



# Laparoscopy is not enough: full ERAS compliance is the key to improvement of short-term outcomes after colectomy for cancer

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## Abstract

**Background** The enhanced recovery after surgery (ERAS) programs and laparoscopic techniques both reduce hospital stay and postoperative morbidity in patients undergoing colorectal cancer surgery. Laparoscopic techniques are an integral part of the ERAS program. However, evidence showing that the implementation of a multimodal rehabilitation program in addition to laparoscopy for colonic cancer would improve postoperative outcomes is still lacking. This study aimed to evaluate the impact of ERAS program on postoperative outcomes after elective laparoscopic colonic cancer resection.

**Methods** This is a single-center observational study from a prospectively maintained database. Two groups were formed from all patients undergoing laparoscopic colonic surgery for neoplasm during a defined period before (standard group) and after introduction of an ERAS program (ERAS group). The primary endpoint was postoperative 90-day morbidity. Secondary endpoints were the total length of hospital stay, readmission rate, and compliance with ERAS protocol.

**Results** A total of 320 patients were included in the analyses, with 160 patients in the standard group and 160 in the ERAS group. There were no differences in the baseline characteristics between the two groups. Overall morbidity was significantly lower in the ERAS group (21.25%) than that in the standard group (34.4%; OR = 0.52 [0.31–0.85],  $p < 0.01$ ). This difference was not due to the reduction in major complications. Mean total hospital stay was significantly lower in the ERAS group (5.8 days) than that in the standard group (8.2 days,  $p < 0.01$ ). There were no differences in readmission rates and anastomotic complications.

**Conclusions** The ERAS pathway reduced the overall morbidity rates and shortened the length of hospital stay, without increasing the readmission rates. A significant reduction in nonsurgical complications was evident, whereas no significant reduction was found for surgical complications.

**Keywords** Enhanced recovery after surgery · Colon cancer · Laparoscopic surgery · Compliance

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Over the last two decades, there have been two major improvements/fundamental developments in perioperative care in the field of colonic surgery, namely the introduction of laparoscopic surgery and the implementation of enhanced recovery after surgery (ERAS) programs, also previously known as fast track (FT) surgery. In comparison with open surgery, the laparoscopic approach significantly reduced length of hospital stay (LOS) as well as postoperative morbidity and pain owing to the reduction of the stress response to surgery, as reported in several randomized controlled trials [1–5]. In parallel, several randomized studies have been performed to assess the impact of ERAS programs on outcomes of elective colorectal surgery, and their implementation also reduces complication rates, shortens the LOS, and accelerates postoperative recovery [6–10].

ERAS programs are not yet widely adopted and may require delay in integrating novel management strategy with highly efficient organization. As a matter of fact, multicentric randomized studies are characterized by nonoptimal or unprecise compliance to the ERAS protocol [6–12].

Moreover, most of the studies about the ERAS programs include heterogeneous groups of patients undergoing open or laparoscopic surgery, both rectal and colonic resections, also creating a potential bias [6, 7, 9, 11, 12].

Thus, the evidence that the implementation of a multimodal rehabilitation program in addition to laparoscopy for colonic cancer would improve postoperative outcomes is therefore still lacking. In our center, we started with colonic and rectal full laparoscopic resection since the early 2000, and we observed a reduced complication rate, a shortened LOS, and an accelerated postoperative recovery [5].

Thus, the aim of this study was to analyze the effect of the ERAS program specifically on patients undergoing laparoscopic colonic surgery in an established laparoscopic center, considering 90-day postoperative morbidity as primary outcome, as well as primary and total LOS, readmission, and compliance with the ERAS protocol.

## Materials and methods

### Patients

From June 2013 to October 2017, we evaluated all the consecutive patients undergoing laparoscopic colonic cancer resection. The inclusion criteria were as follows: patients older than 18 years, and those who underwent elective laparoscopic resection for histopathologically confirmed adenocarcinoma of the large intestine. Patients who needed emergency surgery and those requiring an end or diverting stoma were excluded.

In January 2016, a standardized enhanced recovery protocol for elective colonic resection was implemented at the Paoli-Calmettes Institute and applied systematically (ERAS group). Patients operated from June 2013 to December 2015 (prior to ERAS implementation) served as a baseline (standard group). Informed consent was obtained from all patients before surgery, and the study was approved by the Institutional Review Board and by ethics committee. It was carried out in accordance with the 1989 World Medical Association Declaration of Helsinki.

### Outcomes

The primary outcome was overall postoperative morbidity. Secondary outcomes were postoperative morbidity (Clavien I–II/III–IV), primary LOS, total LOS, readmission rate, postoperative unscheduled consultation, and compliance

with the ERAS protocol. Clinical outcome was evaluated until 90 days postoperatively. Overall 30- and 90-day morbidities were reported according to the Clavien-Dindo classification [13].

### Data collection and follow-up

Pre-, per-, and postoperative data until 90 days postoperatively were recorded routinely into a prospective database. Demographic information included age, gender, Body Mass Index (BMI), American Society Anesthesiologists (ASA) score, comorbidities, and previous abdominal surgery. Surgical information included main procedure (left or right colectomy), surgical approach (laparoscopic multi or single port, robotic), duration, and combined procedures.

Nutritional assessment included measurement of current weight, an estimate of weight loss (whether voluntary or not) compared to normal weight, and calculation of Body Mass Index [ $BMI = \text{weight (kg)} / \text{height}^2 \text{ (m}^2\text{)}$ ].

A patient is considered to be malnourished, if he/she presents with a  $BMI \leq 18.5 \text{ kg/m}^2$  or a  $BMI \leq 21$  in a patient older than 70 or a recent weight loss of more than 10%.

All perioperative care items of our protocol were prospectively recorded for the ERAS group and retrospectively for the standard group.

After hospital discharge, patients in the ERAS group received a medical logbook with emergency telephone number and postoperative instructions to detect early perioperative complication and to assess compliance with the ERAS program. In addition, the postoperative nurse coordinator organized telephone interviews at days 1, 7, and 30 after discharge to record all medical problems and to ensure patient's satisfaction with return home and nursing care. Patients in the standard group only received nurse coordinator and emergency telephone numbers. Both groups attended a follow-up outpatient evaluation at 7–10 days after discharge. Any hospitalization of the patient within 30 days post surgery, after being discharged home, was considered a readmission. Primary LOS was defined as the number of nights spent in hospital after surgery, whereas total LOS was defined as the number of nights spent in the hospital, including nights after readmission within 30 days after surgery. To define the influence of complications on postoperative recovery and hospital stay, all adverse events in the postoperative period were recorded prospectively.

### Enhanced recovery after surgery protocol

Planning for an ERAS protocol in our institution began through the existing multidisciplinary Department of Mini-Invasive Surgery and with the help of a piloting committee, including surgeons, anesthetists, nursing staff, and dieticians. A standardized patient's clinical pathway was developed, in

accordance with the ERAS recommendations and published guidelines [14, 15], and it defined more than 20 perioperative standard care elements (Table 1). Regular meetings were

arranged to allow members of the department to monitor progress and pinpoint impediments to implementation of the core protocol. Overall compliance to 20 items was assessed

**Table 1** Demographic and clinic data

	Overall ( <i>n</i> = 320)		Standard group ( <i>n</i> = 160)		ERAS group ( <i>n</i> = 160)		<i>P</i> value
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	
Gender							
Male	157	49.1	84	52.5	73	45.6	0.22
Female	163	50.9	76	47.5	87	54.4	
Age (years), median (min–max)	67.4	(26–93)	67.5	(28–93)	67.3	(26–91)	0.24
Age group							
< 70 years	190	59.4	94	58.75	96	60.0	0.82
≥ 70 years	130	40.6	66	41.25	64	40.0	
ASA							
Score 1–2	262	81.9	124	77.5	138	86.25	0.04
Score 3–4	58	18.1	36	22.5	22	13.75	
Comorbidity	181	56.6	92	57.5	89	55.6	0.8
Cardiovascular	138	43.1	71	44.4	67	41.9	
Respiratory	59	18.4	30	18.7	29	18.1	
Diabetes	34	21.2	16	10	18	11.2	
BMI (kg/m <sup>2</sup> ), median (min–max)	24.6	(16.6–42.4)	24.6	(16.6–41)	24.8	(16.8–42.4)	0.85
BMI group							
< 30 kg/m <sup>2</sup>	268	83.75	135	84.4	133	83.1	0.76
≥ 30 kg/m <sup>2</sup>	52	16.25	25	15.6	27	16.9	
Previous abdominal surgery	156	48.7	77	48.1	79	49.4	0.82
Neoadjuvant chemotherapy	48	5.1	22	13.8	26	16.3	0.53
Surgical procedure							
Right colectomy	154	48.1	86	53.75	68	42.5	0.04
Extracorporeal anastomosis	70	45.5	49	57	33	48.5	
Intracorporeal anastomosis	84	54.5	37	43	35	51.5	
Left colectomy	166	51.9	74	46.25	92	57.5	
Surgical approach							
Robotic	29	9.1	2	1.3	27	16.9	< 0.01
Multiport laparoscopy	209	65.3	109	68.1	100	62.5	
Single-port laparoscopy	82	25.6	49	30.6	33	20.6	
Combined procedure	63	19.7	34	21.25	29	18.1	0.57
Operative time (min), median (min–max)	222.5	(100–522)	210	(120–413)	248	(100–522)	< 0.01
Conversion to open	14	4.4	9	5.6	5	3.1	0.27
90 D- Postoperative complication	89	27.8	55	34.4	34	21.25	< 0.01
Clavien Dindo I–II	76	23.75	49	30.6	27	16.9	< 0.01
Clavien Dindo III	13	4.1	6	3.75	7	4.4	0.78
Primary hospitalization duration (days), mean (SD)	6.5	(2.8)	7.5	(3.0)	5.4	(2.2)	< 0.01
Total hospitalization duration (days), mean (SD)	7.0	(4.6)	8.2	(5.4)	5.8	(3.1)	< 0.01
Reoperation	8	2.5	5	3.1	3	1.9	0.47
Readmission	23	7.2	10	6.25	13	8.1	0.52
Clavien Dindo I–II	16	5	5	3.1	11	6.9	
Clavien Dindo III	7	2.2	5	3.1	2	1.2	
Non scheduled consultation	22	6.9	10	6.25	12	7.5	0.66

ASA American Society of Anesthesiologists, BMI Body Mass Index, SD standard deviation

and expressed as a percentage, and good compliance was defined as  $\geq 80\%$  score per criterion and/or per patient.

In the ERAS group, postoperative goals are communicated each day with the patient and multidisciplinary care team, aiming for discharge by postoperative day 2, if deemed clinically safe. The following discharge criteria remained unchanged from prior to program implementation: good pain control on oral analgesics (paracetamol, opiate), tolerance of solid food, passage of first flatus, no signs of infection (temperature  $T < 38^\circ\text{C}$ , white blood cells  $< 10,000\text{ G/L}$ , pulse rate  $< 120/\text{min}$ ), adequate mobilization and self-care, and patient accepting discharge.

### Statistical analysis

All statistical analyses were performed at the significance level  $\alpha = 0.05$  and with the SAS<sup>®</sup> 9.3 and R 3.3.2 softwares. Data were summarized by means, medians, ranges, standard deviations (SD), counts, and frequencies as appropriate. Characteristics of the ERAS and standard groups were compared by using Chi-square or Fisher's exact tests for qualitative variables, and Wilcoxon's tests for quantitative variables. Subgroup analyses were performed for postoperative morbidity (overall, Dindo Clavien 1–2 and 3–4), total LOS, readmission rate, and compliance with the ERAS program, in subpopulations defined by risk factors: elderly ( $\geq 70$  years old), male sex, obesity ( $\text{BMI} \geq 30\text{ kg/m}^2$ ), malnutrition, ASA score of 3–4, metastatic disease and/or neoadjuvant chemotherapy, and right colectomy. All risk factors were included as independent variables along with the group (ERAS vs standard) in a multivariate logistic model for overall postoperative morbidity. The Odds Ratios (OR) of overall postoperative morbidity of the ERAS group, compared to the standard, were estimated, respectively in the global population and in the subgroups, along with their Wald's bilateral confidence intervals and  $p$ -values. These estimations were displayed in a forest plot built by using the *forestplot* package v1.7.2 for R. No correction for multiple comparisons was applied.

### Results

A total of 320 consecutive patients underwent elective colorectal cancer resection at the Institut Paoli Calmettes between June 2013 and October 2017. The 160 patients in the standard group (control) received standard care and, from January 2016, 160 patients in the ERAS group underwent the ERAS program. Relevant patient characteristics and operative parameters are shown in Table 1. There were no statistically significant differences in age, sex, and BMI. There was a significantly higher rate of ASA 3–4 patients (22.5% vs. 13.75%,  $p = 0.04$ ) in the standard group.

In general, the study population was mostly elderly and  $\text{ASA} \geq 2$ , reflecting significant comorbidity. Regarding surgical variables, there was a preponderance of right-sided resections in the standard group ( $n = 86$ , 53.8%), compared to the ERAS group ( $n = 68$ , 42.5%) ( $p = 0.03$ ). It probably explains the shorter median operative time in this group (210 min vs. 248 min,  $p < 0.01$ ). A total of 63 combined procedure was performed, involving mainly liver wedge resections and/or cholecystectomy with left gastric artery ligation (to facilitate percutaneous hepatic artery port-catheter insertion) for synchronous metastases ( $n = 17$  in the standard group and 15 in the ERAS group), adnexectomy ( $n = 7$  and 6 respectively), or extended bowel resection ( $n = 7$  and 3, respectively).

### Outcomes

Regarding primary outcome, the overall complication rate was significantly lower in the ERAS group (34.4% vs. 21.25%,  $\text{OR} = 0.52$  [0.31–0.85],  $p = 0.002$ ) up to 90 days after discharge. This conclusion was confirmed and strongly robust in multivariate analysis ( $\text{OR} = 0.56$  [0.33–0.96],  $p = 0.03$ ) (Table 2). The anastomotic complication and reintervention rates are comparable between the two groups. No patient developed Clavien-Dindo grade IV or V complications. The significant decrease in global morbidity is mirrored by the decrease in minor complications.

A significant difference in length of postoperative stay between the two groups was observed. The mean total LOS was 5.8 days for the ERAS group versus 8.2 days for the standard group ( $p < 0.001$ ). Median total LOS was significantly reduced from 7-day (range 4–58) hospital stay before implementation to 5 days (range 2–26) after implementation ( $p < 0.0001$ ). No differences were found in the nonscheduled consultation and readmission rates between the two groups.

**Table 2** Multivariate analysis of the overall postoperative morbidity

Contrast	Odds ratio [95% CI]	$P$ value
ERAS group versus standard group	0.56 [0.33–0.96]	0.03
Elderly versus no elderly (age $< 70$ )	0.77 [0.44–1.33]	0.35
Male versus female	1.58 [0.93–2.68]	0.09
Obese versus no obese ( $\text{BMI} < 30$ )	0.61 [0.29–1.27]	0.18
Malnutrition versus no malnutrition	0.50 [0.20–1.26]	0.14
ASA 3–4 versus ASA 1–2	2.88 [1.50–5.53]	$< 0.01$
Metastatic disease and/or neoadjuvant chemotherapy versus absence	1.26 [0.66–2.39]	0.48
Right colectomy versus left colectomy	1.88 [1.11–3.19]	0.02

ERAS enhanced recovery after surgery, ASA American Society of Anaesthesiologists, BMI Body Mass Index

## Protocol compliance

In the present series, overall median adherence to the ERAS protocol was 90% per patient in the ERAS group and was evaluated a posteriori at 50% in the standard group ( $p < 0.001$ ). Table 3 summarizes results for each specific item.

## Subgroup analysis

We evaluated the results more specifically in patients at risk of medical or surgical complications after colectomy [16, 17]. Analyses from subgroups gave similar results (Table 4) with a significant reduction of overall morbidity in all ERAS subgroups except in obese patients (Fig. 1). There was also a significant reduction of total LOS in all subgroups. Readmission rate was comparable between subgroups, except in metastatic patients. Notably, overall compliance was above 85% in all subgroups.

## Discussion

The present study demonstrates that ERAS implementation in colonic oncological surgery is associated with decreased overall morbidity and LOS, without an increase in readmission rate, even in a high-volume cancer center where laparoscopy has been routinely performed for 15 years.

Despite the existence of high volume and quality of literature regarding ERAS programs in colonic surgery in recent years [6, 18], the recovery benefits following colonic oncological surgery remain controversial when laparoscopy is already implemented [8, 12].

FT programs have been evaluated in large-scale multicenter trials [8, 9, 11, 12, 19], but we believe that randomization is difficult to apply in this specific case. The feasibility of including patients benefiting from the ERAS program or standard care within the same service can be raised. To avoid a cross-over treatment by the nursing staff in the LAFA study [8], patients were admitted either to a ward providing FT care or a ward providing standard care,

**Table 3** ERAS protocol and compliance

	Overall ( <i>n</i> = 320)		Standard group ( <i>n</i> = 160)		ERAS group ( <i>n</i> = 160)		<i>P</i> value
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	
Compliance with ERAS protocol							
Median number of item/patient	15	(6–20)	10	(6–17)	18	(14–20)	< 0.001
Rate	75	(30–100)	50	(30–85)	90	(70–100)	
Specific information	161	50.3	7	4.4	154	96.25	< 0.001
Immunonutrition	306	95.6	150	93.75	156	97.5	0.1
No bowel preparation	203	63.4	92	57.5	111	69.4	0.03
Limited fast	252	78.75	97	60.6	155	96.9	< 0.001
Carbohydrate loading	137	42.8	2	1.25	135	84.4	< 0.001
No long-acting sedation	187	58.4	53	33.1	134	83.75	< 0.001
Antibiotic prophylaxis	320	100	160	100	160	100	
IV Lidocaine	177	55.3	20	12.5	157	98.1	< 0.001
Laparoscopic approach	320	100	160	100	160	100	
Zero fluid balanced	156	48.75	3	1.9	153	95.6	< 0.001
Corticosteroid	192	60	37	23.1	155	96.9	< 0.001
PONV	168	52.5	48	30	120	75	< 0.001
No abdominal or pelvic drainage	243	75.9	120	75	123	76.9	0.69
Normothermia	305	95.6	151	94.4	154	96.3	0.43
Preventive opioid-sparing multimodal analgesia	195	58.1	59	36.9	136	85	< 0.001
Free diet on POD 0	176	55	25	15.6	151	94.4	< 0.001
Early mobilization out of bed on POD 0	284	88.75	125	78.1	159	99.4	< 0.001
Early termination of IV fluid infusion	174	54.4	41	25.6	133	83.1	< 0.001
TED prophylaxis	320	100	160	100	160	100	
Avoidance of nasogastric tube	290	90.6	132	82.5	158	98.75	< 0.001
Early termination of urinary drainage	192	60	54	33.75	138	86.25	< 0.001

PONV postoperative nausea/vomiting, IV intravenous, TED thromboembolic disease

**Table 4** Subgroup analysis

Category	Results	Standard group	ERAS group	<i>P</i> value
Age $\geq$ 70 ( <i>n</i> = 130)	Overall morbidity	25/66 (37.9%)	11/64 (17.2%)	< 0.01 <sup>b</sup>
	Clavien 1–2	23/66 (34.9%)	9/64 (14.1%)	< 0.01 <sup>b</sup>
	Clavien 3–4	2/66 (3.0%)	2/64 (3.1%)	1 <sup>b</sup>
	THS (days)	9.0 days ( $\pm$ 7.3)*	6.3 days ( $\pm$ 4.2)	< 0.01 <sup>a</sup>
	Readmission	3/66 (4.6%)	5/64 (7.8%)	0.49 <sup>b</sup>
	Compliance	51.2% ( $\pm$ 11.2)*	89.8% ( $\pm$ 8.0)	< 0.01 <sup>a</sup>
Male sex ( <i>n</i> = 163)	Overall morbidity	31/76 (40.8%)	22/87 (25.3%)	0.04
	Clavien 1–2	28/76 (36.8%)	19/87 (21.8%)	0.03
	Clavien 3–4	3/76 (4.0%)	3/87 (3.5%)	1
	THS	8.8 ( $\pm$ 6.9)	6.2 ( $\pm$ 3.8)	< 0.01
	Readmission	6/76 (7.9%)	11/87 (12.6%)	0.32
	Compliance	51.5% ( $\pm$ 11.7)	90.5% ( $\pm$ 7.7)	< 0.01
BMI $\geq$ 30 ( <i>n</i> = 52)	Overall morbidity	7/25 (28%)	6/27 (22.2%)	0.63
	Clavien 1–2	5/25 (20%)	6/27 (22.2%)	0.84
	Clavien 3–4	2/25 (8%)	0/27 (0%)	0.23
	THS (days)	8.4 days ( $\pm$ 4.4)	5.3 days ( $\pm$ 1.8)	< 0.01
	Readmission	2/25 (8%)	1/27 (3.7%)	0.6
	Compliance	52.8% ( $\pm$ 14.3)	88.9% ( $\pm$ 6.6)	< 0.01
Malnutrition ( <i>n</i> = 38)	Overall morbidity	6/18 (33.3%)	1/20 (5.0%)	0.04
	Clavien 1–2	5/18 (27.8%)	1/20 (5.0%)	0.05
	Clavien 3–4	1/18 (5.6%)	0/20 (0%)	0.47
	THS	9.7 days ( $\pm$ 12.2)	5.1 days ( $\pm$ 1.5)	< 0.01
	Readmission	1/18 (5.6%)	0/20 (0%)	0.47
	Compliance	51.4% ( $\pm$ 11.4)	90.5% ( $\pm$ 8.1)	< 0.01
ASA score 3–4 ( <i>n</i> = 58)	Overall morbidity	21/36 (58.3%)	7/22 (31.8%)	0.049
	Clavien 1–2	18/36 (50%)	6/22 (27.3%)	0.09
	Clavien 3–4	3/36 (8.3%)	1/22 (4.6%)	1
	THS	11.5 days ( $\pm$ 9.3)	7.1 days ( $\pm$ 4.9)	< 0.01
	Readmission	5/36 (13.9%)	1/22 (4.6%)	0.39
	Compliance	49.6% ( $\pm$ 10.9)	87.7% ( $\pm$ 7.5)	< 0.01
Metastatic disease and/or neoadjuvant chemotherapy ( <i>n</i> = 66)	Overall morbidity	13/27 (48.2%)	7/39 (18.0%)	< 0.01
	Clavien 1–2	12/27 (44.4%)	5/39 (12.8%)	< 0.01
	Clavien 3–4	1/27 (3.7%)	2/39 (5.1%)	1
	THS	9.5 d ( $\pm$ 5.1)	5.5 d ( $\pm$ 2.0)	< 0.01
	Readmission	5/27 (18.5%)	1/39 (2.6%)	0.04
	Compliance	50.2% ( $\pm$ 8.6)	90.1% ( $\pm$ 7.3)	< 0.01
Right colectomy ( <i>n</i> = 154)	Overall morbidity	36/86 (41.9%)	18/68 (26.5%)	0.047
	Clavien 1–2	33/86 (38.4%)	15/68 (22.1%)	0.03
	Clavien 3–4	3/86 (3.5%)	3/68 (4.4%)	1
	THS	8.8 days ( $\pm$ 6.6)	6.1 days ( $\pm$ 3.1)	< 0.01
	Readmission	6/86 (7%)	5/68 (7.4%)	1
	Compliance	52% ( $\pm$ 10.4)	91.9% ( $\pm$ 7.4)	< 0.01

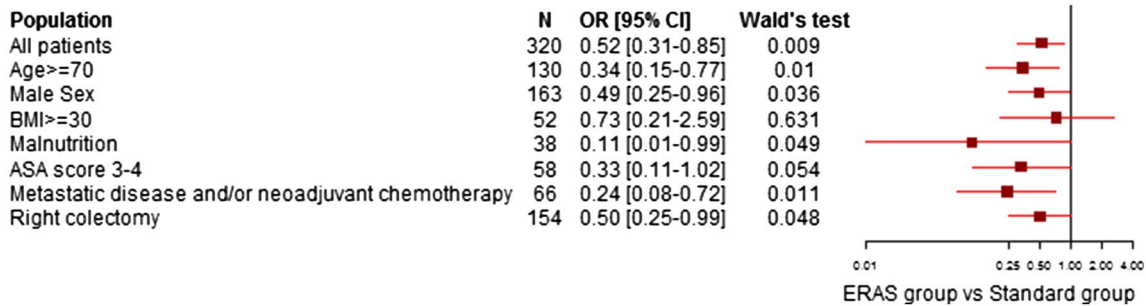
BMI Body Mass Index, ASA American Society of Anaesthesiologists, THS total hospital stay

<sup>a</sup>Mann-Whitney *u* test

<sup>b</sup>Chi-square or exact Fisher's test

\*Mean ( $\pm$  standard deviation)





**Fig. 1** Forest plot of complication rates in subgroup analysis

depending on randomization. It is clear that such binding measures are difficult to apply in most hospitals.

Moreover, it has been demonstrated that improved adherence to the ERAS programs was significantly associated with shorter hospital stay following major colorectal cancer surgery and lower morbidity rate. Thus, the compliance of the ERAS protocol in large-scale multicenter trials including patients operated by laparoscopy and open surgery is low [7, 8, 12] or unknown [15, 20], making the assessment of the impact of ERAS programs over laparoscopy difficult, since they influence each other in reducing morbidity and LOS, confounding the interpretation.

A recent meta-analysis concludes that laparoscopic colorectal resection significantly reduced total LOS and number of complications when compared with open surgery in the settings of suboptimal ERAS programs [18]. However, the benefits of laparoscopic colorectal resection remain to be proved within optimal ERAS programs.

Among the randomized studies, in which patients were optimized within the ERAS program, none actually compared the postoperative results after elective laparoscopic colectomy. The LAFA-trial failed to demonstrate that the combination of laparoscopic surgery and FT protocol is the optimal management for patients undergoing elective colorectal surgery. They reported a significant decrease of postoperative LOS in the FT and laparoscopy groups than in the other groups, but failed to show any impact on postoperative morbidity rate [8]. In this study, the surgeons were not all experienced in laparoscopic colorectal surgery, and there were significant exclusions, including metastatic disease, chemotherapy, comorbidities, and BMI > 30 kg/m<sup>2</sup>.

Our study not only involved experienced surgeons but also included a wide range of patients without exclusion criteria; thus, it is more representative of daily practice. We wanted to evaluate the impact of the implementation of an ERAS protocol in a laparoscopy expert center to “eliminate” the effects of laparoscopy. In our study period, only 11 patients operated by laparotomy were excluded. In addition, we chose to include only colonic resection.

Another potential confounding factor is the disproportionate inclusion of both rectal and colon cancer patients in some studies [9, 11, 12], even though rectal cancer patients are at a higher risk of postoperative short-term complications than colon cancer patients and require a different protocol, notably in relation to diverting stoma. Thus, we only included colonic resection.

In our series, overall compliance rate was at 80–100% according the different criteria and led to a significant reduction of morbidity and LOS. To overcome organizational difficulties, we adopted a collegial approach in implementing our ERAS protocol. Our protocol has been adopted at the same time for all patients undergoing minimal invasive surgery, as part of a hospital project. We believe that the homogenization of practices across all services has made it possible to limit the learning curve of the ERAS program over time, to obtain optimal compliance and to assess its real impact on outcomes in patients undergoing colonic cancer resection.

The majority of the studies describe a reduction in the duration of hospitalization as the main criterion [8–12] but without a significant decrease in postoperative morbidity [8, 9, 12]. Secondary analyses in these studies support the use of laparoscopic resection within an ERAS program as the main factor associated with decreased morbidity, implying that other elements are less important. In the LAFA trial, in addition to laparoscopy, early mobilization and early dietary intake were the only factors independently associated with shortened total LOS. Some authors consider that early mobilization and initiation of oral diet are now the standard of care and the addition of a full multimodal FT management might not reduce postoperative morbidity after laparoscopic colorectal surgery [12].

Certain elements are probably more important than others, but we contend that the implementation of the ERAS program implies a total care reorganization focused on the patient, according to a “clinical pathway.” It includes not only postoperative measures but also better perioperative management of patients with the anticipation of the patient’s “fragilities,” which will limit surgical stress and

its consequences. Thus, the reduction in the LOS is the consequence of a better optimization of the medical and administrative care but especially the consequence of a reduction of the postoperative morbidity. In comparison with the results in the existing literature, overall morbidity was relatively high in the standard group. This can be explained by the complete prospective data collection up to 90 days after surgery and the inclusion of all patients undergoing laparoscopic colonic cancer resection regardless of age, comorbidities, or cancer staging.

We observe no difference in terms of severe morbidity and anastomotic complications, but a significant diminution of minor morbidity Clavien I–II (30.6% vs. 16.9%,  $p < 0.01$ ). Additional Table 5 summarizes the postoperative morbidity of each group.

We believe that only a very high compliance rate will allow us to obtain an additional gain in the patients operated for laparoscopic colon cancer. Our study shows that ERAS is feasible with a very high compliance rate and especially beneficial for all these patients, including the high risk groups often excluded from laparoscopy and ERAS trials (Table 2) (elderly patients, obese [12], metastatic or neoadjuvant chemotherapy [8–10, 12], ASA 3 [9, 15]). Only obese patients have no significant impact on morbidity, but the morbidity has a tendency to decrease in these patients. In fact, as suggested by studies involving older participants [20, 21] and stage IV colorectal cancer [22], frail patients benefit even more from ERAS measures mentioned above, as cultural barriers are more difficult to cross for these patients.

The limitation of this study is that it was not designed as a randomized study but as a historic comparative study; however the compared groups were homogeneous in terms of demographic and clinical characteristics. The implementation of the ERAS protocol required a radical change in care practices in our institution, and it would have been very difficult or impossible for us to manage patient's care according two different protocols in the same period.

## Conclusion

Our results suggest an improvement in terms of outcome compared to pilot series or randomized trial involving selected patients and specific staff inside a department or an institution, which does not necessarily ensure optimal compliance and can represent an additional organizational barrier. The concomitant implementation of an ERAS protocol for all patients undergoing laparoscopic surgery at our institution was a step toward standardization of practices, enabling us to obtain higher compliance rates from the start and to explain our favorable results.

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## Compliance with ethical standards

**Disclosure** H el ene Meillat, Cl ement Brun, Christophe Zemmour, C ecile de Chaisemartin, Olivier Turrini, Marion Faucher, and Bernard Lelong have no conflicts of interest or financial ties to disclose.

## References

- Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazernier G, Bonjer HJ, Haglind E, Pahlman L, Cuesta MA, Msika S, Morino M, Lacy AM (2005) Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol* 6:477–484
- Braga M, Vignali A, Gianotti L, Zuliani W, Radaelli G, Gruarin P, Dellabona P, Di Carlo V (2002) Laparoscopic versus open colorectal surgery: a randomized trial on short-term outcome. *Ann Surg* 236:759–766
- Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, Heath RM, Brown JM (2005) Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet* 365:1718–1726
- Clinical Outcomes of Surgical Therapy Study Group (2004) A comparison of laparoscopically assisted and open colectomy for colon cancer. *N Engl J Med* 350:2050–2059
- Lelong B, Bege T, Esterni B, Guiramand J, Turrini O, Moutardier V, Magnin V, Moges G, Pernoud N, Blache JL, Giovannini M, Delperro JR (2007) Short-term outcome after laparoscopic or open restorative mesorectal excision for rectal cancer: a comparative cohort study. *Dis Colon Rectum* 50:176–183
- Greco M, Capretti G, Gemma M, Pecorelli N, Braga M (2013) Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. *World J Surg* 38:1531–1541
- Kennedy RH, Francis EA, Wharton R, Blazeby JM, Quirke P, West NP, Dutton SJ (2014) Multicenter randomized controlled trial of conventional versus laparoscopic surgery for colorectal cancer within an enhanced recovery programme: EnROL. *J Clin Oncol* 32:1804–1811
- Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF, Gerhards MF, van Wagenveld BA, van der Zaag ES, van Geloven AA, Sprangers MA, Cuesta MA, Bernelman WA (2011) Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). *Ann Surg* 254:868–875
- Gatt M, Anderson AD, Reddy BS, Hayward-Sampson P, Tring IC, MacFie J (2005) Randomized clinical trial of multimodal optimization of surgical care in patients undergoing major colonic resection. *Br J Surg* 92:1354–1362
- Feng F, Li XH, Shi H, Wu GS, Zhang HW, Liu XN, Zhao QC (2014) Fast-track surgery combined with laparoscopy could improve postoperative recovery of low-risk rectal cancer patients: a randomized controlled clinical trial. *J Dig Dis* 15:306–313
- Khoo CK, Vickery CJ, Forsyth N, Vinal NS, Eyre-Brook IA (2007) A prospective randomized controlled trial of multimodal



- perioperative management protocol in patients undergoing elective colorectal resection for cancer. *Ann Surg* 245:867–872
12. Maggiori L, Rullier E, Lefebvre JH, Regimbeau JM, Berdah S, Karoui M, Loriau J, Alves A, Vicaut E, Panis Y (2017) Does a combination of laparoscopic approach and full fast track multimodal management decrease postoperative morbidity? A multicentre randomized controlled trial. *Ann Surg* 266:729–737
  13. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 240:205–213
  14. Lassen K, Soop M, Nygren J, Cox PB, Hendry PO, von Meyenfeldt MF, Fearon KC, Revhaug A, Ljungqvist O, Lobo DN, Dejong CH, Enhanced Recovery After Surgery (ERAS) Group (2009) Consensus review of optimal perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Arch Surg* 144:961–969
  15. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, McNaught CE, MacFie J, Liberman AS, Soop M, Hill A, Kennedy RH, Lobo DN, Fearon K, Ljungqvist O, Enhanced Recovery After Surgery Society, European Society for clinical Nutrition and Metabolism (ESPEN), International Association for Surgical Metabolism and Nutrition (2013) Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *World J Surg* 37:259–284
  16. Parc Y, Reboul-Marty J, Lefebvre JH, Shields C, Chafai N, Tiret E (2016) Factors influencing mortality and morbidity following colorectal resection in France. Analysis of a national database (2009–2011). *Colorectal Dis* 18:205–213
  17. Stillwell AP, Buettner PG, Siu PK, Stitz RW, Stevenson AR, Ho YH (2011) Predictors of postoperative mortality, morbidity, and long-term survival after palliative resection in patients with colorectal cancer. *Dis Colon Rectum* 54:535–544
  18. Zhuang CL, Ye XZ, Zhang XD, Chen BC, Yu Z (2013) Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum* 56:667–678
  19. ERAS Compliance Group (2015) The impact of enhanced recovery protocol compliance on elective colorectal cancer resection: results from an international registry. *Ann Surg* 261:1153–1159
  20. Wang Q, Suo J, Jiang J, Wang C, Zhao YQ, Cao X (2012) Effectiveness of fast-track rehabilitation vs conventional care in laparoscopic colorectal resection for elderly patients: a randomized trial. *Colorectal Dis* 14:1009–1013
  21. Bardram L, Funch-Jensen P, Kehlet H (2000) Rapid rehabilitation in elderly patients after laparoscopic colonic resection. *Br J Surg* 87:1540–1545
  22. Pedziwiatr M, Pisarska M, Kisielewski M, Major P, Wierdak M, Natkaniec M, Budzynski A (2015) Enhanced recovery after surgery (ERAS) protocol in patients undergoing laparoscopic resection for stage IV colorectal cancer. *World J Surg Oncol* 13:330

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