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Impact of a colorectal enhanced recovery program implementation on clinical outcomes and institutional costs: A prospective cohort study with retrospective control☆

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ABSTRACT

Background: The enhanced recovery program for perioperative care of the surgical patient reduces postoperative metabolic response and organ dysfunction, accelerating functional recovery. The aim of this study was to determine the impact on postoperative recovery and cost-effectiveness of implementing a colorectal enhanced recovery program in an Italian academic centre.

Materials and methods: A prospective series of consecutive patients (N = 100) undergoing elective colorectal resection completing a standardized enhanced recovery program in 2013–2015 (ERP group) was compared to patients (N = 100) operated at the same institution in 2010–2011 (Pre-ERP group) before introducing the program. The exclusion criteria were: > 80 years old, ASA score of IV, a stage IV TNM, and diagnosis of inflammatory bowel disease. The primary outcome was hospital length of stay which was used as a proxy of functional recovery. Secondary outcomes included: postoperative complications, 30-day readmission and mortality, protocol adherence, nursing workload, cost-effectiveness, and factors predicting prolonged hospital stay. The ERP group patient satisfaction was also evaluated.

Results: Hospital stay was significantly reduced in the ERP *versus* the Pre-ERP group (4 *versus* 8 days) as well as nursing workload, with no increase in postoperative complications, 30-day readmission or mortality. ERP group protocol adherence (81%) and patient satisfaction were high. Conventional perioperative protocol was the only independent predictor of prolonged hospital stay. Total mean direct costs per patient were significantly higher in the Pre-ERP *versus* the ERP group (6796.76 *versus* 5339.05 euros).

Conclusions: Implementing a colorectal enhanced recovery program is feasible, efficient for functional recovery and hospital stay reduction, safe, and cost-effective. High patient satisfaction and nursing workload reduction may also be expected, but high protocol adherence is necessary.

1. Introduction

The Enhanced Recovery Program (ERP) is a scientific evidence-based perioperative care approach based on a multidisciplinary team employing a multimodal methodology, with the aim to reduce postoperative stress, metabolic response, and organ dysfunction, thereby accelerating recovery [1]. Consequently, the hospital length of stay (LOS) after surgery would be significantly reduced, with no increase in morbidity and mortality rates [2–4] resulting in a potential economic benefit [1,4,5].

Although the concept of implementing specific pathways to enhance recovery after surgery is now widely recognized, ERPs are primarily used in Northwestern Europe, USA, and Canada, and to a lesser extent in Southern Europe, where it prevails in Spain, Portugal [1], and Italy [6].

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The implementation of an ERP protocol relies on a motivated multidisciplinary team including surgeons, anaesthesiologists, and nurses who agree on the endpoints of management, act in close coordination throughout the perioperative phases, and adhere to the ERP protocol that correlates with clinical outcomes [1].

The aim of this study was three-fold: 1) to investigate the impact on postoperative recovery of colorectal ERP implementation in an Italian University hospital, evaluating the efficacy (functional recovery, LOS), safety (postoperative complications, 30-day readmission and mortality), protocol adherence, nursing workload, and cost-effectiveness; 2) to assess the predictive factors of prolonged hospital LOS after colorectal resection; 3) to measure patient satisfaction in the ERP group.

2. Materials and methods

A prospective series of patients (N = 100) undergoing elective colorectal resection and completing a standardized ERP protocol in 2013–2015 (ERP group) at the S. Anna University Hospital Hospital in Ferrara (Italy) was compared to a retrospective series of patients (N = 100) operated at the same institution in 2009–2011 (Pre-ERP group), before the introduction of the ERP methodology. The Italian Ministry of Health funded this study, which began in January 2013. In 2012 the ERP multidisciplinary team was assembled, the ERP protocol was prepared, and informative meetings were scheduled. All consecutive patients between the ages of 18 and 79 years old scheduled for elective colorectal resection were enrolled in the study. The exclusion criteria for both groups were: age > 80 years old, *American Society of Anesthesia* (ASA) score of IV, TNM stage IV, and diagnosis of inflammatory bowel disease.

The criteria adopted for the discharge of ERP and Pre-ERP group patients were the same, specifically: 1) unrestricted oral diet, 2) full intestinal function recovery (i.e. passage of flatus and stool), 3) dynamic pain control (*Numerical Rate Scale* – NRS ≤3) by oral analgesia, 4) independent walking, and 5) no signs of infection.

In order to evaluate the impact on postoperative recovery of implementing the colorectal ERP, the hospital LOS, a proxy of functional recovery, was adopted as primary outcome. Secondary outcomes were postoperative complications, 30-day readmission, mortality, adherence to the protocol, nursing workload, cost-effectiveness, and the predictive factors of prolonged hospital LOS.

All the study data were collected prospectively for the ERP group and retrospectively for the Pre-ERP group.

All *ERP group* patients were extensively informed about the program, including discharge criteria and 4-day planned hospital LOS, by thorough preoperative counselling and an illustrated booklet specifically developed and validated by the multidisciplinary team. The patients were encouraged during hospitalization to follow the perioperative protocol, and were informed about the daily objectives to be achieved, including the discharge home. All ERP elements included in the colorectal protocol were prospectively recorded and checked for successful achievement (i.e. protocol compliance) by an independent observer using a detailed care program for each postoperative day (POD) (Table 1). Although laparoscopy was preferred, alternative surgical approaches were discussed with the patient. A converted laparoscopy was defined as unplanned extension of the surgical incision.

All *Pre-ERP group* patients were treated with the following traditional perioperative care principles: preoperative fasting starting midnight before treatment with no carbohydrate loaded drinks; opioid-based anesthesia with or without thoracic epidural; postoperative intravenous opioids and/or thoracic epidural and/or non-steroidal anti-inflammatory drugs (NSAIDs); nasogastric tube (NGT) removal and oral feeding at restoration of intestinal activity; abdominal drain removal at bowel movements; mobilization at patient's will; and bladder catheter removal at full mobilization. Preoperative counselling focused on patient's training, daily goals assignment or predefined day of discharge were not part of the traditional care plan. The medical records were reviewed to evaluate adherence to any of the 21 elements comprised in the ERP protocol and to determine how much the clinical practice had been modified by its implementation (Table 1).

All surgical procedures in both study groups were performed by staff surgeons trained in colorectal surgery and advanced laparoscopy.

Fulfilment of the predefined discharge criteria was checked by an independent observer in both study groups before discharge from the hospital, and outpatient appointments were scheduled 15 and 30 days after the operation.

The nursing workload was evaluated using the *Project de Recherche en Nursing* (PRN), a standardized and validated point system based on eight groups of activities (respiration, feeding and hydration, elimination, hygiene, mobilization, communication, treatments, and diagnostic procedures) that was developed in Canada to measure the level of patients' nursing care required. The PRN value was compared between groups for the first few days of hospital stay based on the ERP patients' median LOS; a higher PRN point value corresponds to a greater amount of direct care required.

To determine the costs-effectiveness of ERP *versus* traditional care, we collected costs for: 1) ERP implementation; 2) preoperative phase (i.e. preoperative counselling, booklet); 3) direct cost of hospitalizations (i.e. operating room, drugs, exams, visits, LOS); 4) re-hospitalizations.

To evaluate the patient satisfaction, the Patient Satisfaction Consultation Questionnaire (PSCQ-7) [7] and Core Questionnaire Patient Satisfaction (COPS) [8] were administered to all ERP group patients at hospital discharge.

The study was conducted in accordance with the principles of Helsinki Declaration, with approval of the medical ethics review board of S. Anna University Hospital. A written informed consent was obtained from all enrolled patients.

2.1. Statistical analysis

Data were expressed as median (interquartile range – IQR 25-75) and mean ± standard deviation according to distribution assessed by Shapiro-Wilk test. Categorical data were presented as numbers. Data were analysed using Chi-square, t-student, and Mann-Whitney tests as appropriate. As previously reported, the Kaplan-Meier method and the Log-Rank test were used to compare duration of surgical operation, time to functional recovery, and hospital LOS between groups; Cox regression analysis was employed to assess independent predictors of prolonged hospital LOS [9]. Significance was considered for values of $p < 0.05$. Statistical analysis was performed with IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp. Armonk, NY: IBM Corp.).

This report complies with the strengthening the reporting of cohort studies in surgery criteria (STROCSS) [10].

3. Results

The key elements and adherence to the protocol in both groups are illustrated in Table 1. Following ERP implementation, the median compliance with ERP elements was 81.0% (76.2%–85.7%) in the ERP group and 23.8% (19.0%–28.6%) in the Pre-ERP group (Fig. 1).

Demographics and baseline characteristics of all patients are shown in Table 2. Patients were comparable except for those with diabetes, valvular heart disease, and ASA score III who significantly prevailed in the Pre-ERP group.

The intraoperative characteristics and variables are detailed in Table 3. No difference between groups was detected in both disease and operation types, although the number of patients operated on using laparoscopy was significantly higher in the ERP group.

Postoperative variables and outcomes are shown in Table 4. No difference between groups was found in term of postoperative vomiting, re-insertion of NGT, and resumption of intravenous fluids despite a significantly higher number of patients without NGT and with an early oral nutrition in the ERP group (Tables 1 and 4). Complete

Table 1
Key elements of the Enhanced Recovery Program (ERP) protocol.

Variables	Pre-ERP Group (N = 100)	ERP Group (N = 100)	p
Pre-admission counselling (N, %)	0	100	< 0.001
Booklet (N, %)	0	100	< 0.001
No mechanical bowel preparation (N, %)	0	100	< 0.001
No pre-operative fasting (N, %)	0	100	< 0.001
Pre-operative Oral Carbohydrate loading (N, %)	0	95	< 0.001
No premedication (N, %)	92	94	0.568
Mid-thoracic epidural anesthesia (N, %)	21	91	< 0.001
Short-acting anesthetic agent (N, %)	22	88	< 0.001
Avoidance of intraoperative fluid overload (i.o. fluids ≤5 ml/kg/h) (N, %)	0	6	0.014
Intraoperative maintenance of normothermia (N, %)	99	96	0.121
Prevention of nausea and vomiting (N, %)	49	85	< 0.001
Minimally invasive surgery (N, %)	30	89	< 0.001
No abdominal drains (N, %)	7	43	< 0.001
No nasogastric tube (N, %)	2	95	< 0.001
Early mobilization (day ≤ 2) (N, %)	24	59	< 0.001
Post-operative breathing exercises (N, %)	0	94	< 0.001
Mid-thoracic epidural analgesia (N, %)	43	91	< 0.001
Non-opiate oral analgesics/NSAIDs[a] (N, %)	69	85	0.011
Stimulation of gut motility (N, %)	24	39	0.033
Early removal of bladder catheter (day ≤ 2) (N, %)	9	68	< 0.001
Early oral nutrition (day ≤ 1) (N, %)	1	84	< 0.001

[a] Nonsteroidal anti-inflammatory drugs (NSAIDs).

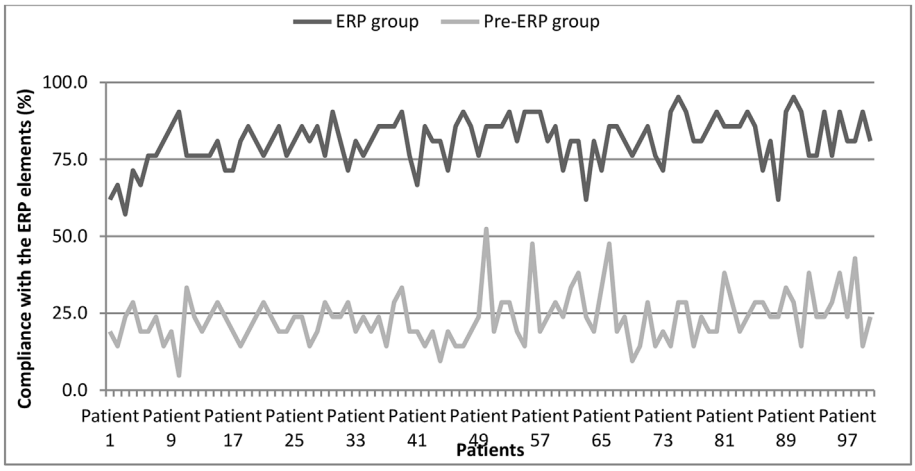

Fig. 1. Compliance with the ERP elements in the ERP and Pre-ERP groups.

functional recovery and pain control on oral analgesics were achieved earlier in ERP as compared to the Pre-ERP group, with no increase in postoperative complications. Hospital LOS was significantly reduced in the ERP group with no increase in 30-day re-admission and mortality (Table 4).

The PRN value per patient was significantly lower in the ERP group compared to the Pre-ERP group in the first four PODs, with a median time saving per ERP patient of 77 min in the POD 1 and 170 min in the POD 4. (Fig. 2, and Table A1).

Total mean direct costs per patient were significantly higher in Pre-ERP patients compared to the ERP group (6796.76 ± 1381.34 euro *vs.* 5339.05 ± 1909.24 euros), despite the higher cost for the laparoscopic equipment in the latter group (Table A2).

Unadjusted Cox regression analysis showed that laparotomy and converted laparoscopy and use of a traditional perioperative care protocol were predictors of prolonged hospital LOS. After adjusting for potential confounders, only use of traditional care was significantly associated with prolonged hospital LOS (Table 5).

Patient satisfaction in the ERP group according to the COPS and PSCQ-7 questionnaire was high and is shown in Tables A3 and A4, respectively.

4. Discussion

In this study, implementing a colorectal ERP protocol resulted in: 1) significant reduction in time to functional recovery and postoperative hospital LOS, with high patient satisfaction; 2) no increase in morbidity, mortality, or 30-day readmissions; and 3) significant decrease in both nursing workload and institutional costs. Finally, adherence to a conventional perioperative protocol was the only independent factor predicting a prolonged hospital LOS.

4.1. How did the implementation of ERP affect the perioperative care?

Implementing ERP may be hindered by barriers, such as lack of awareness or agreement with the evidence, protocol complexity, time limitation and lack of commitment of the multidisciplinary team, limited expertise or resources, or unmet patient expectations [11,12]. We successfully implemented the ERP protocol in our traditional perioperative care setting, although scheduled periodic audits were necessary to define and share the program details for continuing staff education and to maintain high compliance. In addition, high patient satisfaction and lower institutional costs in the ERP group shows that

Table 2
Baseline characteristics.

Variables	Pre-ERP Group (N = 100)	ERP Group (N = 100)	p
Gender (N)			0.321
Male	42	50	
Female	58	50	
Age (years) (N, %)			0.320
< 65	33	42	
65-74	36	35	
≥ 75	31	23	
Body Mass Index[a] (Kg/m^2) (N, %)			0.621
< 25	47	45	
25–29.9	40	38	
≥ 30	12	17	
American Society of Anesthesia score (N, %)			0.026
I	9	2	
II	50	65	
III	41	33	
Diabetes (N, %)	14	4	0.024
Hypertension (N, %)	46	52	0.480
Asthma (N, %)	0	2	0.497
COPD[b] (N, %)	1	3	0.621
Valvular heart disease (N, %)	13	1	0.001
Ischemic heart disease (N, %)	9	8	1.000
Atrial fibrillation (N, %)	5	4	0.748
Hypercholesterolemia (N, %)	16	8	0.126
Chronic renal insufficiency (N, %)	1	1	1.000
Depressive disorder (N, %)	7	13	0.238
MUST[c] score (N, %)			0.081
0	89	91	
1	9	3	
2	2	6	
Pre-operative hemoglobin [median (IQR25-75)]	13.0 (11.1–14.3)	13.1 (11.1–14.5)	0.498

[a] *Body Mass Index* was not available in one patient of the traditional group.
[b] COPD - Chronic Obstructive Pulmonary Disease.
[c] MUST - Malnutrition Universal Screening Tool.

Table 3
Intraoperative characteristics and variables.

Variables	Pre-ERP Group (N = 100)	ERP Group (N = 100)	P
Disease (N, %)			0.361
Cancer	85	84	
Benign tumor	15	14	
Diverticular disease	0	2	
Type of operation (N, %)			0.087
Right colectomy	47	50	
Left colectomy	13	15	
Transverse colon resection	5	4	
Sigmoid resection	26	13	
Rectosigmoid resection	3	13	
Segmental resection	5	4	
Sub-total colectomy	1	1	
New stoma (N, %)	1	1	1.000
Surgical approach (N, %)			< 0.001
Laparotomy	58	5	
Laparoscopy	30	89	
Laparoscopy with conversion	12	6	
Length of procedure (min) [median (IQR25-75)]	197.5 (165.0–224.8)	190.0 (165.8–230.0)	0.925
Intraoperative intravenous fluids (ml/kg/h) [median (IQR25-75)]	15.8 (13.0–20.3)	10.1 (7.5–12.5)	< 0.001
Intraoperative intravenous fluids (ml) [median (IQR25-75)]			
Total	3500 (3000–4500)	2250 (1563–3000)	< 0.001
Crystalloids	3000 (2500–3500)	2000 (1500–2500)	< 0.001
Colloids	500 (500–500)	0 (0–500)	< 0.001
Intraoperative red blood cell transfusion (N, %)	14	8	0.258
Red blood cell transfusion (ml) [median (IQR25-75)]	350 (300–700)	350 (300–365)	0.239
Urine output (ml) [median (IQR25-75)]	865 (600–1270)	500 (300–810)	< 0.001
Prevention of nausea and vomiting (N, %)	49	85	< 0.001

patients and resources were not barriers for implementation.

Recently, Pecorelli et al. demonstrated a positive association between ERP protocol adherence and successful recovery as well as an inverse correlation with LOS, which decreased 11% for every additional protocol element achieved [13]. Furthermore, compliance with at least 70–80% of protocol elements appears to be important to improve outcomes [1,14]. Nelson et al. showed lower overall ERP compliance in patients undergoing open colorectal resection and no significant LOS reduction [15], while a meta-analysis evaluating the role of protocol compliance shows that the outcomes may be achieved regardless of the number, combination, or type of single ERP element [12]. In our study, ERP group patients showed a high (81.0%) protocol adherence, both for open (76.2%) and laparoscopic (81.0%) procedures. A significant improvement in functional recovery was achieved in all ERP patients (median LOS: open 5 days, laparoscopy 4 days) compared to Pre-ERP patients (median LOS: open 8 days, laparoscopy 7 days), which supports the importance of protocol compliance. However, in ERP patients, we registered a low adherence for avoiding intraoperative fluid overload and abdominal drains, probably related to inveterate habits due to training, and for stimulation of gut motility, possibly not adopted due to early recovery of intestinal function in most patients (Table 1). Nevertheless, postoperative functional recovery in the ERP group was improved, which seems to support the importance of adherence to at least 80% of the elements.

As suggested by Fiore et al., functional recovery after colorectal surgery has been traditionally assessed by measuring LOS, which is influenced by health care system, hospital traditions, patient's expectations, and availability of postoperative support [16]. In light of this, they suggested the assessment of time to achieve standardized discharge criteria (i.e. day fit for discharge) as an alternative recovery measure [16]. At our institution, patients were traditionally discharged in the morning, which may explain the gap between day fit for discharge and LOS in the Pre-ERP group (patients completing the discharge criteria in the afternoon, left the hospital on the following day). By contrast, due to the perioperative care change introduced with the program, ERP group patients were discharged as soon as they were fit (Table 4), suggesting that LOS may be a valid surrogate of functional recovery.

Recently, a meta-analysis including 16 randomized trials comparing ERP *versus* traditional care in elective colorectal surgery, has shown a significant reduction of non-surgical complications, shortened LOS, and no increase in readmission rate in patients on ERP, although no decrease in surgical complications could be detected [3]. Pooled data analysis revealed no significant difference in readmission rate between ERP and control groups [16], suggesting safety of early discharge. This is consistent with our study showing a significant reduction in time to functional recovery and LOS, with no increase in either minor or major postoperative complications and 30-day readmissions in ERP patients.

4.2. Was nursing workload affected?

The need of a motivated and dedicated multidisciplinary team involved in patient care and concerns related to possible increase in surgical nurse workload, may contribute to the slow implementation of ERP in clinical practice. However, a recent retrospective study evaluating the nursing workload using PRN showed that the burden for nurses decreased after implementing ERP, with an inverse linear correlation with protocol compliance [17]. Our study confirms the

Table 4
Postoperative variables and outcomes.

Variables	Pre-ERP Group (N = 100)	ERP Group (N = 100)	p
Positioning of (N, %)			
Central venous catheter	77	5	< 0.001
Epidural catheter	43	91	< 0.001
Nasogastric tube (NGT)	98	5	< 0.001
Drainage	93	57	< 0.001
Day of removal of [median (IQR25-75)]			
Epidural catheter	3 (2–3)	3 (3–3)	0.083
NGT	2 (2–3)	1 (0–1)	< 0.001
Abdominal drain	5 (4–7)	3 (3–5)	< 0.001
Foley catheter	4 (4–6)	2 (2–3)	< 0.001
Post-operative red blood cell transfusion (N, %)	4	5	1.000
Vomiting ≤ 24 h (N, %)	5	10	0.283
Vomiting > 24 h (N, %)	9	14	0.376
Re-insertion of NGT (N, %)	6	7	1.000
Resumption of i.v. fluids (N, %)	5	7	0.767
Post-operative i.v. opioids (N, %)	63	5	< 0.001
Post-operative NSAID's[a] (N, %)	69	85	0.011
NRS[b] maximum [median (IQR25-75)]			
Day 0	3 (2–6)	2 (1–5)	< 0.001
Day 1	3 (2–7)	3 (1–6)	0.030
Day 2	2 (2–5)	2 (1–5)	0.012
Day 3	2 (2–3)	1 (1–2)	< 0.001
Day 4	2 (2–3)	1 (0–1)	< 0.001
Stimulation of gut motility (N, %)	24	39	0.033
Time to liquid diet (days)	3 (2–4)	1 (1–1)	< 0.001
Time to solid food (days)	5 (5–7)	3 (2–3)	< 0.001
Time to intestinal activity (days)	4 (3–4)	2 (1–2)	< 0.001
Time to bowel movements (days)	5 (4–6)	3 (2–4)	< 0.001
Time to pain control on oral analgesic (days)	4 (3–5)	3 (3–4)	< 0.001
Time to full mobility and autonomy (days)	3 (3–4)	2 (2–3)	< 0.001
Postoperative day fit for discharge (days)	7 (6–8)	4 (4–5)	< 0.001
Hospital length of stay (days)	8 (7–9)	4 (4–5)	< 0.001
Postoperative complications (Clavien-Dindo) (N, %)			0.663
Grade I	3	7	
Grade II	22	26	
Grade IIIa	1	1	
Grade IIIb	1	1	
In hospital mortality	0	0	–
30-day re-admission (N, %)	6	3	0.498
30-day mortality	0	0	–

[a] Nonsteroidal anti-inflammatory drugs (NSAIDs).
[b] NRS - Numeric Rating Scale.

Table 5
Association between baseline characteristics, intra-operative variable and type of perioperative protocol and prolonged length of hospital stay according to Cox regression analysis adjusted for potential confounders.

Variable	Prolonged hospital length of stay			
	Unadjusted Model		Full Adjusted Model	
	HR (95% CI)	P	HR (95% CI)	p
Gender (ref: female)				
male	0.99 (0.76–1.32)	0.993	0.89 (0.66–1.19)	0.420
Age (ref: < 65 y)				
65-74	0.81 (0.59–1.13)	0.215	0.80 (0.56–1.12)	0.193
≥ 75	0.72 (0.50–1.02)	0.065	0.75 (0.51–1.10)	0.139
BMI[a] (ref: < 25 kg/m^2)				
25–29.9	1.01 (0.74–1.36)	0.997	1.04 (0.76–1.43)	0.813
≥ 30	1.19 (0.79–1.82)	0.408	1.44 (0.92–2.23)	0.108
ASA[b] score (ref: I)				
II	1.11 (0.60–2.07)	0.735	0.93 (0.47–1.83)	0.833
III	0.80 (0.42–1.51)	0.489	0.77 (0.38–1.53)	0.449
MUST[c] score (ref: 0)				
≥ 1	1.06 (0.67–1.70)	0.793	1.33 (0.78–2.25)	0.297
Surgical approach (ref: laparoscopy)				
laparotomy/ laparoscopy with conversion	0.61 (0.46–0.82)	0.001	0.96 (0.66–1.38)	0.811
Perioperative protocol (ref: ERP)				
traditional	0.43 (0.32–0.58)	< 0.001	0.43 (0.29–0.62)	< 0.001

[a] BMI - Body Mass Index.
[b] ASA - American Society of Anesthesia.
[c] MUST - Malnutrition Universal Screening Tool.

possibility to reduce nursing workload with ERP since the early postoperative period, with a steep decrease in the first three PODs (Fig. 2) leads to fast patient functional recovery and autonomy. The study also supports ERP implementation to improve patient care and to reduce resource consumption by modifying hospital staff organization and tailoring nursing activity.

4.3. Are there financial benefits?

A hospitalization direct costs reduction may be expected by

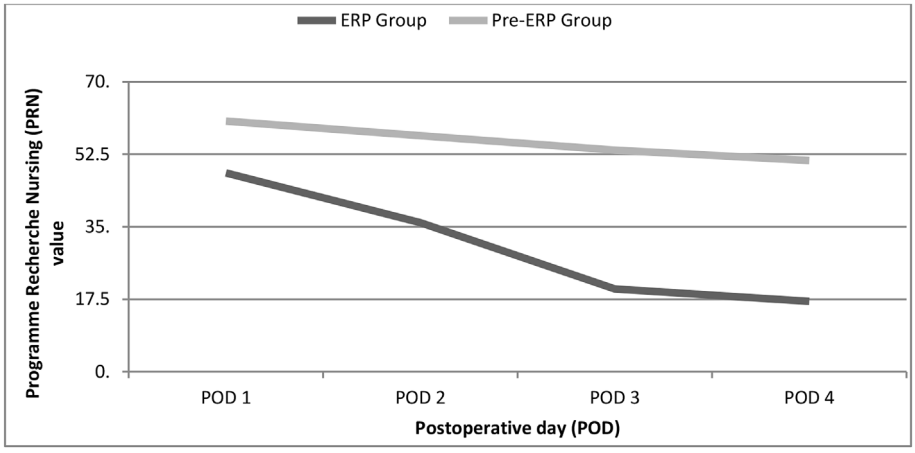

Fig. 2. *Programme Recherche Nursing* (PRN) value during the first four postoperative days in the ERP and Pre-ERP patients.

decreasing hospital LOS without increasing readmission rates. However, a prospective study comparing ERP *versus* traditional care in North America showed significant decrease in societal costs (i.e. productivity loss, caregiver burden, and out-of-pocket expenses) in ERP patients, with no difference in institutional costs, partly explained by ERP implementation costs, prevalence of laparoscopy, health care system costs (i.e. community health service centre, assisted care facility, and physician billing) [5]. However, our study performed in a National Health Care system showed a significant decrease of institutional costs for ERP patients, including implementation costs and prevalence of laparoscopy, showing economic benefit of shortened hospital stay due to faster functional recovery of ERP patients.

4.4. Which factors may predict prolonged hospital LOS?

Slower recovery may be expected in patients undergoing an open rather than laparoscopic colorectal resection. In this study, regression analysis showed that laparotomy and converted laparoscopy were associated to prolonged hospital LOS, but after adjusting for potential confounders, following a traditional perioperative care was the only predictive factor. Thus, perioperative protocol seems more important than surgical approach, although minimal invasive techniques should be preferred and, in our study, almost 90% of ERP patients were operated on by laparoscopy as opposed to 30% in the pre-ERP group. Also, the LAFA trial showed that laparoscopy was the only independent factor to reduce total LOS [18]. In patients undergoing an open colorectal resection, the ERP improved functional recovery and reduced LOS with no increase in readmission rate and, therefore, such a recovery program should always be adopted if a laparotomy is needed [2,18].

4.5. Strengths and limitations

This study has some limitations that need to be addressed. Firstly, the control group was retrospective and selection or information bias may have occurred. To reduce the risk of such bias, we enrolled all consecutive Pre-ERP patients who met the inclusion criteria. Secondly, higher rate of open procedures in Pre-ERP group may have favoured the ERP group, although regression analysis showed no significant effect on prolonged LOS of open approach. Thirdly, patients were discharged according to predefined criteria, but no data on post-discharge daily living activities were available and, therefore, we cannot prove a direct correlation between early discharge and full recovery to baseline status. Nevertheless, patients in the ERP group were highly satisfied of their pathway of care including timing of discharge, suggesting good in-hospital recovery. Unfortunately, due to the retrospective nature of the control group, questionnaires of patient satisfaction were not available in the Pre-ERP group.

5. Conclusion

The implementation of ERP in elective colorectal resection is feasible, efficient, and reduces the time to functional recovery and postoperative hospital LOS, with no increase in morbidity, mortality, or 30-day readmissions, and is cost-effective with significant nursing workload reduction. High patient satisfaction may also be expected, but high protocol adherence is necessary to improve patients' functional recovery.

Appendices

Table A1
Programme Recherche Nursing (PRN) between the groups.

Variables	Pre-ERP Group (N = 100)	ERP Group (N = 100)	p
Programme Recherche Nursing – PRN (value)			
POD 1	60.5 (55.0–65.0)	48.0 (45.0–50.8)	< 0.001

Ethical approval

The study was conducted with approval of the medical ethics review board of the S. Anna University Hospital of Ferrara, Italy (reference number: Prot. N. 52/2011).

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Author contribution

Mattia Portinari: Analysis and interpretation of data, drafting the article, and final approval of the submitted version.

Simona Ascanelli: Conception and design, revising critically the article, and final approval of the submitted version.

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Conflicts of interest

None to declare.

Trial registry number

ClinicalTrials.gov Identifier NCT03382210.

Guarantor

Carlo Feo, Mattia Portinari.

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The study was registered at ClinicalTrials.gov.

POD 2	57.0 (54.0–63.0)	36.0 (29.0–46.0)	< 0.001
POD 3	53.5 (49.0–58.0)	20.0 (17.0–29.0)	< 0.001
POD 4	51.0 (44.3–55.0)	17.0 (15.0–21.0)	< 0.001
Time (min)			
POD 1	302.5 (275.0–325.0)	225.0 (240.0–253.8)	< 0.001
POD 2	285.0 (270.0–315.0)	180.0 (145.0–230.0)	< 0.001
POD 3	267.5 (245.0–290.0)	100.0 (85.0–145.0)	< 0.001
POD 4	255.0 (221.3–275.0)	85.0 (75.0–105.0)	< 0.001

Table A2
Comparison of institutional costs per patient between Pre-ERP and ERP groups.

Variables	Pre-ERP Group (N = 100)	ERP Group (N = 100)	p
Preoperative phase and implementation	12.97	51.1	< .001
Operating room phase			
Pharmacy	189.03 ± 87,90	131.29 ± 71,51	< .001
Equipment	994.68 ± 420.08	1363.90 ± 370.37	< .001
Operating theater	283.59 ± 56.21	286.95 ± 69.49	NS[a]
Surgical ward phase			
Hospital stay	4684.68 ± 1211.64	3134.47 ± 1647.10	< .001
Pharmacy	231.23 ± 137.41	75.21 ± 142.23	< .001
Laboratory	301.64 ± 102.67	200.94 ± 103.18	< .001
Radiology	28.29 ± 35.50	16.43 ± 49.60	< .001
Specialist consultation	4.37 ± 12.53	2.07 ± 7.37	NS
Outpatient clinic and Emergency Department	62.65 ± 101.27	78.14 ± 68.35	NS
Total institutional costs	6796.76 ± 1381.34	5339.05 ± 1909.24	< .001

[a] NS – Not Significant.

Table A3
Core Questionnaire Patient Satisfaction (COPS).

Items	Median (25-75 IQR)
Admission procedure	
Information provided by nurse upon admission	5 (4–5)
Reception at the ward	5 (4–5)
Nursing care	
Expertise of the nursing staff	4 (4–5)
The way nurses helped patients when asked for help	5 (4–5)
The way nurses treated patients	5 (4–5)
Medical care	
The way doctors and nursing staff get along	5 (4–5)
Doctors' expertise	5 (4–5)
Information	
Approachability of hospital staff in case of questions	5 (4–5)
The way information was transferred from one person to another	4 (4–5)
The amount of information	4 (4–5)
Clarity of information given by doctors	5 (4–5)
Patient autonomy	
Patient's ability to participate in treatment decisions	5 (4–5)
Patient being encouraged to be self-sufficient	5 (4–5)
Discharge and aftercare	
The way information was transferred to general practitioner	4 (4–5)
Information provided regarding further treatment	4 (4–5)
The timing of discharge from hospital	5 (4–5)

IQR: interquartile range; A 5-point scale with answering categories unsatisfied (=1), somewhat satisfied (=2), rather satisfied (=3), quite satisfied (=4) and very satisfied (=5) was used.

Table A4
Patient Satisfaction Consultation Questionnaire (PSCQ-7).

Item	Median (25-75 IQR)
All in all, how satisfied are you with your visit to the doctor?	5 (4–5)
Do you think that the doctor understood your health problem?	5 (4–5)
Do you think that your doctor took your health problem seriously?	5 (4–5)
Do you think that the diagnosis given by your doctor applied to your health problem?	5 (4–5)
Did you understand what your doctor told you about your health problem?	5 (4–5)
Do you think that the doctor was thorough?	5 (4–5)
Did you get the impression that the doctor had an extensive knowledge of your health problem?	5 (4–5)

IQR: inte quartile range; A 5-point scale with answering categories unsatisfied (=1), somewhat satisfied (=2), rather satisfied (=3), quite satisfied (=4) and very satisfied (=5) was used.

References

[1] O. Ljungqvist, M. Scott, K.C. Fearon, Enhanced recovery after surgery: a review, JAMA Surg (2017), http://dx.doi.org/10.1001/jamasurg.2016.4952.

[2] K.K. Varadhan, K.R. Neal, C.H. Dejong, et al., The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials, Clin. Nutr. 29 (2010) 434–440, http://dx.doi.org/10.1016/j.clnu.2010.01.004.

[3] M. Greco, G. Capretti, L. Beretta, et al., Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials, World J. Surg. 38 (2014) 1531–1541, http://dx.doi.org/10.1007/s00268-013-2416-8.

[4] M. Adamina, H. Kehlet, G.A. Tomlinson, et al., Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery, Surgery 149 (2011) 830–840, http://dx.doi.org/10.1016/j.surg.2010.11.003.

[5] L. Lee, J. Mata, G.A. Ghitulescu, et al., Cost-effectiveness of enhanced recovery versus conventional perioperative management for colorectal surgery, Ann. Surg. 262 (2015) 1026–1033, http://dx.doi.org/10.1097/sla.0000000000001019.

[6] M. Braga, N. Pecorelli, M. Scatizzi, et al., Enhanced recovery program in high-risk patients undergoing colorectal surgery: results from the PeriOperative Italian society registry, World J. Surg. (2016), http://dx.doi.org/10.1007/s00268-016-3766-9.

[7] L. Frostholm, P. Fink, E. Oernboel, et al., The uncertain consultation and patient satisfaction: the impact of patients' illness perceptions and a randomized controlled trial on the training of physicians' communication skills, Psychosom. Med. 67 (2005) 897–905, http://dx.doi.org/10.1097/01.psy.0000188403.94327.5b.

[8] S.M. Kleefstra, R.B. Kool, C.M. Veldkamp, et al., A core questionnaire for the assessment of patient satisfaction in academic hospitals in The Netherlands: development and first results in a nationwide study, Qual. Saf. Health Care 19 (2010) e24, http://dx.doi.org/10.1136/qshc.2008.030825.

[9] C.V. Feo, M. Portinari, E. Tsolaki, et al., The effect of an Enhanced Recovery Program in elective retroperitoneal abdominal aortic aneurysm repair, J. Vasc. Surg. 63 (2016) 888–894, http://dx.doi.org/10.1016/j.jvs.2015.09.060.

[10] R.A. Agha, M.R. Borrelli, M. Vella-Baldacchino, et al., The STROCSS statement: strengthening the reporting of cohort studies in surgery, Int. J. Surg. 46 (2017) 198–202, http://dx.doi.org/10.1016/j.ijsu.2017.08.586.

[11] Z.M. Alawadi, I. Leal, U.R. Phatak, et al., Facilitators and barriers of implementing enhanced recovery in colorectal surgery at a safety net hospital: a provider and patient perspective, Surgery 159 (2016) 700–712, http://dx.doi.org/10.1016/j.surg.2015.08.025.

[12] L. Gianotti, S. Beretta, M. Luperto, et al., Enhanced recovery strategies in colorectal surgery: is the compliance with the whole program required to achieve the target? Int. J. Colorectal Dis. 29 (2014) 329–341, http://dx.doi.org/10.1007/s00384-013-1802-x.

[13] N. Pecorelli, O. Hershorn, G. Baldini, et al., Impact of adherence to care pathway interventions on recovery following bowel resection within an established enhanced recovery program, Surg. Endosc. 31 (2017) 1760–1771, http://dx.doi.org/10.1007/s00464-016-5169-2.

[14] The impact of enhanced recovery protocol compliance on elective colorectal cancer resection: results from an international registry, Ann. Surg. 261 (2015) 1153–1159, http://dx.doi.org/10.1097/sla.0000000000001029.

[15] G. Nelson, L.N. Kiyang, E.T. Crumley, et al., Implementation of enhanced recovery after surgery (ERAS) across a provincial healthcare system: the ERAS Alberta colorectal surgery experience, World J. Surg. 40 (2016) 1092–1103, http://dx.doi.org/10.1007/s00268-016-3472-7.

[16] J.F. Fiore Jr., I.G. Faragher, A. Bialocerkowski, et al., Time to readiness for discharge is a valid and reliable measure of short-term recovery after colorectal surgery, World J. Surg. 37 (2013) 2927–2934, http://dx.doi.org/10.1007/s00268-013-2208-1.

[17] M. Hubner, V. Addor, J. Slieker, et al., The impact of an enhanced recovery pathway on nursing workload: a retrospective cohort study, Int. J. Surg. 24 (2015) 45–50, http://dx.doi.org/10.1016/j.ijsu.2015.10.025.

[18] M.S. Vlug, J. Wind, M.W. Hollmann, et al., Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study), Ann. Surg. 254 (2011) 868–875, http://dx.doi.org/10.1097/SLA.0b013e31821fd1ce.