# Impact of Enhanced Recovery Program (ERP) on Clinical Outcomes After Elective Colorectal Surgery in a Rural Hospital: A Prospective Cohort Study with Retrospective Control.

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# Abstract

## Introduction:

The main purpose was to determine the impact on postoperative outcome of a standardized enhanced recovery program (ERP) for elective colorectal surgery in a rural hospital.

## Methods

A prospective series of patients (N = 80) undergoing elective colorectal resection completing a standardized ERP protocol in 2018–2020 (ERP group) was compared to patients (N = 80) operated at the same rural hospital in 2013–2015 (pre-ERP group), before the implementation of the program. The exclusion criteria for both groups were: ASA score IV, TNM stage IV, inflammatory bowel disease, emergency surgery, and rectal cancer. The primary outcome was hospital length of stay (LoS) which was used as an estimate of functional recovery. Secondary outcomes included 30-day readmission and mortality rates as well as factors predicting both postoperative complications and prolonged hospital LoS.

## Results

Baseline characteristics were comparable in both groups. Laparoscopic approach was performed in 95% of patients in the ERP group versus 0% in pre-ERP group. The median adherence to ERP protocol elements was 68% as opposed to 12% in the retrospective control group. The median hospital LoS in the ERP-group was significantly lower than in the pre-ERP group (5 *vs.* 10 days) with no increase in 30-day readmission and mortality rates. The Body Mass Index ≥ 30 and the traditional perioperative protocol were the independent predictive factors of postoperative complications, while following a traditional peri-operative protocol was the only factor predicting a prolonged hospital LoS.

## Conclusions

Although limited hospital resources are perceived as a barrier to ERP implementation, the current experience demonstrates how adopting an ERP program in a rural area is feasible and effective, despite it requires greater effort. For patients in such areas, colorectal ERP in elective surgery may also reduce time to functional recovery, postoperative hospital LoS and complications, with no increase in mortality and 30-day re-admissions.

## Introduction

The Enhanced Recovery Program (ERP) is a scientific evidence-based peri-operative care approach centered on a multidisciplinary team aiming to improve postoperative outcomes and to reduce recovery

time in surgical patients, by attenuating the peri-operative metabolic response as well as organ dysfunction [1, 2].

The ERP protocols have primarily been developed and used in urban and academic centers in Europe and North America. Until today, however, there are very few data concerning the application of ERP in elective colorectal surgery in rural and community-based hospitals, serving wide and remote rural areas, where medical resources may be limited [3–6]. People living in a rural environment present many differences from those living in urban areas, in terms of social (e.g., degree of education, health literacy, transportation) and health (e.g., access to medical care, co-morbidities, post-discharge facilities) factors. Furthermore, rural areas are generally larger and less densely populated than urban ones and this implies potential difficulties both for hospital discharge and for patient care in such a context [7, 8]. Another important aspect is the case-volume, which may be lower in rural hospitals, and the higher medical and nursing staff turnover and shortage.

As scientific evidence concerning the effectiveness of ERP in rural contexts is very limited, the primary objective of this study was to determine the impact on postoperative outcomes of a standardized ERP for elective colorectal surgery in a rural hospital using the length of stay (LoS) as a surrogate of functional recovery. The secondary outcomes were to evaluate the 30-day readmission and mortality rates as well as to identify the predictive factors of both postoperative complications and prolonged hospital LoS.

## Materials And Methods

### Study design, setting, participants

A prospective series of consecutive patients (N=80) undergoing elective colorectal resection completing a standardized ERP protocol [17] from November 2018 to July 2020 (ERP group) was compared to patients (N=80) operated at the same rural hospital in Northern-East of Italy from April 2013 to December 2015 (Pre-ERP group), before the implementation of the protocol. The year 2016 was excluded due to organizational changes in the unit which modified the traditional practice, while throughout the year 2017 the ERP protocol was implemented.

Eligible criteria were: age ≥18 years-old, elective colorectal resection, American Society of Anesthesiologists (ASA) score I-III. The exclusion criteria for both groups were: ASA score IV, TNM stage IV, inflammatory bowel disease, emergency surgery, and rectal cancer.

### Variables and Data Sources

Data were recorded prospectively in the ERP group, while they were retrospectively extracted from medical record documentation in the Pre-ERP group by two separate investigators (L.S., V.S.) who were blinded to the study protocol.

All complications were recorded until 30 days after surgery, as well as mortality and hospital readmission.

Patients in the Pre-ERP group underwent an open colorectal resection while to all patients in the ERP group a laparoscopic approach was offered as part of the ERP. All operations in both groups were performed by two distinct surgeons fully trained in colorectal surgery and, in the ERP group, advanced laparoscopy who had well completed their learning curve. Also, the surgeon operating on in the ERP group (C.V.F.) had a consolidated experience implementing ERPs [17-19].

Patients in both groups were discharged after full recovery from the surgical operation. The adopted parameters for patient recovery were as follows: 1) Complete oral feeding recovery, without any restriction, 2) Complete gastrointestinal recovery, defined as the time taken for patients to tolerate solid food and to pass stool, 3) Complete pain control with oral analgesics (i.e., Numerical Rate Scale – NRS ≤3), 4) Return to complete mobilization after surgery, 5) No local or systemic sign of infection.

The Clavien–Dindo grading system [9] was used to classify each patient's most severe encountered complication: no complication (grade 0), minor complication (grades I–II) or major complication (grades III–V).

All ERP items were listed in a specific checklist and were recorded in all postoperative days until patient discharge. During their hospital stay, patients in the ERP group were encouraged to follow the protocol by underlining the potential benefits in terms of post-operative outcomes, as the enhanced recovery principles may not be intuitive.

### Outcome Measures

The primary outcome was the hospital LoS which was used as a surrogate of functional recovery, which included recuperation of intestinal function, toleration of an oral diet, and mobilization.

Secondary outcomes were 30-day readmission and mortality rates and predictive factors of both postoperative complications and prolonged hospital LoS.

### Compliance with ethical standards

The study was carried out in accordance with the International Ethical Guidelines and Declaration of Helsinki. All patients signed a written informed consent before surgery. The study protocol (ID: 354/2019/Oss/AUSLFe) was approved by the local Ethical Committee (*Comitato Etico Area Vasta Emilia Centro– CE-AVEC*).

### Statistical analysis

Clinical parameters were expressed as median [interquartile range (IQR) 25–75)] according to distribution assessed by Shapiro–Wilk test. Categorical data were presented as numbers. Clinical and pathological variables were analyzed with chi-square, and Mann–Whitney tests as appropriate. The Kaplan–Meier test method and Log-Rank test were used to compare the duration of surgical operation, time to complete functional recovery, and hospital LoS between the two groups. A logistic regression analysis was

performed to evaluate the predictive factors of postoperative complications, while the independent predictors of prolonged hospital LoS were determined by using a Cox regression analysis. Of note, hazard ratios (HRs) < 1 correspond to an association of the factor with prolonged hospital LoS, while HRs > 1 correspond to earlier discharge. A p-value <0.05 was considered statistically significant. All collected data were included in an electronic study database and analyzed using the SPSS software (IBM SPSS Statistics for Windows, version 20.0).

## Results

A total of 160 patients undergoing elective colonic resections at our institution were included in this analysis. The investigation group (ERP group) comprised 80 patients operated on *after* the implementation of the colorectal ERP, in 2017, while the control group (Pre-ERP group) included 80 patients operated on *before* starting the ERP.

The applied items included in the protocol, derived from the *fast-track* one proposed by Kehlet and Wilmore in the mid-1990s [2], are listed in **Table 1**. The median adherence to ERP protocol was 68% as opposed to 12% of the retrospective control group. Avoidance of intra-operative fluid overload and delayed early mobilization of patients after surgery were the main elements of lower compliance in the ERP group, as shown in **Figure 1**.

Demographic and clinical data are reported in **Table 2**. Baseline characteristics were comparable in both groups, except for chronic kidney insufficiency which was significantly more frequent in the ERP group. Laparoscopic approach was performed in 95% of patients in the ERP group versus 0% in pre-ERP group (p-value <0.0001). Among intra-operative variables, prophylactic naso-gastric tube and abdominal drains placement were lower in ERP group compared to Pre-ERP group (p-value <0.0001), the rate of intra-operative fluids infusion was about 5*ml/kg/h* lower in ERP group (p-value <0.0001).

All intra-operative variables are shown in **Table 3**.

All the measured post-operative outcomes are reported in **Table 4**. Among them, the complete gastrointestinal recovery was achieved earlier in the ERP group, as well as early mobilization and pain control by oral analgesics (p-value <0.0001). The median hospital LoS in ERP-group was 5 days (4-7 days) versus 10 days (9-14 days) in the pre-ERP group. ERP protocol determined a reduction of 31% in post-operative complications. No significant difference in mortality and 30-days re-admission rates was found between the two groups.

The unadjusted and adjusted analyses are illustrated in **Tables 5-6**. Adjusted logistic regression analysis showed that BMI ≥30 and the conventional peri-operative protocol were associated to increased risk of post-operative complications, while following a conventional peri-operative care protocol was the only factor associated to a prolonged hospital LoS (p<0.0001).

## Discussion

In the current study we evaluated the clinical outcome in patients who underwent elective colorectal resection in a single institution serving a wide low densely populated rural and fishing area *before*, retrospectively, and *after*, prospectively, the adoption of a colorectal ERP. Implementing the protocol in such an area, allowed to improve safely patient's convalescence by reducing time to functional recovery, lowering by half the duration of hospital LoS, and decreasing by almost one third postoperative complications, with no increase in mortality and 30-day re-admissions. Finally, following a traditional perioperative care protocol was the only factor we found to be associated to a prolonged postoperative hospital LoS.

The application of an ERP may be particularly difficult in rural hospitals serving wide areas, as it may be hindered by multiple factors affecting both health care professionals and patients such as: 1) lack of strong scientific evidence supporting the real efficacy outside urban areas and tertiary or academic hospitals, 2) fear of complications due to decrease resources to manage postoperative complications, 3) more difficult access to medical care by the patients, 4) decreased health literacy as ERP principles may not be intuitive, 5) higher medical and nursing staff turnover and shortage, 5) poor familiarity with some elements of ERP protocol by medical and nursing staffs, 6) lack of time and commitment by health care professionals to constitute a multidisciplinary team, 7) limited hospital resources, 8) lower case-volume, 9) patient perplexity about earlier hospital discharge.

Introduction of ERP into clinical practice has been pioneered as *fast-track* surgery by Henrik Kehlet and colleagues in the mid-1990s [1], with the principal objective to optimize postoperative outcomes of the surgical patients. This protocol was initially used in urban and academic tertiary care centers and many hospitals began to adopt it, with a slow progressive dissemination from Northern Europe and North America throughout the world. The core guidelines established by Kehlet were delineated by consensus review [10], until the birth of the Enhanced Recovery After Surgery (ERAS) society in 2010 [11]. The safety and efficacy of colorectal ERP has been established in a few randomized studies and meta-analysis of randomized studies conducted in urban and academic hospitals [12-14]. Until today, however, the evidence regarding the adoption and feasibility of such a program in rural contexts is quite limited [3-8], which may be perceived as a barrier to ERP implementation in those area. Very few experiences from North American rural and community hospitals [6-8] as well as European rural contexts [3-5] have been published in the last decade. Tebala GD *et al.* [3] found age and laparoscopic approach as independent prognostic factors significantly associated with early discharge with a readmission rate of 9.1%. Moreover, they analyzed the influence of the operation day of the week on postoperative recovery: in their study, interestingly, oncologic results were slightly better and postoperative complications were lower in patients operated on Mondays to Wednesdays [3]. Marres CCM *et al.* [4] also found a significant reduction of major post-operative complications and mortality after implementing a quality improvement program in colorectal surgery. Geltzeiler CB *et al.* [6] analyzed the evolution of implementing colorectal ERP from 2009 to 2012 and they found a significant decrease of hospital LoS (6.7 days vs 3.7 days) with a remarkable estimated cost-saving for patients. Archibald LH *et al.* [7] investigated the introduction of a comprehensive care process for enhanced recovery after colon surgery in eight community hospitals and

they concluded that ERP represents the most important factor, more than laparoscopic approach, in decreasing length of stay.

As evidenced from the literature, there is a strong relationship between the adherence to the elements of the protocol and the complete recovery of patients with a remarkable reduction in hospital LoS [15-17]. The median adherence to ERP protocol in our study was 68%. Two important items were not fulfilled: the amount of intra-operative fluids administration and early mobilization after surgery. Concerning the first element, although the amount of intra-operative fluids was reduced with the adoption of the program versus control, the target infusion was not reached, which was probably related to the habits of anesthetists. Early mobilization was probably affected by advanced patients' age [77 years-old (69-83)] as well as the high nurse to patient ratio (1:12 am, 1:12 pm) and limited physiotherapists available for support. However, despite the reduced compliance with these elements, the median time to functional recovery was significantly reduced and the duration of hospital LoS was half among ERP patients (5 days) versus controls (10 days). Furthermore, considering the last quartile of patients in the ERP group (N=20), a further decrease of 1 day in the hospital LoS (4 days) was detected, suggesting that mastering the implementation of ERP improves the outcome.

Another remarkable achievement with the ERP was patient hospital discharge as soon as recovery was complete according to predefined standardized criteria (i.e., fit for discharge), while control patients left the hospital a median of one day after they were fit for discharge.

It could be argued that the improved outcome among ERP patients could be due to the use of laparoscopy (95%) as opposed to open surgery among control patients. Certainly, the laparoscopic approach is a key stress reducing element that should be integrated in ERP to obtain the greatest improvement in recovery [14]. The global peri-operative patient care, however, is fundamental to improve the postoperative outcome regardless of the approach used [18]. A meta-analysis of randomized trials on open colorectal resections showed a significant reduction of hospital LoS by following ERP [20]. Finally, it should be noticed that being on traditional rather than enhanced recovery care was the only independent predictor of prolonged hospital LoS in our study population (N=160).

An interesting point of debate could be the higher postoperative ICU admission rate observed in ERP group (47%) compared to the Pre-ERP group (20%), although the duration of ICU LoS was half [1 (1-1) vs. 2 (1-4), p=0.001]. This reflects, however, the institution of a sub-intensive care unit (SICU) in 2016 to care for the elderly as well as the advanced age in our study population.

Another important aspect of ERP perioperative care is related to health cost-saving. Previous studies show hospital LoS reduction yielding significant cost savings per patient with ERP in colorectal surgery [6,8,17]. Moreover, a prospective study underlined the benefits of an ERP in a North American community hospital in terms of overall wound complications rates [21]. Although not evaluated in our investigation, the decrease in postoperative complications (31%) and duration of hospital LoS (5 days shorter) among patients on enhanced recovery may well suggest a reduction for institutional costs with the ERP.

*Strength and limitations*

This is a single center prospective study with a historical control group used for comparison and, therefore, the results must be interpreted with caution.

Due to profound organizational changes in the unit and the time of implementation of the program there is a two-year interval between the study periods. Also, two different surgeons operated in the ERP group and pre-ERP group, respectively.

Patients in the ERP group may have benefited from the laparoscopic approach as opposed to the open one adopted in the Pre-ERP group. Minimally invasive approaches, however, are an important component of ERPs to reduce the postoperative surgical stress response. Furthermore, at multivariate analysis, being on a traditional perioperative program was the only factor associated to prolonged hospital LoS.

Nonetheless, given the weakness and paucity of scientific evidence about implementation of ERP in colorectal surgery, this study is very useful as it clearly demonstrates the reproducibility of a safe and effective colorectal ERP within a wide agricultural area with a low-density population.

# Conclusion

Although limited resources are perceived as a barrier to ERP implementation, the current experience demonstrated how the use of an ERP in a hospital serving a wide rural low densely populated area is feasible and effective, despite it requires greater effort. Adopting an ERP protocol in elective colorectal surgery in such a context we achieved: 1) significant reduction in time to functional recovery and postoperative hospital LoS, 2) lower postoperative complications, and 3) no increase in mortality and 30-day re-admissions.

# Declarations

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# Tables

Table 1
Key elements of the Enhanced Recovery Program (ERP) protocol.

| Variables | ERP Group (N = 80) | Non-ERP Group (N = 80) | p-value |
|---|---|---|---|
| Pre-admission counselling [N(%)] | 79 (98,7) | 0 (0) | < 0.0001 |
| Information booklet [N(%)] | 79 (98,7) | 0 (0) | < 0.0001 |
| No mechanical bowel preparation [N(%)] | 80 (100) | 28 (35) | < 0.0001 |
| No pre-operative fasting [N(%)] | 80 (100) | 0 (0) | < 0.0001 |
| Pre-operative oral carbohydrate loading [N(%)] | 78 (97,5) | 0 (0) | < 0.0001 |
| No premedication [N(%)] | 71 (88,7) | 80 (100) | 0.003 |
| Mid-thoracic epidural anesthesia [N(%)] | 34 (42,5) | 22 (27,5) | 0.068 |
| Preoperative TAP-block [N(%)] | 44 (55) | 0 (0) | < 0.0001 |
| Short-acting anesthetic agent [N(%)] | 80 (100) | 0 (0) | < 0.0001 |
| Avoidance of intraoperative fluids overload (< 5 ml/kg/h) | 1 (1,25) | 0 (0) | 0.999 |
| Intraoperative maintenance of normothermia [N(%)] | 80 (100) | 80 (100) | 0.999 |
| Prevention of nausea and vomiting [N(%)] | 47 (58,7) | 3 (3,75) | < 0.0001 |
| Minimally invasive surgery [N(%)] | 76 (95) | 0 (0) | < 0.0001 |
| No abdominal drains [N(%)] | 59 (73,7) | 0 (0) | < 0.0001 |
| No nasogastric tube [N(%)] | 51 (63,7) | 7 (8,7) | < 0.0001 |
| Early mobilization (day ≤ 2) [N(%)] | 19 (23,7) | 1 (1,25) | < 0.0001 |
| Post-operative breathing exercises [N(%)] | 80 (100) | 0 (0) | < 0.0001 |
| Mid-thoracic epidural analgesia [N(%)] | 34 (42,5) | 22 (27,5) | 0.068 |
| Non-opiate oral analgesics/NSAIDs [N(%)] | 66 (82,5) | 27 (33,7) | < 0.0001 |
| Stimulation of gut motility [N(%)] | 36 (45) | 1 (27,5) | < 0.0001 |
| Early removal of bladder catheter (day ≤ 2) [N(%)] | 47 (58,7) | 4 (5) | < 0.0001 |
| Early oral nutrition (day ≤ 1) [N(%)] | 55 (68,7) | 0 (0) | < 0.0001 |
| TAP: transverse abdominis plane; NSAIDs: non-steroidal anti-inflammatory drugs. | | | |

## Table 2
### Demographic and baseline characteristics.

| Variables | ERP Group (N = 80) | Non-ERP Group (N = 80) | p-value |
|---|---|---|---|
| **Gender**[N(%)] | | | 0.424 |
| Male | 43 (53,7) | 49 (61,2) | |
| Female | 37 (46,3) | 31 (38,8) | |
| **Age** (years)[N(%)] | | | 0.623 |
| median (IQR 25−75) | 77 (69−83) | 78 (69−83) | |
| < 65 | 15 (18,7) | 13 (16,2) | |
| 65−74 | 21 (26,2) | 17 (21,2) | |
| ≥ 75 | 44 (55,1) | 50 (62,6) | |
| **BMI** (Kg/m$^2$)[N(%)] | | | 0.455 |
| < 25 | 30 | 30 | |
| 25-29.9 | 39 | 33 | |
| ≥ 30 | 11 | 17 | |
| **ASA score**[N(%)] | | | 0.395 |
| I | 2 (2,5) | 3 (3,7) | |
| II | 33 (41,2) | 41 (51,2) | |
| III | 45 (56,3) | 36 (45,1) | |
| **History of Diabetes**[N(%)] | 12 (15) | 16 (20) | 0.533 |
| **Hypertension**[N(%)] | 54 (67,5) | 48 (72,5) | 0.411 |
| **Asthma**[N(%)] | 2 (2,5) | 0 (0) | 0.497 |
| **COPD**[N(%)] | 8 (10) | 6 (7,5) | 0.781 |
| **Valvular heart disease**[N(%)] | 6 (7,5) | 1 (1,25) | 0.117 |
| **Ischemic heart disease**[N(%)] | 9 (11,2) | 7 (8,7) | 0.793 |
| **Atrial fibrillation**[N(%)] | 8 (10) | 14 (17,5) | 0.251 |
| **Hypercholesterolemia**[N(%)] | 19 (23,7) | 11 (13,7) | 0.155 |

BMI, body mass index; ASA, American Society of Anesthesiologists; COPD: Chronic obstructive pulmonary disease; MUST: Malnutrition Universal Screening Tool.

| Variables | ERP Group (N = 80) | Non-ERP Group (N = 80) | p-value |
|---|---|---|---|
| Chronic kidney disease [N(%)] | 11(13,7) | 2 (2,5) | 0.017 |
| Depressive disorder[N(%)] | 7 (8,7) | 6 (7,5) | 0.999 |
| MUST score | | | 0.643 |
| 0 | 54 | 72 | |
| 1 | 15 | 4 | |
| 2 | 9 | 4 | |
| 3 | 1 | 0 | |
| 4 | 1 | 0 | |
| Pre-operative haemoglobin levels [median (IQR 25–75)] | 12.0 (10.9–13.2) | 11.2 (10.0-13.4) | 0.138 |
| BMI, body mass index; ASA, American Society of Anesthesiologists; COPD: Chronic obstructive pulmonary disease; MUST: Malnutrition Universal Screening Tool. | | | |

Table 3
Intraoperative variables.

| Variables | ERP Group (N = 80) | Non-ERP Group (N = 80) | p-value |
|---|---|---|---|
| Disease[N(%)] | | | 0.999 |
| Malignancy | 68 (85) | 69 (86) | |
| Benign tumors/Diverticular disease | 12 (15) | 11 (14) | |
| Type of operation[N(%)] | | | 0.705 |
| Right colectomy | 50 (62) | 52 (65) | |
| Left colectomy | 5 (6) | 3 (4) | |
| Transverse colectomy | 3 (4) | 4 (5) | |
| Segmental colonic resection | 6 (7) | 8 (10) | |
| Sigmoidectomy | 15 (19) | 10 (12) | |
| Rectosigmoid resection | 1 (1,25) | 3 (4) | |
| Preoperative TAP-Block[N(%)] | 44 (55) | 0 (0) | < 0.0001 |
| Formation of new stoma[N(%)] | 4 (5) | 1 (1,25) | 0.367 |
| Surgical approach[N(%)] | | | < 0.0001 |
| Laparotomy | 0 (0) | 80 (100) | |
| Laparoscopy | 76 (95) | 0 (0) | |
| Laparoscopy with conversion | 4 (5) | 0 (0) | |
| Length of procedure (min)* | 170 (153−200) | 80 (65−90) | < 0.0001 |
| Intraoperative intravenous fluids (ml/kg/h)* | 11.5 (8.5−14.6) | 16.1 (12.9−22.2) | < 0.0001 |
| Intraoperative RBC transfusion[N(%)] | 1 (1,25) | 5 (6) | 0.210 |
| * median (IQR25-75); TAP: Tranverse Abdominis Plane; RBC: Red Blood Cells. | | | |

Table 4
Measured postoperative variables and outcomes.

| Variables | ERP Group (N = 80) | Non-ERP Group (N = 80) | p-value |
|---|---|---|---|
| **Positioning of** [N(%)] | | | |
| Central venous catheter | 9 (11) | 19 (24) | 0.060 |
| Epidural catheter | 34 (42) | 22 (27) | 0.068 |
| Prophylactic nasogastric tube (NGT) | 29 (36) | 73 (91) | < 0.0001 |
| Abdominal drain | 21 (26) | 80 (100) | < 0.0001 |
| **Day of removal of** [median (IQR 25−75)] | | | |
| Epidural catheter | 3 (2−3) | 2 (1−3) | 0.207 |
| NGT | 1 (1−2) | 3 (2−4) | 0.001 |
| Abdominal drain | 3 (3−5) | 7 (6−8) | < 0.0001 |
| Foley catheter | 2 (2−3) | 7 (5−9) | < 0.0001 |
| **Post-operative RBC transfusion**[N(%)] | 5 (6) | 21 (26) | 0.001 |
| **Vomiting ≤ 24 h** [N(%)] | 12 (15) | 9 (11) | 0.492 |
| **Vomiting > 24 h**[N(%)] | 7 (9) | 24 (30) | 0.001 |
| **Reactive NGT**[N(%)] | 11 (14) | 12 (15) | 0.999 |
| **Resumption of intravenous fluids**[N(%)] | 4 (5) | 2 (2,5) | 0.443 |
| **Postoperative intravenous opioids** [N(%)] | 14 (17) | 53 (66) | < 0.0001 |
| **ICU admission**[N(%)] | 38 (47) | 16 (20) | < 0.0001 |
| **Median ICU length of stay** (days) [median (IQR 25−75)] | 1 (1−1) | 2 (1−4) | 0.001 |
| Day 0 | 0 (0−3) | 0 (0−3) | |
| Day 1 | 0 (0−2) | 1 (0−2) | |
| Day 2 | 0 (0−0) | 0 (0−2) | |

NGT: nasogastric tube; RBC: red blood cells; ICU: intensive care unit.

| Variables | ERP Group (N = 80) | Non-ERP Group (N = 80) | p-value |
|---|---|---|---|
| Day 3 | 0 (0−0) | 0 (0−1) | |
| Day 4 | 0 (0−0) | 0 (0−0) | |
| Stimulation of gut motility by chewing-gum[N(%)] | 36 (45) | 1 (1,25) | < 0.0001 |
| Oral liquid intake (day) [median (IQR 25−75)] | 1 (1−2) | 5 (4−6) | < 0.0001 |
| Oral solid intake (day) [median (IQR 25−75)] | 3 (2−4) | 7 (6−8) | < 0.0001 |
| Time to intestinal activity (day) [median (IQR 25−75)] | 2 (1−2) | 3 (2−4) | < 0.0001 |
| Time to bowel movements (day) [median (IQR 25−75)] | 3 (2−4) | 5 (4−6) | < 0.0001 |
| Time to optimal pain control with oral analgesics (day) [median (IQR 25−75)] | 3 (3−4) | 4 (3−7) | < 0.0001 |
| Early mobilization (day) [median (IQR 25−75)] | 3 (2−5) | 7 (5−9) | < 0.0001 |
| Fit for discharge (day) | 5 (4−6) | 9 (8−12) | < 0.0001 |
| Hospital lenght of stay (days) [median (IQR 25−75)] | 5 (4−7) | 10 (9−14) | < 0.0001 |
| Postoperative complications (Clavien-Dindo)[N(%)] | | | 0.085 |
| Grade I | 8 (10) | 15 (19) | |
| Grade II | 26 (32) | 33 (41) | |
| Grade IIIa | 2 (2) | 1 (1,25) | |
| Grade IIIb | 1 (1,25) | 4 (5) | |
| Grade IVa | 0 (0) | 2 (2) | |
| Grade IVb | 1 (1,25) | 0 (0) | |
| 30-day re-admission[N(%)] | 3 (4) | 5 (6) | 0.718 |
| 30-day mortality[N(%)] | 0 (0) | 0 (0) | 0.999 |
| Destination at discharge [N(%)] | | | 0.285 |

NGT: nasogastric tube; RBC: red blood cells; ICU: intensive care unit.

| Variables | ERP Group (N = 80) | Non-ERP Group (N = 80) | p-value |
|---|---|---|---|
| Home | 69 (86) | 61 (76) | |
| Long-term care institutions | 8 (10) | 14 (17) | |
| Other hospital ward | 3 (4) | 5 (6) | |
| TNM cancer stage | | | 0.378 |
| In situ | 2 (2,5) | 2 (2,5) | |
| I | 16 (20) | 15 (18,7) | |
| IIa | 22 (32,3) | 27 (39,1) | |
| IIb | 4 (5) | 5 (6) | |
| IIc | 0 (0) | 0 (0) | |
| IIIa | 3 (4) | 1 (1,25) | |
| IIIb | 18 (22,5) | 12 (15) | |
| IIIc | 2 (2,5) | 8 (10) | |
| NGT: nasogastric tube; RBC: red blood cells; ICU: intensive care unit. | | | |

Table 5
Association between baseline characteristics, intraoperative variables, and type of perioperative protocol and prolonged length of hospital stay according to Logistic regression analysis adjusted for potential confounders.

| Any postoperative complication | | | | |
|---|---|---|---|---|
| **Variable** **Unadjusted Model** **Full Adjusted Model** | | | | |
| | OR (95% CI) | P | OR (95% CI) | P |
| **Gender** (ref. female) | | | | |
| male | 1.11 (0.59–2.11) | 0.741 | 1.31 (0.58–2.94) | 0.516 |
| **Age** (ref. < 75 y) | | | | |
| ≥ 75 | 1.97 (1.03–3.76) | 0.041 | 1.76 (0.78–3.99) | 0.174 |
| **BMI*** (ref. < 25 kg/m$^2$) | | | | |
| 25-29.9 | 0.83 (0.41–1.68) | 0.602 | 0.92 (0.39–2.17) | 0.844 |
| ≥ 30 | 5.21 (1.39–19.53) | 0.014 | 5.40 (1.12–25.98) | 0.035 |
| **ASA[a]** (ref. I) | | | | |
| II | 0.34 (0.03–3.93) | 0.388 | 0.32 (0.03–4.06) | 0.376 |
| III | 1.43 (0.12–16.58) | 0.776 | 1.54 (0.11–20.79) | 0.747 |
| **Intraoperative intravenous fluids** (ml/kg/h) (ref. ≤ 10 ml/kg/h) | | | | |
| 10.1–15.0 | 0.61 (0.26–1.45) | 0.261 | 0.399 (0.13–1.23) | 0.107 |
| ≥ 15.1 | 1.22 (0.52–2.84) | 0.649 | 0.88 (0.25–3.03) | 0.833 |
| **Perioperative protocol** (ref. ERP) | | | | |
| traditional | 2.44 (1.27–4.66) | 0.007 | 3.02 (1.22–7.52) | 0.017 |

[*] BMI - Body Mass Index.

[a] ASA - American Society of Anaesthesia.

Table 6

Association between baseline characteristics, intraoperative variables, and type of perioperative protocol and prolonged length of hospital stay according to Cox regression analysis adjusted for potential confounders.

| Prolonged hospital length of stay | | | | |
|---|---|---|---|---|
| Variable | Unadjusted Model | | Full Adjusted Model | |
| | HR (95% CI) | P | HR (95% CI) | P |
| **Gend Gender** (ref. female) | | | | |
| Male male | 0.83 (0.60–1.13) | 0.235 | 0.81 (0.58–1.15) | 0.242 |
| **Age ( Age** (Ref: < 75 ys) | | | | |
| ≥ 75 | 0.74 (0.54–1.02) | 0.067 | 0.88 (0.61–1.27) | 0.489 |
| **BMI* BMI** (ref: < 25 kg/m$^2$) | | | | |
| 25 – 2 25–29,9 | 1.42 (0.99–2.04) | 0.054 | 1.54 (1.05–2.25) | 0.026 |
| 30 ≥30 | 0.97 (0.59–1.57) | 0.887 | 1.11 (0.67–1.83) | 0.695 |
| **ASA[a] ASA score** (ref: I) | | | | |
| III II I | 0.47 (0.15–1.52) | 0.210 | 0.44 (0.13–1.45) | 0.177 |
| IIIIII III | 0.39 (0.12–1.26) | 0.115 | 0.30 (0.09-1.00) | 0.051 |
| **Perio Perioperative protocol** (ref. ERP) | | | | |
| TraditiTraditional | 0.32 (0.23–0.45) | < 0.0001 | 0.28 (0.20–0.40) | < 0.0001 |
| * BMI - Body Mass Index. | | | | |
| [a] ASA - American Society of Anesthesiologists. | | | | |

# Figures
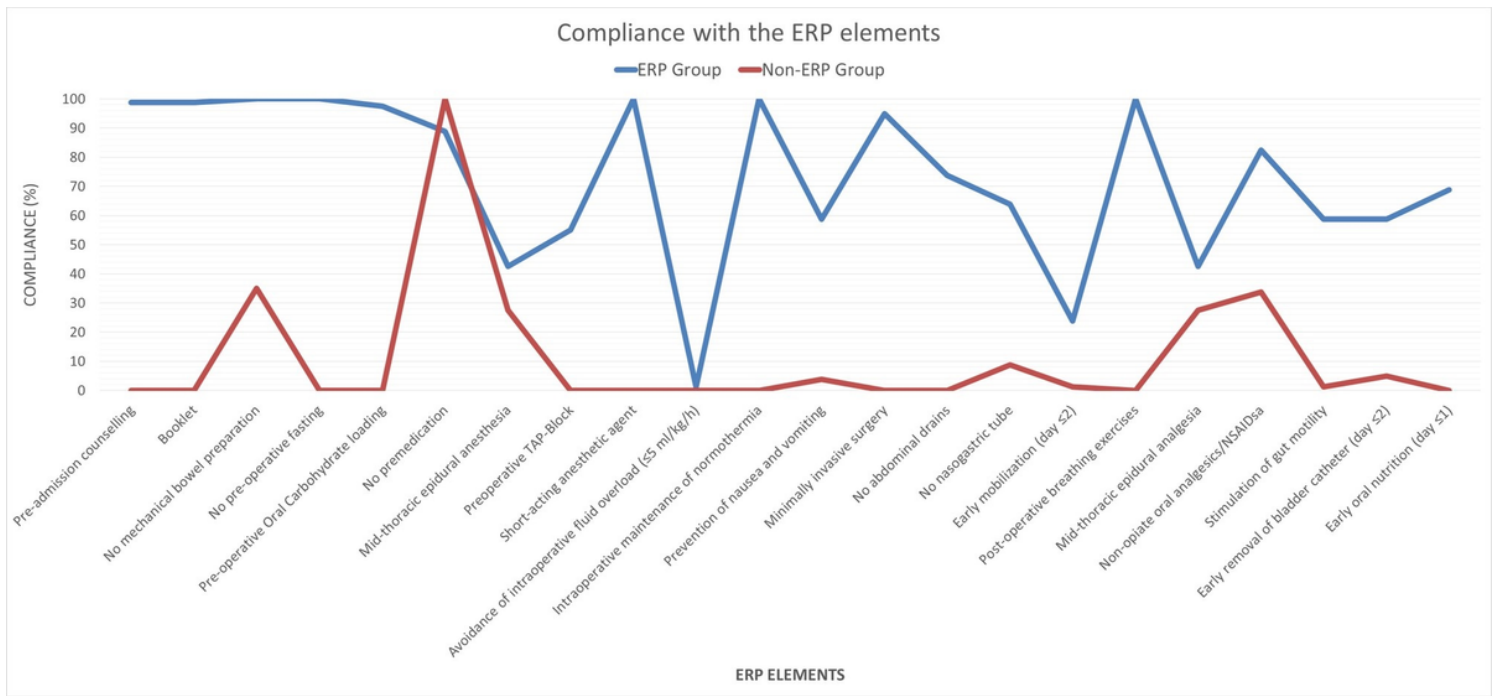
**Figure 1**

Compliance with ERP protocol.