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INFLUENCE OF ERAS PROTOCOL ON POSTOPERATIVE OUTCOMES AFTER ELECTIVE COLORECTAL RESECTION SURGERY: A PROSPECTIVE COHORT STUDY - TWO YEARS SINGLE CENTER EXPERIENCE

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ABSTRACT

Background: ERAS (Enhanced Recovery After Surgery) protocol is a multimodal pathway of perioperative surgical care consisting of evidence-based procedures. ERAS protocol is hard to comply with, because medical staff often opposes well established practice.

Methods: We analyzed length of hospital stay, postoperative complications, time until first stool passage and introduction of normal nutrition in patients undergoing elective colorectal resection surgery in University Hospital Center Split from October 2016. to October 2018. Patients were divided into 4 groups considering operation type (open/laparoscopic) and application of ERAS protocol (good/poor). Application of 60% or more ERAS steps was considered as well performed protocol.

Results: Groups Laparoscopy/ERAS and Open/ERAS had shorter postoperative hospital stay (Median, IQR; days) than groups Laparoscopy/non-ERAS and Open/non-ERAS (LE 5, 4-8 , OE 6, 5-9 vs LNE 7, 5-8,5 , ONE 7, 6-12). Similar difference was shown in times until first stool passage. Patients operated laparoscopically had shorter times until normal food tolerance (Median, IQR; days): LE 3, 2-3, LNE 3, 2-4 than patients who underwent open surgery (OE 3, 3-4, ONE 4, 3-5). In addition, laparoscopically operated patients had lower overall morbidity (P<0.001). Incidence of unplanned operations and hospital readmissions did not differ significantly among groups.

Conclusion: Well-performed ERAS protocol can improve length of hospital stay and time until first stool passage in both open and laparoscopic types of operation. Optimal combination for colorectal resection is laparoscopic surgery with ERAS protocol. If open surgery is done, it should be preferably applied with ERAS protocol as well.

Keywords:

colorectal cancer, colorectal surgery, ERAS protocol

INTRODUCTION

ERAS (Enhanced Recovery After Surgery) is a multimodal, evidence based protocol of perioperative care. The goal of this modality, introduced by Kehlet in early 1990´s, is to standardize perioperative care and combine many scientifically proven steps in order to reduce the length of perioperative stay, surgical stress and number of complications. This way, patient is back in the centre of care rather than individual decisions of a surgeon and other medical staff [1-27]. ERAS protocol in University Hospital Center Split was first introduced in October 2016.

MATHERIALS AND METHODS

Study population and exclusion criteria.

We collected data from a longitudinal, prospective cohort of patients at Department of surgery in University Hospital Center Split in two years period following introduction of ERAS protocol (October 2016. - October 2018.). Only the patients that fulfilled following criteria were included: 1) Pathohistological evidence of malignant disease before hospital admission, 2) Elective colorectal resection surgery was indicated as curative therapy of choice, 3) Patients were part of ERAS protocol with predefined discharge criteria.

The exclusion criteria were following: 1) History of major abdominal operation, 2) History of any operation 30 days before colorectal resection, 3) ASA score >3, 4) Disseminated (metastatic) disease. Every patient was followed three months after day of hospital discharge. All patients were informed about ERAS protocol and agreed to participate in study.

Group formation

Group formation was based on compliance of ERAS protocol (60% or more steps applied were considered as well performed ERAS protocol) and type of operation (open or laparoscopic). Consequently, we divided patients into four groups: Open/non-ERAS (open operations and poorly performed ERAS) or „ONE", Open/

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ERAS (open operations and well performed ERAS) or „OE", Laparoscopy/non-ERAS (laparoscopic operations and poorly performed ERAS) or „LNE" and Laparoscopy/ERAS (laparoscopic operations and well performed ERAS) or „LE" (Figure 1).

Baseline characteristics

For every patient basic set of information (age, gender, BMI, body fat percentage, haemoglobin levels, ASA stage, consumption of tobacco and alcohol, comorbidities), diagnostic workup (cancer site and staging,) and operation data (type, duration, presence of stoma, amount of fluid given during operation) were collected.

ERAS steps

We followed application of 20 ERAS steps in total (8 preoprative, 4 intraoperative and 8 postoperative). ERAS step was considered applied only when it fulfilled strict criteria. All criteria were based on prominent clinical studies and recommendations as shown in Table 1.

Outcomes

Primary outcomes were length of postoperative hospital stay, time of return of bowel function (day of first stool passage and introduction of normal nutrition). All patients were discharged when they complied with these hospital discharge criteria: (1) tolerance of oral intake of fluids and food, (2) passage of first stool, (3) absence of nausea, (4) pain that can be controlled with oral analgesics and (5) patient´s consent.

Secondary outcomes were incidence of major and minor complications, unplanned reoperations, readmissions and in-hospital mortality.

Statistical analysis

For continuous data we tested normality of distribution (Shapiro-Wilk test) and homogeneity of variance (Levene´s test). We expressed our data as arithmetic mean ± standard deviation, median with interquartile range, minimum and maximum value where appropriate. In inferential statistics we used Analysis of Variance (ANOVA-test) and Kruskal Wallis with Mann-Whitney U test. For categorical data we used Chi-squared ($\chi 2$) test. Significance level was set at 5% ($P<0.05$). Statistics were made using software IBM SPSS Statistics 25.0., Chicago, Illinois, USA.

RESULTS

Baseline characteristics

We compared baseline characteristics among groups as seen in Table 2. There were statistically significant differences in haemoglobin and body fat percentage values. In surgical aspects there were significant differences in types of resection and presence of stoma between open and laparoscopic groups. When we compared types of surgical resections and stoma presence in open and laparoscopic groups separately they did not differ significantly.

ERAS steps compliance

We noted 20 ERAS steps in total and compared number of applied steps in each group. In „Open ERAS" group 13,26±1,35 out of the 20 steps and in „Laparoscopic ERAS" group 14,15±1,57 per person was applied. In groups with poorly performed ERAS some of the steps were also applied. In „Open non-ERAS" group 10,04± 1,11 and in „Laparoscopic non-ERAS" 8,79±1,85 was applied successfully (Table 3).

Primary outcomes

Length of postoperative hospital stay was significantly shorter in patients operated laparoscopically with well performed ERAS (LE) comparing to other three groups. On the other hand, patients that underwent open surgery with poorly performed ERAS (ONE) had statistically significant longer postoperative stay than patients in other three groups. Group Open/ERAS (OE) had shorter postoperative stay than Laparoscopy/non-ERAS (LNE), but without statistical significance. Similarly, group Laparoscopy/ERAS (LE) had significantly shorter time until first stool passage than other three groups. Group Open /ERAS (OE) had shorter time until first stool passage than both groups with poorly performed ERAS, but only difference in comparison to group Open/non-ERAS (ONE) was statistically significant. When analysing time until normal food introduction, patients operated laparoscopically (groups LE and LNE) tolerated this kind of food earlier. However, the difference between Laparoscopy/non-ERAS (LNE) and Open/ERAS (OE) was not statistically significant. Open/non-ERAS (ONE) group had significantly longer time until normal food introduction in comparison with other three groups (Table 4).

Secondary outcomes

There was significant difference in overall morbidity and major complications when comparing laparoscopic (LNE and LE) and open (OE and ONE) groups ($P<0,001$) as illustrated in Table 5. Open/ERAS (OE) group showed lower overall morbidity and less major complications when comparing to Open/non-ERAS (ONE) group, but without statistical significance. Similarly, „Laparoscopic ERAS" showed better overall morbidity with less major complications than „Laparoscopic non-ERAS group", but also without statistical significance.

DISCUSSION

Our study showed that combination of laparoscopic surgery and ERAS protocol (group LE) enables significantly faster postoperative recovery (length of postoperative hospital stay, time until first stool passage and induction of normal nutrition) than all three other combinations. Group Open/ERAS (OE) had significantly faster postoperative recovery than group Open/non-ERAS (ONE) and very similar results as group Laparoscopy/non-ERAS (LNE). More precisely, group OE had shorter length of postoperative stay and time until

first stool passage than group LNE, but without statistical significance. Patients in group Open/non-ERAS (ONE) had significantly prolonged postoperative recovery in comparison to all three other groups. Morbidity was significantly lower in patients operated laparoscopically (groups LE and LNE). There was no statistically significant difference in unplanned reoperations, readmissions and in-hospital mortality among groups. In this category ERAS protocol had smaller influence than in postoperative recovery. However, group Open/ERAS (OE) had lower overall morbidity and lower incidence of unplanned reoperations and readmissions in comparison to group Open/non-ERAS (ONE), but without statistical significance. Length of postoperative hospital stay as well as overall morbidity is similar to results given in prominent meta-analyses [27-29]. However, incidence of complications shown in our study is mostly higher than results published in meta-analyses. It can be explained by non-existing upper age limit in our study. Length of postoperative hospital stay was almost equal to prominent LAFA-study by Vlug et al. [30]. Although, when comparing times until first stool passage and normal food tolerance, LAFA study showed much better results. This could be partially explained with fact that we included patients with planned stoma formation (colostoma and ileostoma). Designs of ERAS studies differ dramatically. Therefore, comparison among papers is extremely difficult [27]. Some studies only include operations of the colon without rectum [31-36] or only laparoscopically operated patients [31, 37-44] Also, number and type of ERAS steps applied is different in almost every study [27]. Systematic review of Messenger et al. precisely described mentioned variability by publishing range of 6 to 21 steps applied among 34 analyzed studies [45]. Moreover, it is rarely seen that authors describe exact criteria that they used when deciding which ERAS step was applied. We explained every ERAS step individually with adequate reference, hoping that future studies will also provide this kind of information. Strength of this study is thoroughly described compliance for every ERAS step. This set of information could help discovering which ERAS step is more important in the future. Studies rarely report this result which was mentioned in systematic review by Messenger et al. They noted that only one of all analyzed RCTs reported this kind of data [45]. We conducted audit in accordance to systematic reviews and meta-analysis who constantly pointed out weaknesses of analyzed studies [27-29, 45]. In order to enable easier comparison in the future we also followed audit guidelines of ERAS® society [46]. Limitation of this study is it´s sample size. Moreover, groups are unbalanced in number and in some basic characteristics. Group Laparoscopy/ERAS (LE) had significantly higher level of preoperative haemoglobin and body fat percentage than group Open/non-ERAS (ONE). Body fat percentage is easily explained with higher percentage of females but higher haemoglobin levels remain unexplained. Some types of operations were more common in laparoscopic and some in open type of surgery. It is very hard to say which operation is more severe so the influence of this kind of data is unknown. Except types of operation, presence of stoma was also significantly different when comparing laparoscopic and open surgery. Stomas were more common in laparoscopic surgery. Presence of stoma is linked with worse outcomes, especially regarding stool passage, which could explain why patients in group OE needed less time to achieve this goal than patients in group LNE [47]. Unbalanced group sizes and usage of nonparametric tests in our inferential statistics have lowered the strength and therefore significance in given results could be exaggerated. On the other hand, still relatively low overall compliance and small difference in compliances between ERAS and non-ERAS groups could underestimate it [48,49]. In our study, all patients were part of ERAS protocol, planned to achieve as many steps as possible. That explains smaller difference in compliance between well and poorly performed ERAS groups. We can say that type of operation and ERAS compliance are two most important predictors of surgical outcomes. At the end, we can state that ERAS protocol is a type of perioperative care that will lead to better outcomes in almost every parameter analyzed. Some of the results did not show statistical significance, but we should consider that even unsignificant differences can provide substantial clinical benefit.

CONCLUSION

Our study showed that well performed ERAS protocol can reduce length of postoperative hospital stay and time until first stool passage. The best combination to use when performing colorectal surgery is laparoscopy with well performed ERAS protocol. ERAS is also recommended type of perioperative care in combination with open surgery.

CONFLICT OF INTEREST:

The authors declare that there is no conflict of interest.

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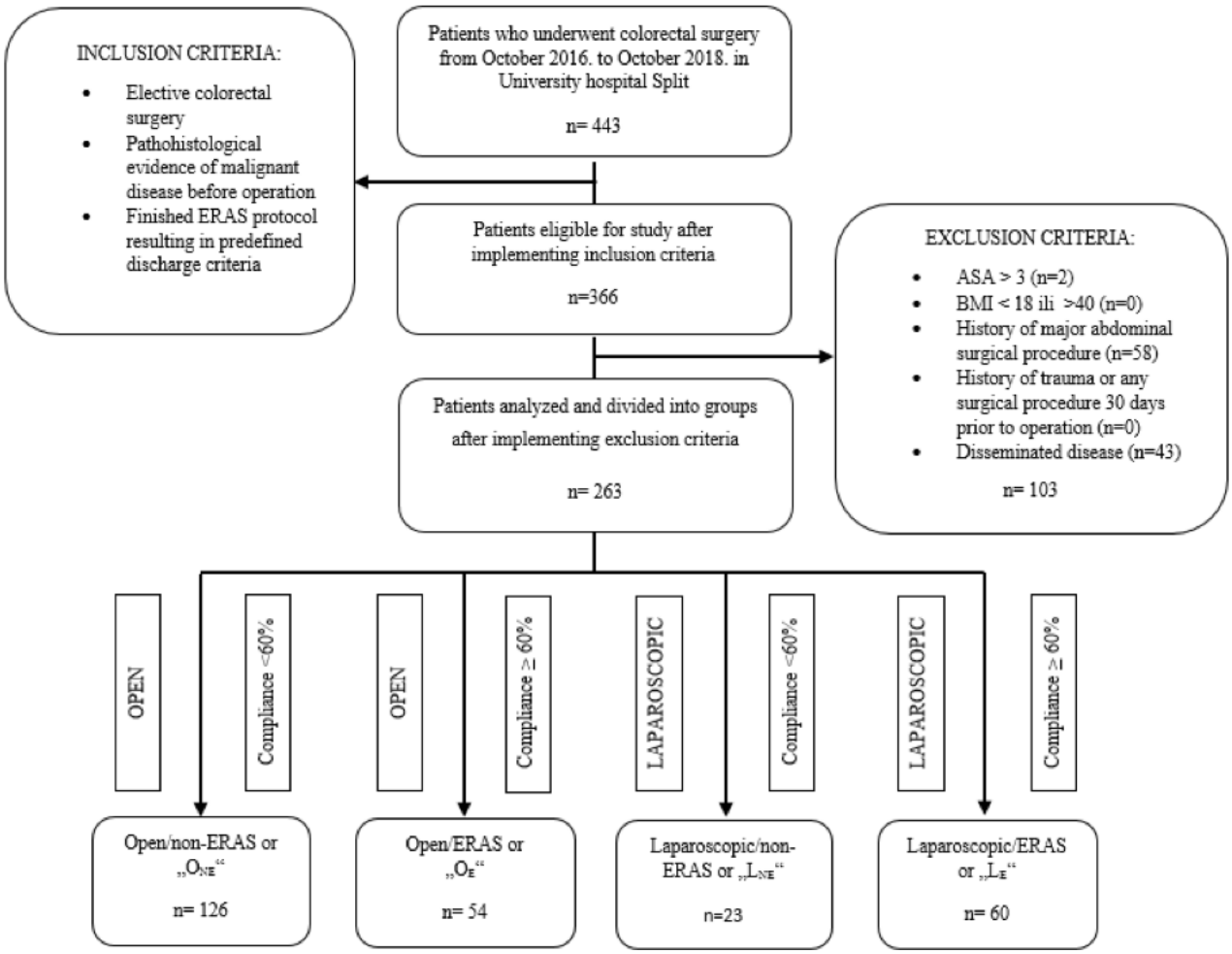

Figure 1. Study flow

ERAS STEP	EVIDENCE BASED CRITERIA
1. Preoperative counselling	Patient is familiar with ERAS steps, expectations, type of operation and risks (3,4).
2. Preoperative nutritional screening	Calculating NRS 2002 score at least two weeks before day of operation. Patients with 3 points or more are scheduled for nutritional intervention with high-protein drinks (5).
3. Bowel preparation	For operations with total mesorectal excision polyethylene glycol is used afternoon before operation and enema morning before operation. For other operations no bowel preparation is used (6,7).
4. Preoperative fasting treatment	Patients are allowed to take solid food up to 6 hours and clear fluids up to 2 hours before induction of anaesthesia (8,9).
5. Preoperative carbohydrate treatment	Patients should ingest >100g of carbohydrates afternoon before and >50g morning before the operation (10).
6. Antibiotic prophylaxis	First generation cephalosporin (cefazolin) and metronidazole are given intravenously 60 minutes before skin incision (11,12).
7. Antithrombotic prophylaxis	Usage of compression socks or intermittent pneumatic compression with low-molecular heparin (13,14).
8. Preanesthetic medication	Routine usage of enteral sedative drugs is avoided. If needed, usage of 5 mg diazepam intravenously is allowed (15).
9. Anaesthetic protocol	Combination of general and regional anesthetics with rapid awakening is used (15).
10. Prevention of intraoperative hypothermia	Patients are warmed under a blanket during procedure with temperature maintained at 34°C (16).
11. Intraoperative fluid management	1-4 mL/kg/h of crystalloid fluid is used for open and laparoscopic surgery (17).
12. Application of nasogastric tube	Routine application as ileus and vomiting prevention should be avoided (18-20).
13. Abdominal drainage	All abdominal drains are removed in first three days after operation.
14. PONVa prophylaxis	For patients with low/mild risk dexamethasone (4-8 mg) with or without metoclopramide (10 mg) is administered. For patients with high risk ondansetron/granisetron is administered (22,23).
15. Postoperative analgesia	Avoidance of opioid analgesics and usage of NSAIDs, paracetamole, metamizole and epidural analgesia (15, 22).
16. Signs of ileus check	Signs of ileus are checked every day.
17. Intake of fluid on the day of operation	Patient should drink (not more than 800 mL) of fluid afternoon after the procedure (23).
18. Early ambulation	Patients are mobilized to sit at the end of the bed or get up and walk short distances (15, 24).
19. High protein ONSb intake	Patients need to take high-protein drinks first four days after the operation (15,25).
20. Urinary drainage management	Urinary catheter is removed in first two days after the operation (26).

[a] *Prophylaxis Of Nausea and Vomiting*
[b] *Oral Nutrition Supplement*

Table 1. ERAS steps and criteria

	Laparoscopy and ERAS (L_E) N=60	Open and ERAS (O_E) N=54	Laparoscopy non-ERAS (L_{NE}) N=23	Open non-ERAS (O_{NE}) N=126	P
Age (AM±SD[a], year)	66,63	67,23	68,17	68,86	0,451*
Gender (M/F)	31/29	35/19	14/9	91/35	0,051†
BMI[b] (AM±SD, kg/m^2)	26,89	25,96	27,05	26,55	0,584*
Body fat (AM±SD, %)	26,77	24,81	26,35	23,43	0,030*
Preoperative haemoglobin (AM±SD, g/L)	131,25	121,74	130,35	125,98	0,037*
Duration of procedure median (IQR[c], min)	135 (117,5-165)	100 (70-130)	140 (120-155)	100 (80-122,5)	<0,001‡
Fluids given during procedure median (IQR, mL)	1000 (800-1250)	1000 (800-1300)	1050 (1000-1600)	1100 (1000-1500)	0,110‡
ASA[d], N (%)					0,576†
I	2 (3,33)	2 (3,7)	0 (0)	3 (2,38)	
II	44 (73,3)	34 (62,96)	18 (78,26)	79 (62,70)	
III	14 (23,33)	18 (33,33)	5 (21,74)	44 (34,92)	
Comorbidities[e]					
Total, N	54	42	22	118	0,734†
Patients with one or more comorbidities, N (%)	39 (65,00)	32 (59,26)	17 (73,91)	82 (65,08)	0,668†
Tobacco, N (%)	8 (14,55)	6 (11,32)	4 (19,05)	24 (19,51)	0,535†
Alcohol, N (%)	1 (1,82)	2 (4,08)	1 (4,55)	5 (4,07)	0,862†
Type of colectomy, N (%)					
Ileocecal resection	2 (3,33)	1 (1,85)	0 (0)	1 (0,79)	
Right hemicolectomy	0 (0)	24 (44,44)	0 (0)	45 (35,71)	
Transversotomy	0 (0)	1 (1,85)	0 (0)	2 (1,59)	
Left hemicolectomy	0 (0)	2 (3,70)	0 (0)	8 (6,35)	
Sigmoidectomy	4 (6,67)	7 (12,96)	1 (4,35)	13 (10,32)	
Hartmann resection	5 (8,33)	8 (13,33)	2 (3,33)	4 (3,17)	
Lower anterior resection	38 (63,33)	9 (16,67)	15 (65,22)	41 (32,54)	
Quenn-Milles (Abdominoperineal resection)	9 (15,00)	2 (3,70)	5 (21,74)	9 (7,14)	
En bloc resections	0 (0)	0 (0)	0 (0)	1 (0,79)	
Total/subtotal colectomy	0 (0)	0 (0)	0 (0)	1 (0,79)	
Other[f]	2 (3,33)	0 (0)	0 (0)	1 (0,79)	
Presence of stoma, N (%)	23 (38,33)	11 (20,37)	7 (30,43)	20 (15,87)	0,006†
T-Stage, N (%)					0,284†
Tis	0 (0)	0 (0)	1 (5,26)	0 (0)	
T_1	7 (14,29)	2 (3,92)	2 (10,53)	6 (5,13)	
T_2	13 (26,53)	10 (19,61)	3 (15,79)	22 (18,80)	
T_3	22 (44,90)	28 (54,90)	9 (47,37)	72 (61,54)	
T_4	7 (14,29)	11 (21,57)	4 (21,05)	17 (14,53)	
N-Stage, N (%)					0,613†
N_0	33 (67,35)	32 (62,75)	13 (68,42)	83 (70,94)	
N_1	9 (18,37)	14 (27,45)	5 (26,32)	27 (23,08)	
N_2	7 (14,29)	5 (9,80)	1 (5,26)	7 (5,98)	

[a] *Arithmetic Mean±Standard Deviation*
[b] *Body Mass Index*
[c] *Interquartile range*
[d] *American Society of Anesthesiologists*
[e] *Hypertension, diabetes type II, COPD, liver cirrhosis, heart failure, history of myocardial infarction and/or CVI, other neurological diseases e.g. epilepsy, mb. Parkinson*
[f] *Transanal total mesorectal excision (TaTME), segmental resections*
** Analysis of variance (ANOVA-test)*
† Chi-squared test
‡ Kruskal-Wallis test

Table 2. Baseline characteristics and surgical aspects per group

ERAS STEPS, N (%)	Laparoscopy and ERAS (L_E) N=60	Open and ERAS (O_E) N=54	Laparoscopy non-ERAS (L_{NE}) N=23	Open non-ERAS (O_{NE}) N=126
Preoperative counselling	49 (81,67)	36 (66,67)	11 (47,83)	45 (35,71)
Preoperative nutritional screening and intervention	29 (48,33)	21 (38,89)	1 (4,35)	17 (13,49)
Bowel preparation	55 (91,67)	45 (83,33)	11 (47,83)	58 (46,03)
Preoperative fasting treatment	58 (96,67)	52 (96,30)	13 (56,52)	62 (49,21)
Preoperative carbohydrate treatment	47 (78,33)	47 (87,04)	12 (53,17)	64 (50,79)
Antibiotic prophylaxis	60 (100)	54 (100)	23 (100)	124 (98,41)
Antithrombotic prophylaxis	59 (98,33)	54 (100)	20 (86,96)	113 (89,68)
Preanesthetic medication	5 (8,33)	3 (5,55)	1 (4,35)	11 (8,73)
Anaesthetic protocol	35 (58,33)	39 (72,22)	12 (53.17)	62 (49,21)
Prevention of intraoperative hypothermia	23 (38,33)	19 (35,19)	4 (17,39)	25 (19,84)
Intraoperative fluid management	0 (0)	0 (0)	0 (0)	0 (0)
Application of nasogastric tube	59 (98,33)	53 (98,15)	22 (95,65)	113 (89,68)
Abdominal drainage	39 (65,00)	26 (48,15)	4 (17,39)	9 (7,14)
PONV prophylaxis	28 (46,67)	15 (27,78)	4 (17,39)	13 (10,32)
Postoperative analgesia	49 (81,67)	47 (87,04)	16 (69,57)	64 (50,79)
Signs of ileus check	59 (98,33)	54 (100)	23 (100)	125 (99,21)
Intake of fluid on the day of operation	37 (61,67)	31 (57,41)	10 (43,48)	49 (38,89)
Early ambulation	53 (88,33)	34 (62,96)	13 (56,52)	41 (32,54)
High protein ONS intake	54 (90,00)	49 (90,74)	19 (82,61)	91 (72,22)
Urinary drainage management	51 (85,00)	37 (68,52)	12 (52,17)	21 (16,67)
TOTAL, AM±SD	14,15±1,57	13,26±1,35	10,04±1,11	8,79±1,85

Table 3. Protocol compliance

Length of postoperative hospital stay, days				L_E	O_E	L_{NE}	O_{NE}
GROUP	Median (IQR)[a]	Min[b]	Max[c]	P<0,001*			
Laparoscopy and ERAS (L_E) N=60	5 (4-6)	2	23	/	0,001	0,001	<0,001
Open and ERAS (O_E) N=54	6 (5-9)	3	16	0,001	/	0,374	<0,001
Laparoscopy non-ERAS (L_{NE}) N=23	7 (5-8,5)	5	19	0,001	0,374	/	0,034
Open non-ERAS (O_{NE}) N=126	7 (6-12)	4	25	<0,001	<0,001	0,034	/
Day of first stool passage				L_E	O_E	L_{NE}	O_{NE}
GROUP	Median (IQR)	Min	Max	P<0.001*			
Laparoscopy and ERAS (L_E) N=60	3 (2-4)	1	10	/	0,004	<0,001	<0,001
Open and ERAS (O_E) N=54	4 (3-5)	1	9	0,004	/	0,077	0,011
Laparoscopy non-ERAS (L_{NE}) N=23	5 (4-6,5)	2	8	<0,001	0,077	/	0,269
Open non-ERAS (O_{NE}) N=126	4 (3-5)	1	14	<0,001	0,011	0,269	/
Day of normal food introduction				L_E	O_E	L_{NE}	O_{NE}
GROUP	Median (IQR)	Min	Max	P<0,001*			
Laparoscopy and ERAS (L_E) N=60	3 (2-3)	1	5	/	<0,001	0,070	<0,001
Open and ERAS (O_E) N=54	3 (3-4)	2	7	<0,001	/	0,077	<0,001
Laparoscopy non-ERAS (L_{NE}) N=23	3 (2-4)	1	5	0,070	0,077	/	<0,001
Open non-ERAS (O_{NE}) N=126	4 (3-5)	2	14	<0,001	<0,001	<0,001	/

[a] *Median (Interquartile range)*

[b] *Minimal value*

[c] *Maximal value*

** Kruskal-Wallis test. Groups were individually compared by Mann-Whitney U test*

Table 4. Primary outcomes

	Laparoscopy and ERAS (LE) N=60	Open and ERAS (OE) N=54	Laparoscopy non-ERAS (LNE) N=23	Open non-ERAS (ONE) N=126	P*
Overall morbidity < 30 days, N (%)	20 (33,33)	38 (70,37)	9 (39,13)	92 (73,02)	<0,001
Patients with one or more major complication, N (%)	4 (6,67)	15 (27,78)	3 (13,04)	51 (40,48)	<0,001
Total no. of major complications	5	15	4	59	
Pathological ileus	3	15	3	45	
Anastomotic leakage	1	0	0	5	
Anastomotic fistula	1	0	0	2	
Wound dehiscence	0	0	0	2	
Peritonitis	0	0	0	1	
Intraabdominal abscess	0	0	0	2	
Haemoperitoneum	0	0	0	1	
Othera	0	0	1	1	
Patients with one or more minor complication, N (%)	16 (26,67)	23 (42,59)	6 (26,09)	41 (32,54)	0,278
Total no. of minor complications	17	28	6	46	
Wound infection	6	13	3	23	
Wound haematoma	0	1	0	1	
Urinary tract infection	2	4	0	5	
Pneumonia	0	1	0	1	
Nausea and vomiting	7	6	2	13	
Otherb	2	3	1	3	
Unplanned reoperations, N (%)	3 (5,00)	2 (3,70)	1 (4,35)	13 (10,32)	0,375
Total no. of readmissions, N (%)	3 (5,00)	1 (1,85)	0 (0)	6 (4,76)	0,568
< 1 month	3	1	0	5	
< 3 months	0	0	0	1	
In-hospital mortality, N (%)	0 (0)	0 (0)	0 (0)	0 (0)	

[a] *Necrosis of skin around stoma*
[b] *Blood in stool*
* *Chi-squared test*

Table 5. Secondary outcomes