Conditions Associated with Worse Acceptance of a Simplified Accelerated Recovery after Surgery Protocol in Laparoscopic Colorectal Surgery: A Randomized Controlled Trial.

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Abstract

Background: Accelerated Recovery after Surgery Programs were initially applied to colorectal surgery and used a multimodal care approach to relieve the response to surgical stress. An important factor that negatively impacts the success of these programs is the non-tolerance of patients to certain items in the adopted protocol, especially with regard to post-operative measures. The identification of these factors may help to increase the success rate of such programs, ensuring that benefits reach a greater number of patients and that resources are better allocated. Thus, the aims of this study were to assess the results of the implementation of a Simplified Accelerated Recovery Protocol (SARP) and to identify possible factors associated with failure to implement postoperative protocol measures in patients submitted to laparoscopic colorectal surgery.

Methods: 161 patients were randomly divided into two groups. The SARP group (n = 84) was submitted to the accelerated recovery program and the CC group (n = 77), to conventional postoperative care. The SARP group was further divided into two subgroups: patients who tolerated the protocol (n=51) and those who did not (n=33), in order to analyze factors contributing to protocol nontolerance.

Results: The groups had similar sociodemographic and clinical characteristics. The SARP group had a shorter hospital stay, better elimination of flatus, was able to walk and to tolerate a diet sooner ($p < 0.0001$). The rates of complications and of returns to the emergency room were similar between groups. In the multivariate analysis of the subgroups, we found that prolonged surgical time, stoma creation, and the development of complications were variables that placed program acceptance at risk ($p < 0.0001$).

Conclusions: The accelerated postoperative recovery program that was adopted, although simplified, was able to improve recovery from laparoscopic colorectal surgery and proved to be safe for patients. Extensive surgeries, occurrence of complications, and the need for ostomy were variables associated with program non-acceptance.

Trial registration: Trial Registry: RBR2b4fyr - Date of registration: 03 October 2017.

Background

Enhanced Recovery After Surgery™ (ERAS) programs aim to replace traditional perioperative practices, which have long been adopted and used, with interventions that have proven to be beneficial, based on solid scientific evidence. ERAS programs were initially applied to colorectal surgery and used a multimodal care approach to relieve the response to surgical stress, accelerating postoperative recovery and reducing costs for both public and private health systems.[1,2] However, in spite of their scientifically-proven advantages and of the widespread adoption of minimally-invasive techniques, one their main features, ERAS™ protocols are used in less than one-third of surgical procedures in the United States and the United Kingdom[2,3,4,5]. This is mainly due to operational difficulties, initial costs for implementation and also due to the complexity and number of interventions advocated by most of the described

protocols, which make it unfeasible for many institutions to adopt these measures in their daily practice.[6,7]

The use of simplified protocols, with a smaller number of interventions, could facilitate the adoption of such measures by a greater number of institutions, mainly in developing countries, where resources are scarce. Few studies in the literature have carried out a randomized analysis of the benefits of simplified protocols for accelerated recovery after surgery. Another important factor that negatively impacts the success of accelerated recovery programs after colorectal surgeries is the non-tolerance of patients to certain items in the adopted protocol, especially with regard to post-operative measures, which have a non-acceptance rate of up to 40%[8]. The identification of factors related to non-tolerance may help to increase the success rate of such programs, ensuring that benefits reach a greater number of patients and that resources are better allocated. Thus, the aims of this study were to assess the results of the implementation of a Simplified Accelerated Recovery Protocol (SARP) and to identify possible factors associated with failure to implement postoperative protocol measures in patients submitted to laparoscopic colorectal surgery.

Methods

This is a prospective randomized study that compared two groups of patients. One was submitted to simplified accelerated recovery protocol (SARP), focusing on postoperative measures (Table 1), while the other group underwent conventional postoperative care (CC) (Table 2). The choice was made to focus on postoperative measures, because these would allow for better control throughout the study; further, some preoperative measures associated with accelerated recovery programs had already been implemented in our service in recent years. Patients over 18 years of age were included, as per classifications I and II of the American Society of Anesthesiology (ASA). These patients underwent elective laparoscopic colorectal surgery with anastomosis, with or without protective ostomy. The study excluded patients with end-stage colorectal cancer, mental or psychiatric disorders, and those with contraindications to laparoscopic surgery. Also excluded were pregnant patients and those who had previously undergone esophageal, gastroduodenal, or pancreatic surgery, as well as those who refused to participate in the study. All participants signed a statement of Informed Consent.

Table 1. Simplified accelerated postoperative recovery program (SARP)

1. Removal of the nasogastric catheter prior to extubation
2. Restricted liquid diet approximately 8 h postoperatively, soft diet on the 1st POD, and free diet on the 2nd POD
3. Suspension of serum therapy on the 1st POD, with maintenance of the salinized venous catheter

4. Early mobilization, starting 6-8 h postoperatively, with assistance of the physiotherapy team
5. Food quantification performed by the nutrition team
6. Removal of the urinary catheter within 24 h postoperatively
7. Removal of abdominal drains within 48 h postoperatively

Table 2. Conventional postoperative care (CC)

1. Maintenance of the nasogastric catheter until effective peristalsis or reduction of flow
2. Restricted liquid diet initiated only after elimination of gas and/or presence of bruit
3. Daily gradual progression of oral diet
4. Removal of drains after 4 days, if there were no signs of complications
5. Removal of the urinary catheter within 48 h postoperatively
6. Maintenance of serum therapy until adequate acceptance of a soft diet
7. Mobilization, according to the patient's request

The patients underwent surgery at the Colorectal Surgery Department of Felício Rocho Hospital, a tertiary referral hospital in Belo Horizonte, Brazil, over a two-year period. Initially, 250 patients were considered eligible; 71 patients were excluded for not meeting the inclusion criteria, while three were excluded for refusing to participate in the study. Of the 176 participating patients who underwent colorectal resections by video-assisted laparoscopy, 13 (7.4%) and 2 (1.1%) patients were excluded due to conversion and data collection failures, respectively. The remaining 161 patients were included in the data analysis. The distribution of patients and of analyzed groups is presented in the CONSORT diagram[9] (Fig. 1).

Colon preparation was performed with oral sodium phosphate. A regular diet was maintained until eight hours before surgery and patients were encouraged to ingest clear liquids up to three hours before surgery. All patients received standardized anesthetic care and antimicrobial prophylaxis was administered in a single dose of ceftriaxone 2 g and metronidazole 1.5 g, thirty minutes before skin incision. Urinary and nasogastric catheters were placed at the start of surgery to monitor urine output and to achieve gastric decompression, respectively.

All procedures were started using video-assisted laparoscopy, with two 10 mm portals and three 5 mm portals. Creation of larger than necessary longitudinal or transverse incisions, to allow for the removal of

surgical specimens (> 8 cm) was considered to be a conversion.

Randomization of patients was performed at the end of surgery by a simple draw between groups (SARP or CC). Groups were compared to assess their similarities and to assess the implementation results for the simplified accelerated recovery protocol. Moreover, patients in the SARP group were divided into two subgroups, according to their tolerance or non-tolerance to SARP, in order to assess possible factors working against the adoption of the protocol. In this case, as was done in other studies, hospital discharge eligibility by the third postoperative day (POD) was considered a tolerance criterion to SARP[10,11,12]. Patients who were not discharged by the third POD, according to these criteria, were considered intolerant to the program. The established criteria for discharge were stable vital signs, an alert and oriented mental status, absence of symptoms and of suspected complications, unassisted walking, tolerance to a soft or solid diet, satisfactory elimination of flatus, spontaneous diuresis, good pain control with oral analgesics, self-sufficiency in basic daily activities, and the patient's expressed desire to go home.

In the SARP group, the "tolerant" subgroup (patients discharged by the third POD) and the "non-tolerant" subgroup (those discharged after the third POD) were compared to each other. The variables potentially involved in tolerance or non-tolerance to program items were presence of complications, need for ostomy, operative time, body mass index (BMI), age, sex, ASA classification 1 or 2, presence of comorbidities, malignant or benign disease, and type of surgery. Regarding the type of surgery, two groups were formed: patients who underwent surgery involving only the colon (colectomies) and those who underwent surgeries that involved the rectum, that is, proctectomies (total or partial excision of the mesorectum).

Upon discharge, oral and antispasmodic analgesics (hyoscine and dipyrone or paracetamol) were prescribed to the patients, and the use of enoxaparin at 40 mg/day for four weeks was recommended. Patients were guided on how to contact the team in case of intercurrent events, such as abdominal pain or distension, fever, an interruption in the elimination of flatus and feces, among others. All patients were instructed to return for postoperative consultation seven to ten days after discharge, or as needed.

Postoperative complications were considered to be those that developed by the thirtieth POD, categorized according to the Clavien-Dindo classification[13].

This study was approved by the Research Ethics Committee of our institution and by the Research Ethics Committee of the Federal University of Minas Gerais. It was registered on the Brazilian Platform of Research under CAAE number 43719015.4.0000.5149. It is enrolled in the Brazilian Clinical Trials Registry, linked to the International Clinical Trials Registry of the World Health Organization under number RBR-2b4fyr.

Statistical analysis

The sample size was determined using Epi Info software version 7.2, with power equal to 0.80, a margin of error of 5%, an expected tolerance percentage of 0.12, and a confidence level of 95%. The statistical

analysis of the variables was performed using the SPSS program (IBM - version 20.0, 2011). To compare the quantitative measures, the Mann-Whitney U test was used for non-normal distributions, and Student's t-test for abnormal distributions, with verification by the Shapiro-Wilk test. Pearson's asymptotic and exact chi-square tests were used to compare category variables. Multivariate logistic regression was used to analyze association. Variables with an association at the 0.20 level were considered candidates for the multivariate model. They were jointly analyzed until only those with significance at the 0.05 level remained. The quality of the adjustment was analyzed using the Hosmer-Lemeshow test. A p-value < 0.05 was considered statistically significant.

Results

Of the 161 patients included in the final analysis, 84 (52.2%) were allocated to the SARP group and 77 (47.8%), to the CC group. Ninety-six patients were female (59.6%). Age ranged from 25 to 95 years, with an average of 57.4 ± 12.6 years. BMI ranged from 18.0 to 51.0 kg/m^2, with a median of 25.5 kg/m^2.

The two groups were similar with respect to demographic characteristics, as well as to the type and to the duration of the surgery performed, as shown in Table 3.

Table 3
Demographic, clinical, and surgical characteristics of patients in the SARP and CC groups (n = 161)

Variables	SARP (n = 84)	CC (n = 77)	*p*-value
Age	55.01 ± 12.60	58.39 ± 13.86	0.074[1]
Mean ± SD	55.5 (48.0; 61.8)	58.0 (51.0; 70.0)	
Median (Q1; Q3)			
Sex, n (%)	51 (53.1)	45 (46.9)	0.769[2]
Female	33 (50.8)	32 (49.2)	
Male			
BMI	25.41 ± 5.14	25.89 ± 4.91	0.890[1]
Mean ± SD	25.47 (22.54; 28.41)	25.24 (22.60; 27.97)	
Median (Q1; Q3)			
ASA, n (%)	41 (51.9)	38 (48.1)	0.945[2]
1	43 (52.4)	39 (47.6)	
2			
Disease, n (%)	57 (49.6)	58 (50.4)	0.295[2]
Malignant	27 (58.7)	19 (41.3)	
Benign			
Type of surgery, n (%)	70 (83.33)	59 (76.62)	0.084[2]
Colectomy	14 (16.67)	18 (23.28)	
Proctectomy			
Duration of the surgery, min	234.25 ± 67.11	249.81 ± 77.34	0.274[1]
Mean ± SD	240.00 (180.00; 270.00)	240.00 (195.00; 300.00)	
Median (Q1; Q3)			

[1]Mann Whitney U test; [2]asymptotic chi-square test; [3]exact chi-square test

SARP, simplified accelerated postoperative recovery program; CC, conventional postoperative care; BMI, body mass index; SD, standard deviation; Q1; Q3, interquartile range

Variables	SARP (n = 84)	CC (n = 77)	*p*-value
Concomitant resection of other organs, n (%)	25 (50.0)	25 (50.0)	0.711[2]
Yes	59 (53.2)	52 (46.8)	
No			
Need for ostomy, n (%)	14 (37.8)	23 (62.2)	0.061[3]
Ileostomy	69 (56.1)	54 (43.9)	
No			
[1]Mann Whitney U test; [2]asymptotic chi-square test; [3]exact chi-square test			
SARP, simplified accelerated postoperative recovery program; CC, conventional postoperative care; BMI, body mass index; SD, standard deviation; Q1; Q3, interquartile range			

The median time of surgical procedures was 240.0 min and did not differ between groups ($p = 0.274$). The most common surgical indication was colorectal cancer, with 115 cases (71.4%). Thirty-seven patients (23%) required ostomy.

A total of 39 patients developed complications, with an overall rate of 24.2%. The SARP group presented a rate of 25% (21/84), while the CC group presented a rate of 23.4% (18/77) ($p = 0.810$). One patient in the SARP group died on the sixth POD due to an anastomotic fistula, resulting in an overall mortality rate of 0.62%. Four patients, with three belonging to the CC group, returned to the emergency room after discharge and were readmitted to the hospital. One patient presented with an anastomotic fistula, one with dehydration, and two with nausea and vomiting caused by an adynamic ileus. The median length of hospital stay was 3.0 days in the SARP group and 5.0 days in the CC group ($p < 0.0001$). In addition to a shorter hospitalization period, patients in the SARP group started walking, expelling gas, and tolerating a diet sooner. On the other hand, patients in this group relied more heavily on analgesics (Table 4).

Table 4
Comparative analysis of postoperative results among patients in the SARP and CC groups (n = 161)

Variables	SARP (n = 84)	CC (n = 77)	*p*-value
	n %	n %	
Hospitalization time Median (Q1; Q3)	3.00 (2.0; 4.00)	5.00 (5.0; 7.00)	**< 0.0001**[1]
Hospital discharge	51 (60%)	0 (0.0)	**< 0.0001**[2]
≤ 3 days	33 (40%)	77 (100%)	
> 3 days			
Nausea	30 (44.8)	37 (55.2)	0. 113[2]
Yes	54 (57.4)	40 (42.6)	
No			
Vomiting	19 (46.3)	22 (53.7)	0.387[2]
Yes	65 (54.2)	55 (45.8)	
No			
Walking (days)	64 (65.3)	34 (34.7)	**< 0.0001**[2]
1st POD	20 (31.7)	43 (68.3)	
After 1st POD			
Elimination of gas (days)	49 (65.3)	26 (34.7)	**0.002**[2]
1st POD	35 (40.7)	51 (59.3)	
After 1st POD			
Bowel movements	56 (52.8)	50 (47.2)	0.817[2]
Up to 3rd POD	28 (50.9)	27 (49.1)	
After 3rd POD			
Tolerance to free diet (days)	72 (97.3)	2 (2.7)	**< 0.0001**[2]
Up to 3rd POD	12 (13.8)	75 (86.2)	
After 3rd POD			

[1]Mann-Whitney U test; [2]asymptotic chi-square test; [3]exact chi-square test

SARP, simplified accelerated recovery program; CC, conventional postoperative care; CD, Clavien-Dindo; POD, postoperative day

Variables	SARP (n = 84)	CC (n = 77)	*p*-value
	n %	n %	
Use of analgesics, anti-inflammatory drugs, and opioids	82 (54.7)	68 (45.3)	**0.019**[2]
Yes	2 (18.2)	9 (81.8)	
No			
Return to the hospital and rehospitalization after discharge	1 (25.0)	3 (75.0)	0.350[3]
Yes	83 (52.9)	74 (47.1)	
No			
Postoperative complications (Clavien-Dindo)	63(51.6)	59(48.37)	0.810
No complications	21(53.8)	18(46.2)	
Complication, CD ≥ 1			
[1]Mann-Whitney U test; [2]asymptotic chi-square test; [3]exact chi-square test			
SARP, simplified accelerated recovery program; CC, conventional postoperative care; CD, Clavien-Dindo; POD, postoperative day			

In the SARP group, 51 of 84 patients were discharged by the third POD, resulting in a success rate of 60% for the implementation of SARP, according to the criteria adopted in the present study (Table 4).

When comparing the two subgroups in the SARP group, (i.e., patients who tolerated and those who did not tolerate the protocol), univariate analysis demonstrated that the development of complications, the need for ostomy, a longer operative time, and the performance of proctectomies were all factors associated with nontolerance to SARP (Table 5).

Table 5
Results of the univariate analysis of the possible variables that influenced the tolerance or nontolerance to the accelerated recovery program in the subgroups of the SARP group (n = 84)

Variables	Tolerance to "SARP" (n = 51)	Nontolerance to "SARP" (n = 33)	*p*-value
Postoperative complications (Clavien-Dindo), n (%)	4 (19.0)	17 (81)	**< 0.0001**[2]
Yes, CD ≥ 1	47 (74.6)	16 (25.4)	
No			
Need to perform ostomy, n (%)	2 (14.3)	12 (85.7)	**< 0.0001**[2]
Yes	49 (70)	21 (30.0)	
No			
Duration of surgery, min	217.87 ± 56.86	262.00 ± 75.89	**0.004**[4]
Mean ± SD	252.50 (210.00; 305.00)	210.00 (180.00; 240.00)	
Median (Q1; Q3)			
Type of surgery, n (%)	49 (70.0)	21 (30.0)	**< 0.0001**[2]
Colectomy	2 (14.3)	12 (85.7)	
Proctectomy			
BMI, n (%)	14 (50)	14 (50)	0.069[2]
< 25	30 (71.4)	12 (28.6)	
≥ 25			
BMI, n (%)	13 (46.4)	14 (53.6)	0.064[2]
Eutrophic	20 (70.7)	10 (29.3)	
Overweight	9 (90)	1 (10)	
Obese			

[1]Mann-Whitney U test; [2]asymptotic chi-square test; [3]exact chi-square test; [4]Student's t-test

[*]Pearson's chi-square test

SARP, simplified accelerated postoperative recovery program; RC, right colectomy; TME, total mesorectal excision; CD, Clavien-Dindo; SD, standard deviation; Q1; Q3, interquartile interval; ICU, intensive care unit; ASA, American Society of Anesthesiology

Variables	Tolerance to "SARP" (n = 51)	Nontolerance to "SARP" (n = 33)	*p*-value
Age, n (%)	45 (65.2)	24 (34.8)	0.566[2]
< 65 years	8 (57.1)	6 (42.9)	
≥ 65 years			
Age range, n (%)	6 (66.7)	3 (33.3)	0.406[3]
< 40 years	32 (62.7)	19 (37.3)	
40 to 60 years	10 (66.7)	5 (33.3)	
60 to 70 years	3 (33.3)	6 (66.7)	
> 70 years			
Sex, n (%)	32 (62.7)	19 (37.3)	0.790[1]
Female	21 (65.6)	11 (34.4)	
Male			
ASA classification, n (%)	24 (60.0)	16 (40.0)	0.481[1]
1	29 (67.4)	14 (32.6)	
2			
Presence of comorbidity, n (%)	33 (63.5)	19 (36.5)	0.923[2]
Yes	20 (64.5)	11 (35.5)	
No			
Disease, n (%)	31 (54.4)	26 (45.6)	0.084[2]
Malignant	20 (74.1)	7 (25.9)	
Benign			
Surgical time, n (%)	0 (0.0)	0 (0.0)	-
≤ 3	51 (60.7)	33 (39.3)	
> 3			

[1]Mann-Whitney U test; [2]asymptotic chi-square test; [3]exact chi-square test; [4]Student's t-test

*Pearson's chi-square test

SARP, simplified accelerated postoperative recovery program; RC, right colectomy; TME, total mesorectal excision; CD, Clavien-Dindo; SD, standard deviation; Q1; Q3, interquartile interval; ICU, intensive care unit; ASA, American Society of Anesthesiology

Variables	Tolerance to "SARP" (n = 51)	Nontolerance to "SARP" (n = 33)	*p*-value
ICU time, n (%)	46 (62.2)	28 (37.8)	0.477[3]
Up to 1 day	7 (77.8)	2 (22.2)	
More than 1 day			
Use of opioids, n (%)	41 (62.1)	25 (37.9)	0.517[2]
Yes	12 (70.6)	5 (29.4)	
No			
[1]Mann-Whitney U test; [2]asymptotic chi-square test; [3]exact chi-square test; [4]Student's t-test			
*Pearson's chi-square test			
SARP, simplified accelerated postoperative recovery program; RC, right colectomy; TME, total mesorectal excision; CD, Clavien-Dindo; SD, standard deviation; Q1; Q3, interquartile interval; ICU, intensive care unit; ASA, American Society of Anesthesiology			

In multivariate analysis, the development of complications, a longer operative time, and the need for ostomy were identified as predictors of non-tolerance to SARP items (Table 6).

Table 6
Results of the multivariate analysis of the variables that influenced the tolerance or nontolerance of the SARP items (n = 84)

Variables	OR (95% CI OR)	P-value
Type of surgery	2.74 (0.06; 121.57)	0.602
Complications (Clavien-Dindo)	14.78 (3.42; 63.93)	**< 0.0001**
Surgical time	1.01 (1.002; 1.021)	**0.015**
Need for ostomy	11.20 (1.65; 75.89)	**0.0013**
Age	1.04 (0.98; 1.09)	0.181
Sex	1.84 (0.51; 6.68)	0.356
Neoplasm	1.25 (0.31; 4.99)	0.757
Hosmer-Lemeshow test (p = 0.930). Adjustment quality test of the logistic regression model.		
SARP, simplified accelerated postoperative recovery program		

Discussion

The purpose of this study was to evaluate the results of the implementation of a simplified accelerated recovery protocol (SARP) in patients submitted to laparascopic colorectal surgery and to identify possible factors related to implementation failure. Only postoperative measures were adopted, as they were considered the most important and because many pre- and perioperative measures, already shown to be beneficial, had been adopted in our department previously, and it was not considered ethical to not adopt them in one of the groups.

The results obtained with regard to the length of hospital stay, the conversion rate, morbidity, and mortality are all comparable to those of other studies[14,15].

The median length of hospital stay in the SARP group was significantly lower, and patients started walking, expelling gas, and tolerating a diet sooner, confirming the main advantages of the several accelerated postoperative recovery programs. Complication and rehospitalization rates, as well as returns to the emergency room, were not different between groups. Therefore, we conclude that the implementation of an accelerated recovery protocol, even if simplified (SARP), was beneficial and safe for patients, as it shortened hospital stays without increasing the risk of complications or rehospitalizations[10,16].

In addition, the present study was able to demonstrate a 60% acceptance rate for SARP, which matches the rates described in the literature, despite the wide variation observed. Some pilot studies describe more than 90% acceptance[8], while others observe very low rates of adherence to accelerated recovery programs[17]. Nygren et al. reported the importance of maximizing adherence to ERAS™ protocols, but this adherence is often hampered by their complexity[7,14]. The present study, as is the case with a few others described in the literature,[18,19] aims to simplify the protocol, adapting it to the actual circumstances of our institution. In this way, a simplified protocol was adopted (Table 1) and, even though it counted only seven items, the success rate remained at 60%. This result demonstrates that four out of ten patients did not benefit from SARP, making it clear that it is still possible to improve the cost-benefit ratio by increasing the acceptance rate of these protocols. The identification of these patients, as well as the reasons for non-tolerance, certainly makes it possible to achieve even better results in the future.

In univariate analysis, by comparing patients who tolerated SARP with those who did not, we demonstrated that the development of postoperative complications, the need for ostomy, a prolonged operative time, and the performance of proctectomies were the variables associated with non-tolerance to the program. In multivariate analysis, development of complications, the need for ostomy, and a prolonged operative time, but not the type of surgery performed, influenced the non-acceptance of the protocol.

Of the patients who had complications, 81% did not tolerate SARP ($p < 0.0001$). The possible reasons associated with non-tolerance to the program are a long hospital stay, immobilization over an extended period, greater difficulty in accepting a diet due to a longer ileum recovery, and uncertainty of being discharged after the complication.

Patients who required ostomy had a significantly higher failure rate. Only 14.3% of patients with ostomy tolerated SARP ($p < 0.0001$), which matches the results from other studies that analyzed this finding[20,21]. According to Delaney et al[22], the need for ostomy is an independent risk factor for prolonging hospital stay after colorectal surgery. Some studies have shown that setting up an educational program prior to discharge, with guidelines on how to care for the stoma, can shorten the hospital stay. These educational programs are even more effective if performed in the preoperative period, particularly with the involvement of a specialized physician or a stomatherapist[23,24,25]. Therefore, educational programs are an excellent investment of resources, in order to optimize the acceptance of accelerated postoperative recovery protocols.

Prolonged operative time was another factor that influenced the acceptance of SARP. The mean surgical time in the group that tolerated SARP was significantly lower than the mean in the group that did not. Adoption of measures that reduce surgery length, such as the strict standardization of the surgical technique and the participation of a senior surgeon in surgeries during the learning period, can not only contribute to reducing surgery time, but may also positively influence the implementation of SARPs.

In univariate analysis, another factor that significantly influenced the acceptance of the program was the type of surgery: patients who underwent rectal surgeries had worse tolerance to the program than those who underwent colectomies. In patients who underwent colectomies, the acceptance rate of SARP was 78.6%, while in patients who underwent proctectomies, the acceptance rate decreased to 14.3%. The ERAS Compliance Group[26] also reported poor results in patients who underwent rectal surgery, with a lower rate of adherence to the protocol, longer hospital stays, and higher readmission rates.

However, as demonstrated by multivariate analysis, the type of surgery itself was not statistically related to tolerance or non-tolerance to the implementation of the program. Nevertheless, patients who underwent rectal resections had longer surgeries and more complications and required ostomies more frequently; these variables were significant in multivariate analysis. Accordingly, proctectomy is a procedure more likely to result in non-tolerance to SARP. In other words, proctectomies in the present study met the conditions for worse acceptance of SARP and should be investigated by the team, in search of better results.

Other variables that were analyzed, such as age, BMI, sex, and type of disease (whether benign or malignant), did not influence the acceptance of SARP. These data demonstrate that SARPs can be adopted even in elderly patients and in those with high BMI, as demonstrated previously by the study of the ERAS Compliance Group[26], which found no differences between these variables in the acceptance of the ERAS protocol.

The ERAS™ philosophy has gained wider acceptance in the scientific community. Recently, the ERAS Society[16], as well as the American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons, published the guidelines for clinical practice for enhanced recovery after surgery in colorectal surgery[27]. In a meta-analysis of sixteen randomized, controlled

studies, Greco et al.[28] demonstrated that hospital stays were shortened by 2.28 days and that the complication rate decreased by 40% with the adoption of accelerated postoperative recovery programs. Moreover, Lee et al.,[4] among other authors,[29,30], found that ERAS™ allowed patients to get back to work sooner and to be less dependent on caregivers, without impairing quality of life.

In Brazil, in a study with over 5,000 patients who underwent large abdominal surgeries, Bicudo-Salomão et al.[31] demonstrated that operation costs, length of hospital stay, and complication rates were reduced in patients submitted to the ACERTO™ accelerated recovery protocol, compared to patients submitted to conventional postoperative care.

However, for the programs to succeed, it is essential that measures be well-tolerated by the patients[32]. In that regard, this study was able to identify variables that negatively influence patients' acceptance of SARPs.

Conclusions

The adoption of an accelerated recovery program, albeit simplified and focused on postoperative measures, was safe and brought benefits to patients tolerant to the program. The development of complications, prolonged operative time, and the need for ostomy adversely impacted tolerance to SARP. Therefore, the adoption of specific and targeted measures to reduce the negative impact of these variables on the acceptance of SARPs can lead to better acceptance by specific groups of patients, improving results and making them more cost-effective.

Strengths

It is randomized controlled trial. A simplified protocol of accelerated postoperative recovery was used, which can be easily implanted.

Limitations

The main limitations of the present study were a reduced number of patients for the comparative analysis of some variables, such as rehospitalization and reoperation rates, use of a single criterion (length of hospital stay) to define the success of the adopted program, and a lack of individual analysis of the acceptance or non-acceptance of each variable of the program.

Abbreviations

ACERTO™ accelerated recovery protocol. ASA
American Society of Anesthesiologists; BMI:body mass index; CC conventional postoperative care; CD, Clavien-Dindo; ERAS™:Enhanced Recovery After Surgery; ICU, intensive care unit; POD:postoperative day;

Q1; Q3, interquartile range; SARP:Simplified Accelerated Recovery Protocol; SD:standard deviation TME:total mesorectal excision.

Declarations

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Consent to publication

Not Applicable.

Authors' contributions

Fábio Lopes de Queiroz: data acquisition, analysis and interpretation; draft and critical revision of article for important intellectual content; final approval of version to be published.

Antonio Lacerda-Filho: data analysis and interpretation; draft and critical revision of article for important intellectual content; critically revised article for important intellectual content, final approval of version to be published.

Adriana Cherem Alves: data acquisition, analysis and interpretation.

Fábio Henrique de Oliveira: data acquisition, analysis and interpretation.

Paulo Rocha França Neto: data acquisition.

Rodrigo de Almeida Paiva: data acquisition.

All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are available in http://www.ensaiosclinicos.gov.br/rg/RBR-2b4fyr and from the corresponding author on reasonable request.

Ethics approval and consent to participate

The ethics committee of the Federal University of Minas Gerais approved this study.

Competing interests

The authors declare that they have no competing interests.

References

1. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78:606–17.
2. Fearon KC, et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. Clin Nutr. 2005;24:466–77.
3. Thanh NX, et al. An economic evaluation of the Enhanced Recovery After Surgery (ERAS) multisite implementation program for colorectal surgery in Alberta. Can J Surg. 2016;59:415–21.
4. Lee L, et al. Cost-effectiveness of enhanced recovery versus conventional perioperative management for colorectal surgery. Ann Surg. 2015;262:1026–33.
5. Stowers MD, Lemanu DP, Hill AG. Health economics in Enhanced Recovery After Surgery programs. Can J Anaesth. 2015;62:219–30.
6. Lyon A, Payne CJ, Mackay GJ. Enhanced recovery program in colorectal surgery: does one size fit all? World J Gastroenterol. 2012;18:5661–3.
7. Springer JE, Doumouras AG, Lethbridge S, Forbes S, Eskicioglu C. A provincial assessment of the barriers and utilization of enhanced recovery after colorectal surgery. J Surg Res. 2019;235:521–8.
8. Vlug MS, 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. 2011;254:868–75.
9. Moher D, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomized trials. BMJ. 2010;340:c869.
10. Andersen J, et al. Readmission rates after a planned hospital stay of 2 versus 3 days in fast-track colonic surgery. Br J Surg. 2007;94:890.
11. Bardram L, Funch-Jensen P, Kehlet H. Rapid rehabilitation in elderly patients after laparoscopic colonic resection. Br J Surg. 2000;87:1540–5.
12. Gustafsson UO, et al. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. ArchSurg. 2011;146:571–7.
13. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240:205–13.
14. Nygren J, et al. An enhanced-recovery protocol improves outcome after colorectal resection already during the first year: a single-center experience in 168 consecutive patients. Dis Colon Rectum. 2009;52:978–85.
15. Teeuwen PH, et al. Enhanced recovery after surgery versus conventional perioperative care in rectal surgery. Dis Colon Rectum. 2011;54:833–9.

16. Gustafsson UO, Scott MJ, Hubner M, et al. Guidelines for perioperative care in elective colorectal surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations: 2018. World J Surg. 2019;43:659–95.
17. Bona S, et al. Introducing an enhanced recovery after surgery program in colorectal surgery: a single center experience. World J Gastroenterol. 2014;20:17578–87.
18. Fonseca LM, et al. A simplified rehabilitation program for patients undergoing elective colonic surgery-randomized controlled clinical trial. Int J Colorectal Dis. 2011;26:609–16.
19. Aguilar-Nascimento JE, et al. Multimodal approach in colorectal surgery without mechanical bowel cleansing. Rev Col Bras Cir. 2009;36:204–9.
20. Cartmell MT, et al. A defunctioning stoma significantly prolongs the length of stay in laparoscopic colorectal resection.*SurgEndosc.*2008;22:2643–2647.
21. Ulrich AB, et al. Diverting stoma after low anterior resection: more arguments in favor. Dis Colon Rectum. 2009;52:412–8.
22. Delaney CP, et al. Prospective, randomized, controlled trial between a pathway of controlled rehabilitation with early ambulation and diet and traditional postoperative care after laparotomy and intestinal resection. Dis Colon Rectum. 2003;46:851–9.
23. Danielsen AK, Burcharth J, Rosenberg J. Patient education has a positive effect in patients with a stoma: a systematic review. Colorectal Dis. 2013;15:276–83.
24. Altuntas YE, et al. The role of group education on quality of life in patients with a stoma. Eur J Cancer Care (Engl). 2012;21:776–81.
25. Forsmo HM, Pfeffer F, Rasdal A, Sintonen H, Körner H, Erichsen C. Pre- and post operative stoma education and guidance within an enhanced recovery after surgery (ERAS) program reduces length of hospital stay in colorectal surgery. *Int J Surg.*2016;**3**:**121–126**.
26. ERAS Compliance Group. The impact of enhanced recovery protocol compliance on elective colorectal cancer resection: results from an international registry. Ann Surg. 2015;261:1153–9.
27. Carmichael JC, et al. Clinical practice guidelines for enhanced recovery after colon and rectal surgery from the American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons. Dis Colon Rectum. 2017;60:761–84.
28. Greco M, et al. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. World J Surg. 2014;38:1531–41.
29. Smart NJ, et al. Deviation and failure of enhanced recovery after surgery following laparoscopic colorectal surgery: early prediction model. Colorectal Dis. 2012;14:727–34.
30. Steele SR, et al. Improving outcomes and cost-effectiveness of colorectal surgery. J Gastrointest Surg. 2014;18:1944–56.
31. Bicudo-Salomão A, et al. Impact of the ACERTO project in the postoperative morbi-mortality in a university hospital. Rev Col Bras Cir. 2011;38:3–10.

32. Arrick L, Mayson K, Hong T, Warnock G. Enhanced recovery after surgery in colorectal surgery: impact of protocol adherence on patient outcomes. J Clin Anesth. 2018;21:7–12.

Figures

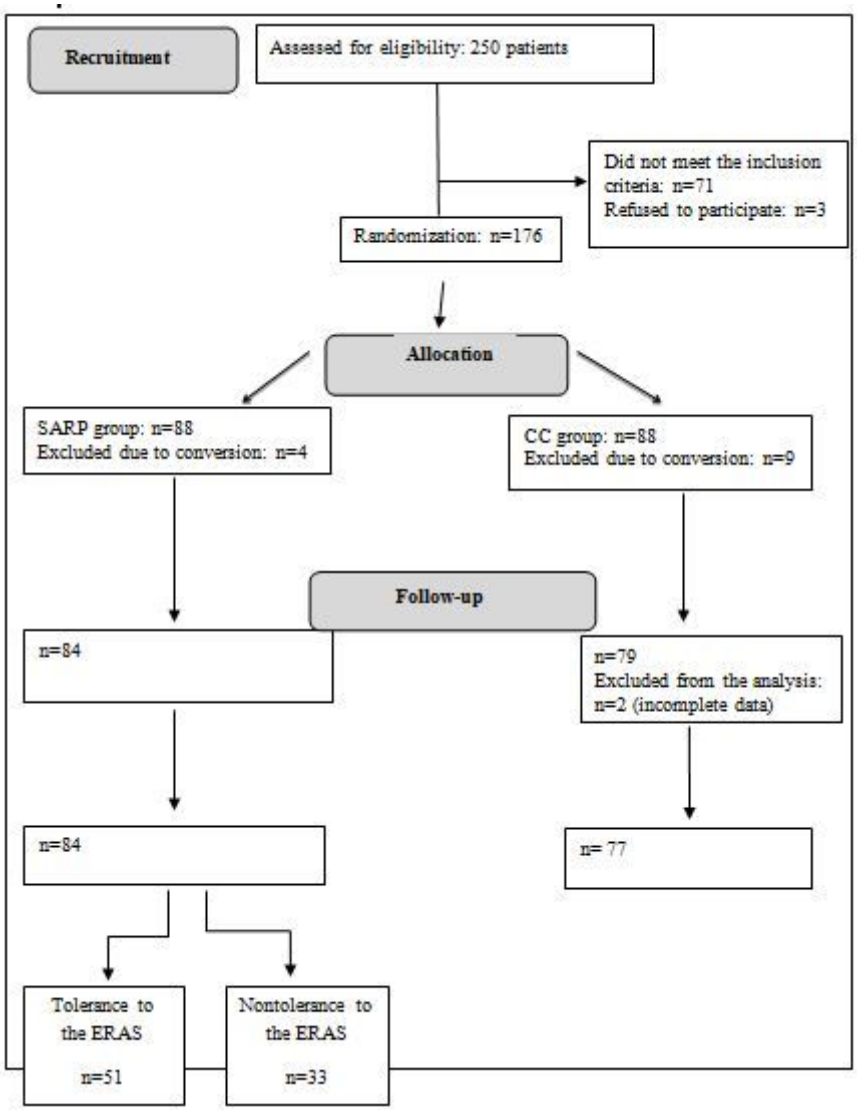

Figure 1

CONSORT diagram of patient allocation.

Supplementary Files

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- CONSORT2010Checklist.doc