



“Optimal recovery” after colon cancer surgery in the elderly, a comparative cohort study: Conventional care vs. enhanced recovery vs. prehabilitation[☆]

Carlos Cerdán Santacruz,^a Mireia Merichal Resina,^b Ferney David Gómez Báez,^b Lucía Milla Collado,^{c,*} María Belén Sánchez Rubio,^d Óscar Cano Valderrama,^e José Luis Morales Rul,^f Ester Sebastián Vigatá,^g Gemma Fierro Barrabés,^h Jordi Escoll Rufino,^a José Enrique Sierra Grañón,^a Jorge Juan Olsina Kissler^b

^a Colorectal Surgery Department at Hospital Universitario Arnau de Vilanova de Lleida, Lleida, Spain

^b General Surgery Department, Hospital Universitario Arnau de Vilanova, Lleida, Spain

^c Thoracic Surgery Department, Hospital Universitario Arnau de Vilanova, Lleida, Spain

^d Universidad de Lleida, Spain

^e Hospital Clínico Universitario de Vigo, Vigo, Spain

^f Internal Medicine, Hospital Universitario Arnau de Vilanova, Lleida, Spain

^g Psychiatrist, Hospital Universitario Arnau de Vilanova, Lleida, Spain

^h Oncological Nurse, Hospital Universitario Arnau de Vilanova, Lleida, Spain

ARTICLE INFO

Article history:

Received 17 March 2022

Accepted 5 June 2022

Available online 17 June 2022

Keywords:

Prehabilitation

Enhanced recovery after surgery

Conventional care

Optimal recovery

Elderly patients

Colon cancer

ABSTRACT

Background: Colon cancer in elderly patients is an increasing problem due to its prevalence and progressive aging population. Prehabilitation has experienced a great growth in this field. Whether it is the best standard of care for these patients has not been elucidated yet.

Methods: A retrospective comparative cohort study of three different standards of care for elderly colon cancer patients (>65 years) was conducted. A four-weeks trimodal prehabilitation program (PP), enhanced recovery program (ERP) and conventional care (CC) were compared. Global complications, major complications (Clavien-Dindo ≥ 3), reinterventions, mortality, readmission and length of stay were measured. Optimal recovery, defined as postoperative course without major complications, no mortality, hospital discharge before the fifth postoperative day and without readmission, was the primary outcome measure. The influence of standard of care in optimal recovery and postoperative outcomes was assessed with univariate and multivariate logistic regression models.

Results: A total of 153 patients were included, 51 in each group. Mean age was 77.9 years. ASA Score distribution was different between groups (ASA III-IV: CC 56.9%, ERP 25.5%, PP 58.9%; $p = 0.014$). Optimal recovery rate was 55.6% (PP 54.9%, ERP 66.7%, CC 45.1%; $p = 0.09$). No

[☆] Please cite this article as: Cerdán Santacruz C, Merichal Resina M, Báez Gómez FD, Milla Collado L, Sánchez Rubio MB, Cano Valderrama O, et al. “Recuperación óptima” tras cirugía por cáncer de colon en el paciente añoso. Resultados de un estudio de cohorte: Cuidados convencionales, Recuperación intensificada y programa de prehabilitación. Cir Esp. 2022

* Corresponding author.

E-mail address: luciamillacollado@hotmail.com (L. Milla Collado).

differences were found in major complications ($p = 0.2$) nor reinterventions ($p = 0.7$). Un-
eventful recovery favors ERP and PP groups ($p = 0.046$ and $p = 0.049$ respectively).

Conclusions: PP and ERP are safe and effective for older colon cancer patients. Fewer overall
complications and readmissions happened in ERP and PP patients. Major complications
were independent of the standard of care used.

© 2022 Published by Elsevier España, S.L.U. on behalf of AEC.

“Recuperación óptima” tras cirugía por cáncer de colon en el paciente añoso. Resultados de un estudio de cohorte: Cuidados convencionales, Recuperación intensificada y programa de prehabilitación

R E S U M E N

Palabras clave:

Prehabilitación
Recuperación Intensificada tras
Cirugía del Adulto
Cuidados convencionales
Recuperación óptima
Pacientes ancianos
Cáncer de colon

Introducción: El cáncer de colon (CC) en pacientes de edad avanzada es un problema
creciente por su prevalencia y envejecimiento progresivo de la población. La prehabilitación
ha experimentado un gran crecimiento en este campo sin haberse dilucidado si es el mejor
estándar de cuidados para estos pacientes.

Métodos: Estudio retrospectivo comparativo de cohortes de tres estándares diferentes de
cuidados para pacientes mayores de 65 años con CC. Se compararon un programa de
prehabilitación (PP) trimodal de cuatro semanas, uno de recuperación intensificada (RI) y
cuidados convencionales (CC). Se midieron complicaciones globales, complicaciones mayo-
res (Clavien-Dindo ≥ 3), reintervenciones, mortalidad, reingresos y estancia hospitalaria. La
recuperación óptima fue la medida de resultado primaria. La influencia del estándar de
atención en la recuperación óptima y los resultados postoperatorios se evaluó con modelos
de regresión logística univariante y multivariante.

Resultados: Se incluyeron 153 pacientes, 51 por grupo. La edad media fue 77,9 años. La
distribución del ASA fue diferente entre los grupos (ASA III-IV: CC 56,9%, RI 25,5%, PP 58,9%;
 $p = 0,014$). La tasa de recuperación óptima fue del 55,6% (PP 54,9%, RI 66,7%, CC 45,1%;
 $p = 0,09$). No se encontraron diferencias en complicaciones mayores ($p = 0,2$) ni reinterven-
ciones ($p = 0,7$). La recuperación sin incidencias favorece a los grupos RI y PP ($p = 0,046$ y
 $p = 0,049$ respectivamente).

Conclusiones: PP y RI son seguros y efectivos para pacientes mayores con CC. Las compli-
caciones generales y reingresos en pacientes con RI y PP fueron menores. Las complica-
ciones mayores resultaron independientes del estándar de cuidados utilizado.

© 2022 Publicado por Elsevier España, S.L.U. en nombre de AEC.

Introduction

Colon cancer in elderly population is a current relevant
worldwide problem due to its increasing prevalence, progres-
sive aging and frailty of this population group¹.

The best standard of care for elderly colon cancer patients
has been extensively discussed and it is still arguable:
laparoscopy vs. open approach²⁻⁴, the feasibility of enhanced
recovery programs (ERP)⁵⁻⁷, and potential advantages of
prehabilitation programs (PP)^{8,9}.

Some encouraging results have been published concerning
PP in elderly patients after colon cancer surgery^{8,10,11}, and
therefore, an increasing interest is evident in the scientific
community in the last few years^{12,13}.

Despite these results, a recently published randomized
controlled trial challenges previous evidence, and therefore,
the role of PP could be questioned, mainly when compared to
ERP¹⁴.

In this context, we designed a study to compare the
postoperative outcome after colon cancer surgery in elderly

patients following three different standards of perioperative
care: conventional care (CC), ERP and PP.

Material and methods

Study design

A comparative Cohort study of consecutive patients included
in a prehabilitation program was done. Comparison groups
were two historical cohorts of patients with same inclusion
and exclusion criteria who had been consecutively attended at
our colorectal surgery unit of a tertiary referral center
following ERP and CC. All the patients were included in the
prehabilitation program. The same number of consecutive
patients in the ERP and CC cohorts were included from a
prospectively maintained data base. The study period was
October 2016–May 2019.

Ethical permission for this analysis was provided by the
local hospital ethics committee (22/21-4658).

Study participants

Inclusion criteria were colon cancer patients, 15 cm or above from anal verge, age of 65 or older, and operated on an elective surgery. The main selection criteria for patients to undergo PP, was a score ≤ 14 in the frailty screening tool G8 scale¹⁵. Exclusion criteria were stage IV disease, inability to understand ERP or PP preoperative and postoperative instructions or disabled patients who were unable to do any physical activity.

Prehabilitation program

A trimodal design was used, embracing physical exercising, nutritional supplementation and psychological assessment. Apart from this, during operation and postoperative management, these patients were managed following ERP criteria. A multidisciplinary team of psycho-oncologists, dietitians and endocrinologists, physiatrists, anesthesiologists, internal medicine doctors, oncology nurses and colorectal surgeons was set up.

Nutritional counseling and supplementation

Patients were evaluated following the Malnutrition Universal Screening Tool (MUST)¹⁶. Advice of appropriate nutrition and counseling for prehabilitation phase were given. Every patient was orally supplemented with immune-nutrient based shakes (Atempero, Vegenat®), 200 mL twice a day during the preoperative week. Those patients at risk of malnutrition were derived to an exhaustive malnutrition diagnosis protocol and individualized assessment.

Physical exercise

The physiatrist's visit always took place after nutritional screening. Anemia screening and diabetic profile, when indicated, were done. When severe malnutrition or poor cardiorespiratory conditions were diagnosed, physical exercise was considered contraindicated. Those cases were further discussed in order to establish if they were suitable candidates for surgery or if they were considered appropriate to be discarded.

Patients with normal screening tests were designated an individualized multi-task exercise program during a personal interview in an outpatient visit. Exercise routine consisted of strengthening of respiratory muscles, muscle stretching exercises, moderate aerobic activity counseling with 3-5 weekly sessions and strengthening limb exercises.

Psychological assessment

During surgical interview with the colorectal surgeon the hospital anxiety and depression scale (HADS)¹⁷ was undertaken. Those with an altered score were referred to personal evaluation with the psycho-oncologist; patients with normal punctuation were forwarded to a group meeting where meditation and stress managing tools were explained and put into practice.

ERP

ERP has been implemented within our hospital since 2015. Very strict inclusion criteria were considered at the early

beginning of the program, when elderly colorectal cancer patients were considered, just fit or healthy patients (e.g. ASA II, non-diabetic) were included in the program.

A 70% adherence was required to be included in the ERP group according to the last ERAS Guidelines for colorectal surgery^{18,19}.

Conventional care

Conventional care was considered for all those patients that were not included in the ERP or PP preoperatively.

Outcome and measures

The recorded clinical variables included standard of care, demographic variables, comorbidities, past surgery, substance abuse, chronic medications, ASA score, tumor location, surgical technique, surgical approach, intraoperative complications, and postoperative outcome variables such as anastomotic leak, postoperative ileus, surgical site infection, reintervention and readmission. Postoperative complications were classified according to Clavien-Dindo²⁰. Major complications were defined as Clavien-Dindo \geq III.

Our primary outcome was optimal recovery, which had been previously defined as the postoperative recovery with hospital discharge prior to postoperative day 5 and absence of major complication, nor mortality nor readmission at 30-days²¹. Secondary outcomes were global rate of complications, length of stay, overall mortality, failure to rescue rate and readmission rate. Failure to rescue had been previously defined as the death of a patient after one or more potentially treatable complications.

Statistical method

Continuous variables with a normal distribution are shown as mean and standard deviation (SD); those with non-normal distribution are shown in median and range. Categorical variables are shown in number and percentage.

The relation among continuous variables was studied with the Mann-Whitney test. The relation among categorical variables was studied with χ^2 -Test (or Fisher exact test when necessary).

Univariate analysis with χ^2 -Test for categorical variables was done. Clinically relevant variables and those with a p value < 0.1 were introduced in a multivariate logistic regression model with calculation of odds ratio [(OR) (95% CI)]. In multivariate model variables were introduced with a full-model strategy and automatic step selection.

The statistical package used for the analysis was Stata 13.1 (StataCorp, Texas, USA).

Results

A total of 153 patients were analyzed, 51 in each standard of care group: PP, ERP and CC. Mean age was 77.9 (SD 6.8), with 87 male and 66 female patients (56.9% and 43.1% respectively).

Demographic variables, comorbidities and ASA score classification in the whole sample and in each standard of care group is represented in [Table 1](#). Patients in ERP had a

Table 1 – Demographic variables and distribution of comorbidities in the global sample, and in each group of care regimen.

| | Total (n = 153) | Conventional care (n = 51) | ERP (n = 51) | Prehabilitation (n = 51) | p |
|----------------|-----------------|----------------------------|---------------|--------------------------|-------|
| Sex | | | | | |
| Male | 87 (56.9) | 27 (52.9) | 28 (54.9) | 32 (62.7) | 0.57 |
| Female | 66 (43.1) | 24 (47.1) | 23 (45.1) | 19 (37.3) | |
| Age* | 77.9 (+/-6.8) | 79.2 (+/-6.3) | 75.8 (+/-7.1) | 78.6 (+/-6.5) | 0.028 |
| ASA | | | | | |
| I | 9 (5.9) | 2 (3.9) | 4 (7.8) | 3 (5.9) | 0.014 |
| II | 72 (47.1) | 20 (39.2) | 34 (66.7) | 18 (35.3) | |
| III | 70 (45.8) | 28 (54.9) | 13 (25.5) | 29 (56.9) | |
| IV | 2 (1.3) | 1 (2) | 0 (0) | 1 (2) | |
| Obesity | 52 (34) | 14 (27.5) | 17 (33.3) | 21 (41.2) | 0.34 |
| Heart disease | 44 (28.8) | 17 (33.3) | 13 (25.5) | 14 (27.5) | 0.66 |
| COPD | 31 (20.3) | 9 (17.6) | 11 (21.6) | 11 (21.6) | 0.85 |
| Diabetes | 55 (35.9) | 20 (39.2) | 15 (29.4) | 20 (39.2) | 0.49 |
| Liver disease | 3 (2) | 3 (2) | 0 (0) | 0 (0) | 0.035 |
| Kidney disease | 25 (16.3) | 7 (13.7) | 9 (17.6) | 9 (17.6) | 0.83 |
| Alcohol use | 13 (8.5) | 3 (5.9) | 4 (7.8) | 6 (11.8) | 0.55 |
| Tobacco abuse | | | | | |
| Never | 121 (79.1) | 45 (88.2) | 39 (76.5) | 37 (72.5) | 0.3 |
| Past smoker | 28 (18.3) | 5 (9.8) | 10 (19.6) | 13 (25.5) | |
| Current smoker | 4 (2.6) | 1 (2) | 2 (3.9) | 1 (2) | |

* Data are shown in mean and SD. ANOVA was used for comparison.

Table 2 – Operative data in the global sample and in each standard of care group.

| | Total (n = 153) | Conventional care (n = 51) | ERP (n = 51) | Prehabilitation (n = 51) | p |
|-------------------------------------|-----------------|----------------------------|--------------|--------------------------|--------|
| Previous Surgery | | | | | |
| Yes | 59 (38.6) | 27 (52.9) | 20 (39.2) | 12 (23.5) | 0.09 |
| No | 94 (61.4) | 24 (47.1) | 31 (60.8) | 39 (76.5) | |
| Surgical Approach | | | | | |
| Laparoscopy | 116 (75.8) | 29 (56.9) | 45 (88.2) | 42 (82.4) | 0.0001 |
| Open | 20 (13.1) | 16 (31.4) | 2 (3.9) | 2 (3.9) | |
| Conversion | 17 (11.1) | 6 (11.8) | 4 (7.8) | 7 (13.7) | |
| Surgical Technique | | | | | |
| Right Hemicolectomy | 89 (58.2) | 28 (54.9) | 31 (60.8) | 30 (58.8) | 0.37 |
| Extended Right Hemicolectomy | 9 (5.9) | 3 (5.9) | 4 (7.8) | 2 (3.9) | |
| Left Hemicolectomy | 14 (9.2) | 3 (5.9) | 2 (3.9) | 9 (17.6) | |
| Sigmoidectomy | 33 (21.6) | 13 (25.5) | 12 (23.5) | 8 (15.7) | |
| Subtotal Colectomy | 2 (1.3) | 0 (0) | 1 (2) | 1 (2) | |
| Total Colectomy | 1 (0.7) | 0 (0) | 0 (0) | 1 (2) | |
| Segmental Colectomy | 3 (2) | 2 (3.9) | 1 (2) | 0 (0) | |
| Hartmann Procedure | 1 (0.7) | 1 (2) | 0 (0) | 0 (0) | |
| Right Hemicolectomy + Sigmoidectomy | 1 (0.7) | 1 (2) | 0 (0) | 0 (0) | |

lower age and a significantly higher rate of ASA I-II patients, compared to the other two groups ($p < 0.01$). The distribution of the rest of comorbidities among the three groups is equivalent, with the only exception of liver disease that is significantly higher in the CC group (0.03).

Surgical details, such as previous interventions, surgical technique and surgical approach are summarized in [Table 2](#). The highest rate of laparoscopic surgery was found in ERP (88.2%), followed by PP (82.4%) and CC (75.8%) in third place. The lower conversion rate was also seen in the ERP group (7.8%), being PP (13.7%) and CC (11.8%) quite similar.

All the patients that were included in the ERP had an over 70% accomplishment of ERAS items as described in the methods section. PP were managed also following ERAS guidelines, although it was not considered a necessary criterion for inclusion in PP group. [Table 3](#) represents each

ERAS items criterion considered and its accomplishment in each ERP and PP groups. There only existed statistically significant differences in the preoperative items: preoperative information, optimization, nutrition and anemia screening ($p < 0.01$), favoring PP patients.

According to the adopted definition, 85 patients, 55.6% of the total sample, experienced an optimal recovery. No differences among the three groups were found ($p = 0.09$), although when compared by pairs differences existed between the ERP group and the CC one. Uneventful postoperative course, meaning no complications happening, was more frequent in both the ERP (68.6%) and PP (66.7%), compared to the CC group (49%) ($p = 0.047$). Overall complications classified according to Clavien-Dindo's were similar in the three groups. Major complications happened in 15 patients, 9.8% of the sample, of whom nine patients (5.9%) required a

Table 3 – ERAS items accomplishment in the ERAS (ERP) and Prehabilitation (PP) Cohorts. ERAS items categorization exactly reproduces last version of ERAS Colorectal Surgery Guidelines²⁰.

| ERAS items | | ERP | PP | p |
|-------------------------|--------------------------------------|----------|----------|-------|
| | | n (%) | n (%) | |
| Preadmission Items | Preoperative information | 44 (87) | 51 (100) | 0.01 |
| | Optimization | 34 (67) | 51 (100) | <0.01 |
| | Prehabilitation | 0 (0) | 51 (100) | n.a. |
| | Nutrition | 39 (76) | 51 (100) | <0.01 |
| Preoperative Items | Anemia screening | 39 (76) | 51 (100) | <0.01 |
| | Prevention of nausea and vomiting | 49 (96) | 47 (92) | 0.67 |
| | Selective premedication | 29 (57) | 34 (67) | 0.41 |
| | Prophylactic antibiotics | 51 (100) | 51 (100) | n.a. |
| | No bowel preparation | 35 (68) | 32 (63) | 0.83 |
| Intraoperative Items | Maintaining euvolemia | 49 (96) | 51 (100) | 0.49 |
| | Avoid fasting and carbohydrate drink | 47 (92) | 49 (96) | 0.67 |
| | Standard anesthetic protocol | 51 (100) | 51 (100) | n.a. |
| | Fluid normovolemia | 31 (61) | 36 (70) | 0.4 |
| | Normothermia | 33 (65) | 37 (72) | 0.52 |
| Postoperative Items | Minimal invasive surgery | 45 (88) | 42 (82) | 0.57 |
| | No drainage | 30 (59) | 33 (65) | 0.68 |
| | No gastric drainage | 51 (100) | 51 (100) | n.a. |
| | Multimodal analgesia | 33 (65) | 35 (69) | 0.67 |
| | Thromboprophylaxis | 47 (92) | 49 (96) | 0.67 |
| | Fluid normovolemia | 31 (61) | 36 (70) | 0.4 |
| | Urinary catheter early removal | 45 (88) | 47 (92) | 0.74 |
| | Prevent Hyperglycemia | 24 (47) | 29 (57) | 0.32 |
| Postoperative nutrition | 45 (88) | 44 (86) | 0.98 | |
| Early mobilization | 42 (82) | 39 (76) | 0.62 | |

Data shown represents total number of patients and percentages.
n.a.: Not applicable.

Table 4 – Postoperative results in the global sample and in each standard of care group.

| | Total (n = 153) | Conventional care (n = 51) | ERP (n = 51) | Prehabilitation (n = 51) | p |
|--------------------|-----------------|----------------------------|--------------|--------------------------|-------|
| Optimal Recovery | | | | | |
| Yes | 85 (55.6) | 23 (45.1) | 34 (66.7) | 28 (54.9) | 0.09 |
| No | 68 (44.4) | 28 (54.9) | 17 (33.3) | 23 (45.1) | |
| No complications | 94 (61.4) | 25 (49) | 35 (68.6) | 34 (66.7) | 0.047 |
| Clavien-Dindo | | | | | |
| I | 13 (8.5) | 6 (11.8) | 6 (11.8) | 1 (2) | 0.15 |
| II | 31 (20.3) | 14 (27.5) | 8 (15.7) | 9 (17.6) | |
| IIIa | 3 (2) | 1 (2) | 0 (0) | 2 (3.9) | |
| IIIb | 10 (6.5) | 4 (7.8) | 2 (3.9) | 4 (7.8) | |
| IVa | 1 (0.7) | 0 (0) | 0 (0) | 1 (2) | |
| IVb | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| V | 1 (0.7) | 1 (2) | 0 (0) | 0 (0) | |
| Mayor Complication | 15 (9.8) | 6 (11.8) | 2 (3.9) | 7 (13.7) | 0.2 |
| Reintervention | 9 (5.9) | 3 (5.9) | 2 (3.9) | 4 (7.8) | 0.7 |
| Readmission | 6 (3.9) | 5 (9.8) | 0 (0) | 1 (2) | 0.048 |
| Length of stay* | 7.7 (6.7) | 9.5 (8.6) | 5.9 (3.8) | 7.8 (6.7) | 0.030 |

* Data are shown in mean and SD. ANOVA was used for comparison.

reoperation and there was just one case of mortality. Length of hospital stay and readmission rates also favors both ERP and PP against CC; differences between ERP and PP programs are not significant. Every postoperative outcome measure and their distribution in every standard of care group are represented in Table 4.

Likewise, Fig. 1 shows a graphic representation of the most relevant postoperative outcome measures and the p values of χ^2 -Test of the three groups and when they are compared by

pairs (CC vs. ERP, CC vs. PP and ERP vs. PP). A significant higher rate of complications was diagnosed in the CC group vs. both ERP and PP groups ($p = 0.046$ and 0.049 respectively), with no differences between ERP and PP ($p = 0.8$).

Table 5 represents the results of univariate and multivariate logistic regression analysis to determine a possible relation between the standard of care and optimal recovery. In univariate analysis the factors related to optimal recovery were age, ASA score and surgical approach; none of them was

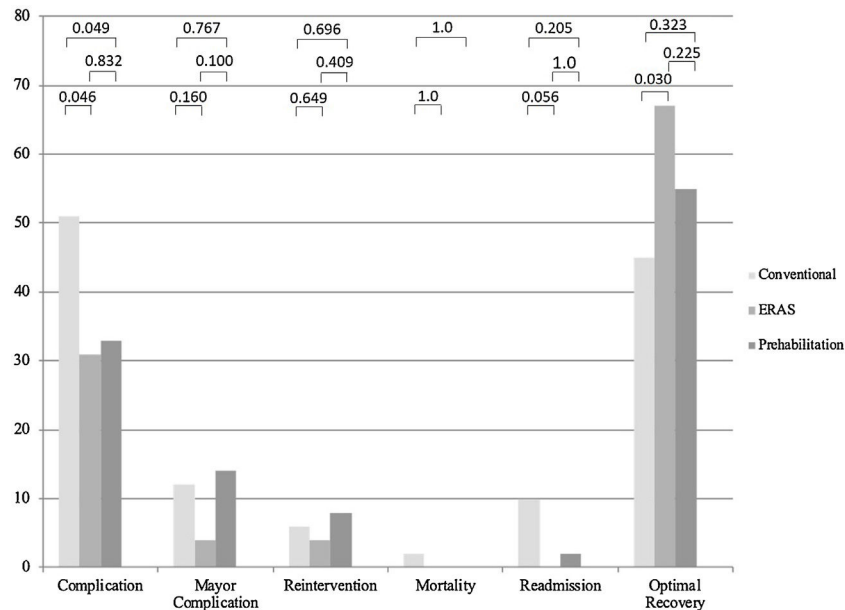


Figure 1 – Bar graphic of postoperative outcomes. Chi-square test was used for comparisons among the three groups by pairs (CC vs. ERP, CC vs. PP and ERP vs. PP).

still significant in multivariate analysis. Standard of care shows a clinical trend in univariate analysis but this relation disappeared in multivariate analysis.

Discussion

Optimal recovery, considered as postoperative course with no major complications, hospital discharge before the fifth postoperative day, no mortality and no readmission, as it

had been previously defined²¹, was achieved in a 55.6% of elderly colon cancer patients attended at our unit. When comparing among groups, CC clearly obtained the lower rate (45.1%) vs. 54.9% in the PP group and 66.7% among the ERP patients. Although there are not many other references to compare with, as this concept has not been widely used, the authors who originally described it, reported a 49.7% in a mixed cohort of colon and rectal cancer patients of any age. Total complication rates and readmissions favors ERP and PP programs, without differences between them, and being

Table 5 – Univariate and multivariate analysis of possible factors influencing postoperative Optimal Recovery.

| | Optimal Recovery | | | | |
|-------------------|------------------|-------|------|--------------|-------|
| | Univariate | | OR | Multivariate | |
| | n (%) | p | | 95% CI | p |
| Standard of Care | | | | | |
| Conventional Care | 23 (45.1) | 0.09 | 1 | | |
| ERP | 34 (66.7) | | 1.3 | 0.53–3.3 | 0.545 |
| Prehabilitation | 28 (54.9) | | 1.1 | 0.47–2.70 | 0.786 |
| Age* | 76.6 (7.0) | 0.007 | 0.96 | 0.91–1.01 | 0.094 |
| ASA | | | | | |
| I–II | 52 (65) | 0.01 | 1 | | 0.113 |
| III–IV | 33 (45.2) | | 0.56 | 0.27–1.14 | |
| Surgical Approach | | | | | |
| Laparoscopy | 73 (62.9) | 0.005 | 1 | | |
| Open | 6 (30) | | 0.33 | 0.11–1.04 | 0.057 |
| Conversion | 6 (35.3) | | 0.43 | 0.14–1.29 | 0.131 |

* Data are shown in mean and SD. ANOVA was used for comparison.

clearly lower and significantly different to the CC group. Patients without any complications have been over 60% in our series, what shows to be higher than other available data in equivalent patients¹⁴; specifically, patients managed according to our prehabilitation regimen experienced a difference higher than a 10% of uneventful postoperative stay compared to those of Carli et al.¹⁴. Major complications and readmission rates are comparable, although our LOS is higher, probably because of a higher rate or reinterventions in our PP group. In this sense, a possible explanation might be that they included in this group a 27.7% of patients with primary created stomas, some of whom might be protective ileostomies that could prevent from clinically relevant anastomotic leaks and reinterventions, or even definitive colostomies in rectal cancer patients.

Our results highlight the problem that still exists for proper patient selection for the most advantageous standard of care in each case among this elderly population. As a whole, postoperative outcome in this sample of elderly patients have kept within the quality standards proposed at a national level for colorectal surgery units, considering these standards as global, not only in the elderly population²².

Patients included in both groups of ERP and PP were managed trying to follow scrupulously the ERP Guidelines published at each time^{18,19}. Although CC group might be influenced by some of ERP learnings at some point, it clearly poses a totally different standard of care as it is reflected in the much higher rate of open surgery compared to the two other groups. It is also quite obvious that every preadmission and preoperative items are impossible to be followed without a proper planification, including avoiding fasting, bowel preparation, optimization, nutritional screening and intensification or treating anemia.

Following our PP, reserving it for the frailest patients attended at our unit, we were able to obtain equivalent postoperative results to those obtained with ERP in a quite healthier population. Although these results are not statistically significant to those in CC, a clear clinical difference of 10% rate of optimal recovery was observed. It is probable that these differences did not reach statistical significance, because not enough study population.

It is noticeable that many of the studies carried out on PP are not based on strict inclusion and exclusion criteria, and patients of all ages are admitted, without any selection according to frailty or morbidity^{20,23-26}. Thus, the beneficial results of PP may be questionable, especially with the recently published results obtained by Carli et al.¹⁴. Nevertheless, although it is a randomized clinical trial, it is not exempt of certain limitations, like a 40% of the prehabilitation group patients having to be excluded from the per-protocol analysis because of low accomplishment with the prehabilitation program. In this sense, our PP cohort showed quite higher rates, as it is shown in the preadmission items of ERAS recorded in Table 3.

Thus, even taking into account the selection bias present in the present work, we consider PP results as quite positive as long as it has probably opened the ERP door to a group of patients who, otherwise, would have been managed by the CC and could not have benefitted from the virtues of none of ERP or PP.

Major complications, most of the times, are related to technical issues and therefore it is not clear in which manner they can be avoided depending on the standard of care applied in every case, and therefore in most series major complications are the same in every group of comparison^{8,14,27}.

One of the great uncertainties concerning perioperative care in colon cancer surgery at this moment is an adequate selection of patients for just ERP or previous prehabilitation. Conventional care at this moment should be avoided, as results are worse in terms of overall complications or readmission rates^{27,28}, and there should not be any more concerns about the applicability of ERP nor PP in elderly patients.

Further research in this field is still needed. Appropriate patients' selection for PP has not been elucidated yet. Some issues that have been investigated with contradictory results include duration^{25,29}, possibility of ambulatory performing^{8,30}, or its eventual ability to modify oncological outcome of certain types of tumors¹⁰; definitely a very exciting field for research.

This paper has some limitations such as the obvious selection bias of patients to be included in the ERP and CC and its retrospective data collection in both historic cohorts. Nevertheless, it has some important strengths, as being the first paper in which CC, ERP and PP groups are compared in terms of postoperative results in elderly patients having surgery for colon cancer. Selection biases have also been overcome with the rigorous statistical analysis using a multivariate logistic regression model to depict confounders.

Conclusions

This study demonstrates that older colon cancer patients benefit from new standards of care such as ERP or PP better than conventional care, with good results in terms of applicability and safety, with 66.7% and 54.9% of optimal recovery respectively, with fewer overall complications and readmissions in ERP and PP patients.

Additional benefit of prehabilitation to ERP could not be elucidated from our experience, therefore, further work for appropriate selection of patients is warranted.

Funding

No funding was received for the present study.

Conflicts of interest

The authors of the article do not have any commercial association that might pose a conflict of interest in relation to this article.

Ethics approval

The study protocol was approved by the Local Ethics Committee.

Disclosures

None of the authors have any conflicts of interest nor disclosure.

REFERENCES

- Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. *CA Cancer J Clin.* 2020;0:1-20. <http://dx.doi.org/10.3322/caac.21601>.
- Cerdán Santacruz C, Frasson M, Flor-Lorente B, et al. Laparoscopy may decrease morbidity and length of stay after elective colon cancer resection, especially in frail patients: results from an observational real-life study. *Surg Endosc.* 2017;31:5032-42. <http://dx.doi.org/10.1007/s00464-017-5548-3>.
- Horie T, Shida D, Takamizawa Y, et al. Laparoscopic versus open colectomy for elderly patients with colon cancer: a propensity score analysis with the Controlling Nutritional Status (CONUT) Score. *Nutr Cancer.* 2020;7:1-6.
- Rossi BW, Labib P, Ewers E, Leong S, Coleman M, Smolarek S. Long-term results after elective laparoscopic surgery for colorectal cancer in octogenarians. *Surg Endosc.* 2020;34:170-6. <http://dx.doi.org/10.1007/s00464-019-06747-5>.
- Tejedor P, Pastor C, Gonzalez-Ayora S, Ortega-Lopez M, Guadalajara H, Garcia-Olmo D. Short-term outcomes and benefits of ERAS program in elderly patients undergoing colorectal surgery: a case-matched study compared to conventional care. *Int J Colorectal Dis.* 2018;33:1251-8.
- Zhuang CL, Ye XZ, Zhang XD, Chen BC, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a metaanalysis of randomized controlled trials. *Dis Colon Rectum.* 2013;56:667-78. <http://dx.doi.org/10.1097/DCR.0b013e3182812842>.
- Joris J, Hans G, Coimbra C, Decker E, Kaba A. Elderly patients over 70 years benefit from enhanced recovery programme after colorectal surgery as much as younger patients. *J Visc Surg.* 2020;157:23-31. <http://dx.doi.org/10.1016/j.jvisc Surg.2019.07.011>.
- Van Rooijen SJ, Molenaar CJL, Schep G, et al. Making patients fit for surgery: introducing a four pillar multimodal rehabilitation program in colorectal cancer. *Am J Phys Med Rehabil.* 2019;98:888-96. <http://dx.doi.org/10.1097/PHM.0000000000001221>.
- Mayo NE, Feldman L, Scott S, et al. Impact of preoperative change in physical function on postoperative recovery: argument supporting prehabilitation for colorectal surgery. *Surgery.* 2011;150:505-14. <http://dx.doi.org/10.1016/j.surg.2011.07.045>.
- Trépanier M, Minella E, Paradis T, et al. Improved disease-free survival after prehabilitation for colorectal cancer surgery. *Ann Surg.* 2019;270:493-501. <http://dx.doi.org/10.1097/SLA.0000000000003465>.
- Minnella EM, Liberman AS, Charlebois P, et al. The impact of improved functional capacity before surgery on postoperative complications: a study in colorectal cancer. *Acta Oncol.* 2019;58:573-8. <http://dx.doi.org/10.1080/0284186X.2018.1557343>.
- Van Rooijen S, Carli F, Dalton S, et al. Multimodal prehabilitation in colorectal cancer patients to improve functional capacity and reduce postoperative complications: The first international randomized controlled trial for multimodal prehabilitation. *BMC Cancer.* 2019;19:1-11. <http://dx.doi.org/10.1186/s12885-018-5232-6>.
- Tew GA, Bedford R, Carr E, et al. Community-based prehabilitation before elective major surgery: the PREP-WELL quality improvement project. *BMJ Open Qual.* 2020;9e000898. <http://dx.doi.org/10.1136/bmj-oq-2019-000898>.
- Carli F, Bousquet-Dion G, Awasthi R, et al. Effect of multimodal prehabilitation vs postoperative rehabilitation on 30-day postoperative complications for frail patients undergoing resection of colorectal cancer: a randomized clinical trial. *JAMA Surg.* 2020;155:233-42. <http://dx.doi.org/10.1001/jamasurg.2019.5474>.
- Bruijnen CP, Heijmer A, van Harten-Krouwel DG, et al. Validation of the G8 screening tool in older patients with cancer considered for surgical treatment. *J Geriatr Oncol.* 2021;12:793-8. <http://dx.doi.org/10.1016/j.jgo.2020.10.017>. Epub 2020 Nov 8.
- Boléo-Tomé C, Monteiro-Grillo I, Camilo M, Ravasco P. Validation of the Malnutrition Universal Screening Tool (MUST) in cancer. *Br J Nutr.* 2012;108:343-8. <http://dx.doi.org/10.1017/S000711451100571X>.
- Zigmond A, Snaith R. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983;67:361-70. <http://dx.doi.org/10.1111/j.1600-0447.1983.tb09716.x>.
- Gustafsson UO, Scott MJ, Schwenk W, et al. Enhanced Recovery After Surgery (ERAS) Society, for Perioperative Care; European Society for Clinical Nutrition and Metabolism (ESPEN); International Association for Surgical Metabolism and Nutrition (IASMEN). Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *World J Surg.* 2013;37:259-84. <http://dx.doi.org/10.1007/s00268-012-1772-0>.
- Gustafsson UO, Scott MJ, Hubner M, et al. Guidelines for perioperative care in elective colorectal surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations: 2018. *World J Surg.* 2019;43:659-95. <http://dx.doi.org/10.1007/s00268-018-4844-y>.
- Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg.* 2009;250:187-96.
- Aarts MA, Rotstein OD, Pearsall EA, et al. Postoperative ERAS interventions have the greatest impact on optimal recovery: experience with implementation of ERAS across multiple hospitals. *Ann Surg.* 2018;267:992-7. <http://dx.doi.org/10.1097/SLA.0000000000002632>.
- de la Portilla F, Builes S, García-Novoa A, et al. Analysis of quality indicators for colorectal cancer surgery in units accredited by the Spanish Association of Coloproctology. *Cir Esp.* 2018;96:226-33. <http://dx.doi.org/10.1016/j.ciresp.2018.02.008>.
- Mora López L, Pallisera Llovera A, Serra-Aracil X, et al. A single-center prospective observational study on the effect of trimodal prehabilitation in colorectal surgery. *Cir Esp.* 2020;98:605-11. <http://dx.doi.org/10.1016/j.ciresp.2020.03.023>. Epub 2020 May 17.
- Minnella EM, Awasthi R, Gillis C, et al. Patients with poor baseline walking capacity are most likely to improve their functional status with multimodal prehabilitation. *Cent Surg Assoc.* 2016;160:1070-9. <http://dx.doi.org/10.1016/j.surg.2016.05.036>.
- Gillis C, Li C, Lee L, et al. Prehabilitation versus Rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. *Anesthesiology.* 2014;121. 937-7.
- Li C, Carli F, Lee L, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. *Surg Endosc.* 2013;27:1072-82. <http://dx.doi.org/10.1007/s00464-012-2560-5>.

27. Meillat H, Brun C, Zemmour C, et al. Laparoscopy is not enough: full ERAS compliance is the key to improvement of short-term outcomes after colectomy for cancer. *Surg Endosc.* 2020;34:2067–75. <http://dx.doi.org/10.1007/s00464-019-06987-5>.
28. Hawkins AT, Geiger TM, King AB, et al. An enhanced recovery program in colorectal surgery is associated with decreased organ level rates of complications: a difference-in-differences analysis. *Surg Endosc.* 2019;33:2222–30. <http://dx.doi.org/10.1007/s00464-018-6508-2>.
29. Loughney L, West MA, Dimitrov BD, Kemp GJ, Grocott MP, Jack S. Physical activity levels in locally advanced rectal cancer patients following neoadjuvant chemoradiotherapy and an exercise training programme before surgery: a pilot study. *Perioper Med.* 2017;6:1–8. <http://dx.doi.org/10.1186/s13741-017-0058-3>.
30. Bruns E, Argillander T, Schuijt H, et al. Fit4SurgeryTV at-home prehabilitation for frail older patients planned for colorectal cancer surgery a pilot study. *Am J Phys Med Rehabil.* 2019;98:399–406. <http://dx.doi.org/10.1097/PHM.0000000000001108>.