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Original article

Implementation of a perioperative multimodal rehabilitation protocol in elective colorectal surgery. A prospective randomised controlled study☆

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A B S T R A C T

Introduction: Multimodal rehabilitation (MMR) consists of a combination of several methods for management of the surgical patient, designed to reduce the response to surgical stress and a more comfortable and earlier recovery.

Objective: To assess the implementation of an MMR protocol in a Colorectal Surgery Unit, and to compare the results with the traditional model, as well as assessing its efficacy as regards recovery and hospital stay.

Material and methods: A total of 119 patients who received elective surgery for colorectal diseases in a period during 2009-2010 were prospectively and randomly analysed. The patients were divided into 2 groups: 58 patients were assigned to the traditional group and 61 to the MMR group. The MMR group protocol consisted of, preoperative education, early feeding and mobilisation.

Results: Both groups were homogeneous as regards the preoperative variables evaluated, the type of disease and the procedures carried out. The nasogastric tube was kept in place for 4 (1-9) days compared to 1 day (0-2) in the MMR group, with no differences in the number of re-insertions. Significant differences were found in the introduction of a liquid diet (3 [1-5] days traditional versus 0 [0-2] MMR) (P<.001), and passing of first flatulence (3 [1-6] days traditional versus 1 [1-3] MMR) (P<.001). The MMR group had a postoperative stay of 4.15±2.18 versus 9.23±6.97 days in the traditional group (P<.001). No significant differences were found in complications or readmissions.

Conclusions: MMR in colorectal surgery in the Spanish public health system is feasible and enables surgical patients to have a faster recovery without increasing complications, leading to an earlier hospital discharge.

☆Registration: this study has been registered on ClinicalTrials.gov, number NCT01148394.

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Implantación de un protocolo de rehabilitación multimodal perioperatoria en cirugía colorrectal electiva. Estudio prospectivo, aleatorizado y controlado

Palabras clave:
Cirugía colorrectal
Rehabilitación multimodal perioperatoria
Alimentación precoz

RESUMEN

Introducción: La rehabilitación multimodal (RMM) consiste en la combinación de varios métodos para el manejo del paciente quirúrgico encaminados a disminuir la respuesta al estrés quirúrgico y una recuperación más cómoda y precoz.
Objetivo: Valorar la implantación de un protocolo de RMM en una unidad de cirugía colorrectal y comparar los resultados con el modelo tradicional, valorando su eficacia en cuanto a recuperación y estancia.
Material y métodos: Se analizó prospectiva y aleatorizadamente a 119 pacientes intervenidos de forma electiva por enfermedad colorrectal entre 2009 y 2010. Se asignó a 58 pacientes al grupo tradicional y 61 al grupo RMM. La RMM consistió en educación preoperatoria, alimentación y movilización precoz.
Resultados: Ambos grupos eran homogéneos en cuanto a variables preoperatorias valoradas, el tipo de enfermedad y los procedimientos realizados. La sonda nasogástrica se mantuvo en el grupo tradicional 4 (1-9) días frente a 1 (0-2) días en el grupo RMM, sin diferencias en la reinserción de la sonda. Se encontraron diferencias significativas en el inicio de la dieta líquida —3 (1-5) días tradicional, frente a 0 (0-2) con RMM ($p < 0,001$)— y expulsión de la primera ventosidad —3 (1-6) días tradicional, frente a 1 (1-3) con RMM ($p < 0,001$)—. Los pacientes en el grupo RMM tuvieron una estancia postoperatoria de 4,15 ± 2,18, frente a 9,23 ± 6,97 días del grupo tradicional ($p < 0,001$). No se encontraron diferencias significativas en las complicaciones o reingresos.
Conclusiones: La RMM en cirugía colorrectal en el sistema sanitario público español es factible y permite una más rápida recuperación de los pacientes operados sin aumentar las complicaciones, permitiendo un alta hospitalaria precoz.

Introduction

"Fast-track" surgery or multimodal rehabilitation consists of combining several different methods for surgical patient care before, during, and immediately after the procedure, and is targeted towards reducing the adverse response to surgical stress and the organ dysfunction that this causes in order to make patient recovery a more comfortable and speedy process.[1] Several different studies have been published in the last decade that support changes to the traditional treatment given to surgery patients,[2] and that based on the current scientific evidence available, propose certain measures that are a source of controversy among many surgeons in Spain. For these reasons, it was proposed that these concepts be put into practice in our professional field.[3,4]

The primary objective of our clinical study was to evaluate the possibility of applying a multimodal patient management protocol in order to improve postoperative recovery in a colorectal surgery unit of the Spanish public health system, comparing this new method with traditional patient care by evaluating its efficacy with regard to early postoperative recovery, reduced morbidity, and shorter hospitalisation time.

Material and methods

We performed a prospective, randomised study between June 2009 and February 2010. We recruited patients from the *Hospital Clínico Universitario de Valencia* (Valencia university clinical hospital) that were operated on by the same groups of six surgeons that make up the *Unidad de Coloproctología* (coloproctology unit) in the general surgery department. The hospital ethics committee gave previous approval to our study.

Inclusion criteria

Patients older than 18 years, American Society of Anaesthesiologists (ASA) score between 1 and 4, elective abdominal surgery requiring colon/rectum resections (including reoperations) using laparotomy or laparoscopy, living in the metropolitan area of Valencia and informed consent.

Exclusion criteria

Patients without an independent daily lifestyle (patients unable to walk, bathe, or eat on their own) and those undergoing emergency surgical procedures, such as for perforations with peritonitis, intestinal occlusion, or massive haemorrhage of the lower GI tract.

Study protocol

We recruited coloproctological patients from outpatient care clinics, where they were asked to participate in the study after being informed in detail as to the nature of the

research. Once the informed consent was signed, patients were randomly assigned into the following groups using sealed envelopes: traditional postoperative management techniques and multimodal rehabilitation (MMR).

MMR group

Preoperative period

We asked the patients in the MMR group to return for a second visit with a nurse that was being funded by the study. The patient and his/her family were given both verbal and written information of the recommendations and actions to be taken by themselves and the hospital staff during the postoperative period. Patients were admitted to the hospital on the day prior to the surgery and were administered low molecular weight heparin subcutaneously based on their weight, and antibiotic prophylaxis according to current guidelines. Patients consumed a normal diet until the night before the surgery, with no colon preparation. Within this group, those patients that were to undergo an intraoperative colonoscopy or might require a loop ileostomy received an antegrade mechanical bowel preparation with Fosfosoda®.

Immediate postoperative period (day 0)

We removed the nasogastric tube before extubation, and the MMR group patients were administered high doses of oxygen (80%) intraoperatively and during the first 2 hours after the operation. Patients in the MMR group were encouraged to drink water *ad libitum* 6 hours after the procedure and to get out of bed if possible, and were prescribed i.v. ondansetron at 4 mg/8 h.

Day 1 following operation

The first day following the operation, the patients commenced soft diet tolerance if liquid tolerance was established, without waiting for signs of intestinal motility. We recommended walking and respiratory physical therapy. The urinary catheter was removed.

Day 2 following operation

Perfusions were removed and the patient commenced a normal diet if adequate tolerance to the soft diet had been established. Drains were removed as appropriate.

Day 3 following operation

Patients were discharged from the hospital if they complied with the criteria established in Table 1 (these criteria are the same for both patient groups).

Table 1 – Criteria for hospital discharge

Absence of any kind of postoperative complication
Expulsion of gas and/or faeces
Sufficient oral analgesia
Independence for daily activities (walking, feeding, washing, etc.)
Having tolerated three or more solid meals
Patient agreement
Controlled output in patients with a stoma

Traditional group

Preoperative period

Patients were admitted to the hospital on the day prior to the surgery without the examination by the previously mentioned nurse. Patient was administered low molecular weight heparin subcutaneously based on their weight, and antibiotic prophylaxis according to current guidelines. The colon was prepared before surgery with a liquid diet 2 days prior to the operation and antegrade mechanical bowel preparation with Fosfosoda®.

Immediate postoperative period (day 0)

The nasogastric tube was maintained and oxygen administered through nasal cannula at 2 l/min. No antiemetics were prescribed as they had the nasogastric tube.

Day 1 following operation

Patients in the traditional group remained on nasogastric tubes and complete fasting for the first day. Tolerance was not commenced until signs of recovered intestinal transit appeared, such as bowel sounds or flatulence.

Day 2 following operation

In the traditional group, the urinary catheter and drains were removed and water tolerance was commenced if the previously described signs of recovered intestinal transit were present.

Day 3 following operation and afterwards

The patients moved on to liquid diets when appropriate and intake progressed according to tolerance and in the presence of signs of recovered intestinal transit. The patient also commenced mobility. The patient was discharged from the hospital when compliant with all criteria set forth in Table 1 (which are the same for both groups of patients).

Readmission to the hospital was defined as a patient that has been discharged and returns for at least 1 day of hospitalisation. We did not consider those patients that sought occasional emergency treatment in this category.

The follow-up period lasted for 30 days after the operation.

Economic costs were calculated according to the cost of the total number of days spent in the hospital. These data were obtained using official records supplied by the financial department of the *Hospital Clínico Universitario*, Valencia. The current cost of hospital stay is currently 341.70 Euros per day.

Anaesthetic protocol

The same anaesthesiologist treated all patients in the study. Anaesthesia was induced using 5mg/kg sodium thiopental, 0.5 mg/kg atracurium besylate, and 0.1μg/kg fentanyl, and was then maintained using 1.4%-2.5% sevoflurane, with dosage varying based on patient age. Additional fentanyl was administered on demand. During the surgical procedure, we administered fluids at 15 ml/kg/h with the objective of maintaining systolic pressure above 90 mm Hg and diuresis of at least 80 ml/h.

Initial blood losses were compensated for using colloids or crystalloids. Body temperature was maintained using a heating blanket. After extubation, the patient was transferred to a post-anaesthesia recovery room. The anaesthesiologist decided on the type of postoperative analgesia. In both groups, postoperative pain was managed using an intravenous infusion pump controlled by the patient (Hospira® pump) with morphine at 0.5 mg/ml, continuous perfusion at 1 ml/h, and bolus administration at 2 ml/h and a 15 min lockout time, according to the general analgesic guidelines for the management of postoperative pain endorsed in October 2006 by the *Servicio de Anestesiología* (anaesthesiology department) of the *Hospital Clínico de Valencia*, or an epidural catheter with bupivacaine at 0.125% with continuous perfusion at 10 ml/h. For the study and evaluation of postoperative pain, all patients were required to rate their level of pain using a visual analogue scale from the first day following the operation until discharge from the hospital. On the second day following the operation, the intravenous/epidural PCA was removed in both groups, and intravenous paracetamol at 1 g/8 h, alternating every 4 h with intravenous magnesium metamizol at 2 g/8 h, was administered.

Statistical analysis

We performed an intention to treat analysis of our results. The sample size was calculated using previously published studies as a model.[5] Assuming an expected difference between the two groups of 2.5 hospital days and a standard deviation of 4.8 days, the sample size would be set at 58 patients in each group, with a statistical power of 80%. We used Mann-Whitney tests, Kruskal-Wallis tests, Fisher's exact tests with likelihood ratio, and Pearson's chi-square tests as appropriate. All statistical analyses were performed using SPSS® software version 15.0 for Windows (SPSS, Inc.; Chicago, Illinois, USA).

Results

Our study included 135 consecutive patients as seen in the study profile in Figure. We excluded 10 patients due to non-compliance with inclusion criteria (1 hospitalised patient and 9 emergencies: 2 cases of perforated sigmoiditis, 4 cases of occluding colorectal cancer, 1 case of ischaemic colitis, 1 case of sigmoid volvulus, and 1 patient did not give consent for participation in the study). We also excluded 2 patients from the traditional group and two from the MMR group due to failure of the PCA pump, and 2 patients from the MMR group due to extravasation from the epidural catheter. Lastly, we analysed the data from the 58 patients left in the traditional group and 61 in the MMR group. Both groups were homogeneous with regard to demographical and preoperative patient values (Table 2). Patient characteristics related to the operation from both groups are displayed in Table 3. We observed no significant differences between the two groups with regard to the rate of re-insertion of the nasogastric tube, vomiting, or postoperative ileus. Although the patients from the MMR group did have a higher incidence of postoperative nausea, the nasogastric tube did not have to be re-inserted or oral tolerance delayed. We did observe a significant decrease in mean hospital stay between the patients in the traditional and MMR groups ($P<.001$). However, we did not observe significant differences between the two groups with regards to readmissions to the hospital, or in the rate of complications. Complications of the surgical wound were defined as evisceration or infection. Urinary catheter complications were defined as acute urine retention or urinary infections. We observed a significantly greater rate of complications of the urinary catheter in the traditional group (Table 4). Extravasation and phlebitis were considered to be complications of the peripheral intravenous access point, and respiratory complications were defined as respiratory infections and pulmonary thromboembolism (Table 4).

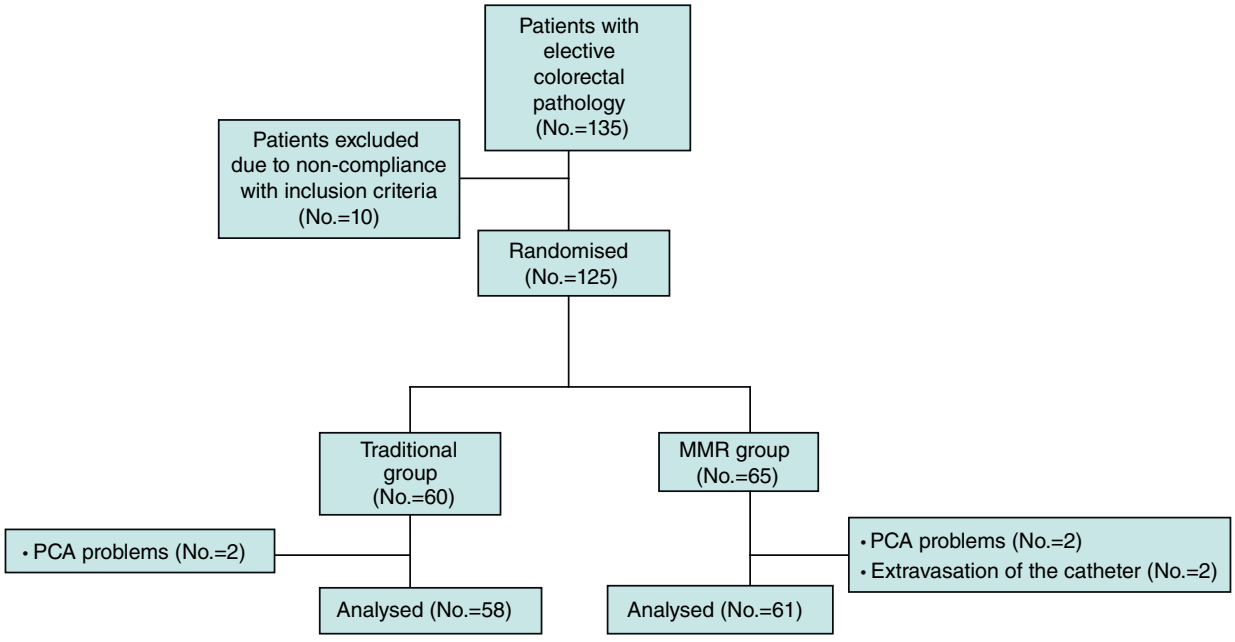

Figure – Distribution of patients included in the study.

Table 2 – Characteristics of each group

	Traditional (No.=58)	MMR (No.=61)	P
Age, years	60 (28-88)	62 (27-85)	.493
Sex, male/female	32 (55.3)/26 (44.7)	40 (65.5)/21 (34.5)	.127[a]
Body mass index	28.06 (17-34)	27.33 (18-35)	.565[b]
ASA			.304[c]
1	4 (7)	2 (3)	
2	22 (38)	26 (43)	
3	25 (43)	30 (49)	
4	7 (12)	3 (5)	
Physiological POSSUM	16.01 (12-31)	14.26 (12-22)	.254[b]
*Surgical POSSUM**	11.21 (7-26)	10.93 (9-19)	.585[b]
Disease			.360[c]
Cancer	40 (68)	46 (75)	
Diverticular	9 (16)	10 (16)	
Chronic IBD	9 (16)	5 (8)	
	4 (5)	2 (3)	.125[d]
Neoadjuvant chemo/radiation therapy			
Tobacco	18 (32)	15 (25)	.293[d]
Alcohol	6 (11)	4 (7)	.091[d]

ASA indicates American Society of Anaesthesiologists score; IBD: inflammatory bowel disease.
Values are expressed as no. (%) or median (interval).
[a]Pearson's chi-square test.
[b]Mann-Whitney; Student's t test.
[c]Likelihood ratio.
[d]Fisher's test.

Table 3 – Data regarding the operations

	Traditional (No.=58)	MMR (No.=61)	P
Duration of surgery, min	135 (80-240)	164 (90-315)	.086[a]
Surgeon			.102[b]
1	17 (29)	15 (25)	
2	12 (21)	10 (16)	
3	7 (13)	6 (10)	
4	5 (9)	5 (8)	
5	12 (21)	16 (26)	
6	5 (7)	9 (15)	
Antegrade bowel preparation	53 (91)	12 (20)	<.001[c]
Laparotomy/laparoscopy	42 (72)/16 (28)	39 (64)/22 (36)	.098[c]
Procedure			.544[b]
Right hemicolectomy	7 (13)	10 (16)	
Left hemicolectomy	14 (25)	13 (21)	
AR	10 (16)	11 (18)	
LAR/ULAR	20 (34)	23 (38)	
Amputation	7 (13)	4 (7)	
Nasogastric tube, days	4 (1-9)	1 (0-2)	.003[a]

AR indicates anterior resection of the sigmoid colon; LAR, low anterior resection; ULAR, ultra-low anterior resection.
Values are expressed as no. (%) or median (interval).
[a]Mann-Whitney test.
[b]Likelihood ratio.
[c]Pearson's chi-square test.

Discussion

This study was designed to test whether the application of MMR in colorectal surgery provides a better and speedier patient recovery. The current scientific evidence appears to indicate that these techniques do improve symptoms that are secondary to surgical aggression, and could lead to reduced morbidity and health costs incurred, an earlier

Table 4 – Results from the analysis of both groups

	Traditional (No.=58)	MMR (No.=61)	P
Postoperative ileus	11 (19)	12 (20)	.166[a]
Vomiting	10 (17)	12 (20)	.217[a]
Re-insertion of the NGT	9 (16)	7 (12)	.106[a]
Start of liquid diet (day following the operation)	3 (1-5)	0 (0-2)	<.001[b]
First gas passed (day following the operation)	3 (1-6)	1 (1-3)	<.001[b]
Defecation (day following the operation)	4 (2-8)	3 (3-7)	.309[b]
Epidural/intravenous analgesia	4 (7)/54 (93)	3 (5)/58 (95)	.577[a]
Pain (visual analogue scale)			.265[c]
Day 1 following operation	5 (1-10)	4 (1-9)	
Day 2 following operation	4 (2-8)	4 (1-8)	
Day 3 following operation	3 (1-7)	3 (1-6)	
Morphine administered by PCA, mg	105±46	149±34	.109[d]
Wound complications	12 (21)	9 (15)	.105[a]
Urinary catheter complications	4 (7)	1 (1)	.021[a]
Peripheral intravenous access point complications	2 (3)	2 (3)	.502[a]
Anastomotic leak/number of sutures	6-50	4-51	.65[a]
Pulmonary complications	4 (7)	2 (3)	.159[a]
Hospital stay, days	9.23±7	4.15±2.2	<.001[d]
Readmission rate, days	2 (3)	3 (5)	.507[a]
Hospital costs, Euros	3.153.9±2.381.7	1.418.1±745	<.001[d]

PCA indicates patient-controlled analgesia.
Values are expressed as no. (%), median (interval) or mean (standard deviation).
[a]Fisher's test.
[b]Mann-Whitney test.
[c]Kruskal-Wallis test.
[d]Student's t-test.

discharge from the hospital, and a more rapid return to normal activity.

The duration of hospital stay after colorectal surgery remains too lengthy. A multicentre review indicated that the mean postoperative hospital stay was 11.8 days.[6] Over 10 years ago, the use of a multimodal approach was suggested for significantly reducing postoperative hospital stays in laparoscopic surgery.[7] Kehlet et al[8] published a clinical pathway that reduced the median hospital stay to 2 days, and a return to gastrointestinal functioning within 2-3 days in over 90% of patients, with no cardiopulmonary complications and a readmission rate of 15% in a group of 60 patients. In 2005, this same group published another study in which they analysed the preoperative care provided to patients in 295 different European hospitals.[9] Over 85% of patients underwent mechanical bowel preparation before the procedure. The nasogastric tube was removed in 78% of patients that underwent a laparoscopy on the same day as the surgical procedure, whereas this only occurred in 33% of patients that underwent a laparotomy. Epidural analgesia was used in only 8% of hospitals in France, 12% in Italy and Spain, 27% in the United States and Germany, and 67% in the United Kingdom. In Spain, the mean delay for commencing liquid tolerance was 5.3 days, and 6.9 days for normal ingestion. After 5 days, 82% of the patients undergoing laparoscopic surgery had recovered intestinal functioning, as opposed to 53% of patients undergoing open surgery. In Europe, the majority of patients (mean: 53%) could walk three days after the procedure, whereas in the United States, 71% were walking on the second day and 85% on the third. In Europe, patients undergoing laparoscopic surgery had a shorter hospital stay than those undergoing a laparotomy (8.7 vs 11.9 days), with a mean hospital stay of 11.8 days in patients that were converted to open surgery.[9]

The results of our study reflect the possibility of successfully implementing an MMR protocol in Spain with comparable results to those described by other authors. Mean hospital stay and the rates of readmissions and postoperative morbidity are within the lower limits described in the literature for both the MMR and traditional groups. In the MMR group, mean postoperative hospital stay was 4.23 days for the *Hospital Clínico Universitario de Valencia* (*HCUV*), as opposed to 3.3-6.6 days as described by other authors, and the rate of readmissions to the *HCUV* was 4.91 days as opposed to the 3.1-21.3 days cited in the literature.[5,8,10-13] We also obtained good postoperative morbidity rates in our study. Only 6% of patients in our study received postoperative epidural analgesia, which is below the 12% reported by the survey carried out by Kehlet et al.[9] These rates reflect the difficulty of and resistance to the introduction of epidural analgesia for treating postoperative pain in our system. Currently, the health system overload and the lack of suitable operating rooms limits the length of time available for the anaesthesiologist to place an epidural catheter. Additionally, the perception of both surgeons and anaesthesiologists is that this is not a necessary procedure. Even so, with the use of epidural analgesia being the reference method for controlling postoperative pain, our results have not suffered

from the use of intravenous analgesia in the majority of our patients. These results are similar to those described by Delaney et al[5] in their study on epidural versus intravenous analgesia in MMR protocol. We observed significantly higher rates of complications from the urinary catheter in the traditional group. This could explain why urinary catheters were maintained the traditional group longer than in the MMR group. Advancements made in perioperative pathophysiology have shown that several different factors contribute to increasing postoperative morbidity and prolonging hospital stay and convalescence of surgical patients.[14] However, we do not yet know which the key points in an MMR protocol are and which steps are secondary.

One of the main concerns regarding early discharge from the hospital is the safety of releasing patients 3-5 days after surgery. The medical literature on this subject has indicated that anastomotic leaks occur rarely in patients using MMR, and until now, no studies have indicated adverse effects when instructing the patient to seek hospital attention if suspicious symptoms develop at home.[7,12] We do not believe that early discharge is inappropriate or unsafe, since the proximity to the hospital (inclusion criteria) and a close outpatient monitoring during the first week out of the hospital allow for readmission within a few hours if any signs of complications arise. One could argue that colon surgery with MMR patient care could imply a greater rate of readmissions according to the literature, but over 65% of these readmissions occur after the fifth day following the operation, and as such, could not have been prevented with a longer hospital stay.[15] In to our study, the rate of readmission was not significantly different between the two groups.

The criteria for patient discharge in our protocol are the same as in traditional methods, except that in our case these criteria are achieved earlier. Additionally, the hospital costs incurred are significantly less when applying the MMR even when readmissions are taken into account,[10-12] which is fundamental to providing high quality and efficient health care services. The implementation of these programmes requires a coordinated effort from all health care staff, not only from doctors and nurses. It also involves a learning curve because the results and compliance with MMR improve as the professionals carry out these programmes gain experience.[16] The available scientific evidence appears to indicate that these protocols improve the biological functioning of the patient in response to the surgery by reducing postoperative complications, thus diminishing morbidity rates and providing the patient with a more comfortable postoperative recovery. Additionally, the introduction of multimodal recovery programmes reduces the hospital stay and the costs incurred by patients subjected to general surgical procedures. Therefore, these programmes are of great interest for those involved in hospital management, who generally seek to reduce the costs of patient care. However, we must not forget that the first and most important objective is always to provide the highest standards of quality in patient care.[17]

The application of MMR in colorectal surgery within the Spanish health system is quite feasible and allows for improved and more rapid recovery of surgical patients without increasing rates of complications and leads to an early discharge of the patient from the hospital.

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Conflict of interest

The authors declare that they have no conflict of interest.

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