Journal of Gastrointestinal Surgery (2019) 23:587–594
https://doi.org/10.1007/s11605-018-3943-2

ORIGINAL ARTICLE

Enhanced Recovery Program for Colorectal Surgery: a Focus on Elderly Patients Over 75 Years Old

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Received: 9 February 2018 / Accepted: 20 August 2018 / Published online: 5 September 2018

Abstract

Background An enhanced recovery after surgery (ERAS) protocol can effectively improve perioperative outcomes in surgical patients by reducing complication rates and hospital stay. However, its application in elderly patients has yielded contradictory results. The aim of this study was to evaluate surgical outcomes in a cohort of elderly patients undergoing colorectal resection in our unit before and after the introduction of ERAS.

Methods From 328 patients undergoing colorectal surgery in our unit over a 2-year period (2015–2016), 114 patients ≥ 75 years of age were selected. The patients were categorized according to perioperative treatment as pre-ERAS and ERAS patients (respectively, 53 vs 61 patients), and the groups were compared for statistical purposes. Outcome measures included length of hospital stay, recovery of bowel functions, oral feeding, postoperative complications, and readmissions. Compliance with the ERAS protocol was also measured.

Results Groups were homogeneous for all the clinical-surgical variables, with the sole exception of the Charlson index, which was more severe in the ERAS group ($p = 0.012$). Compared with control patients, ERAS patients reported improved functional recovery (time to first flatus, stool, and oral feeding; $p < 0.001$). Hospital stay was reduced in ERAS patients overall and by side of resection, excluding rectal procedures. No differences were observed regarding postoperative complications. Of note, an optimal adherence to the protocol was reported, with 79% of items respected.

Conclusions ERAS can be considered safe in elderly patients undergoing colorectal surgery with a high comorbidity index, providing a reduction in hospital stay and improving short-term postoperative outcomes. Finally, the protocol application was feasible, with a high adherence to the items in this subset of patients.

Keywords Enhanced recovery after surgery · ERAS · Colorectal surgery · Elderly patients · Outcomes

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Introduction

Initially proposed by Professor Henrik Khelet in Denmark, enhanced recovery after surgery (ERAS) is a multidisciplinary program of care delivered to patients in order to obtain a rapid recovery after surgical interventions.[1,2]

To date, a number of studies have widely documented that fast-track rehabilitation could improve perioperative management by reducing stress and postoperative complications, shortening the length of hospital stay, and reducing health-related costs.[3–6]

Current fast-track protocols combine multidisciplinary perioperative care strategies, including no pre-operative mechanical bowel preparation, a minimal number of invasive tests, short-acting anesthetics, adequate perioperative fluid management, postoperative analgesia, early oral feeding, early

removal of urinary catheters, and immediate postoperative deambulation. Accordingly, the application of an ERAS program requires a dedicated multidisciplinary team composed of surgeons, anesthesiologists, nurses, physiotherapists, dieticians, and stoma therapists.[3–6]

With respect to colorectal surgery, ERAS has been recognized as the gold standard of care to manage patients, improving short-term postoperative outcomes, reducing morbidity, and decreasing complication rates.[7,8]

Despite these benefits, the application of ERAS in elderly populations have produced contradictory results: indeed, a number of studies have documented that elderly patients have a low adherence to the protocol, in particular, failing to achieve early feeding, early catheter removal and early mobilization, and requiring, as a consequence, a longer hospital stay.[8–10] Moreover, a few concerns have been raised regarding the feasibility of the ERAS approach in this subgroup, in relation to their comorbidities and poorer nutritional status.[9]

Indeed, the unique assistance that elderly patients require is a matter of concern for health care providers due to the decreased physiological reserve and increased perioperative risks in such patients. In addition, more than 70.0% of colorectal cancers are currently primarily diagnosed among patients over 65 years of age,[11] and the rate of elderly patients in surgical departments is increasing accordingly.

Finally, despite some recent studies reporting fewer laparoscopic procedures in patients over the age of 79 years[10] as well as the lower tolerance for refeeding/early mobilization and lower compliance with postoperative instructions exhibited by elderly patients,[9–12] current ERAS guidelines do not differentiate the perioperative approaches in this subgroup.[8]

On the basis of this background, the aim of this study was to analyze the safety, feasibility, and efficacy of an enhanced recovery program after colorectal surgery in patients over 75 years of age.

Materials and Methods

Study Design and Population This study was reported according to the STROBE guidelines for retrospective studies.[13]

A retrospective review of prospectively collected data was performed, and the study population included all consecutive patients who underwent colorectal surgery between January 2015 and December 2016 at the General Surgery 1 Unit, Fondazione Policlinico Universitario "Agostino Gemelli" in Rome. Inclusion criteria for this study were as follows: age of 75 years or more, treated with elective laparoscopic/open colorectal surgery for benign or malignant disease. Patients assessed as ASA IV and patients who underwent emergency resections were excluded. Of note, our institution has been certified as a high-volume center for colorectal surgery by the Italian National Health Authorities[14] and meets all the requirements for quality cancer care according to ECCO standards, including weekly multidisciplinary decision team (MDT) meetings for colorectal cancer patients and a dedicated team of colorectal surgeons.[15]

We collected and reviewed patient demographics (age, sex), clinical data (BMI, ASA score, Charlson index score, Charlson age-comorbidity index (CACI)), surgical records (operative procedure, operative time), pathologic data, and postoperative outcomes. All records were included in a database for statistical purposes and analysis.

Patients were categorized according to the perioperative treatment protocol received. Patients treated from January to December 2015 received standard perioperative care; subsequently, all consecutive patients admitted from January to December 2016 were managed according to an ERAS protocol. All patients were admitted between 12 and 24 h before the surgical procedure (Institutional Review Board (IRB) approval code for the ERAS study: 1808).

Pre-ERAS Protocol The pre-ERAS protocol included mechanical bowel preparation for left colectomy and rectal resection, perioperative fasting (beginning 8 h before surgery), routine use of drainages and a nasogastric tube, a noncoded anesthesiology protocol, removal of drainage after stool canalization, and oral feeding starting with the first passage of gas or stool.

Discharge criteria included tolerance for a normal diet without nausea or vomiting, adequately controlled pain, return of flatus or stool passage, no evidence of surgical complications, absence of both fever and tachycardia, ability to perform activities of daily living (ADLs), and willingness to be discharged. Information regarding adherence to the protocol with the pre-operative, intraoperative, and postoperative phase was collected.

ERAS Protocol The ERAS protocol was introduced at our institution in January 2016, led by an MDT including surgeons, anesthesiologists, nurses, and dieticians with regular reviews of the protocol and audits of the results. Since then, all patients undergoing elective colorectal surgery have been managed according to this protocol.

The protocol includes a nutritional status evaluation involving Nutritional Risk Screening (NRS) 2002, anthropometric measures, bioelectrical impedance analysis (BIA), and nutritional counseling beginning 3 weeks before admission. A nutritional re-evaluation is performed at admission. Anthropometric measures and BIA are performed at discharge and 1 month afterwards.[16]

Patients are encouraged to follow a tailored dietary regimen with an overall caloric intake of 2200 kcal for men and 2000 kcal for women, as follows: 3 days before admission, the patients are encouraged to follow a normal caloric, low-residue dietary regimen. A carbohydrate supplement drink (powder maltodextrin-based drink) is added starting from

3 days before hospital admission up to 3 h before the surgical operation. An immune-modulating compound is added starting from 2 days before hospital admission up to 2 days before the surgical operation.[16]

For left and right colon resections, bowel preparation is achieved by two enemas. For anterior resections (ARs), bowel preparation is achieved with the addition of an oral compound.

Compression stockings and subcutaneous low-dose unfractionated heparin or subcutaneous low-molecular-weight heparin are used for thrombo-prophylaxis. Antibiotic prophylaxis, consisting of a second-generation cephalosporin and metronidazole, is administered 30–60 min prior to skin incision.

Intraoperative fluid restriction is achieved with the administration of a crystalloid and colloid solution at an infusion rate of 5 and 3 ml/kg/h, respectively.

Postoperative pain control is achieved by intraoperative placement of intravenous patient-controlled analgesia (IV PCA) with tramadol 300 mg/24 h after priming with morphine and the administration of 100 mg of ketoprofen by the end of the surgical procedure. Transversus abdominis plane (TAP) block is performed in a sterile setting under ultrasound guidance at the end of the surgical procedure.

The urinary catheter is removed on postoperative day (POD) 1 for right and left colon resections and on POD 2 for rectal resections. Nasogastric tubes are not routinely used, and an oro-gastric tube is used intraoperatively only if needed. Drains are placed according to the intraoperative setting and the patient's characteristics, i.e., for ultralow colorectal anastomoses or in patients at risk of bleeding, and are removed at the time of first flatus in the former case and on POD 1 in patients at risk of bleeding.

Intravenous infusions are suspended on POD 1 if possible. Per oral feeding is encouraged on POD 1 by using a liquid, low-residue diet with an overall caloric intake less than 1000 kcal and a 13% protein composition. On POD 2, the diet is administered in a semiliquid fashion, with a low residue and an overall caloric intake of 1450 kcal and a protein fraction of 14.0%. Starting from POD 3, until discharge, the diet is administered to reach a caloric intake of 1800 kcal (18.0% proteins).[16]

Mobilization is encouraged from POD 1 with patients walking at least 300 m and spending 6-h sitting.

Discharge criteria are the same as those applied during the pre-ERAS protocol.

Outcome Measures Postoperative outcomes included bowel recovery (time to first flatus and time to stool, measured in days), time to oral feeding (measured in days), perioperative complications (measured using the Clavien-Dindo classification),[17] postoperative hospital stay (measured in days, starting from POD1), 30-day mortality, late morbidity (defined by 90-day complications), and readmission rate.

Follow-Up The follow-up was conducted with clinical visits and physical examinations 1 month after discharge, followed by telephone interviews every 3 to 6 months thereafter.

Statistical Analysis Baseline characteristics and operative and postoperative variables were compared using a bivariate analysis. Categorical variables were analyzed using frequency and percentage, whereas continuous variables were analyzed using means and standard deviations (SDs). The chi-squared test was used for comparing categorical variables. The *t* test or Mann-Whitney test was used depending on the data distribution into the analyzed population. The tests were performed two-tailed, and a p value < 0.05 was considered statistically significant. Statistical analysis was conducted using SPSS 22.0 software for Windows (SPSS Inc., Chicago, IL) and MedCalc for Windows, version 10.2.0.0 (MedCalc Software, Mariakerke, Belgium). A post hoc analysis was performed for evaluating the power of the tests using G*Power software version 3.1.2.[18]

Results

Patients Of 328 patients undergoing colorectal surgery at our unit from January 2015 to December 2016, 114 patients met the inclusion criteria; 61 of them were included in the ERAS group, and 53 were included in the pre-ERAS group (Fig. 1). Table 1 lists the clinical and surgical features in the two groups. No statistically significant differences were documented between the two groups with respect to age, sex, and BMI. Regarding comorbidities, no differences were reported for ASA scores; patients in the ERAS protocol group had greater mean Charlson index values (5.05 vs 3.81; $p = 0.012$) and CACI scores (6.8 vs 6.2; $p = 0.080$) than the pre-ERAS patients.

Groups were homogeneous for operative procedures and techniques (side of resection and use of laparoscopy, $p =$ ns; Table 1).

Postoperative Outcomes Postoperative outcomes and early complications are documented in Table 2. Overall, we reported statistically significant differences in bowel recovery, with a significant improvement in the meantime to first flatus ($p < 0.001$) and time to stool ($p < 0.001$) in the ERAS group compared with those in the controls.

Subgroups analyses revealed that, although the time to first stool passage was comparable, the time to oral feeding was accelerated in the ERAS group also according to the side of resection in right colectomies, left colectomies, and rectal resections.

Indeed, the time to oral feeding was reduced by almost 2 days in ERAS patients ($p < 0.001$) for all types of surgical procedures.

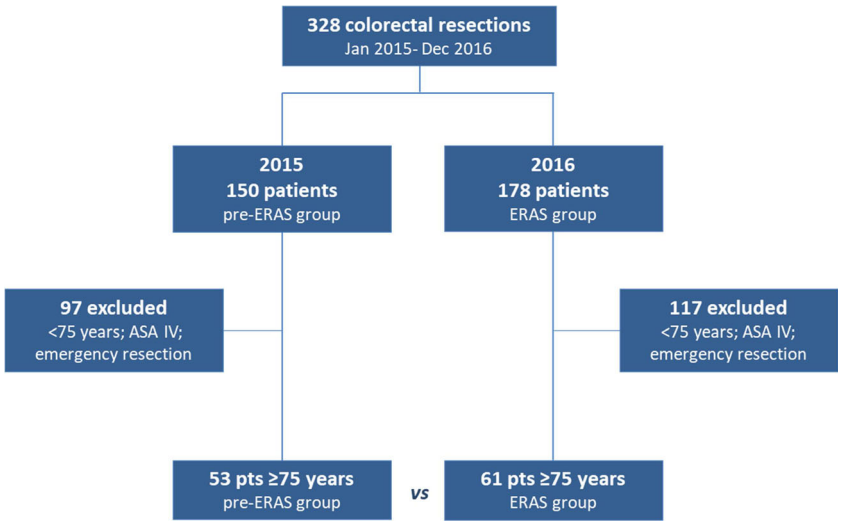

Fig. 1 Study flow chart and study design

The mean postoperative hospital stay was shorter in the ERAS group (overall, 5.40 ± 2.68 vs 6.26 ± 2.45; $p < 0.001$) and by side of resection, with the sole exception of rectal procedures.

Table 1 Clinical and surgical features of study population

	Pre-ERAS group ($n = 53$ patients)	ERAS group ($n = 61$ patients)	p value
Sex			
M/F	29.0/24.0	26.0/35.0	0.840[a]
Age, years			
Mean ± SD (range)	80.0 ± 3.7 (75–90)	80.2 ± 3.8 (75–91)	0.879[d]
BMI			
Mean ± SD (range)	25.8 ± 4.2 (18.3–34.6)	26.0 ± 4.0 (17.3–37.7)	0.975[d]
ASA, *n* (%)			
ASA1	1.0 (1.9%)	1.0 (1.6%)	
ASA2	43.0 (81.1%)	39.0 (64.0%)	0.108[b]
ASA3	9.0 (17%)	21.0 (34.4%)	
Charlson index			
Mean ± SD (range)	3.8 ± 2.0 (1.0–12.0)	5.0 ± 2.5 (1.0–13.0)	0.012[d]
CACI score			
Mean ± SD (range)	6.2 ± 1.5 (5.0–11.0)	6.8 ± 1.7 (5.0–13.0)	0.080[d]
Diagnosis, *n* (%)			
Malignant disease	51.0 (96.2%)	58.0 (95.1%)	
Benign disease	2.0 (3.8%)	3.0 (4.9%)	0.872[a]
Surgical procedure, *n* (%)			
Right hemicolectomy	19.0 (35.8%)	28.0 (45.9%)	
Left hemicolectomy	10.0 (18.9%)	13.0 (21.3%)	0.573[c]
AR/Hartmann/Miles	21.0 (39.6%)	18.0 (29.5%)	
Others	3.0 (5.7%)	2.0 (0.3%)	
Surgical technique, *n* (%)			
Mini-invasive surgery	42.0 (79.2%)	54.0 (90.2%)	
Open surgery	11.0 (20.7%)	7.0 (9.8%)	0.175[b]

AR anterior resection

[a] Chi-squared test. Total sample size 114 patients; effect size *w* 0.31, alpha error 0.05, power (1-beta) 0.91

[b] Chi-squared test. Total sample size 114 patients; effect size *w* 0.31, alpha error 0.05, power (1-beta) 0.85

[c] Chi-squared test. Total sample size 114 patients; effect size *w* 0.31, alpha error 0.05, power (1-beta) 0.80

[d] *t* test. effect size *d* 0.51, alpha error 0.05, power (1-beta) 0.81

Table 2 Postoperative outcomes in elderly patients

	Pre-ERAS group ($n = 53$ patients)	ERAS group ($n = 61$ patients)	p value
Time to first flatus, days			
Overall, mean ± SD (range)	2.6 ± 0.9 (1.0–5.0)	2.1 ± 0.9 (1.0–5.0)	< 0.001[a]
Time to stool, days			
Overall, mean ± SD (range)	3.4 ± 1.1 (1.0–6.0)	2.7 ± 1.2 (1.0–6.0)	< 0.001[a]
Right hemicolectomy, mean ± SD	3.8 ± 0.8	3.15 ± 1.1	0.124[a]
Left hemicolectomy, mean ± SD	2.8 ± 1.1	2.6 ± 1.1	0.797[a]
AR/Hartmann/Miles, mean ± SD	3.3 ± 1.3	2.1 ± 1.3	0.825[a]
Time to oral feeding, days			
Overall, mean ± SD (range)	4.0 ± 2.1 (2.0–13.0)	2.3 ± 1.2 (2.0–9.0)	< 0.001[a]
Right hemicolectomy, mean ± SD	4.0 ± 1.8	1.1 ± 0.3	*0.025*[a]
Left hemicolectomy, mean ± SD	3.5 ± 0.7	1.0 ± 0.0	< 0.001[a]
AR/Hartmann/Miles	4.5 ± 2.8	1.1 ± 0.2	< 0.001[a]
Complications, *n* (%)			
Clavien-Dindo grade I-II	16.0 (30.2%)	17.0 (27.9%)	
Clavien-Dindo grade III-IV	4.0 (7.5%)	2.0 (3.3%)	0.707[b]
Complications (Clavien-Dindo I-IV), *n* (%)			
Right hemicolectomy	6 (11.3%)	8 (13.1%)	0.825[b]
Left hemicolectomy	2 (3.8%)	4 (6.6%)	0.560[b]
AR/Hartmann/Miles	11 (20.8%)	7 (11.5%)	0.399[b]
Postoperative hospital stay			
Overall, mean ± SD (range)	6.3 ± 2.4 (4.0–15.0)	5.4 ± 2.7 (3.0–17.0)	< 0.001[a]
Right hemicolectomy, mean ± SD (range)	6.3 ± 2.5 (4.0–14.0)	5.0 ± 2.1 (4.0–14.0)	0.001[a]
Left hemicolectomy, mean ± SD (range)	5.5 ± 0.9 (5.0–8.0)	4.6 ± 1.3 (3.0–8.0)	0.026[a]
AR/Hartmann/Miles, mean ± SD (range)	6.8 ± 2.9 (4.0–15.0)	6.5 ± 3.7 (3.0–17.0)	0.282[a]
30-day mortality, *n* (%)			
	1.0 (1.9%)	1.0 (1.6%)	0.538[b]
90-day complications, *n* (%)			
	4.0 (7.5%)	1.0 (1.6%)	0.565[b]
Readmission rate, *n* (%)			
	2.0 (3.7%)	3.0 (4.9%)	0.872[b]

AR anterior resection

[a] *t* test. effect size *d* 0.51, alpha error 0.05, power (1-beta) 0.81

[b] Chi-squared test. Total sample size 114 patients; effect size *w* 0.31, alpha error 0.05, power (1-beta) 0.91

The incidence of postoperative complications was similar in the two groups, and the prevalence of severe adverse events was low, independently of the type of perioperative care employed.

In line with this finding, the groups were also comparable with respect to late morbidity and readmission rates. All analyses were documented with an optimal power (1-β > 0.80).

Compliance With the ERAS Protocol Protocol adherence is reported in Table 3. A median number of 15 out of 18 ERAS items (78.9%) (range, 12–16) was fulfilled in the cohort of elderly patients. Significant compliance with the preoperative instructions was also achieved for the vast majority of intraoperative and postoperative items.

Discussion

Currently, there is no generally accepted definition of the term "elderly" in the scientific literature, and the World Health Organization (WHO) along with the Colorectal Cancer Collaborative Group defines an elderly individual as anyone aged 65 years or older.[19]

Of note, the number of elderly patients, especially in developed countries, is steadily increasing, with an estimation that they will constitute 20% of the population in future years.[20]

Recent studies have documented the prevalence of elderly patients among individuals undergoing abdominal surgery.[21]

Table 3 Adherence to ERAS protocol in elderly patients

Pre-operative ERAS items, *n* (%)	
Pre-admission counseling	55.0 (90.2%)
Fluid and carbohydrate loading	61.0 (100.0%)
No prolonged fasting	61.0 (100.0%)
Antibiotic prophylaxis	61.0 (100.0%)
No pre-medication	61.0 (100.0%)
No/selective bowel preparation	47.0 (77.0%)
Thromboprophylaxis	61.0 (100.0%)
Intra-operative ERAS items, *n* (%)	
No nasogastric tube	59.0 (96.7%)
Prevention of nausea and vomiting	59.0 (96.7%)
Avoidance of salt and water overload	61.0 (100.0%)
Maintenance of normothermia	61.0 (100.0%)
Standard anesthetic protocol	44.0 (72.1%)
No drains	3.0 (4.9%)
Laparoscopic surgery	48.0 (89.0%)
Postoperative ERAS items, *n* (%)	
Early mobilization	61.0 (100.0%)
Early removal of bladder catheter	57.0 (93.4%)
Early oral nutrition	61.0 (100.0%)
Stimulation of gut motility	0.0 (0.0%)

Advanced age has traditionally been associated with increased postoperative morbidity and mortality following colorectal surgery due to a lack of organ function or reserve—as measured by the ASA class and Charlson index,[22,23] and elderly patients usually exhibit a longer recovery with increasing hospital and social costs. To the same extent, recent literature has focused on patients with frailty syndrome, particularly with respect to postoperative outcomes.[22]

Patients presenting frailty syndrome have worse CACI scores[23]; according to recent literature, a CACI greater than 5.8 is consistent with intermediate frailty, whereas values greater than 6.7 indicate severe frailty profiles.[24]

According to our results, patients treated through the ERAS protocol at our institution presented worse Charlson index values and a trend toward more severe CACI scores (mean 6.2), being at greater risk for frailty and complications. In this manuscript, we also document that elderly patients could be safely treated with the ERAS protocol. Indeed, although exhibiting higher mean Charlson and CACI index values than the pre-ERAS period, the patients displayed improvements in postoperative functional recovery and hospital stay.

The reduction in surgical stress by the application of an ERAS protocol might be highly effective in elderly individuals who could benefit more from a less invasive perioperative care pathway.[25–30]

Despite the documented benefit of the ERAS program, its implementation and adherence to the protocol remain a challenge.

Different studies have shown that a greater compliance to the protocol is associated with a shorter length of hospital stay,[31–34] fewer complications,[33] a lower 30-day morbidity, and fewer readmissions.[31]

A systematic review conducted by Bagnall et al.[35] evaluated the ERAS program in elderly patients undergoing colorectal surgery; although the program was reported as safe, among 16 manuscripts analyzed, only two were randomized trials, and only five were rated as good quality papers. Moreover, the ERAS protocols were not homogeneous among these studies. Furthermore, important outcomes such as readmission or reoperation rates were seldom analyzed.[36,37]

Few studies have reported data on adherence to ERAS components,[9,11,12] and overall compliance to the protocol decreases with increased patient age. Particularly, elderly patients have a lower tolerance for the postoperative early liquid or solid diet, are less likely to have their catheters removed early, and do not achieve the same level of mobilization during the postoperative period as younger patients do[9–12]; however, abdominal drains are commonly used in patients over 75 years of age,[10,38] probably because of a greater risk of bleeding associated with cardiovascular disease. Nevertheless, in our series, a high adherence to the protocol (over the 70%) was registered for most of the pre-operative, intraoperative, and postoperative items. Baek did not report any significant differences in postoperative outcomes between younger and older groups of patients[39] after the introduction of ERAS.

In keeping with our findings, a recent study reported that elderly patients do not require a specifically tailored ERAS protocol. The authors also documented that a laparoscopic approach is associated with increased adherence to ERAS and improved short-term postoperative outcomes.[38]

In our series, postoperative care was fully achieved in the elderly group, including the early resumption of liquid and oral feeding and early mobilization. Postoperative stay was shorter in the ERAS group, excluding patients undergoing rectal resections. The reasons why the ERAS protocol did not reduce the length of hospitalization is probably due to the peculiar features characterizing this procedure and its perioperative management. In particular, a stoma was necessary for most patients, pre-operative mechanical bowel preparation could lead to patient dehydration, and the subgroup of rectal resections also included Miles' procedures.

This series had some limitations: first, it was a single-center retrospective series with a relatively small sample size. Second, the patients were homogeneous for the vast majority of clinical and surgical features, and the retrospective period was limited to 2 years. Third, the selection of 75 years of age as a cutoff for elderly patients is arbitrary. Furthermore, our center is a referral institution for colorectal surgery, and the rate of mini-invasive procedures is high (greater than 75%).

Conclusion

Our study has shown that enhanced recovery after colorectal surgery is feasible and safe in elderly patients undergoing colorectal surgery, providing a benefit in terms of hospital stay and functional recovery.

The results of this study emphasize that elderly patient "per se" should not be acknowledged as a high-risk patient and that probably severe comorbidities and other surgical risk factors are more indicative of a frailty condition.

Future implementations of ERAS program for colorectal patients should be toward the development of a tailored protocol based on differences between colon and rectal surgery and on patient comorbidities rather than specifically on age.

Authors' Contributions 1. Conception and design: all authors.
2. Provision of study materials or patients: Maria Carmen Lirosi, Cristina Larotonda, and Flavio Tirelli.
3. Collection and assembly of data: Maria Carmen Lirosi, Cristina Larotonda, Flavio Tirelli, and Laura Lorenzon.
4. Data analysis and interpretation: Maria Carmen Lirosi, Cristina Larotonda, Flavio Tirelli, and Laura Lorenzon.
5. Manuscript writing: Maria Carmen Lirosi, Cristina Larotonda, Flavio Tirelli, Laura Lorenzon, and Alberto Biondi.
6. Final approval of the manuscript: all authors.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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