study suggest that the ERAS program was superior to conventional postoperative care for patients undergoing elective colonic or rectal resection. Patients treated according to the ERAS program developed significantly fewer complications and had shorter hospital stay. However, no differences in mortality were found.

Postoperative complications occur in up to one-third of patients undergoing colorectal surgery.¹ The most common

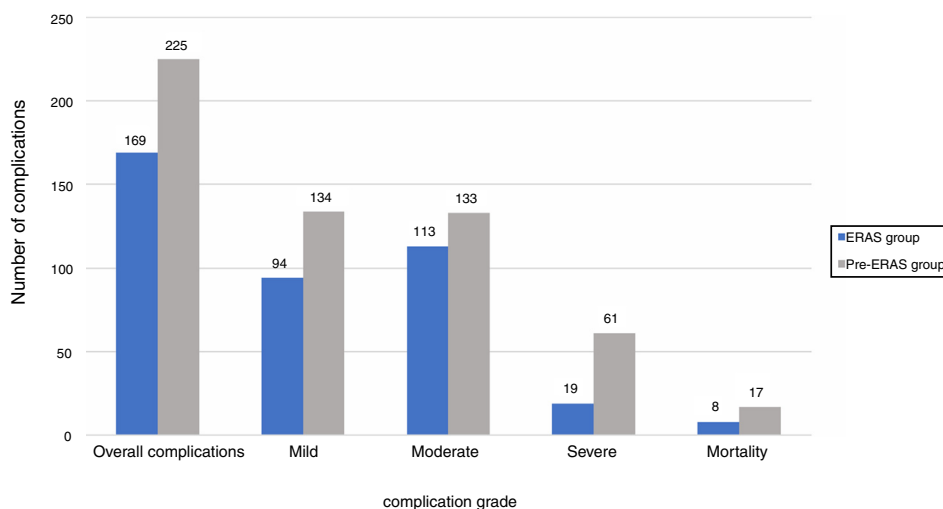


Figure 3 Overall complications.

Table 3 Demographic and perioperative characteristics of included patients.

	Pre-ERAS group	ERAS group
Age (years) mean (SD)	68.5 (13.6)	70.5 (12.4)
Gender, n (%)		
Female	120 (33.3)	137 (42.9)
Male	240 (66.7)	182 (57)
Body mass index ($\text{kg}\cdot\text{m}^{-2}$) Mean (SD)	27.8 (4.2)	27.8 (4.7)
ASA grade, n (%)		
I	37 (10.2)	23 (7.2)
II	204 (56.6)	173 (54.2)
III	117 (32.5)	116 (36.3)
IV	2 (0.5)	7 (2.2)
Hypertension, n (%)	201 (55.8)	199 (62.4)
Diabetes, n (%)	91 (25.3)	76 (23.8)
COPD, n (%)	57 (15.8)	47 (14.7)
Chronic renal disease, n (%)	35 (9.7)	22 (6.9)
Ischemic heart disease, n (%)	40 (11.1)	29 (9.1)
Preoperative Hb ($\text{g}\cdot\text{dL}^{-1}$) Mean (SD)	12.7 (1.8)	12.7 (2.0)
Preoperative Albumin ($\text{g}\cdot\text{dL}^{-1}$) Mean (SD)	3.8 (0.6)	3.7 (0.7)
Surgery, n (%)		
Open approach	167 (46.4)	116 (36.4)
Laparoscopic approach	193 (53.6)	203 (63.6)
Conversion to open, n (%)	16 (4.4)	15 (4.7)
Epidural, n (%)	76 (21.2)	25 (7.8)
Length of surgery (min) Mean (SD)	147.2 (54.1)	121.4 (49.2)
Intraoperative fluids (milliliters) Mean (SD)	2466.9 (1033.5)	1731.9 (702.8)
24 h fluids (milliliters) Mean (SD)	5463.7 (1687.2)	4356.4 (1236.6)
24 h balance (milliliters) Mean (SD)	2717.1 (1714.1)	2056.3 (1375.3)

ASA, American Society of Anesthesiologists physical status classification; COPD, chronic obstructive pulmonary disease; h, hours; BMI, body mass index.

complications reported are infectious, wound infection or organ space infection, and Gastrointestinal (GI) motility complications, including ileus and bowel obstruction.¹⁹ In a recent meta-analysis, Geco et al. showed that ERAS pathway was associated to a reduction of overall morbidity (Relative Ratio [RR] = 0.60; 95% CI 0.46–0.76), particularly with

respect to no surgical complications; and the ERAS pathway shortened two-day LOS, without increasing readmission rates.²⁰

In our study, we found similar results that were previously reported, fewer patients presented infectious complications, ileus, and anastomotic breakdown. In the

Table 4 Postoperative complications after colorectal surgery.

	Pre-ERAS group	ERAS group	p-value
AKI, <i>n</i> (%)	34 (9.4)	29 (9.1)	0.895
ARDS, <i>n</i> (%)	13 (3.6)	4 (1.2)	0.082
Acute myocardial infarction, <i>n</i> (%)	1 (0.3)	0 (0)	1.000
MINS, <i>n</i> (%)	5 (1.4)	1 (0.3)	0.221
Arritmia, <i>n</i> (%)	34 (9.4)	33 (10.3)	0.701
Cardiac arrest, <i>n</i> (%)	5 (1.4)	4 (1.2)	1.000
Cardiogenic pulmonary edema, <i>n</i> (%)	11 (3.1)	6 (1.8)	0.462
DVT, <i>n</i> (%)	0 (0)	1 (0.3)	0.469
PE, <i>n</i> (%)	2 (0.5)	1 (0.3)	1.000
Stroke, <i>n</i> (%)	3 (0.8)	0 (0)	0.252
Infection, source uncertain, <i>n</i> (%)	35 (9.7)	25 (7.8)	0.418
Infection, laboratory confirmed, <i>n</i> (%)	47 (13.1)	15 (4.7)	0.000
Surgical site infection (superficial), <i>n</i> (%)	46 (12.8)	26 (8.1)	0.060
Surgical site infection (deep), <i>n</i> (%)	42 (11.6)	11 (3.4)	0.000
Surgical site infection (organ/space), <i>n</i> (%)	39 (10.8)	15 (4.7)	0.004
Anastomotic breakdown, <i>n</i> (%)	36 (10)	15 (4.7)	0.012
Urinary tract infection, <i>n</i> (%)	13 (3.6)	7 (2.2)	0.364
Pneumonia, <i>n</i> (%)	13 (3.6)	10 (3.1)	0.833
Gastrointestinal bleed, <i>n</i> (%)	11 (3.1)	18 (5.6)	0.127
Postoperative Haemorrhage, <i>n</i> (%)	84 (23.3)	80 (25.1)	0.653
Paralytic ileus, <i>n</i> (%)	121 (33.6)	61 (19.1)	0.000
Delirium, <i>n</i> (%)	39 (10.8)	18 (5.6)	0.018
LOS Mean (SD)	13 (17)	11 (10)	0.034

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; MINS, myocardial injury after non-cardiac surgery; DVT, deep vein thrombosis; PE, pulmonary embolism; LOS, length of stay.

Post-ERAS group, patients received better perioperative management of fluids, both intraoperatively, and in the immediate postoperative period. Volume overload was associated with postoperative complications^{21,22} and mortality²³; while GDHT had shown that it could reduce the incidence of postoperative complications; its role within the ERAS program was recently questioned.^{24,25} Nonetheless, Gustafsson et al. identified restriction of intravenous fluid and use of a preoperative carbohydrate drink as major independent predictors of success.¹² Similarly, a restrictive perioperative fluid therapy, was the only individual ERAS item associated with a reduction of postoperative complications in the metacentre ERAS registry data, after analysing more than 2000 patients undergoing colorectal surgery.²⁶ Our study data provide further evidence that perioperative fluid management -in particular to prevent volume overload, is an important predictor of outcome, which underscores the need to keep this item on clinical pathways,²⁷ despite particular controversies,²⁸ and contradictory results of recent meta-analysis.²⁴

In our study, we found that restrictive fluid administration was associated with a reduction of complications; however, due to the 100% compliance in GDHT, we cannot draw conclusions regarding its usefulness.

The relationship between the onset of postoperative complications or LOS, and the rate of compliance to the ERAS protocol is subject to discussion. A high ERAS adherence has been shown to be associated with a significant reduction in LOS,²⁹ Nevertheless, its association with a reduction of complications is less evident.²⁹ Meaningfully, LOS is an irrelevant resource of measure, and has often been used as

a surrogate measure for postoperative complications.³⁰ It is not necessarily directly related to postoperative morbidity. Even though, in our study, despite not found a decrease in mortality, we found a significant decrease in moderate and severe complications.

A single-center prospective cohort study showed a significant decrease in postoperative complications (OR = 0.73; 95% CI 0.55–0.98). Following an overall increase in preoperative and perioperative adherence to the ERAS protocol from 43.3% to 70.6%.¹² Similarly, The United Kingdom Enhanced Recovery Partnership Program (ERPP) found that a $\geq 80\%$ ERAS compliance was associated with a shorter median LOS by two days,³¹ and recently, the Francophone Group for Enhanced Recovery after Surgery (“Groupe francophone de réhabilitation améliorée après chirurgie” [GRACE]) found a statistically significant relationship between protocol compliance and LOS for colorectal surgery, in a large multicentre prospective study including 490 patients; the threshold value of 68% of the elements applied was associated with a statistically significant effect on LOS.³² A high compliance to the items of the protocol, has been evoked to be essential to obtain the best outcomes.³³ Our results are similar to those previously published.

A limitation of the present study is that the analysis was retrospective and the results should have been interpreted as such. Despite this, database entry was done prospectively, which minimized data loss. Another limitation of this study included a relatively small sample size, and low risk patients. Moreover, both groups were not balanced in terms of population size, gender and open surgical vs. laparoscopic approach. Especially the greater number of patients with a

Table 5 Multivariable analysis of complications development after colorectal surgery in all included patients (pre-ERAS and ERAS groups).

	Correlation	Lower end 95% CI	Upper end 95% CI	p-value
<i>Patients with complications (all severity)</i>				
ERAS	-0.08	-0.15	-0.01	0.030
Age	0.15	0.07	0.22	<0.001
ASA	0.21	0.13	0.27	<0.001
Laparoscopy	-0.26	-0.32	-0.18	<0.001
Female	0.09	0.01	0.16	0.020
Epidural	0.08	0.01	0.15	0.035
Duration	0.18	0.11	0.26	<0.001
Intraoperative fluids	0.21	0.14	0.28	<0.001
24 h fluids	0.25	0.18	0.32	<0.001
24 h fluid balance	0.26	0.19	0.33	<0.001
<i>Patients with complications (moderate or severe)</i>				
ERAS	-0.10	-0.17	-0.02	0.008
Age	0.11	0.04	0.19	0.002
ASA	0.17	0.10	0.25	<0.001
Laparoscopy	-0.23	-0.30	-0.15	<0.001
Female	0.16	0.09	0.24	<0.001
Epidural	0.08	0.01	0.16	0.021
Duration	0.19	0.12	0.26	<0.001
Intraoperative fluids	0.23	0.16	0.30	<0.001
24 h fluids	0.22	0.15	0.30	<0.001
24 h fluid balance	0.20	0.13	0.27	<0.001
<i>Patients with complications (severe)</i>				
ERAS	-0.16	-0.23	-0.09	<0.001
Age	0.09	0.01	0.16	0.017
ASA	0.12	0.04	0.19	0.001
Laparoscopy	-0.15	-0.22	-0.07	<0.001
Female	0.14	0.07	0.21	<0.001
Epidural	0.04	-0.03	0.11	0.283
Duration	0.18	0.11	0.25	<0.001
Intraoperative fluids	0.16	0.08	0.23	<0.001
24 h fluid balance	0.18	0.10	0.25	<0.001

ERAS, Enhanced Recovery After Surgery; ASA, American Society of Anesthesiologists physical status classification; CI, confidence interval; ERAS, Enhanced Recovery After Surgery.

laparoscopic approach may have been influenced to obtain better outcome, however, the routine application of this approach constitutes a measure of the ERAS protocol itself. The use of Esophageal Doppler and Vigileo/Flotrac was not protocolized. Studies have shown that there is a limited concordance between the two devices to measure cardiac output and preload sensitive parameters and their response to clinical interventions.³⁴ This difference could be a source of misleading intraoperative management. However, due to the pragmatic features of this study, this limitation may be considered unimportant.

Conclusions

ERAS program is feasible, and its results are superior to conventional postoperative care for patients undergoing elective colonic or rectal resection. Patients treated according to an ERAS program develop significant fewer

complications and have shorter hospital stay. However, no difference in mortality has been found.

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Conflicts of interest

The authors declare no conflicts of interest.

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