ORIGINAL ARTICLE

Does enhanced recovery improve the survival rates of patients 3 years after undergoing surgery to remove a tumor in the colon?

P. Viannay [1,2] · A. Hamy [1,2,3] · R. Jaouen [1,2] · F. X. Caroli-Bosc [2,3,4] · C. Luel [2] · S. Vasseur [2] · M. Levaillant [5] · J. F. Hamel [2,5] · Aurélien Venara [1,2,3,6]

Abstract

Purpose The advantages of enhanced recovery programs (ERP) after colorectal surgery for morbidity and length of stay are well known. On a longer term, evidence is much more limited. The aim of this study is to determine the impact of ERP on survival after 3 years of follow-up, following colorectal cancer surgery.

Methods All the patients undergoing resection for colorectal cancer between the years 2010 and 2014 were included. Patients were classified according to their compliance with the ERP (< 70 or $\geq 70\%$).

Results Among the 206 patients included during the period, 129 were male (62.6%). The 3-year overall survival rate was 70.4% (145 patients) and relapse-free survival was 59.2% (122 patients). The survival after 3 years was influenced by the initial metastatic status ($p < 0.0001$), operative morbidity ($p < 0.001$), and the presence of peritumoral emboli ($p = 0.006$). However, the compliance with the ERP $\geq 70\%$ did not influence overall survival ($p = 0.63$), nor relapse-free survival ($p = 0.93$). The same observations were found among the "at-risk" population (synchronous metastasis and postoperative complication).

Conclusion The ERP does not seem to influence the 3-year relapse-free survival after colorectal resection for cancer.

Keywords Enhanced recovery · Colorectal cancer · Global survival · Disease-free survival

Introduction

Bowel resection surgery is common, with 40,000 colon resection procedures every year in France, 70% of which are aimed at removing cancer [1]. The outcomes of this surgery, which initially had a morbidity rate of 2 to 20%, of which 2 to 6% concerned fistulas, have changed thanks to enhanced recovery after surgery (ER) programs that were introduced in the 1990s by H. Kehlet [2]. Their many short-term, postoperative benefits are well known, such as reduced morbidity, mortality, time spent in hospital, and cost of treatment [3–5]. In fact, the literature reports that hospitalization periods have reduced by 2.94 days and the cost of treatment per patient has reduced by 1600 euros [6], as well as a 50% reduction in morbidity (CI [0.35; 0.72]) by reducing the rate of readmissions from 22 to 9% [3, 4, 7, 8].

The longer-term benefits are still under review. These programs, which were initially developed for bowel surgery, reduced postoperative immunodepression and inflammation [9–11]. This could also be beneficial for cancer surgeries as it reduces the risk of relapse in the medium to long-term. As far as we know, there are currently only two studies that report the long-term benefits. Gustafsson et al. [12] also concluded that 70% compliance with ER programs could reduce the risk of death after 5 years with a hazard ratio (HR) of 0.58 (95% confidence interval (95% CI) = 0.39–0.88). Furthermore, Curtis et al. [13] note that a combined approach of a laparoscopy and an ER program would increase the chances of survival after 5 years with an HR of 1.55 (95% CI = 0.16–2.06).

✉ Aurélien Venara
  auvenara@yahoo.fr

1 Department of Visceral and Endocrinal Surgery, CHU Angers, 4 rue Larrey, 49933 Angers Cedex 9, France

2 Département de Médecine, UFR Santé d'Angers, Angers, France

3 EA HIFIH, Angers, France

4 Department of Digestive and Liver Disease, CHU Angers, 4 rue Larrey, 49933 Angers Cedex 9, France

5 Department of Biostatistics, CHU Angers, 4 rue Larrey, 49933 Angers Cedex 9, France

6 UMR INSERM 1235, TENS, Université de Nantes, Rue Alexis Ricordeau, 44000 Nantes, France

Therefore, improving the chances of long-term survival could be added to the many advantages of ER programs and provide new arguments in favor of extending these programs to other areas in current practice. However, there are not enough of these high-quality studies, which still need to be verified on other sample groups.

The primary objective of this study was to evaluate the impact of following a postoperative enhanced recovery program on surviving 3 years after surgery.

The secondary objectives were to evaluate the impact that following an ER program has on survival without relapse for 3 years after surgery, to evaluate the factors influencing survival for 3 years after surgery, and to evaluate the impact of ER programs on at-risk groups.

Equipment and method

Patients

This monocentric, retrospective study included all patients who underwent a colectomy as a result of cancer in the visceral surgery department of our university hospital. The colectomy may have been a scheduled surgery or an emergency procedure. The cancer diagnosis was confirmed by the anatomic pathology department. The inclusion period was from January 1, 2010 to December 31, 2014. The list of patients was taken from the hospital's encrypted electronic database.

Patients were excluded if they did not meet our inclusion criteria, declined to participate in the study, or did not have a follow-up after 3 years (Fig. 1).

The design of this study was approved by our local ethics committee and the database is registered with the *Commission Nationale de l'Informatique et des Libertés* (CNIL—National Commission for Informatics and Liberties) under the number 2017-MR-03-11.

Methodology

The main evaluation criterion was overall survival for 3 years and was defined by whether the patient was living or deceased 3 years after surgical treatment.

The secondary evaluation criterion was survival without relapse for 3 years, defined by the date of relapse assessed by a CT scan of the thoracic, abdominal, or pelvic regions carried out every 6 months, as recommended by the *Fédération Française de Cancérologie Digestive* (French Federation for Digestive Oncology) [14].

Data concerning survival, relapses, and the date and cause of death was immediately recorded in files when it became available or was gathered by telephone from the patients' general practitioners, oncologists, or gastroenterologists.
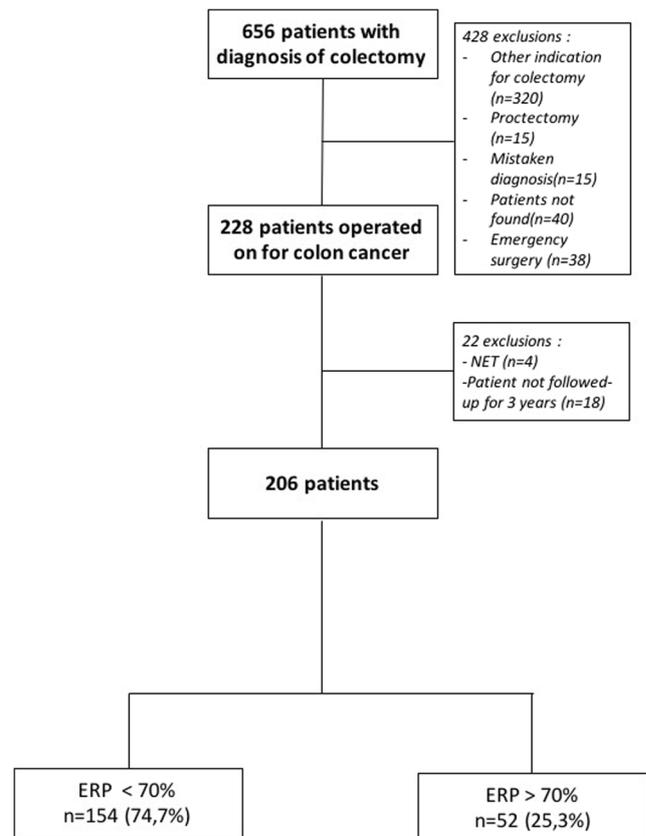

Fig. 1 Flow-chart of our population. NET, neuroendocrine tumor

Data

The following data was collected:

– Demographic information such as age, sex, body mass index (BMI), medical history, American Society of Anesthesiology (ASA) score, and use of anticoagulants.
– Surgical data such as the surgical approach and type of surgery.
– Anatomic pathology data such as the quality of resection (R status), the presence of peritumoral emboli or perineural invasions, and the status of microsatellite instability (MSI).
– Short- and medium-term follow-up: postoperative morbidity, compliance with enhanced recovery programs, date of relapse, and date of death.

Postoperative morbidity was defined as anything other than normal and expected outcomes that occurred within 30 days of surgery. Complications that were not directly linked to surgical procedures were classed as medical complications.

Perioperative care

An ER program was introduced into the department in June 2012. It follows the recommendations of the *Société*

Française de Chirurgie Digestive (SFCD—French Society of Digestive Surgery) and the French Society of Anesthesia & Intensive Care Medicine (SFAR) [15].

In order to assess compliance, the percentage of compliance was calculated using the data recorded in Table 1 (number of items followed/number of markers ($n = 13$)).

The literature concludes that enhanced recovery programs are considered to have been followed if at least 70% of the recommendations were followed, which could result in reduced morbidity and mortality by decreasing the instances of postoperative ileus [16]. Thus two groups were defined based on this 70% threshold:

- Enhanced recovery program in which more than 70% is followed ($n = 52$). This means that adherence to the different criteria chosen by SFAR and SFCD, according to current recommendations, was higher than 70%.
- Enhanced recovery program in which less than 70% is followed ($n = 154$). This means that adherence to less than 70% of the different, recommendations stated above was observed.

Statistical analysis

Qualitative variables were recorded as percentages and compared using a Chi^2 test or Fisher's exact test. Quantitative variables were recorded as averages (+/− standard deviation) and compared using the Student's t test or the Mann-Whitney U test.

The survival rates of the different groups were compared using the logrank test and were represented by Kaplan-Meier's survival curve.

A value of $p < 0.05$ was considered significant.

Results

Two hundred six patients were included in the study, 129 of whom were men (62.6%). Average body mass index and age were 26.7 kg/m^2 (± 5.5) and 70.9 years (± 12.1), respectively. One hundred four patients had a right hemicolectomy (50%) and 90 had a left hemicolectomy or a sigmoid colectomy (43.7%).

Factors influencing survival

In our sample group, demographic characteristics were not associated with survival 3 years after surgery (Table 2).

On the other hand, factors that did influence survival 3 years after surgery included the stage of the tumor ($p < 0.0001$) and the presence of synchronous metastases ($p < 0.0001$) or peritumoral emboli ($p = 0.006$). Perineural invasions were more common in patients who did not survive the 3 years (43.75 vs 26.09%), but the difference was not significant ($p = 0.08$). The short-term outcomes of surgery, and morbidity in particular, were equally linked to a reduced survival rate in the 3 years after surgery ($p < 0.001$).

Relapses after 1, 2, and 3 years were associated with reduced survival rates in the 3 years after surgery ($p < 0.0001$, $p < 0.0001$, and $p < 0.0001$, respectively) (Table 3).

Comparison of the groups ER < 70% and ER ≥ 70%

There were no differences in demographics or characteristics of the tumors between the two groups (Table 4). Table 5 records postoperative morbidity within the two groups. In the short term, a reduction in the average period of hospitalization was observed in the group ≥70% (15.7 days (± 10) vs 12.2 days (± 12) ($p = 0.047$)). Furthermore, overall morbidity and the rate of postoperative anastomotic fistulas were not significantly impacted by the ER program ($p = 0.34$ and $p = 0.83$, respectively). There were fewer medical complications in the sample group ER ≥ 70% (9.6%) compared to the group ER < 70% (20.9%), but this was not significant ($p = 0.07$).

The length of hospitalization was significantly longer in the group ER < 70% than in the group ER ≥ 70% ($p = 0.047$).

Table 1 Enhanced recovery program implemented in our department

Preoperative	Intraoperative	Postoperative
Patient information[a]	Laparoscopy[a]	Premature removal of the urinary catheter[a]
No extended fasting period[a]	Prevention of nausea	Removal of the nasogastric tube in the operating theater[a]
No bowel preparation[a]	No drain[a]	Mobilization at day 0[a]
Preoperative intake of carbohydrates[a]	Multimodal analgesia	Premature removal of catheter[a]
No systematic premedication	Personalized fluid replacement plan	Respiratory stimulation
Immunonutrition	Prevention of hypothermia	Thromboprophylaxis[a]
	Dexamethasone	

[a] Data retained to assess compliance with enhanced recovery

Table 2 Surviving 3 years after surgery according to demographic information, medical history, and treatments

	Surviving 3 years (N = 145)		Not surviving 3 years (N = 61)		p value
	Mean/ actual	Standard deviation/ percentage	Mean/ actual	Standard deviation/ percentage	
Age	70.5	12.5	71.9	11	0.44
BMI	27.2	5.8	25.8	5.1	0.21
Sex					
Female	64	44.1%	23	37.7%	0.44
Male	81	55.9%	38	62.3%	
Diabetes					
Present	25	17.4%	10	16.4%	1.00
Absent	119	82.6%	51	83.6%	
Dyslipidemia					
Present	32	22.2%	17	27.9%	0.47
Absent	112	77.8%	44	72.1%	
ASA score					
1	21	14.5%	4	6.6%	0.23
2	69	47.6%	26	42.6%	
3	54	37.2%	30	49.2%	
4	1	0.7%	1	1.6%	
Hypertension (HTN)					
Present	65	44.8%	27	44.2%	1.00
Absent	80	55.2%	34	55.8%	
COPD					
Present	6	4.2%	2	3.3%	1.00
Absent	138	95.8%	59	96.7%	
Procedure carried out:					
Right hemicolectomy	72	49.7%	32	52.5%	0.45
Transverse colectomy	3	2.1%	2	3.3%	
Left hemicolectomy	40	27.6%	14	22.9%	
Sigmoidectomy	27	18.6%	9	14.7%	
LAR	3	2.1%	3	4.9%	
Hartmann's procedure	0	0%	1	1.6%	
Postoperative chemotherapy					
Present	66	45.8%	28	47.5%	0.88
Absent	78	54.2%	31	52.5%	
Anticoagulant					
Present	12	8.3%	7	11.5%	0.44
Absent	133	91.7%	54	88.5%	
Length of hospital stay	14.4	9	15.7	14.1	0.43

BMI body mass index (kg/m^2), *ASA* American Society of Anesthesiologists score, *HTN* arterial hypertension, *COPD* chronic obstructive pulmonary disease, *LAR* lower anterior resection

Survival in the 3 years after surgery

After 3 years, 145 patients were still alive (70.4%) and 122 patients had not had a relapse (59.2%). Table 6 records the survival data according to the subgroups of the sample group. Thus, ≥ 70% adherence to an ER program did not significantly improve the chances of surviving 3 years after surgery, either for the whole sample group (p = 0.63) (Fig. 2a), for patients with metastatic cancer (p = 0.67) (Fig. 2b), or for the patients with surgical complications (p = 0.61) (Fig. 2c).

There was also no change to the chances of survival without relapse in 3 years for the group that adhered fully to the

Table 3 Surviving 3 years after surgery according to the effects of surgery and anatomic pathology information

	Surviving 3 years		Not surviving 3 years		*p* value
Complications	62	42.8%	42	68.8%	*0.001*
No complications	83	57.2%	19	31.1%	
Anastomotic fistula	13	9%	5	8.2%	1
No fistula	132	91%	56	91.8%	
Resection margin					
R0	145	10%	58	98.3%	0.289
R1	0	0%	1	1.7%	
Stage					
0	2	1.4%	0	0%	*p < 0.0001*
1	18	12.8%	6	10%	
2	47	33.3%	9	15%	
3	56	39.7%	16	26.7%	
4	18	12.8%	29	48.3%	
Stage M					
M0	127	87.6%	31	50.8%	*p < 0.0001*
M1	18	12.4%	30	49.2%	
MSI					
No loss of expression	29	85.3%	6	66.7%	0.332
Loss of expression	5	14.7%	3	33.3%	
Perineural invasions	24	26.1%	14	43.7%	0.076
Peritumoral emboli	42	34.4%	29	58%	*0.006*
Relapse 1 year	11	7.6%	19	47.5%	*p < 0.0001*
Relapse 2 years	23	15.9%	22	71%	*p < 0.0001*
Relapse 3 years	23	15.9%	25	100%	*p < 0.0001*

Italic emphasis is for significant results

recovery program, whether in the overall sample group ($p = 0.93$), the patients with metastatic cancer ($p = 0.79$), or the patients with surgical complications ($p = 0.86$).

Discussion

This monocentric, retrospective study included 206 patients who underwent a colectomy as a result of cancer. Out of the study's overall sample group, 145 patients (70.4%) were still alive after 3 years and 122 had not had a relapse after 3 years (59.2%). Risk factors affecting chances of survival 3 years after surgery include advanced-stage tumors ($p = <0.0001$), synchronous metastases ($p < 0.0001$), peritumoral emboli ($p = 0.006$), and surgical complications ($p < 0.001$). The length of hospitalization was significantly longer in the group ER < 70% than in the group ER ≥ 70% ($p = 0.047$). In conclusion, whether for the overall sample group or the groups separated according to the initial status of metastatic cancer or the development of a postoperative complication, a 70% threshold of adherence to the ER program did not influence the chances of surviving the 3 years after surgery.

Firstly, our study records an overall survival rate of 70% and a survival rate without relapses of 59.2% 3 years after surgery. This is similar to the literature, which records an overall survival rate of 60% and a survival rate without relapses of 30 to 55% in the 5 years after surgery, depending on the stage of the tumor [17, 18]. In our study, the main risk factors contributing to relapses reported in the literature, such as the stage of the tumor, peritumoral emboli, synchronous metastases, or surgical complications, were closely associated with survival in our study [19]. However, the presence of perineural invasions did not significantly increase the risk of relapse in our study ($p = 0.08$) despite the fact that this was reported as a risk factor in the literature [20]. This disparity with the literature is most likely explained by the volume of missing data due to the fact that these have only recently been included as a factor in anatomic pathologists' reports.

Secondly, we have assessed the impact that long-term adherence to the program has on survival. In our overall sample group, total survival, or survival without relapse, was not influenced by following the ER program ($p = 0.63$ and $p = 0.93$, respectively). These findings conflict with the literature. In fact, Gustafsson et al. [12] note a reduced risk of death 5 years after surgery with a HR of 0.58 (95% CI = 0.39–0.88) associated with adherence of ≥ 70%. Furthermore, Curtis et al. [13] note that a combined approach of a laparoscopy and an ER program would increase the chances of survival after 5 years with an HR of 1.55 (95% CI = 0.16–2.06). This disparity may be explained by the fact these two studies include follow-ups

Table 4 Adherence to recommendations of enhanced recovery according to demographic information, medical history, and treatments

Adherence to the recommendations	Ratio ≥ 70%		Ratio < 70%		p value
	Mean/ actual	Standard deviation/ percentage	Mean/ actual	Standard deviation/ percentage	
Age	68.2	12.6	71.8	11.8	0.06
BMI	27.6	6.5	26.1	4.8	0.13
Sex					
Female	19	36.5%	68	44.2%	0.42
Male	33	63.5%	86	55.8%	
Diabetes					
Present	10	19.2%	25	16.3%	0.67
Absent	42	80.8%	128	83.7%	
Dyslipidemia					
Present	16	30.8%	33	21.6%	0.19
Absent	36	69.2%	120	78.4%	
ASA score					
1	4	7.7%	21	13.7%	0.10
2	23	44.2%	72	47.1%	
3	23	44.2%	60	39.2%	
4	2	3.9%	0	0%	
Hypertension (HTN)					
Present	25	48.1%	67	43.5%	0.63
Absent	27	51.9%	87	56.5%	
COPD					
Present	4	7.8%	4	2.6%	0.11
Absent	47	92.2%	150	97.4%	
Procedure carried out:					
Right hemicolectomy	27	51.9%	77	50%	0.61
Transverse colectomy	0	0%	5	3.2%	
Left hemicolectomy	13	25%	41	26.6%	
Sigmoidectomy	9	17.3%	27	17.5%	
LAR	3	5.8%	3	1.9%	
Hartmann's procedure	0	0%	1	0.6%	
Postoperative chemotherapy					
Present	24	47.1%	70	46.1%	1
Absent	27	52.9%	82	53.9%	
Anticoagulant					
Present	9	17.3%	10	6.5%	0.27
Absent	43	82.7%	144	93.5%	
Length of hospital stay	12.2	12	15.7	10.2	*0.047*

BMI body mass index (kg/m^2), *ASA* American Society of Anesthesiologists score, *HTN* arterial hypertension, *COPD* chronic obstructive pulmonary disease, *LAR* lower anterior resection

for 5 years instead of 3 years. However, since our study reveals no signs of improved survival rates for the 3 years after surgery, it is therefore unlikely that an improvement would be noted after 5 years. The differences between the ER programs analyzed in these reports may also explain this disparity. In fact, Gustafsson et al. [13] analyze a program that mainly comprises of epidural analgesia and controlling the replenishment of preoperative intravenous fluid. The preoperative intravenous fluid could in fact serve as an individual predictive factor for surviving 5 years after surgery [21], but we were unable to use this due to a considerable lack of data as a result of the retrospective nature of this study.

As the ER program did not have an impact on the survival of our overall sample group, we assessed its effect on subgroups of the sample population that were more at risk of relapse, as defined in our findings. Thus, overall survival and survival without relapse in patients with metastatic cancer and in patients with postoperative complications were

Table 5 Adherence to recommendations of enhanced recovery by ≥ or < 70%, according to operative morbidity and anatomic pathology data

	Ratio ≥ 70%		Ratio < 70%		p value
Overall morbidity	23	4.4%	81	5.2%	0.337
Anastomotic fistula	8	15.4%	10	6.5%	0.83
Intraperitoneal accumulation	4	7.7%	20	13%	0.30
Internal abscess	1	1.9%	3	1.9%	1
Medical complication	5	9.6%	32	20.8%	0.07
Postoperative ileus	7	13.5%	12	7.8%	0.27
Infection/bladder obstruction	2	3.8%	14	9.1%	0.37
Pulmonary infection	1	1.9%	9	5.8%	0.25
Death	1	1.9%	5	3.2%	1
Resection margin					
R0	51	100%	153	99.4%	1
R1	0	0%	1	0.6%	
Stage					
0	3	5.8%	3	1.9%	0.34
1	9	17.3%	15	9.7%	
2	12	23.1%	44	28.6%	
3	17	32.7%	55	35.7%	
4	11	21.2%	37	24%	
Stage M					
M0	42	80.8%	116	75.3%	0.46
M1	10	19.2%	38	24.7%	
MSI					
No loss of expression	13	86.7%	22	78.6%	0.69
Loss of expression	2	13.33%	6	21.4%	
Perineural invasions	7	21%	31	34.4%	0.19
Peritumoral emboli	16	34%	55	44%	0.30
Relapse 1 year	7	15.2%	23	16.5%	1
Relapse 2 years	12	26.7%	33	25.2%	0.84
Relapse 3 years	13	30.2%	35	28%	0.84

MSI microsatellite instability

compared according to the extent to which they adhered to the ER program. As the ER program reduced postoperative immunodepression, inflammation, and surgical stress, it was anticipated that the latter two sample groups would benefit from the advantages of ER programs. Surprisingly, there was no evidence that following this recovery program resulted in different survival rates in the two subgroups 3 years after surgery.

Although our study does not agree with the literature regarding the long-term benefits of ER programs, our findings are unlikely to have been influenced by a selection bias since the differences between the groups < and ≥ 70% following the recovery program in the short-term were comparable to those in the literature.

In fact, the group of patients following the ER program ≥ 70% did not differ greatly from the group of patients who followed it < 70% with regard to demographic characteristics or the cancer treatment and its characteristics. This made the two groups comparable. It is interesting to note that the short-term benefits of ER programs reported in the literature were confirmed in our study. Hence, a reduction in the average hospitalization period was observed ($p = 0.047$). The literature notes a reduction in the hospitalization period by 2 days as a result of ER programs [22]. Similarly, we noted a reduction in

Table 6 Estimated overall survival rate and without relapse in the general sample group and in patients with metastatic cancer or postoperative complications

General sample group					
Overall survival	> 70% (N = 52)		< 70% (N = 154)		p value
Surviving 3 years	38	(73.1%)	107	69.5%	0.632
Not surviving 3 years	14	(26.9%)	47	30.5%	
Surviving without relapse for 3 years					
Present	30	(57.7%)	92	59.7%	0.931
Absent	22	(42.3%)	62	40.3%	
Patients with metastatic cancer					
Overall survival	> 70% (N = 10)		< 70% (N = 38)		p value
Surviving 3 years	3	30.00%	15	39.47%	0.668
Not surviving 3 years	7	70.00%	23	60.53%	
Surviving without relapse for 3 years					
Present	2	20.00%	8	21.05%	0.795
Absent	8	80.00%	30	78.95%	
Complications					
Overall survival	> 70% (N = 23)		< 70% (N = 81)		p value
Surviving 3 years	15	65.22%	47	58.03%	0.615
Not surviving 3 years	8	34.78%	34	41.97%	
Surviving without relapse for 3 years					
Present	12	52.17%	41	50.62%	0.856
Absent	11	47.83%	40	49.38%	

Fig. 2 Estimation of 3-year global survival according to the compliance with the enhanced recovery program (< or ≥ 70%) **a** in overall population, **b** in the population of patients with metastasis, **c** in the population of patients experiencing postoperative morbidity
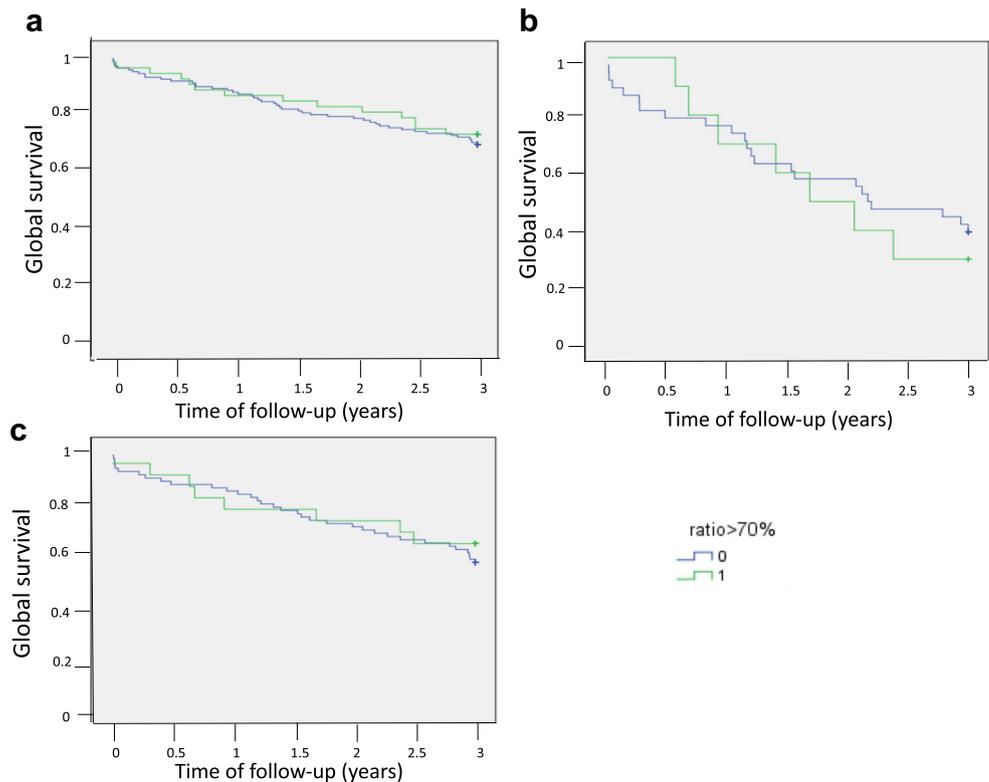
the instances of non-surgical morbidities ($p = 0.07$). The fact that the difference was not significant is most likely linked to a collection bias as the data was collected from reports on file. Surgical morbidity, which is generally not as serious, may be underestimated as it is probably not reported as extensively in discharge reports. However, despite this collection bias, our findings are in line with the literature as a recent meta-analysis also recorded a reduction in the instances of non-surgical morbidities [RR = 0.71; CI 95% 0.60–0.86], without an improvement to mortality or surgical morbidity [23].

Nonetheless, this study is limited due to its retrospective nature. In fact, some of the data on surgical morbidity may have been underestimated in the sample group before 2012 as it was recorded on paper, making it more difficult to compile than after 2012, when it began to become available electronically.

However, the primary and secondary evaluation criteria were compiled prospectively, therefore limiting this bias.

Similarly, it was not possible to collect some significant information on enhanced recovery, such as information on fluid replacement techniques adapted according to the case. This could reduce the impact of our recovery program on surviving 3 years after surgery. Finally, since an insufficient number of the ER group returned for follow-ups, we were only able to assess survival to 3 years. However, evidently this only presents a minor bias since the survival curves do not tend to diverge after 3 years.

Conclusion

The introduction of an enhanced recovery program with a compliance rate of ≥ 70% brings short-term benefits, such as a reduction in hospitalization periods and non-surgical morbidity. In contrast, in our study, ≥ 70% adherence did not result in improving overall survival rates, or in reducing relapses in the overall sample group or in the at-risk patients who underwent surgery for bowel cancer. Although these findings still need to be confirmed in other sample groups, this should not impede the implementation of ER programs as their short-term, postoperative benefits, on healthcare spending, for example, are huge and have been widely documented.

Compliance with ethical standards

References

1. Alves A (2005) Postoperative mortality and morbidity in French patients undergoing colorectal surgery: results of a prospective multicenter study. Arch Surg 140:278–283 discussion 284
2. Kehlet H (1997) Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth 78:606–617
3. Ljungqvist O, Scott M, Fearon KC (2017) Enhanced recovery after surgery: a review. JAMA Surg 152:292–298
4. Grant MC, Yang D, Wu CL, Makary MA, Wick EC (2017) Impact of enhanced recovery after surgery and fast track surgery pathways on healthcare-associated infections: results from a systematic review and meta-analysis. Ann Surg 265:68–79
5. Slim K (2016) The benefits of enhanced recovery after surgery. J Visc Surg 153:S41–S44
6. Roulin D, Donadini A, Gander S, Griesser AC, Blanc C, Hübner M, Schäfer M, Demartines N (2013) Cost-effectiveness of the implementation of an enhanced recovery protocol for colorectal surgery. Br J Surg 100:1108–1114
7. Miller TE, Thacker JK, White WD, Mantyh C, Migaly J, Jin J, Roche AM, Eisenstein EL, Edwards R, Anstrom KJ, Moon RE, Gan TJ, Enhanced Recovery Study Group (2014) Reduced length of hospital stay in colorectal surgery after implementation of an enhanced recovery protocol. Anesth Analg 118:1052–1061
8. Thiele RH, Rea KM, Turrentine FE, Friel CM, Hassinger TE, Goudreau BJ, Umapathi BA, Kron IL, Sawyer RG, Hedrick TL, McMurry TL (2015) Standardization of care: impact of an enhanced recovery protocol on length of stay, complications, and direct costs after colorectal surgery. J Am Coll Surg 220:430–443
9. Venara A, Duchalais E, Dariel A, Aubert P, Durand T, Meurette G, Rolli-Derkinderen M, Hamy A, Neunlist M (2018) Anti-inflammatory effects of enhanced recovery programs on early-stage colorectal cancer surgery. World J Surg 42:953–964
10. Cabellos Olivares M, Labalde Martínez M, Torralba M, Rodríguez Fraile JR, Atance Martínez JC (2018) C-reactive protein as a marker of the surgical stress reduction within an ERAS protocol (Enhanced Recovery After Surgery) in colorectal surgery: a prospective cohort study. J Surg Oncol 117:717–724
11. Mari G, Costanzi A, Crippa J et al (2016) Surgical stress reduction in elderly patients undergoing elective colorectal laparoscopic surgery within an ERAS protocol. Chir Buchar 111:476–480
12. Gustafsson UO, Oppelstrup H, Thorell A, Nygren J, Ljungqvist O (2016) Adherence to the ERAS protocol is associated with 5-year survival after colorectal cancer surgery: a retrospective cohort study. World J Surg 40:1741–1747
13. Curtis NJ, Taylor M, Fraser L, Salib E, Noble E, Hipkiss R, Allison AS, Dalton R, Ockrim JB, Francis NK (2018) Can the combination of laparoscopy and enhanced recovery improve long-term survival after elective colorectal cancer surgery? Int J Color Dis 33:231–234
14. Lecomte T, André T, Bibeau F, Blanc B, Cohen R, Lagasse JP, Laurent-Puig P, Martin-Babau J, Panis Y, Portales F, Taieb J, Vaillant E. «Cancer du côlon non métastatique». Thésaurus National de Cancérologie Digestive, 11–2017, [En ligne] http://www.tncd.org
15. Mariette C, Alves A, Benoist S, Bretagnol F, Mabrut JY, Slim K (2005) Perioperative care in digestive surgery. Guidelines for the French society of digestive surgery (SFCD). Ann Chir 130:108–124
16. Grass F, Slieker J, Jurt J, Kummer A, Solà J, Hahnloser D, Demartines N, Hübner M (2017) Postoperative ileus in an enhanced recovery pathway—a retrospective cohort study. Int J Color Dis 32:675–681
17. Manfredi S, Bouvier AM, Lepage C, Hatem C, Dancourt V, Faivre J (2006) Incidence and patterns of recurrence after resection for cure of colonic cancer in a well defined population. Br J Surg 93:1115–1122
18. Manfredi S, Benhamiche AM, Meny B, Cheynel N, Rat P, Faivre J (2001) Population-based study of factors influencing occurrence and prognosis of local recurrence after surgery for rectal cancer. Br J Surg 88:1221–1227
19. Haga Y, Ikejiri K, Wada Y, Ikenaga M, Koike S, Nakamura S, Koseki M (2015) The EPOS-CC score: an integration of independent, tumor- and patient-associated risk factors to predict 5-years overall survival following colorectal Cancer surgery. World J Surg 39:1567–1577
20. Tougeron D, Sickersen G, Mouillet G et al (2015) Predictors of disease-free survival in colorectal cancer with microsatellite instability: an AGEO multicentre study. Eur J Cancer 51:925–934
21. Asklid D, Segelman J, Gedda C, Hjern F, Pekkari K, Gustafsson UO (2017) The impact of perioperative fluid therapy on short-term outcomes and 5-year survival among patients undergoing colorectal cancer surgery—a prospective cohort study within an ERAS protocol. Eur J Surg Oncol 43:1433–1439
22. Sarin A, Litonius ES, Naidu R, Yost CS, Varma MG, Chen L-L (2016) Successful implementation of an Enhanced Recovery After Surgery program shortens length of stay and improves postoperative pain, and bowel and bladder function after colorectal surgery. BMC Anesthesiol 16:55
23. Nicholson A, Lowe MC, Parker J, Lewis SR, Alderson P, Smith AF (2014) Systematic review and meta-analysis of enhanced recovery programmes in surgical patients. Br J Surg 101:172–188