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ORIGINAL ARTICLE

Short-term outcomes and benefits of ERAS program in elderly patients undergoing colorectal surgery: a case-matched study compared to conventional care

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Abstract

Purpose The aim of the study was to evaluate the benefits of implementing Enhanced Recovery After Surgery (ERAS) protocols in elderly patients undergoing elective colorectal surgery.

Methods A retrospective non-randomized cohort study was conducted from September 2012 to December 2016. We included patients ≥ 70 years undergoing elective colorectal surgery. Outcome measures, compliance with interventions, and postoperative complications of patients treated under ERAS were case-matched (based on gender, age, type of surgery, and the presence/absence of a temporal stoma) to a retrospective group of patients ≥ 70 years treated under conventional care.

Results A total of 312 patients (156 ERAS vs. 156 non-ERAS) were included in the study. The ERAS group had a significant reduction of grade III/IV Dindo-Clavien's postoperative complications when compared with conventional care. ERAS had a positive effect in reducing anastomotic leakage (14.7% non-ERAS vs. 9%) and postoperative mortality (11.5% non-ERAS vs. 1.9% ERAS; $p = 0.001$). A reduction of 2 days in length of hospital stay was achieved after implementing ERAS (8 (6.75) vs. 6 (5.25); $p < 0.0001$), while readmission rates remained unaffected. The average of global compliance (GC) with all ERAS interventions was 42%. GC was significantly lower in patients with permanent/temporary stomas and in patients in whom an open approach was performed.

Conclusion In our experience, ERAS should be implemented without reservations in elderly patients expecting the same goals and benefits as with other age groups. Barriers in achieving a high compliance rate are common and will require a great effort in patient's education, an intensive perioperative care, and sometimes a change in the surgeons' practice.

Keywords ERAS · Elderly · Colorectal cancer surgery · Multimodal · Enhanced recovery after surgery

Introduction

Enhanced Recovery After Surgery (ERAS) programs are an assortment of evidence-based perioperative interventions that have been widely implemented within the surgical community with the aim of promoting a better postoperative recovery [1]. Focused on colorectal surgery, evidence-based studies and clinical trials have demonstrated over the last decade that ERAS compared to the traditional postoperative way of care reduces medical and surgical complications with a significant reduction in the length of hospital stay [2–5].

The ERAS programs should ideally be targeted to those patients to whom the expected benefit may be greater. For instance, elderly patients undergoing surgery for colorectal cancer should be a target population since over 50% of cases in our daily practice are above 70 years old. Some studies have demonstrated the feasibility of ERAS in elderly populations; however, they have described significant barriers in implementing ERAS interventions, and so, the real effect in this particular population has not yet been described [6, 7]. This is due to the fact that compliance within all interventions may be difficult to achieve with each patient, which may worsen end results. Our group previously published a

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prospective multicenter study showing the feasibility on ERAS in elderly patients undergoing elective colorectal surgery. Patients were treated under the same protocol and compliance with ERAS was 56%; however, the exact impact on this particular population could not be measured as there was a lack of comparison to a retrospective group of elderly patients treated under non-ERAS care [8].

The aim of this study is to evaluate the impact of ERAS in elderly patients after colorectal surgery compared to a retrospective case-control matched group of patients treated under the conventional way of care.

Methods

A retrospective review was performed over a prospectively maintained database selecting patients ≥ 70 years old who underwent elective surgery for colorectal cancer at a tertiary center (Fundacion Jimenez Diaz University Hospital, Madrid, Spain) between September 2012 and December 2016. We divided patients into two groups based on the "intention to treat" protocol applied after surgery. The first group, named ERAS group, included all patients treated under ERAS programs (2015–2016). This group was case-matched to a retrospective non-ERAS group in which patients were treated under traditional postoperative protocols (2012–2014). A case control 1:1 design was applied based on gender, age (stratified by the following: between 70 to 75, 75 to 80, 80 to 85, and over 85 years old), type of surgery (colon vs. rectum), and the presence/absence of a temporal stoma. The study was initiated after obtaining approval by the local institutional review board committee.

In the ERAS group, a group of 10 interventions were implemented in the study on the basis of our previously published protocols as shown in Table 1 [8]. By definition, we targeted in the ERAS group the discharge day at the 4th or 5th postoperative day (POD) for colon or rectal surgery, respectively. Compliance with interventions were combined and expressed as the percentage of patients who had a correct intervention documented in the medical history. We defined global compliance (GC) as the rate of patients for whom compliance was achieved with all postoperative interventions of ERAS protocol. Additional data included for analysis was related to patient's preoperative characteristics (age, gender, previous comorbidities, preoperative anemia and nutritional status, and neoadjuvant therapies) and surgery records (type of intervention and stoma creation). Short-term postoperative complications were graded in minor vs. major categories by using the Clavien-Dindo classification [9]. The length of hospital stay (LOS) and rates and causes of readmissions during the first 30-day postoperative period were also documented.

Statistical analysis

Descriptive statistics were calculated with mean and standard deviation (SD) or median and interquartile range (IQR) for quantitative variables. Comparison of differences between group means was carried out using ANOVA for variables with normal distribution and the Mann-Whitney *U* test for quantitative variables with non-parametric distribution. We used chi-squared analysis with Fisher's exact test when any value observed in the contingency table was less than 5 to compare proportion variables. A Kruskal-Wallis test was performed to explore the impact of compliance within interventions on the

Table 1 Enhanced recovery program

Preoperative period	Information of the complete process
	Nutritional optimization, anemia, and comorbidities
	Pre-assessment visit with the nurse in case stoma is necessary
	Bowel mechanical preparation (rectum surgery)
	Supplemental nutritional drinks throughout the day before
Intraoperative period	Thrombo-embolic deterrent stockings
	Antibiotic prophylaxis
	Epidural sited (if open surgery)
	Urinary catheter sited
	No nasogastric drainage
	Minimal perioperative IV fluid
	Normothermia
Postoperative period	IV fluids discontinued if patient drinking adequately
	Thrombo-embolic prophylaxis
	Enforced mobilization
	Urinary catheter removed
	Early intake
	Respiratory physiotherapy

length of stay. Odds ratios (OR) were computed for dichotomous and continuous risk factors between groups and logistic regression was performed, selecting those variables that showed a $p < 0.25$ in the univariate analysis. Sample size calculations estimated that 142 patients would be required in each group to detect statistical results, assuming an expected difference of 10% in major complications between groups ($\alpha = 0.05$, $\beta = 0.20$).

All statistical analyses were conducted using SPSS® version 22 software (SPSS, Inc., Chicago, IL) and p values of < 0.05 were considered statistically significant.

Results

A total of 312 patients over 70 years old who underwent surgery for colorectal cancer were included in the study: 156 patients in the ERAS group vs. 156 in the non-ERAS group. Of them, 184 (59%) were men while 128 (41%) were women, with a mean age for the whole group of 78.9 ± 5 years of age. Demographics, patient's baseline characteristics, and surgical procedures are presented in Table 2. Right hemicolectomies (43 vs. 44%) were the most common surgery done, followed by sigmoidectomies and low anterior resections (19% each), left hemicolectomies (12 vs. 18%), Hartmann procedures (4 vs. 8%), abdominoperineal resections (3 vs. 5%), and 3 subtotal colectomies (1.6%). Laparoscopic surgery was performed in 59% of patients in ERAS groups, vs. 21% in non-ERAS groups ($p < 0.000$). There were no differences between groups in the pre-surgery hemoglobin values (ERAS 12.6 ± 1.7 g/dL vs. 12.2 ± 1.8 g/dL non-ERAS). The preoperative nutritional status, based on mean albumin values, was significantly better for patients under ERAS treatment when compared to the non-ERAS group (4 ± 0.3 g/dL vs. 3.8 ± 0.5 g/dL, $p = 0.002$) respectively.

A significant reduction in major postoperative complications was observed in the ERAS group when compared to the traditional non-ERAS group (21.8 vs. 10.3%; $p = 0.02$). Anastomotic leakage showed a clinically relevant reduction when patients were treated under ERAS vs. non-ERAS (9 vs. 14.7%). Mortality rate has also decreased from 11.5 to 1.9% in ERAS group ($p = 0.001$). Both groups have similar percentage of postoperative ileus (21.8% ERAS group vs. 24.4% non-ERAS group). A more detailed analysis of postoperative complications is shown in Table 3.

In Table 4, we presented the results of the univariate and the multivariate analysis about the variables of the study that may have had an influence on Dindo-Clavien complications. In the results of the multivariate analysis, the ERAS protocol remained as the only variable that demonstrated to be an independent, protective factor in decreasing complications (OR 0.4, 95%CI 0.19, 0.83, $p = 0.015$).

Data was measured independently for each intervention in the ERAS group as is presented in Table 5. By definition, we avoided mechanical preparation in colonic surgeries and all patients received preoperative dietary recommendations and a carbohydrate-rich drink at 2–4 h before surgery. A central line was placed in 26% of patients, as multimodal analgesia was employed via epidural catheter for 32% of cases. Early intake of clear liquids at 6 h after surgery and early mobilization were the most successfully carried out interventions in over 90% of patients. On the other hand, stopping intravenous fluids and early removal of urinary catheter rates presented lower adherence with 62 and 67%, respectively.

Table 2 Patient baseline characteristics and surgical techniques

Variable	ERAS ($n = 156$)	NO ERAS ($n = 156$)	p value
Age (mean ± SD) (years)	78.7 ± 5	79 ± 5	NS
Sex (F:M)	64:36	54:46	NS
Preop albumin level (g/dL)	4 ± 0.3	3.9 ± 0.5	NS
Preop hemoglobin level (g/dL)	12.6 ± 1.7	12.2 ± 1.8	NS
Surgical technique			
Right hemicolectomy	67 (43%)	69 (44%)	NS
Sigmoidectomy	33 (22%)	20 (13%)	
Anterior resection	29 (19%)	30 (19%)	
Left hemicolectomy	12 (8%)	18 (12%)	
Hartmann	6 (4%)	12 (8%)	
Miles	8 (5%)	5 (3%)	
Subtotal colectomy	1 (0.6%)	2 (1%)	
Neoadjuvant therapy	23 (15%)	20 (13%)	NS
Laparoscopic surgery	92 (59%)	33 (21%)	$p < 0.0001$
Stoma	33 (21%)	39 (25%)	NS
Drainage	114 (73%)	114 (73%)	NS

NS non-significant results

Table 3 Postoperative outcomes

Postoperative complications	ERAS group ($n = 156$)		Non-ERAS group ($n = 156$)		p value
	Colon ($n = 113$)	Rectum ($n = 43$)	Colon ($n = 109$)	Rectum ($n = 47$)	
No complications	67 (59%)	27 (63%)	61 (56%)	18 (38%)	
Clavien-Dindo					
Grades I–II	35 (31%)	11 (26%)	23 (21%)	20 (43%)	$p = 0.02$
Grades III–V	11 (10%)	5 (12%)	25 (23%)	9 (19%)	
Postoperative ileus	26 (23%)	12 (28%)	21 (19%)	13 (28%)	NS
Anastomotic leakage*	9 (8%)	5/29 (17%)	15 (14%)	8/30 (27%)	NS
Reoperations	11 (10%)	5 (12%)	12 (11%)	2 (4%)	NS
Mortality	3 (3%)	0%	14 (13%)	4 (9%)	$p = 0.001$
Hospital length of stay (days − IQR)	5 (4)	7 (6)	7 (5)	10 (6)	$p = 0.000$
Readmissions	6 (5%)	1 (2%)	6 (6%)	5 (11%)	NS
Hospital length of stay + readmissions (days − IQR)	5 (6)	7 (6)	8 (5)	11 (12)	$p = 0.000$

NS non-significant results

*Anastomotic leakage includes clinical and radiological leaks, excluding Hartmann and Miles procedures from the rectum surgery group

Overall, there was a GC rate of 42% of ERAS group patients for whom compliance was achieved with all postoperative measured interventions. Performing laparoscopic surgery achieved a higher GC percentage (46% laparoscopic surgery vs. 38% open surgery; $p > 0.05$). Patients who underwent rectal surgery had lower GC rates when compared to colon surgery (31 vs. 46%; $p > 0.05$). In addition, a creation of either a temporary or definitive stoma also decreased GC rates (45% without stoma vs. 33% with stoma; $p > 0.05$).

Patients with GC > 50% presented lower median of LOS (5 [2] days vs. 10 [9] days, $p = 0.000$) as shown in Fig. 1a. Total LOS, including readmission rate, was also reduced as the percentage of compliance with the elements of the protocol increases ($p = 0.000$) (Fig. 1b). Global compliance including the expected day of hospital discharge (4th POD for colonic surgery and 5th for rectal surgeries) was 38.9%. Readmissions in 30 days after surgery were similar in both groups. Total LOS (including readmissions days) was lower in ERAS group ($p < 0.05$) (Table 4).

Discussion

Our study showed a significant impact on decreasing major postoperative complications, anastomotic leakage, postoperative mortality, and LOS when ERAS was applied to a prospective cohort of patients > 70 years old who underwent colorectal cancer surgery, compared to a retrospective control group under non-ERAS care. Our data showed that 60% of patients in the ERAS group had no complications vs. 51% in the non-

Table 4 Results from the univariate and multivariate analysis on variables influencing postoperative complications

	Minor complications ($n = 89$)	Major complications ($n = 50$)	p value Univariate analysis	p value Multivariate analysis
Sex (M:F)	49:40 (55:45%)	30:20 (60:40%)	NS	–
Age (mean ± SD)	79.9 ± 5	79.7 ± 5.8	NS	–
Colon	57 (77%)	34 (74%)	NS	–
Rectum	17 (23%)	12 (26%)		
Laparoscopy surgery	30 (34%)	13 (26%)	$p = 0.35$*	NS
Open surgery	59 (66%)	37 (74%)		
Stoma	27 (30%)	10 (20%)	$p = 0.19$*	NS
Non-stoma	62 (70%)	40 (80%)		
ERAS	46 (52%)	16 (32%)	$p = 0.025$*	$p = 0.015$
Non-ERAS	43 (48%)	34 (68%)		
Albumin (mean ± SD)	3.9 ± 0.4	3.8 ± 0.4	NS	–
Hemoglobin (mean ± SD)	12.1 ± 1.7	12.1 ± 1.9	NS	–

NS non-significant results

*Variables included in the multivariate analysis

Table 5 Compliance rates with ERAS interventions

Variable	*n* (%)
Mechanical bowel preparation	151 (96.8%)
Early intake	141 (90.4%)
Early suspension of intravenous fluids	97 (62.2%)
Early mobilization	137 (87.8%)
Early urinary catheter removal	107 (68.6%)
Discharged ERAS	67 (42.9%)
Discharged ERAS+1	27 (17.3%)
Global compliance	66 (42.3%)

ERAS group. There were less minor grades I and II in the ERAS group vs. non-ERAS 30 vs. 28%, respectively, while major grades III and IV were significantly lower in the ERAS group (10%) vs. non-ERAS group (22%).

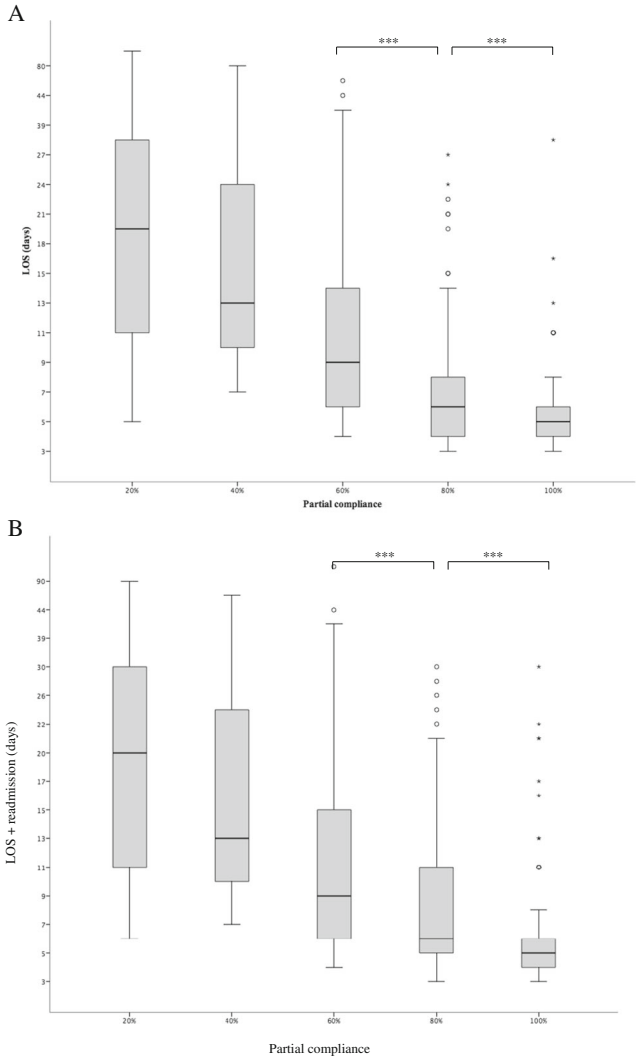

Fig. 1 Influence of compliance with ERAS measures in LOS (**a**) and LOS + readmission (**b**) (Kruskal-Wallis test). < 50% of < 50% of GC LOS: 10 [4-90] vs. >50% of GC LOS 5 [3-30]; p=0.000

In Table 6, we described the current studies that have been published in the literature about the feasibility and benefits of ERAS programs in colorectal surgery in elderly patients compared to younger patients; however, to date, only a few have focused on ERAS vs. non-ERAS exclusively in elderly patients, which we believe are more reliable [6, 10–22]. Of them, the most evidence-based experience comes from two randomized clinical trials published in 2011 by Jia et al. [19] and in 2014 by Wang et al. [14]. Both studies showed a decrease in LOS and a significant reduction in postoperative complications under ERAS protocols; however, some complications appeared to be underrated. For example, the incidence of anastomotic leakage following a colectomy in elderly patients is reported between 5 and 10% [23, 24] in the clinical practice, and both studies reported a near to zero incidence as shown in Table 6. In contrast, we reported a significant decrease in anastomotic leakage from 14.7 to 9% in non-ERAS vs. ERAS, respectively. We believe that there are several factors in the study contributing to these results in terms of reduction of anastomotic leakage. Since we introduced the ERAS program in our study, we implemented a prehabilitation protocol in which a nutritional preoperative evaluation (by Malnutrition Universal Screening Test) and a screening of anemia were given to every patient. Those patients where malnutrition or anemia < 10 g/dL was confirmed were sent to an intensive preoperative treatment program. As a result, preoperative albumin and hemoglobin values were higher in the ERAS group and this may explain the lower rate of anastomotic leakage.

Secondly, patients in the ERAS group were treated under individualized goal-directed fluid therapy with the aim to adjust the intraoperative volume. In addition, the goal of stopping intravenous fluids on the 1st POD was a major intervention in the ERAS protocol that was achieved in 62% of cases. Restriction and early suspension of IV fluids has been reported to reduce cardiopulmonary complications and seems beneficial for anastomotic healing [25]. Thirdly, the implementation of ERAS protocol provides for better patients' supervision, which leads to an early detection of leakage and the opportunity to establish an appropriate treatment. For example, patients in the ERAS group were under a standardized postoperative monitoring of early detection laboratory markers such as the C-reactive protein (CRP) analysis on the 2nd and 4th POD. When CRP levels and clinical signs were atypical, a CT scan was performed to detect postoperative complications. Finally, the increase of the percentage of laparoscopy procedures may have a positive influence on our results, as it is an essential part of the ERAS program. The exact impact of any intervention itself on decreasing postoperative complications has been explored in a multivariate analysis, showing that the ERAS protocol (taken into consideration as a block of interventions) was the only independent factor to reduce postoperative complications.

Table 6 ERAS program in elderly population. Literature review

Author, year	Groups	Number	Dindo-Clavien I–II (%)	Dindo-Clavien III–V (%)	Anastomotic leak (%)	Median LOS (IQR) or mean ± SD	Readmissions (%)	Death (%)
Hendry et al. 2009 [10]	ERAS ≥ 80	194	33	7 (5–11)	5.1	–	3.1	1.3
	ERAS < 80	839	27.3	6 (4–8)		–	1.3	3.1
Rumstad et al. 2009 [11]	ERAS ≥ 80	207	61.6	2.3	1.4	11 (1–53)	2.4	0.9
	ERAS 70–79	535	35.9	0.8	3.5	8 (2–83)	4.6	1.1
Naef et al. 2010 [12]	ERAS ≥ 70	176	57		3.5	–	–	3.4
	ERAS < 70	114	33			–	–	2.6
Walter et al. 2011 [13]	ERAS ≥ 80	68	38	7	4.3	7 (6–10)	4	4
	ERAS < 80	332	39	10		6 (5–10)	9	2
Wang et al. 2012 [14]	ERAS ≥ 65	40	5	–	0	5.5 (5–6)	–	5
	No-ERAS ≥ 65	38	21.1	–	0	7 (6–8)	–	2.6
Pawa et al. 2012 [6]	ERAS ≥ 80	130	26.2		2.3	8 (5–14)	6.2	16.2
	ERAS < 80	558	9.3		3	6 (3–8)	9.1	2.5
Verheijen et al. 2012 [15]	ERAS ≥ 80	81	–	10	5	10	5	–
	ERAS < 80	267	–	10		7	11	–
Feroci et al. 2013 [16]	ERAS ≥ 75	204	37.2		3.3	7 (3–43)		6.3
	ERAS < 75	402	21.4			5 (3–56)		1.2
Keller et al. 2013 [17]	ERAS ≥ 70	153	16.9		0.7	5 ± 4.9	4.6	0
	ERAS < 70	302	12.6		1	4.5 ± 5.7	5.6	0
Baek et al. 2013 [18]	ERAS ≥ 70	77	26		2.6	12 (7–31)	11.7	0
	ERAS < 70	226	31.9		8.4	12 (5–109)	4	0
Jia et al. 2014 [19]	ERAS ≥ 70	117	27.4	2.6	2.6	9 ± 2	–	–
	No-ERAS ≥ 70	116	58.6	2.6	1.7	13.2 ± 1	–	–
Kisialeuski et al. 2015 [20]	ERAS > 65	49	26.5	8.2	4.1	5.5 (2–18)	6.1	–
	ERAS ≤ 65	43	27.9	7	4.7	4.5 (2–13)	2.3	–
Forsmo et al. 2017 [21]	ERAS ≥ 80	19	42.1	10.5	10	7 (3–50)	21.1	5.3
	ERAS 66–79	56	25	16.1	10.9	5.5 (2–36)	25	3.6
	ERAS ≤ 65	79	31.6	8.9	6.6	5 (2–47)	15.2	0
Pirrera et al. 2017 [22]	ERAS ≥ 76	203	11.9	9.4	3.4	4.7 ± 5	4.9	1.5
	ERAS 66–75	175	12.2	8.5	4	4.7 ± 4	4.6	0.6
	ERAS ≤ 65	211	10.4	8.1	3.8	3.9 ± 3	4.7	0
Tejedor et al. 2017 (present study)	ERAS ≥ 70	156	29.5	10.3	9	6 (5.25)	4.5	1.9
	No-ERAS ≥ 70	156	27.6	21.8	14.7	8 (6.75)	7.1	11.5

As a combined impact of these commented measures, a positive outcome of ERAS was also observed in postoperative mortality showing a statistically significant reduction of 11.5 to 1.9% ($p = 0.001$).

One of the common critiques on implementing ERAS in elderly patients is that there is a lack of information about the adherence of compliance with the ERAS interventions, and so, the final impact of ERAS may be unreliable. Previous studies have reported worthy in compliance with preoperative and intraoperative ERAS interventions, but reduced adherences during the postoperative phase [1]. In our data, we defined the variable GC as the rate of patients for whom compliance was achieved with all the postoperative interventions. The GC in the ERAS group was 42%. We believe that this measure is a useful tool to detect implementation barriers as patients who underwent rectal surgery (31% rectal surgery vs. 46% colon surgery) or surgeries with a stoma creation (45% without stoma vs. 33% with stoma) had a lower GC rates. Therefore, these kinds of patients may require a special supervision from the care team with the aim to achieve better results. Of note, we observed that the higher percentage of laparoscopic surgery presented with better results in GC (46% laparoscopic surgery vs. 38% open surgery). GC had also significant effects on the LOS. As shown in the results, after a revision of the literature about ERAS in elderly patients undergoing colorectal surgery, there is a range of median LOS between 2 and 12 days. We reported a significant reduction in the median LOS of 6 (5.25) days in the ERAS group. The LOS in the ERAS group was significantly lower when compared to 8 (6.75) days in the non-ERAS group, and readmission rates to the hospital after discharge were the same independently of ERAS treatments. Taking into account the LOS and the readmission days, there was an economic impact in decreasing cost as patients under ERAS stayed a median of two less days in the hospital. Important to highlight, we observed a significant positive correlation of GC in decreasing LOS especially when a 50% or over of GC was achieved. We consider that, based on the study population of elderly patients, these LOS and readmission rates are considerably good to support the idea that ERAS is a feasible and secure option for this particular population.

Limitations

This study has some limitations that deserve to be mentioned. Firstly, our study is not a randomized controlled trial, although both groups are homogeneous and present with a large number of patients in each group. Secondly, we did not apply frailty risk stratification [26], instead of the age-range, in order to obtain a more objective classification as a predictor of outcomes. We feel that age is not as good of an indicator as frailty index, which has demonstrated to correlate better with complications, overall survival, and length of stay [27]. An evaluation of weakness in elderly patients is needed and has to be taken into account preoperatively; thus, a geriatric assessment before surgery will be introduced in our center.

Conclusions

Based on our results, ERAS is a feasible program and obtains better outcomes compared to the traditional way of care after colorectal surgery and should be implemented without reservations in elderly patients. We believe that efforts in further studies on ERAS and elderly patients should be directed to predict patients at risk of failure to adopt the program, to identify implementation barriers in this particular population, and to achieve a higher grade of adherence to these protocols.

In order to achieve a high compliance rate within this age group, major efforts will be required, associated with patient education and social factors. Goals and benefits expected in this population would be the same as found in other age groups.

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Compliance with ethical standards

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

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