

The ERAS Protocol is at the forefront of the peri-operative pathway in colorectal surgery: monocentric clinical study

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SUMMARY: The ERAS Protocol is at the forefront of the peri-operative pathway in colorectal surgery: monocentric clinical study.

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Introduction. Colon cancer is one of the most common neoplastic diseases, with onset in old age; the benefits of the ERAS protocol were evaluated in the peri-operative treatment of patients affected by this neoplasm.

Methods. We studied 90 cases of colorectal neoplasia observed at the General Surgery UOC of the San Camillo de Lellis Hospital between September 2014 and April 2016, undergoing laparoscopic surgery and to which the ERAS protocol was applied; key points were the preoperative oral feeding, the epidural anesthesia, the reduced or failed hydro-electrolytic overload, the early mobilization and recovery of the feeding, the non-use of drainage. The most important parameters

considered were the reduced duration of the operating hospital stay, the lower occurrence of early and distant complications.

Results. 85 surgical procedures were performed with laparoscopic technique (94.4%) and 5 with traditional open technique (5.6%). The conversion rate was 5.8% (5/85). 29 surgical procedures of right hemicolectomy (32.2%) and 26 of anterior resection of the rectum (28.9%) were performed; in another 29 patients (32.2%) an intervention with an open traditional technique was performed. A balanced anesthesia was performed in 41 patients (45.6%); epidural anesthesia in 32 cases (35.6%); the Tap Block in 17 subjects (18.9%). The average volume of liquid infusion was 1664cc \pm 714; the average post-operative hospital stay of 4.3 \pm 0.9 days.

Conclusions. The ERAS protocol reduces the duration of the post-operative hospitalization, involves a lower incidence of precocious and remote complications, in particular if associated with a minimally invasive surgical method; it is easily applicable and reproducible in a hospital environment, with a marked reduction in healthcare management costs.

KEY WORDS: ERAS - Colorectal cancer - Fast-track surgery - Laparoscopy - Post-operative hospitalization.

Introduction

Some fundamental innovations in abdominal surgery have led to a significant improvement in the post-operative outcomes in recent years: the capillary diffusion of laparoscopy, which currently represents the gold standard in most surgical interventions, further improved by the advent of the robotic

technique and the emergence of Enhanced Recovery After Surgery (ERAS) protocols. The introduction of minimally invasive surgery has certainly revolutionized abdominal surgery, significantly reducing surgical stress and postoperative complications, resulting in a faster recovery of the patient. The second revolutionary change was the introduction of the ERAS protocols into clinical practice. These protocols represent a real epoch-making shift from traditional treatments to a new model of collaboration in the healthcare sector that has as its final objective the achievement of an optimization of the patient's perioperative path, with a faster postoperative recovery and a better level of satisfaction.

This process also involves a reduction in postoperative medical-surgical complications and a

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significant saving in terms of medium and long-term health care costs (1-3). An ERAS protocol represents the set of peri-operative actions related to clinical practice with the clear aim of combining multiple interventions, which individually applied alone would give poor results, to reduce surgical stress and promote early postoperative recovery (4, 5). The main philosophy of ERAS involves the reduction of metabolic stress caused by the surgical trauma, favoring a rapid recovery of the operated patient (6-8). The implementation of these strategies implies a modification of the factors that influence the biological response to the surgical stress by the patient, ultimately reducing significantly the postoperative complications, the morbidity, the mortality, the hospital stay and ultimately in a significant way, health costs (11-16).

The ERAS is not in fact based on the single specialist doctor, but on the patient. It does not represent a simple standardization of a peri-operative

protocol, but a real multidisciplinary collaboration of a team, which also involves the patient in the creation of a management audit (30-32). The establishment of a multidisciplinary team is the key to its success. With this type of approach, thanks to a combination of different measures in daily clinical practice, a drastic reduction in morbidity, mortality and duration of postoperative hospitalization is obtained, with a reduced waste of resources (17-20). The standardized process facilitates the decisions for all the medical and nursing staff involved (33-35).

In 2013 Nygren et al. published the latest updated guidelines for the implementation of the ERAS protocol in colorectal surgery (9, 10). The various peri-operative steps to be followed in the ERAS protocol (Figure 1) are carefully defined with the differences to be implemented in case of Colon Surgery or Rectal Surgery (21). The different items to be executed are shown in Table 1, A and B (22, 23). In particular, it is important to underline the use of peripheral anesthetic

TABLE 1 A - ERAS SOCIETY GUIDELINES FOR PERI-OPERATIVE TREATMENT IN COLON ELECTIVE SURGERY.

ERAS ITEM	Colon Surgery	Rectal Surgery
Consueing and preoperative information	essential	essential with attention to the possible colostomy
Optimization of medical therapy	correct any anemia and malnutrition status. Cessation of smoking	identical but evaluation more blood loss - neoadjuvant therapies - more complex surgery
Mechanical Intestinal Preparation	to avoid	indicated the preparation of the colon after any ostomy
Peri-operative Glucidic Load	indicated	indicated
Preoperative feeding	recommended	recommended
Pre-anesthesia	to avoid long acting BDZ	to avoid long acting BDZ
Anesthesiological techniques	epidural / locoregional	epidural / locoregional
Prevention of hypothermia	recommended	recommended
Fluid Restriction	recommended	recommended

TABLE 1 B - ERAS SOCIETY GUIDELINES FOR PERI-OPERATIVE TREATMENT IN COLORECTAL SURGERY.

Use of Postoperative Morphine	to avoid	to avoid
Nausea and Vomiting Post-Operators	treat and prevent according to guidelines	treat and prevent according to guidelines
Naso-gastric basin	to avoid	to avoid
Use of laxatives	recommended to reduce the ileum	No in case of ostomy
Laparoscopic approach	recommended	recommended for benign pathology and selected cases
Drenaggio addominale	to avoid	no clinical evidence
Immediate re-admission	recommended	recommended
Immediate removal of the bladder catheter	recommended in the first day p.o.	recommended
Immediate mobilization	recommended	recommended

techniques for the control of analgesia with a substantial reduction in the use of opioids, which are strongly discouraged. It also highlights the centrality of early mobilization and nutrition in order to reduce and prevent the occurrence of “post-operative nausea and vomiting” (PONV) to a minimum. Post-operative results are significant (24-28). These highly positive results have certainly contributed to the development and large scale application of the ERAS protocol: minimizing the post-operative admission period, in fact, can lead to positive results on the patient, as prolonged hospitalization can in itself bring an increase in the risk of morbidity (61).

With regard to medical, bronchopulmonary and cardiovascular complications, they are decidedly less when the ERAS protocol is applied (56). The fast track provides in fact the control and the restriction of the volume of infused fluids injecting, the early mobilization, the non-positioning of the nasogastric tube (SNG) in the post-operative, the use of epidural anesthesia, the non-use of long-acting opiate drugs; all factors that seem to have a positive influence on the reduction in the onset of short-term internship complications; the removal of the SNG at the end of the intervention, associated with early mobilization, seems to significantly reduce the risk of the onset of respiratory complications during the post-operative hospitalization; furthermore, the restriction of intravenous infusional fluid therapy in the intraoperative period which in the immediate postoperative period is associated with a marked improvement in cardiac and pulmonary function. Another important factor is the early removal of the bladder catheter (CV) which certainly leads to a reduction in the risk of infections of the urinary tract (23). Within the ERAS protocol, a significant reduction in the onset of nausea and vomiting in the postoperative period (PONV) was also demonstrated; this is most likely linked to early mobilization and non-use of opioids, factors that positively affect the rapid recovery of a valid and adequate intestinal peristalsis. In conclusion, the application of the ERAS protocol seems to have led to a clear reduction in the incidence of post-operative medical and surgical complications (55).

With regard to health management, the benefits and advantages deriving from the application of the

ERAS protocol are undoubtedly represented by the reduction in resource consumption and avoidable complications (37, 38). All this translates into an improvement in the quality of the therapies implemented and a reduction in overall healthcare costs (39, 40). The gradual but progressive adoption of ERAS strategies has confirmed the difficulties in moving from a traditional approach to an innovative one based on evidence, although the benefits for patients and the economy produced by the fast track path are now fully demonstrated. The fast track has been adopted, with substantial economic benefits, since the year 2000 in several countries all over the world and has led to a marked reduction in the duration of hospitalization with a consequent reduction in healthcare costs (6, 64, 65): reducing the length of hospitalization means that more patients can be treated on the same beds, increasing the turnover and the efficiency of the department also in economic and management terms. With this in mind, the use of the ERAS protocol is the ideal means to improve assistance and at the same time lower costs. It is clear from several studies that the ERAS protocol associated with laparoscopic techniques clearly reduces the duration of hospitalization by 2-5 days (66-68).

It should be remembered, however, that laparoscopic technique alone already contributes greatly to the reduction of hospitalization, as numerous scientific studies have shown (69, 70). Cakir et al. have in fact verified how the application of laparoscopic surgery together with some specific interventions of the ERAS protocol, such as the removal of the naso-gastric tube before extubation, the mobilization within the first 24 h postoperative, the use of anti-inflammatory drugs steroids, the use of epidural anesthesia, are independent predictors of the duration of the post-operative course (71). The reduction of the postoperative intestinal ileum is another fundamental factor to shorten the time of discharge, leading to a reduction in costs (72) and also the control of pain appears directly associated with a more rapid discharge (73, 74). The laparoscopic approach reduces the incidence of surgical wound infections significantly (75, 76). Moreover, the reduction in hospitalization according to the guidelines of the ERAS path, is another factor able to reduce this incidence with a

further evident advantage in terms of management and reduction of health expenditure.

Materials and methods

In Italy, on the initiative of the San Raffaele Institute of Milan and the Vita Salute University, a multi-center study on the ERAS protocols started in 2015. The Lazio Region adheres to this study proposal and identifies in three University Polyclinics (Sant'Andrea, Tor Vergata, Biomedical Campus) and in the AO San Giovanni - Addolorata centers where this study must be conducted at the regional level. Despite this, it did not exist in the A.S.L. of Rieti a true ERAS protocol approved and working for patients undergoing Colorectal Surgery. Regardless of this initiative, from September 2014 the U.O.C. of General Surgery of the San Camillo de Lellis Hospital of Rieti has created a perioperative management protocol based on the principles and recommendations of the Enhanced Recovery After Colorectal Surgery with the aim of expanding the criteria of the Short Cycle Surgery, improving the peri-operative patient care and reducing healthcare costs.

The aim of the present study was to analyze the results of the application of the ERAS Protocol in Colorectal Surgery at the General Operative Unit of General Surgery, paying particular attention to the evaluation of post-operative outcomes such as the length of hospital stay and the incidence of complications. Starting from September 2014, a perioperative management protocol was written and implemented following the dictates of the ERAS for all patients undergoing Colorectal Surgery at the General Surgery Unit of the San Camillo de Lellis Hospital. Up to April 2016, 90 patients undergoing colorectal surgery for benign and malignant disease were included in the study.

Data collection

All patients admitted to the General Oncological Surgery Department of the Provincial General Hospital "San Camillo de Lellis" of Rieti for rectal and benign malignant pathology, candidates for resective surgery with a traditional approach, were

included in the protocol open, both minimally invasive laparoscopy. All patients had to sign an informed consent to the surgery and to the proposed postoperative management protocol. Parameters such as age, sex, tumor site and stage, anesthesia evaluation were included; the type and duration of surgery; blood loss and intraoperative fluid infusion. Only patients defined as ASA IV were excluded from the protocol during the preoperative evaluation by the anesthesiologist.

In this study, 90 patients with a mean age of 62.7 ± 13.2 years and an average BMI of 26.3 ± 4.7 , 44 male patients (48.9) and 46 females (51.1%) were included. Of these, 71 patients had at least one comorbidity (78.9%) with an ASA average score of 2.5 ± 0.6 . Malignancy was the most frequent cause of intervention (78.9%, $n = 71/90$), while 19 patients were treated for benign pathology (21.1%), represented by the diverticular pathology (sigma stenosis) and prolapse complete of the rectum, treated with resection of the sigma and suspension of the rectum (intervention of Frykam-Goldberg). The analyzed sample was subsequently divided into two groups: first 45 cases (period I) and subsequent 45 cases (period II). A comparative analysis between the two groups was performed in order to evaluate the changes and the evolution over time of the selected results and the efficiency of the protocol (Table 5). An out-patient follow-up was performed 7 and 15 days after the intervention, followed by a telephone follow-up 30 days after the intervention.

All patients operated for neoplastic pathology were subsequently contacted for the evaluation of the oncological follow-up. The morbidity, the type of postoperative and distant complications, and the need for re-hospitalization in all patients included in the study were evaluated. The duration of the post-operative stay was evaluated, assessing all patients who completed the protocol. The differences in terms of duration of the intervention, type of intraoperative infusional therapy performed, VAS recorded upon awakening and on the first postoperative day, mean dose of daily administration of paracetamol, and duration of hospitalization in patients > 65 years, BMI > 25 Kg / m², neoplastic pathology and in the male gender were evaluated. The impact of the ASA score on the variables analyzed was also assessed.

Statistic analysis

All data were collected prospectively and analyzed using version 2.0 of the IBM SPSS Statistics program (version 2.0 Armonk, NY; IBM Corporation) for MacOSX. Continuous variables were presented as mean + or - standard deviation for parametric or median for nonparameters. The categorical variables were instead represented as a percentage frequency. The analysis of the one-way variance (ANOVA) test and the Student test were used, when appropriate, for the analysis of the parametric variables. The Wilcoxon test, the Kuskal-Wallis test and the Mann-Withney test were instead used for the analysis of non-parametric variables. The significance level was set at $p < 0.05$.

Pre-operative protocol

The pre-operative study was performed between one and two weeks before the surgical intervention by emato-chemical tests: blood cell count, hydro-electrolyte structure, coagulation structure, renal function, liver function and nutritional status, evaluated by the assay of albuminemia and total proteins; radiological evaluation using standard thorax RX and/or total body TAC staging, as needed. Other in-depth investigations (such as liver MRI, chest HRCT, ECO with contrast medium) were carried out in case of need; preoperative surgical visit; preoperative cardiologic evaluation; evaluation of nutritional status: distributing to patients a minimum screening questionnaire (Mini Nutritional Assessment - MNA). Additional evaluations were carried out (pneumological examination and Respiratory Functionality Testing - PFR, gastroenterological examination, etc.) when deemed necessary.

All patients were provided with an information leaflet regarding the type of intervention proposed, the risks and the advantages of the ERAS protocol and the rules to be followed and respected in order to complete a correct protocol. If the evaluation team considered it necessary, family members were involved in the patient's acceptance and participation path to the protocol. It has been carefully illustrated to the patient: the organization of the

department and nursing assistance; pain management and other postoperative needs; the management of possible post-operative complications; the organization of post-discharge ambulatory controls. No intestinal mechanical preparation was performed in the pre-operative period. All patients followed exclusively a slag-free diet regimen for one week prior to surgery. Patients with alterations of the alvus were not subjected to special preparations, unless strictly necessary. Patients with pathology of the medium-low rectum or in the case of a programmed ileus or colostomy, performed an evacuating enema the evening before surgery and the very morning of the operation, before access to the ward.

During the pre-operative cardiology evaluation, antithrombotic prophylaxis was given according to international guidelines. All patients had to be hospitalized the morning of the surgery at 7.00 am and were able to take home therapy and clear liquids up to 2 hours before surgery. No pre-operative antibiotic prophylaxis was performed unless strictly necessary and indicated for any patient associated pathologies, such as cardiac valvular disease. Only peri-operative antibiotic prophylaxis was administered at the time of the surgical incision. The continuation during the postoperative period was dependent on the outcome and outcomes of the intervention and the patient's comorbidities. Local-regional anesthesia has been preferred in all its forms, from local infiltration to peripheral and central blocks, in association with general anesthesia. General anesthesia had its miorisolution as its main purpose, as intra-operative analgesia was normally achieved with the use of regional anesthesia techniques. This reduces the consumption of opioid drugs for the benefit of anti-emesis and the early recovery of intestinal peristalsis. Infusion of intra-operative fluids was reduced in the normovolemic patient, and limited only to the exclusive replacement of blood loss, diuresis and *perspiratio insensibilis*. In this way, a marked reduction in the formation of tissue edema at the surgical wound and the surgical site is obtained, avoiding the cardio-respiratory overload of the operated patient.

During the surgery, the normovolemia in the patient has been properly maintained with the use of external devices and the administration of heated fluids. All patients were treated with laparoscopic

minimally invasive method, unless it was performed due to the presence of medical and/or surgical contraindications. In the case of laparoscopic approach, an access technique with 4 trocars (one/two of 5 mm and two/three of 12 mm) was routinely used. The surgical specimen was normally removed through a mini-laparotomy, obtained by extending up to 3.5 cm the incision performed for the placement of the umbilical trocar. In the case of a traditional open approach, a median or transverse longitudinal laparotomy incision was performed, depending on the type of intervention to be performed. The naso-gastric tube (SNG) was usually placed at the beginning of surgery and was removed at the end of the operation, always before extubation and patient awakening. The bladder catheter (CV) has been routinely positioned.

The intra-abdominal drainage tube was normally positioned only in the case of extra-peritoneal anastomosis packaging after rectal surgery, in the absence of protective colostomy. The surgeon has always had to specify the motivation of intra-abdominal drainage placement, in particular cases in whom he has had to perform, for example, a high risk of bleeding. A protective ileostomy was packaged regularly in patients with neoplasm localized in the middle-lower rectum and undergoing chemo-radio neoadjuvant therapy.

Post-operative protocol

The patient undergoing surgery was followed in the immediate postoperative period in the Operating Room Recovery Room, where the vital parameters, the evaluation of postoperative pain, recovery of cognitive ability were constantly monitored. A standard post-operative management card has been set up to be performed in the ward. Control blood tests were performed routinely on the 1st and 3rd postoperative days. Postoperative pain was also assessed on Day 1 in all patients, using the VAS scale. The epidural catheter, if present, was removed on the morning of the first postoperative day. Just as the bladder catheter was removed on the morning of the first postoperative day; at this point the accurate monitoring of diuresis has started for the following 24 hours. The permanence of the

bladder catheter was indicated only in case of oligo-anuria and/or macroscopic haematuria. The repositioning of the bladder catheter was performed only in case of acute post-operative urinary retention and a specialized urological consultation was performed in order to evaluate and organize the discharge of the patient from the hospital with the catheter in place, with programmed postponed attempt of outpatient removal.

In order to optimize the early recovery of therapy and oral feeding, together with the simultaneous suspension of intravenous parenteral therapy, accurate monitoring of postoperative nausea and vomiting (PONV) was performed. Finally, a post-operative antalgic therapy was set up by the extension of the analgesic blocks already taken during the operation. If necessary, in addition paracetamol and/or ketoralac were used intravenously, avoiding the use of opioids as much as possible. Post-operative antalgic therapy was continued for 24-48 hours immediately after the operation, according to the patient's individual needs. For the first 12 hours immediately following surgery, crystalloid infusion therapy is established at a rate of about 0.7-1.0 ml/kg/h. Any changes in the amount of perfused liquids have been dependent on any patient co-morbidities and urinary output. For this purpose, the patient's hydro-electrolyte balance is normally recorded, which also includes the fluids administered to the patient in the operating room during surgery. At the distance of 6 hours from the awakening, the patient can take water when needed, if well tolerated. For patients who return to the ward after 5.00 pm on the afternoon of surgery, the first meal is breakfast the next morning. The use of chewing gum from the evening of the day of surgery was usually encouraged, especially in cases of nausea and vomiting. On the first postoperative day, intravenous infusion therapy was reduced or stopped and the patient was able to drink at least 1-1.5 L of water within 24 hours; he could also take tea and biscuits, both for lunch and dinner. Particularly important in this regard is that all meals have been consumed by patients, sitting at the table and not lying in bed. The eventual extension of the infusion fluid-therapy has occurred and has been indicated in case of oliguria, nausea and vomiting, and the needs determined by the possible associated

pathologies. In patients who underwent right hemicolectomy, with an intra-operative finding of plentiful fecal stasis in the colonic lumen, an evacuating cleaning enema was performed on the second postoperative day. In the following days of hospitalization, the patient gradually and gradually resumed normal oral feeding.

The patient, once back in the ward, after 4 hours from the surgery was mobilized and immediately placed in a sitting position, to be maintained for at least 60 minutes. On the first postoperative day, the patient had to stay out of bed for at least 6-7 hours, walk around, go and come back from the bathroom and walk for at least half of the corridor of the ward. When necessary, family members were involved for the first mobilization in the morning and for the walk to be performed in the late morning or early afternoon. On the second day, the patient had to try to resume his normal daily activity, almost autonomously. All patients were advised to obtain before surgery of a post-surgical elastic belly, to be worn before getting out of bed and in a sitting and orthostatic position. From the second postoperative day, the patient must be able to maintain the sitting or semi-seated position even in bed during the day. The patient to be dischargeable must: be apiretic and with arterial pressure and blood tests in the standard; have good post-operative pain control with oral analgesic therapy; having reacquired and obtained: adequate motor autonomy; an adequate resumption of oral nutrition; adequate recovery of intestinal canalization.

Results

A balanced anesthesia with infiltration of surgical accesses was performed in 41 patients (45.6%). Epidural anesthesia was instead practiced in 32 patients (35.6%), while the Tap-Block in 17 cases (18.9%) in association with general anesthesia. The mean of intra-operative infusions performed was 1664 ± 714 without differences compared to the anesthetic techniques used ($p = 0.15$; Table 2). No intraoperative intra-transfusion were performed. With a mean VAS on waking, in the whole series, of 2.4 ± 0.6 , the analysis of the differences compared to the various anaesthesiological techniques performed, showed a significant reduction of VAS in patients undergoing epidural or Tap-Block anesthesia, compared to those treated with only Balanced Anesthesia [$p = 0.001$; Table 2, 85 surgical procedures were performed with laparoscopic technique (94.4%) and 5 with traditional open technique (5.6%)]. The conversion rate was 5.8% (5/85) and the causes were strictly due to an oncological nature in 2 patients and related to the presence of intra-peritoneal adhesions in the remaining 3 cases. The interventions carried out with the respective operating times are shown in Table 3. 29 right hemicolectomy (32.2%) and 26 for the anterior resection of the rectum were performed (28.9%). In 29 other patients (32.2%) a left colonic surgery was performed, consisting of 16 cases in a left hemicolectomy and the remaining 13 patients with a sigmoidectomy. In addition, 6 abdominal-perineal amputations according to Miles

Table 2: assessment of the VAS upon awakening with respect to the anesthetic techniques used

Anesthesia Technique	Infused liquids i.o. (1)	VAS awakening (2)
Balanced	1821.9 +- 713.6	2.9+-0.6
Epidural	1531.2 +- 561.8	2.2+-0.4
Tab-Block	1528.1 +-759.1	2.1+-0.3
(1) $p = 0,15$		(2) $p < 0.001$ Balanced vs Tap-Block/Epidural

Table 3: interventions performed with respective average operating times

Intervention	Number	%	Operating Time (min)
Miles	6	6.7	231.3+-44.8
Right Hemicolectomy	29	32.2	132.6+-45.7
Left Hemicolectomy	16	17.8	150.8+-33.1
Sigmoidectomy	13	14.4	122.9+-17.9
Anterior resection of the rectum	26	28.9	197.2+-61.8

Table 4: Duration of hospital stay compared to the interventions performed

Intervention	Average hospitalization p.o. (days)
Miles	4.8±0.7
Right Hemicolectomy	3.8±1.0
Left Hemicolectomy	4.1±0.3
Sigmoidectomy	4.1±0.4
Anterior resection of the rectum	4.7±1.2

were performed for neoplastic pathology. The packaging of a colostomy was necessary in 13 patients (14.4): 6 definitive colostomies were performed, in patients undergoing Miles, while 7 temporary colostomies of protection were packaged in patients operated on anterior resection of the rectum for neoplastic pathology and Treated Neoadjuvant Radiotherapy.

The duration of the intervention and the intra-operative infusions did not show significant differences in patients aged >65 years, BMI >25 kg/m², with neoplastic and male pathologies. Analysis of the VAS recorded upon awakening showed significantly increased values in male patients (2.6 ± 0.6 vs 2.3 ± 0.5 ; $P = 0.05$), as well as those with BMI >25Kg / m² (2.6 ± 0.7 vs 2.3 ± 0.4 ; $p = 0.02$). No significant difference was found in patients aged >65 years and those operated for neoplastic pathology. Finally, no substantial difference was observed in the intraoperative variables analyzed compared to the ASA Score. All patients were admitted on the day of the operation. Of these, 86 patients (95.6%) completed the whole protocol. The reasons for non-completion in the remaining 4 patients are to be found in the need for admission in UTIC or UTIPO for more than two nights (respectively for intraoperative onset of AMI and elevation of troponins on the first postoperative

day); ureteral lesion resulting in leakage in the 2nd day p.o., which required placement of a ureteral stent; lesion of the dura mater during an epidural with onset of pain in the fronto-occipital and consequent need of bed for 3 days. Considering the patients who completed the protocol, an average post-operative hospital stay of 4.3 ± 0.9 days was recorded. All patients were mobilized on the evening of the operation or on the 1st day p.o. The mean VAS was in the 1st day of 2.6 ± 0.8 with an average daily consumption of paracetamol equal to 0.5 (0-1.2) grams, considering the entire duration of the hospitalization. In one case it was necessary to reposition the SNG in the first day due to the onset of a mechanical sub-occlusion of the colostomy, which was resolved in the 2nd day with subsequent removal of the tube. The bladder catheter was removed with an average of 1.2 ± 0.7 days. With a recovery of intestinal peristalsis, obtained after a period of time with an average of 1.02 ± 0.1 days, the canalization to gases was observed after a period of time with an average of 1.9 ± 0.7 days, while the canalization to the feces instead after an average of 3.3 ± 1.2 days. In all cases a complete canalization was obtained at the time of discharge. The analysis of the duration of the average post-operative hospital stay, compared to the type of intervention

Table 5: Analysis of the differences observed in the two time periods

Parameters analyzed	period 1	period 2	p
Balanced Anesthesia	62.2% (28/45)	28.8% (13/45)	<0.01
Epidural Anesthesia	22.2% (10/45)	48.85% (22/45)	0.02
Tap-Block	15.5% (7/45)	22.3% (10/45)	0.4
VAS at awakening	2.7±0.6	2.2 ±0.4	0.001
VAS in 1 ^o day p.o.	2.7±0.9	2.5±0.6	0.2
Paracetamol/day	1.0±0.7	0.5±0.4	0.02
Operating time (min)	158.2±48.2	159.7±62.7	0.9
Intraoperative infusion (ml)	1689.4±650.2	1635.7±786.4	0.7
Postoperative Hospital stay (days)	4.3±0.9	4.3±0.9	0.9

performed, is reported in Table 4. It was observed that the lower average hospital stay was obtained after right hemicolectomy (3.8 ± 1 days).

In patients treated for diseases of the left colon with left hemicolectomy or sigmoidectomy, the median duration of admission was 4.1 days. Taking into account all types of interventions performed, the average hospital stay was included in the 5 post-operative days.

Discussion

The application of the ERAS protocol in patients undergoing colorectal surgery significantly affects the post-operative outcomes, resulting in a reduction in both hospitalization and post-operative pain, with a more rapid recovery of normal daily activity by the patient. Certainly the principles of the ERAS protocol have been devised and formulated to bring the greatest advantages in patients undergoing open traditional surgery, but currently it has been extensively demonstrated by the LAFA trial, as the association ERAS Protocol - Laparoscopic Minimally Invasive Surgery translates into optimization of medical and surgical outcomes. It should also be emphasized that the best results of the ERAS protocol were obtained in the complex patients, the older subjects and those with multiple co-morbidities (41, 42).

To obtain positive results, it is essential to obtain the most accurate adherence to the numerous items expected by the ERAS (24). This need is certainly very difficult to maintain outside of a scientific study and could discourage the adoption of the ERAS protocol in non-university structures and centers. The formulation and application of an ERAS protocol are in fact complex and require a long period of time. Furthermore, it should be considered that the ERAS protocol, when applied alone, is not sufficient on its own to ensure excellent results in the short term and at a distance (43-45). All participants in the protocol involved (doctors, nurses and patients) must also have an active role in the implementation of the protocol (57, 58). We must know perfectly the principles that underlie the ERAS, have full confidence in the protocol and the strong, determined will to change and change some old traditional behaviors of common clinical practice (29). Above all, in

particular, it is absolutely necessary to set up a well-coordinated and well-functioning multidisciplinary team that has common and shared objectives. Furthermore, the patient's conviction, the preoperative counseling, the standardization of the treatment process and the possibility to modify the protocol itself, at any time, on the basis of new scientific acquisitions, represent essential prerequisites and fundamental characteristics that are integral part to this important process of change, which can rightly be defined as a real epochal transition (46-48).

The integrity of the ERAS system in the elderly patient, which is compliant, has the greatest advantages in terms of post-operative results. It should be noted that in these patients, adequate fluid therapy, which avoids hyperhydration, and an early mobilization result in an improvement in the respiratory and cardio-circulatory function of the patient operated, with a faster recovery of normal daily activities and a lower impact negative from surgical stress (49, 50). In fact, in our experience, no postoperative respiratory complications were reported, which are very frequent and common in traditional post-operative management. As for sex, our sample was equally divided between male and female patients. The analysis of the peri-operative results has given a significant success. Surely they point out a more painful possibility of pain on the part of women, as indeed very often, considered in normal daily clinical practice, even on our part (51, 52). It's always happened, it's never been easier to think of a greater onset (in the case of women it is mainly localized at subcutaneous level) of postoperative morbidity.

In our experience, however, no difference in terms of postoperative morbidity compared to sex was observed (53, 54). The BMI greater than 25 kg/m² was the only factor that led to a significant increase in the average dose of paracetamol administered during the post-operative period; moreover, the VAS on waking was also higher in these patients, while no significant differences were recorded in the other post-operative results analyzed. Regarding the type of pathology treated with surgery, most of the interventions performed in our series have involved neoplastic diseases. Malignant neoplasms did not result in significantly worse outcomes than benign neoplasms. This result in our series is probably influenced by the contained

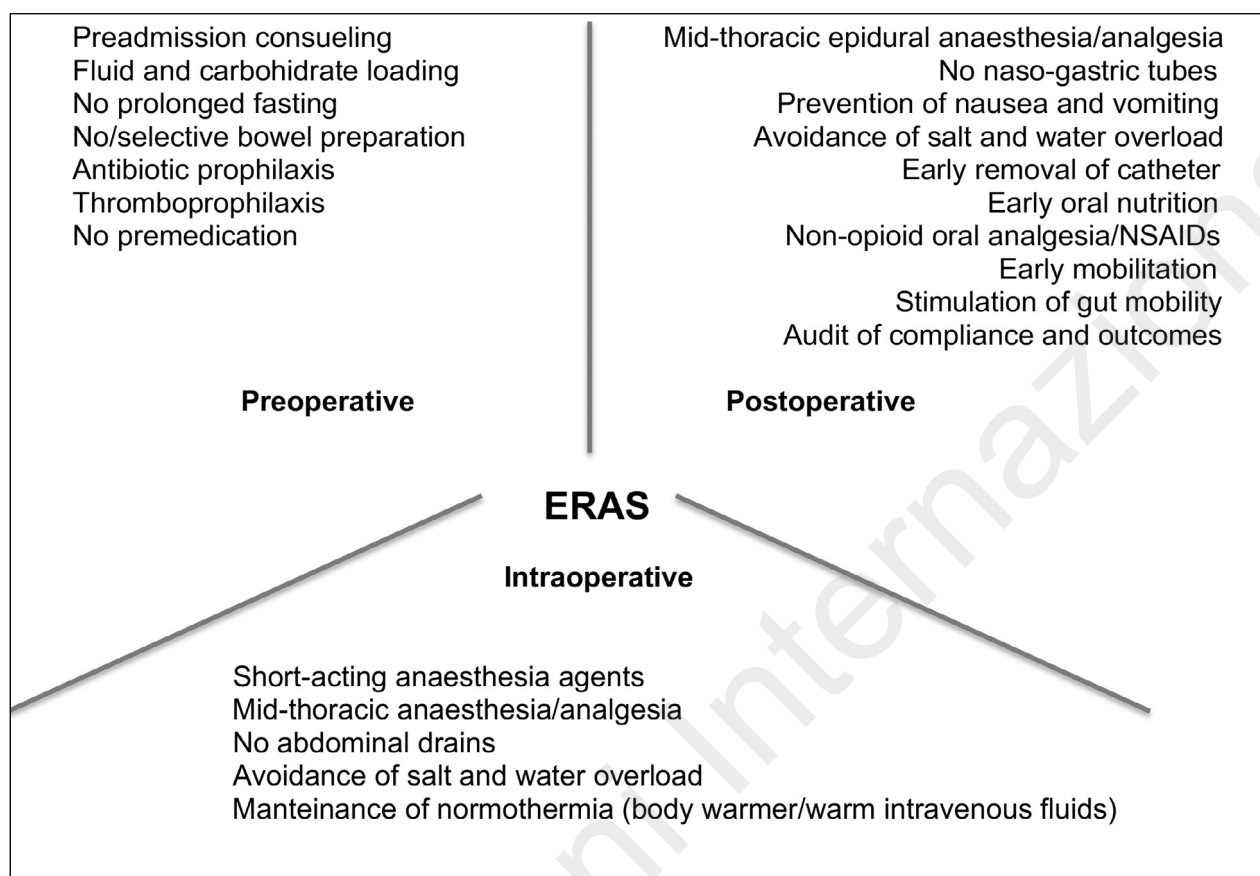


Figure 1 - The ERAS perioperative path.

presence of benign neoplasms in our series, object of the study. Regarding the anesthesiological techniques practiced, in our experience the additional use of local-regional anesthesia techniques, such as the epidural and the Tap-Block “has allowed a significant reduction of post-operative pain, both at waking and during hospitalization. The choice of anesthesia is of fundamental importance for the implementation and correct implementation of an ERAS protocol. The ultimate goal is to reduce operative stress and achieve adequate analgesia control” without the use of opioid drugs. In fact, drugs of this type involve an increased risk of post-operative nausea and vomiting and a delayed recovery of normal peristalsis, resulting in a lengthening of hospitalization times. In addition, no episodes of nausea or vomiting were found in our series and no patient needed the placement of the naso-gastric tube, with the exception of a case where it was necessary for the presence of a sub-occlusion state in a patient with colostomy, resolved in the 2nd day after an endoscopy examination (59, 60).

Our results further underline how the close collaboration between surgeon and anesthesiologist represents a fundamental cornerstone in the management and application of an ERAS protocol. Regarding the intra-operative results of our series, most of the patients underwent laparoscopic surgery, with a low conversion rate, linked to the presence of tenacious visceral adhesions, or to purely oncological reasons. The duration of the intervention obviously presented substantial differences compared to the interventions performed, while it was not influenced by any of the factors analyzed, such as in particular the BMI > 25 Kg/m² and the type of pathology treated. The intra-operative infusions were absolutely in line with those described and recommended in the literature and no transfusion was performed during the operation. It is widely demonstrated that, following these management lines scrupulously, peri-operative hyper-hydration is completely avoided, thus significantly improving the speed of recovery of the patient in the first 24 hours immediately follow-

ing surgery (1-3). However, the fundamental objectives of the ERAS protocol are certainly the reduction of hospitalization time and the improvement of post-operative outcomes (62, 63). However, a fundamental factor for the correct evaluation of the quality of an ERAS protocol is represented by the incidence of late post-operative complications, which occur after discharge from the hospital and which require re-hospitalization within 30 days from surgery (4, 5). In our series, the protocol was completed in almost all patients. The different steps to be completed in the first 48 hours after the intervention must be considered in all respects fundamental steps to be followed to obtain an adequate achievement of the ERAS objectives (79). This is also true because the first two post-operative days often represent 50% or 2/3 of the total length of stay; not being able to adequately start the protocol, inevitably involves a significant lengthening of hospital stay times (6-8).

In our case series, all patients were mobilized the same evening as surgery, or at least the morning of the following day, the first postoperative day, immediately after the removal of the bladder catheter and the epidural catheter (if present). Considering all the patients who completed the protocol, we obtained an average hospital stay of about 4 days post-operatively, absolutely in line with the international literature. Instead, by evaluating the different types of operations performed, we observed normal differences in duration, obviously linked to surgical technical aspects. It is obvious, for example, that a right hemicolectomy is burdened by less surgical stress for the patient, with a lower risk of complications than rectal surgery. Nevertheless, for all the surgical procedures performed, an average hospital stay of less than 5 days post-operative was obtained. To obtain this remarkable result was made possible thanks to the achievement, within 5 days from the intervention, of the different eligibility criteria indicated in the protocol, which made the patients "fit to discharge", i.e. suitable for discharge; in particular, the early recovery of normal peristaltic intestinal activity and of the gas channeling allowed to obtain an early re-feeding, with a complete recanalization to the faeces obtained in all the patients studied, before discharge. Finally, in our series we did not observe any hospital re-entry after 30 days from the intervention due to the onset of late complications at home (80-82).

Conclusions

In conclusion, in the international literature the application of ERAS protocols has not shown a clear reduction of post-operative complications, but results comparable to those of traditional post-operative management are reported. In our series, no anastomotic dehiscences were observed and 30-day re-hospitalizations with better results than those reported in the literature. This result is certainly linked to the number of the sample, but at the same time the possibility to perform the interventions always with the same surgical and anesthetic team has a positive influence on the post-operative outcomes, as already demonstrated in other series published in the literature (36). Moreover, the optimization of the peri-operative and management process involves a reduction of the surgical stress suffered by the patient throughout the care path, starting from the pre-operative assessment, until the end of the hospital course. In our ward, patients are hospitalized the same day of surgery and are operated in a nutritional and emotional state, as much as possible optimized. All the factors involved in this process lead to an improvement in the patient's general condition, including nutritional status and acceptance of hospitalization and of the disease itself, resulting in a significant improvement in medical and surgical outcomes. In particular, the possibility of eating normally at home until the time of surgery, (following only a diet that is free of waste for 5 days before the intervention), is honestly a fundamental factor for achieving an improvement in the management of these patients.

An increase in post-operative morbidity could however occur with the increase in casuistry. Certainly, the first adverse events and the first failures, represented by the early re-hospitalization, should not change the trust in the ERAS Protocol and the desire to continue to progress, innovate and improve. In conclusion, in our experience the conception and application of an ERAS protocol in colorectal surgery involved an optimization of the entire peri-operative care and management path, with a significant reduction in hospitalization and post-operative complication times. The achievement of these results also leads to a sharp reduction in management costs and an improvement in the level of

patient satisfaction, the hospital structure and all professionals, doctors and nurses, involved in the

care and management path represented by the ERAS Protocol.

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