# Enhanced recovery pathways, patient-reported outcomes and return to intended oncological therapy after colorectal surgery: the Italian ColoRectal Anastomotic Leakage study group (iCral 3).

## BACKGROUND

The ultimate goal of any surgery is to return the patient to at least their baseline functional status, if not an improved functional status compared with their preoperative state, as rapidly as possible and with the least amount of intercurrent disability. Enhanced Recovery After Surgery (ERAS) is a multimodal and multifactorial approach to the optimization of perioperative management (1, 2). In order to modify and improve the response to surgery-induced trauma, the program relies on a series of evidence-based items related to pre-, intra- and post-operative care (3). Several meta-analyses on ERAS showed a significant reduction of morbidity rates and length of stay after colorectal surgery (4-6). However, program implementation outside clinical trials is still extremely variable (7-9), as the necessary multidisciplinary involvement makes the program vulnerable to various areas of failure, that explain the great variation in adherence rates to program items (10-12).

During the early phase of program implementation, adherence rate to program items rarely goes beyond 50% (13), needing to reach at least 70% in order to significantly improve results (faster recovery and reduced morbidity). A recent cohort study conducted in 80 Spanish centers on about 2,000 patients recruited in 2 months (14) reported a mean adherence rate to ERAS items at 63.6%, reaching 72.7% in centers that declared to have an institutional program. A large multicenter study conducted on 2,352 patients undergoing colorectal resection in 13 centers in 6 different European countries also showed a mean overall adherence rate to ERAS items at 75% (15). In other studies, adherence to ERAS items was higher, reaching up to 90% (16, 17).

Moreover, a clear and significant dose-effect curve between adherence rate to ERAS program items and early outcomes was demonstrated (18-20), and recent evidence deriving from retrospective studies suggests that ERAS programs may also offer a definite advantage over long-term survival after colorectal resection for malignancy (21-23). While many studies to date have focused on early outcomes (i.e. earlier return of bowel function, lower complication rates, and/or shorter length of inpatient stay), for the majority of oncologic operations, however, postoperative recovery carries the additional demand of returning the patient to adjuvant oncologic therapies. It is still unclear if ERAS program could improve the failure to "return to intended oncologic therapy" (RIOT) after cancer surgery due to complications and lingering poor performance status (24), that is strongly associated with worse oncologic outcomes, including shortened overall survival (25, 26). Measuring patient-reported outcomes (PROs) addresses the gap in enhanced recovery assessment by incorporation of patient-centered quality into our global assessment of outcomes (27). Taken together, these data establish a paradigm for association of perioperative medical care to long-term oncologic outcomes—revealing how the perioperative care team's actions over a relatively short number of days and hours around the time of a cancer surgery can improve cancer-specific survival. The concept is that various perioperative techniques, protocols, and agents will blunt the patient's perioperative stress response, reduce complications, and improve functional recovery after surgery. Together, these effects allow more people to RIOT in a more timely fashion and in a more complete way. To the extent that the combination of preservation of immune competence and more reliable return to adjuvant therapies then reduce recurrence rates, longer and more meaningful survivals may be achieved.

Therefore, we planned this study to prospectively evaluate the impact of adherence to ERAS program items after colorectal resections on PRO in the whole population and on failure to RIOT for malignant disease.

**METHODS**

Prospective enrollment from November 2020 to October 2021 in 60 Italian surgical centers. All patients undergoing elective or delayed urgency colorectal surgery with anastomosis will be included in a prospective database after written informed consent. A total of 3,000 patients is expected based on a mean of 50 cases per center.

***Inclusion criteria***

1. Patients submitted to laparoscopic/robotic/open/converted ileo-colo-rectal resection with anastomosis, including planned Hartmann's reversals.
2. American Society of Anesthesiologists' (ASA) class I, II or III
3. Elective or delayed urgency surgery
4. Patients' written acceptance to be included in the study.

***Exclusion criteria***

1. American Society of Anesthesiologists' (ASA) class IV-V
2. Emergent surgery
3. Pregnancy
4. Hyperthermic intraperitoneal chemotherapy for carcinomatosis.

***Outcome measures***

1. Preoperative risk factors for morbidity (age, gender, obesity, nutritional status, diabetes, cardiovascular disease, chronic liver disease, renal failure, inflammatory

bowel disease, perioperative steroid therapy, ASA class I-II vs III, SARS-CoV-2 infection)

2. Operative parameters (approach, procedure, anastomotic technique, length of operation, pTNM stage)
3. Adherence to ERAS program (28, 29) items (Tab.1).

***Endpoints***

*Primary*

1. Patient-related outcomes measures (PROMs):
    a. Euro-QoL Group EQ-5D-5L (EQ-5D-5L, 32);
    b. MD Anderson Symptom Inventory for gastrointestinal surgery patients (MDASI-GI, 33);
    c. Functional Assessment of Cancer Therapy – Colorectal (FACT-C, 34)
2. Return to intended oncologic therapy (RIOT, 24)

*Secondary*

3. Anastomotic leakage rate
4. Minor and major complication rates according to Clavien-Dindo (35, 36) and JCOG (37) classification
5. Overall length of postoperative hospital stay (including any readmission)
6. Difference between date of readiness for discharge (RFD, 38) and date of actual discharge
7. Readmission and reoperation rates
8. Comparison of two nutritional status scores, MNA-SF (30) and PNI (31), regarding anastomotic leakage, minor and major complication rates and RIOT (24)

9. Impact of anastomotic testing through air-leak test (ALT) and near-infrared fluorescence (NIR) narrow-band imaging (NBI) using indocyanine green (ICG) on anastomotic leakage rates

***Recorded data and follow-up***

Potential patient-specific and intraoperative risk factors will be recorded: gender, body mass index, nutritional status, frailty (39), surgical indication (cancer, polyps, chronic inflammatory bowel disease, diverticular disease), use of steroids, renal failure and dialysis, cardiovascular or respiratory disease, American Society of Anesthesiologist class, bowel preparation, type of approach, level of anastomosis and technique (mechanical or hand-sewn, intra- or extra-corporeal), operative time, presence of drainage, and perioperative blood transfusion(s). During the postoperative period, patients will be examined by the attending surgeon daily. Fever (central temperature > 38 °C), pulse, abdominal signs, bowel movements, volume and aspect of drainage (if present) will be recorded daily. The local attending surgeon will make any decision for complementary exams and imaging according to his own criteria, the only exception being the creation of a proximal diverting stoma at operation, that mandates routine check of anastomotic integrity through an intraluminal contrast exam (standard x-rays or CT scan), MRI, or direct endoscopic evaluation three to six weeks after the operation. The rate of any adverse event will be calculated and graded according to Clavien-Dindo criteria (35, 36) and to Japan Clinical Oncology Group Postoperative Complications (JCOG-PC) extended criteria (37), including all anastomotic leaks, wound infection (according to the definitions of the Centers for Disease Control and Prevention and wound culture, 40), pneumonia (clinical symptoms, and physical and radiological examinations), central line infection (positive blood culture), urinary tract infection (positive urine

culture with bacterial count). Patients will be followed-up in the outpatient clinic up to 8 weeks after discharge from the hospital.

Anastomotic dehiscence (any deviation from the planned postoperative course related to the anastomosis, or presence of pus or enteric contents within the drains, presence of abdominal or pelvic collection in the area of the anastomosis on postoperative CT scan, leakage of contrast through the anastomosis during enema or evident anastomotic dehiscence at reoperation for postoperative peritonitis) will be defined and graded according to international consensus guidelines (41). Anastomotic testing will be performed intraoperatively with the air-leak test (ALT) and using ICG-NIR-NBI with a standard protocol *[ICG 25 mg diluted in 10 mL water (2.5 mg/mL); first bolus i.v. injection of 4 mL (10 mg) after vascular control and mesenteric division, just before proximal and/or distal bowel division; second bolus i.v. injection of 4 mL (10 mg) just before joining anastomotic stumps; third (optional) bolus i.v. injection of 2 mL (5 mg) after the anastomosis is completed; NIR-NBI observation within 120-180" after every ICG injection (direct, laparoscopic or endoscopic)].*

PROM questionnaires (32-34) will be administered to all enrolled patients four to one week before the planned operation, on the day of discharge, and 6 weeks after the operation.

RIOT (24) rates will be recorded in all patients submitted to surgery for malignancy, according to national guidelines for colorectal cancer (42).

After anonymization, all data of each single case will be prospectively uploaded by local investigator(s) on a protected web-based database and incorporated into a spreadsheet for data analysis, checking for any discrepancy, that will be addressed and solved through strict cooperation between chief investigator, data manager and participating centers.

***Ethics and dissemination***

The study will be conducted according to the Helsinki declaration and to the Guideline for good clinical practice E6(R2) principles. This study protocol will be submitted to the coordinating

center ethics committee (Comitato Etico Regionale delle Marche - C.E.R.M.) for approval and then registered at ClinicalTrials.gov (NCT04397627). Thereafter, all the participating centers will obtain authorization to participate from the local institutional review board. The results of the study are intended to be presented at national and international medical congresses on corresponding fields of interest (colorectal surgery, abdominal surgery). Written publications of the results are planned within surgical journals. The authorship for written publications is confirmed to all participating investigators, only being granted in the case of substantive contributions to the design, conduct, data analysis, collection and interpretation. Anonymized participant-level datasets will be available after study completion upon reasonable request by contacting the principal investigator.

***Statistical Analysis***

Quantitative values will be expressed as mean ± standard deviation (SD), median and range; categorical data with percentage frequencies. For categorical data, analysis will include the use of cross tabulation, chi squared or Fisher's exact test where indicated. Continues or discrete variables will be analyzed using Student's two-sided t test (allowing for heterogeneity of variances) or with a non-parametric test (Mann-Whitney U test or Kruskal-Wallis test as indicated). Joint and conditional multivariate association between all variables shown to be significant on univariate analysis will be assessed using binary logistic or multiple linear regression. The odds ratio (OR) will be presented followed by 95% confidence interval (95% CI). Concerning comparison of nutritional status scores, areas under the receiver-operating characteristics curve (AUC-ROC) will be calculated for all endpoints, considering values from 0.7 to 0.8 as acceptable, 0.8 to 0.9 excellent, and above 0.9 as outstanding (43). Differences in AUC-ROC curves will be analyzed with the chi-squared test. Optimal cut-off points will be obtained applying Youden's Index (Sensitivity+Specificity-1), choosing those values of the AUC-ROC curve where this index is

maximal. Negative predictive values (NPV) and positive predictive values (PPV) will also be calculated; finally, a logistic regression model will be built using the presence/absence of endpoint as dependent variable, and nutritional scores ≤ or > the cut-off values as explanatory factors; using logistic transformation of the linear predictors, the probabilities of the endpoint related to the different combinations of factors level will be obtained (44). For all statistical tests the significant level is fixed at $p < .05$. Statistical analyses will be carried out using STATA software (Stata Corp. College Station, Texas, USA).

***Sample size***

Adherence to at least 70% of the ERAS program items was identified as a cut-off for significant improvement of outcomes (18), with a 2:1 expected ratio below:above the cut-off. Estimating a reduction of postoperative PRO from preoperative baseline (1.0) at 0.7 for adherence above the cut-off and at 0.64 for adherence below the cut-off (44), alpha 0.04, beta 0.8, the required sample size is n=2,406 (802 cases above 70% adherence and 1,604 below 70% adherence). Reported rates for failure to RIOT and ERAS program items adherence below or above 70% are 13 and 6.5%, respectively (27); the required sample size for evaluation of failure to RIOT is n=885 (295 cases above 70% adherence and 590 below 70% adherence). Based on previous iCral observational study on colorectal surgery in Italy (44, 46, 47), the expected ratio of malignant:benign indications to surgery is 70:30 (2,100 resections for malignancy and 900 resections for benign disease on the basis of 3,000 expected cases).

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**Acronyms**

ALT: Air leak test

ASA: American Society of Anesthesiologists

EQ-5D-5L: Euro-QoL Group EQ-5D-5L

ERAS: Enhanced Recovery after Surgery

FACT-C: Functional Assessment of Cancer Therapy – Colorectal

ICG: indocyanine green

JCOG: Japan Clinical Oncology Group

JCOG-PC: Japan Clinical Oncology Group Postoperative Complications

MDASI-GI: MD Anderson Symptom Inventory for gastrointestinal surgery patients

MNA-SF: mini nutritional assessment – short form

MRI: magnetic resonance imaging

NBI: narrow-band imaging

NIR: near-infrared

PNI: prognostic nutritional index

PROs: patient-reported outcomes

PROMs: patient-reported outcomes measures

RFD: readyness for discharge

RIOT: return to intended oncologic therapy

Tab. 1: Definition of adherence to ERAS program items (28, 29).

| | ITEM | Adherence criteria |
|---|---|---|
| Preoperative | Nutritional status screening | Patient submitted to nutritional screening through Mini Nutritional Assessment Short Form (MNA-SF) (30) and Prognostic Nutritional Index (PNI) (31) |
| | Nutritional Prehabilitation | All patients showing MNA-SF < 12 (malnourished or suspect for malnutrition) and BMI > 30 (obesity) receive specific nutritional consultation |
| | Physical Prehabilitation | Patient receives a standard protocol of physical activity to be accomplished in the preoperative period; frail and limited motility patients are submitted to specific geriatrician/physiatrist consultation and personalized activity program |
| | Psychologic Prehabilitation | Patient and his familiars/caregivers are screened by the case-manager; in case of anxiety/depression concerning diagnosis and related procedure psychologic consultation is warranted |
| | Counseling | Patient and his familiars/caregivers receive full information and suggestions regarding perioperative program from surgeon, anesthesiologist and case-manager |
| | Preoperative Immunonutrition | Patient is administered Impact Oral ™ (Nestlè Health Science, Italy) 330 ml per os, three briks per day during 5 days preceding surgery or two bricks per day during 7 days preceding surgery |
| | Management of anemia | Patient with Hb concentration < 130 g/L for men and <120 g/L for nonpregnant women receive correction of anemia before surgery preferably through intravenous iron preparations (ferric carboxymaltose) and blood transfusion(s) in strictly necessary cases |
| | Antithrombotic prophylaxis | Patient receives graduate compression stockings and/or pneumatic compression device, together with prophylaxis with low molecular weight heparin during the perioperative period, to be extended up to 28 days after surgery in case of malignancy |
| | Antibiotic prophylaxis | Patient is administered i.v. antibiotic 30 to 60 minutes before incision, according to local protocols |
| | No bowel preparation | No routine bowel preparation is used, except in case of anticipated need for covering stoma |
| | Oral carbohydrates load | Carbohydrates rich beverage (12.5% maltrodextrins, PreOp™, Nutricia Italy) is given preoperatively (800 ml on the evening before surgery and 400 ml 2 to 3 hours before surgery) |
| | Preoperative fasting | Preoperative fasting is limited to two hours for clear liquids (water, coffee, tea) and to 6 hours for milk and solid food |
| Intraoperative | No premedication | No long- or medium-action sedatives. Short and ultra-short acting sedatives (e.g. Lorazepam, Midazolam, Methohexital, Dexmedetomidine, Ketamine) are allowed before performing spinal, epidural or loco-regional anesthesia |
| | PONV prophylaxis | Postoperative nausea/vomiting prophylaxis is administered according to individual risk assessment (Apfel score) through a multimodal approach |
| | Normothermia | Body temperature is monitored during surgery, utilizing fluid warmers and/or thermic blankets as necessary |
| | Standard anesthetic protocol | General anesthesia through short-acting anesthetics, cerebral activity monitoring to enhance recovery and to reduce postoperative delirium, anesthesia level monitoring and complete reversal of neuromuscular blockade |
| | Intraoperative fluid management | Restrictive fluid therapy (defined as maintenance fluids at <2 ml/kg/h) or goal-oriented fluid therapy (stroke volume) |
| | Multimodal analgesia | Use of more than two drugs or analgesia strategies (TAP-block or spinal anesthesia for minimally invasive surgery; thoracic epidural anesthesia for open surgery) in order to reduce the use of opiates |
| | Minimally invasive surgery | Patient submitted to laparoscopic, robotic or video-assisted surgery (conversions to open surgery included on a intention-to-treat basis) |
| Postoperative | No major opiates | Patient receives no major opiates in the postoperative period |
| | No nasogastric tube | Nasogastric tube, if used, is removed at the end of surgery |
| | No drain | No drain is placed in the abdominal cavity (pelvic drain allowed for pelvic surgery with low colorectal anastomosis) |
| | Bladdder catheter | Urinary catheter removed on POD 1 (up to POD 2 in case of pelvic surgery) |
| | Early mobilization | Patient receives passive mobilization on POD 0, active mobilization on POD 1 |
| | Early oral feeding | Patient receives liquid oral diet starting 6 hours after surgery and semisolid diet starting on POD 1 |
| | Pre-discharge check | Patient is checked just before discharge at home concerning adequate oral intake, bowel function, adequate pain control, active mobilization, no clinical/serological evidence of any postoperative complication, full agreement to go home |
| | Audit | All data regarding patients included in the program are reviewed by the local investigator(s) before uploading into the database; any adverse event is reviewed and discussed |

## Appendix 1 **CLAVIEN-DINDO CLASSIFICATION (35, 36)**

| **Grade** | **Definition** |
|---|---|
| Grade I | Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside |
| Grade II | Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included |
| Grade III | Requiring surgical, endoscopic or radiological intervention |
| Grade IIIa | Intervention not under general anesthesia |
| Grade IIIb | Intervention under general anesthesia |
| Grade IV | Life-threatening complication (including CNS complications)* requiring IC/ICU management |
| Grade IVa | Single organ dysfunction (including dialysis) |
| Grade IVb | Multiorgan dysfunction |
| Grade V | Death of a patient |

*Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks.
CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

| **Grades** | **Organ System** | **Examples** |
|---|---|---|
| Grade I | Cardiac | Atrial fibrillation converting after correction of K_-level |
| | Respiratory | Atelectasis requiring physiotherapy |
| | Neurological | Transient confusion not requiring therapy |
| | Gastrointestinal | Noninfectious diarrhea |
| | Renal | Transient elevation of serum creatinine |
| | Other | Wound infection treated by opening of the wound at the bedside |
| Grade II | Cardiac | Tachyarrhythmia requiring _-receptor antagonists for heart rate control |
| | Respiratory | Pneumonia treated with antibiotics on the ward |
| | Neurological | TIA requiring treatment with anticoagulants |
| | Gastrointestinal | Infectious diarrhea requiring antibiotics |
| | Renal | Urinary tract infection requiring antibiotics |
| | Other | Same for I followed by tx with antibiotics for phlegmonous infection |
| Grade IIIa | Cardiac | Bradyarrhythmia requiring pacemaker implantation in local anesthesia |
| | Neurological | See grade IV |
| | Gastrointestinal | Biloma after liver resection requiring percutaneous drainage |
| | Renal | Stenosis of the ureter after kidney transplantation treated by stenting |
| | Other | Closure of dehiscent noninfected wound in the OR under local anesthesia |
| Grade IIIb | Cardiac | Cardiac temponade after thoracic surgery requiring fenestration |
| | Respiratory | Bronchopleural fistulas after thoracic surgery requiring surgical closure |
| | Neurological | See grade IV |
| | Gastrointestinal | Anastomotic leakage after descendorectostomy requiring relaparotomy |
| | Renal | Stenosis of the ureter after kidney transplantation treated by surgery |
| | Other | Wound infection leading to eventration of small bowel |
| | Grade IVa | Cardiac Heart failure leading to low-output syndrome |
| | Respiratory | Lung failure requiring intubation |
| | Neurological | Ischemic stroke/brain hemorrhage |
| | Gastrointestinal | Necrotizing pancreatitis |
| | Renal | Renal insufficiency requiring dialysis |
| Grade IVb | Cardiac | Same as for IVa but in combination with renal failure |
| | Respiratory | Same as for IVa but in combination with renal failure |
| | Gastrointestinal | Same as for IVa but in combination with hemodynamic instability |
| | Neurological | Ischemic stroke/brain hemorrhage with respiratory failure |
| | Renal | Same as for IVa but in combination with hemodynamic instability |

Suffix “d” Cardiac Cardiac insufficiency after myocardial infarction (IVa–d)
Respiratory Dyspnea after pneumonectomy for severe bleeding after chest tube placement (IIIb–d)
Gastrointestinal Residual fecal incontinence after abscess following descendorectostomy with surgical evacuation. (IIIb–d)
Neurological Stroke with sensorimotor hemisyndrome (IVa–d)
Renal Residual renal insufficiency after sepsis with multiorgan dysfunction (IVb–d)
Other Hoarseness after thyroid surgery (I–d)
TIA, transient ischemic attack; OR, operating room.

## Appendix 2 **Mini Nutritional Assessment Short Form (MNA-SF®) (30)**

**A Presenta una perdita dell' appetito? Ha mangiato meno negli ultimi 3 mesi? (perdita d'appetito, problemi digestivi, difficoltà di masticazione o deglutizione)**
0 = Grave riduzione dell'assunzione di cibo
1 = Moderata riduzione dell'assunzione di cibo
2 = Nessuna riduzione dell'assunzione di cibo

**B Perdita di peso recente (<3 mesi)**
0 = perdita di peso > 3 kg
1 = non sa
2 = perdita di peso tra 1 e 3 kg
3 = nessuna perdita di peso

**C Motricità**
0 = dal letto alla poltrona
1 = autonomo a domicilio
2 = esce di casa

**D Nell' arco degli ultimi 3 mesi: malattie acute o stress psicologici?**
0 = sì 2 = no

**E Problemi neuropsicologici**
0 = demenza o depressione grave
1 = demenza moderata
2 = nessun problema psicologico

**F1 Indice di massa corporea (IMC) = peso in kg / (altezza in m)$^2$**
0 = IMC <19
1 = 19 ≤ IMC < 21
2 = 21 ≤ IMC < 23
3 = IMC ≥ 23

SE L' IMC NON E' DISPONIBILE, SOSTITUIRE LA DOMANDA F1 CON LA DOMANDA F2.
NON RISPONDERE ALLA DOMANDA F2 SE LA DOMANDA F1 E GIA' STATA COMPLETATA

**F2 Circonferenza del polpaccio (CP in cm)**
0 = CP inferiore a 31
3 = CP 31 o superiore

**Valutazione di screening** (max.14 punti) **12-14** punti**:** stato nutrizionale normale; **8-11** punti**:** a rischio di malnutrizione; **0-7** punti**:** malnutrito.

## Appendix 3 **Prognostic Nutritional Index (PNI) (31)**

PNI = Serum albumin (g/L) + (0.005 x total lymphocyte count/µL)
**Valutazione di screening ≥50:** stato nutrizionale normale; **45-50:** a rischio di malnutrizione; **<45:**malnutrito.

Appendix 4 Questionario sulla salute – Versione Italiana **Euro-QoL Group EQ-5D-5L™ (32)**

Data compilazione ___/___/____; preop □; dimissione □; tardivo □

Sotto ciascun argomento, faccia una crocetta sulla casella (UNA SOLA) che descrive meglio la sua salute OGGI.

**CAPACITÀ DI MOVIMENTO**

| | |
|---|---|
| Non ho difficoltà nel camminare | ❑5 |
| Ho lievi difficoltà nel camminare | ❑4 |
| Ho moderate difficoltà nel camminare | ❑3 |
| Ho gravi difficoltà nel camminare | ❑2 |
| Non sono in grado di camminare | ❑1 |

**CURA DELLA PERSONA**

| | |
|---|---|
| Non ho difficoltà nel lavarmi o vestirmi | ❑5 |
| Ho lievi difficoltà nel lavarmi o vestirmi | ❑4 |
| Ho moderate difficoltà nel lavarmi o vestirmi | ❑3 |
| Ho gravi difficoltà nel lavarmi o vestirmi | ❑2 |
| Non sono in grado di lavarmi o vestirmi | ❑1 |

**ATTIVITÀ ABITUALI** (*per es. lavoro, studio, lavori domestici,attività familiari o di svago)*

| | |
|---|---|
| Non ho difficoltà nello svolgimento delle attività abituali | ❑5 |
| Ho lievi difficoltà nello svolgimento delle attività abituali | ❑4 |
| Ho moderate difficoltà nello svolgimento delle attività abituali | ❑3 |
| Ho gravi difficoltà nello svolgimento delle attività abituali | ❑2 |
| Non sono in grado di svolgere le mie attività abituali | ❑1 |

**DOLORE O FASTIDIO**

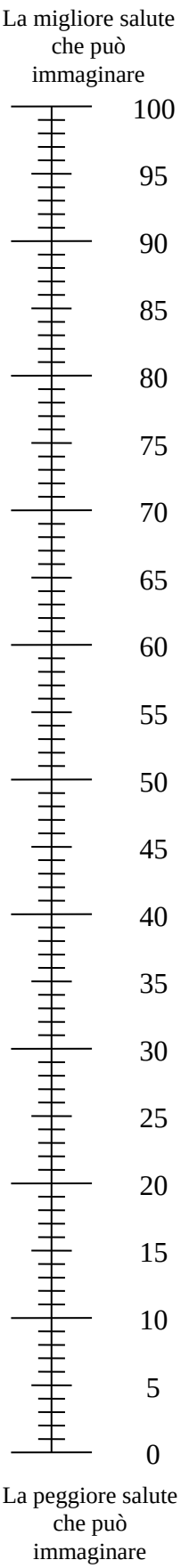
| | |
|---|---|
| Non provo alcun dolore o fastidio | ❑5 |
| Provo lieve dolore o fastidio | ❑4 |
| Provo moderato dolore o fastidio | ❑3 |
| Provo grave dolore o fastidio | ❑2 |
| Provo estremo dolore o fastidio | ❑1 |

**ANSIA O DEPRESSIONE**

| | |
|---|---|
| Non sono ansioso/a o depresso/a | ❑5 |
| Sono lievemente ansioso/a o depresso/a | ❑4 |
| Sono moderatamente ansioso/a o depresso/a | ❑3 |
| Sono gravemente ansioso/a o depresso/a | ❑2 |
| Sono estremamente ansioso/a o depresso/a | ❑1 |

- Vorremmo sapere quanto è buona o cattiva la sua salute OGGI.
- Questa è una scala numerata che va da 0 a 100.
- 100 rappresenta la migliore salute che può immaginare.
  0 rappresenta la peggiore salute che può immaginare.
- Segni una X sul punto della scala per indicare com'è la sua salute OGGI.
- Poi, scriva nella casella qui sotto il numero che ha segnato sulla scala numerata.

LA SUA SALUTE OGGI = ☐



Appendix 5 **MD Anderson Symptom Inventory for gastrointestinal surgery patients (MDASI-GI) (33)**

Data compilazione ___/___/____; preop □; dimissione □; tardivo □

I Parte: Come sono I tuoi sintomi? Le chiediamo quanto ritiene che i suoi sintomi siano stati forti nelle ultime 24 ore. Per favore selezioni per ogni elemento un numero da 0 (sintomi assenti) a 10 (sintomi presenti al massimo).

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Dolore | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 2 | Stanchezza | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 3 | Nausea | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 4 | Sonno disturbato | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 5 | Non sentirsi a proprio agio | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 6 | Affanno | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 7 | Non ricordare le cose | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 8 | Mancanza di appetito | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 9 | Sonnolenza | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 10 | Secchezza delle fauci | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 11 | Tristezza | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 12 | Vomito | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 13 | Formicolii | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 14 | Stitichezza | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 15 | Diarrea (feci liquide) | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 16 | Difficoltà a deglutire | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 17 | Alterazione del gusto | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 18 | Sensazione di gonfiore | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

II Parte: Quanto i suoi sintomi hanno interferito con la sua vita? Quanto i suoi sintomi hanno interferito con i seguenti elementi nelle ultime 24 ore? Per favore selezioni per ogni elemento un numero da 0 (i sintomi non hanno interferito) a 10 (i sintomi hanno interferito completamente).

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | Attività quotidiana | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 20 | Umore | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 21 | Lavoro (anche domestico) | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 22 | Rapporto con altre persone | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 23 | Camminare | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 24 | Godimento della vita | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

Appendix 6 **Functional Assessment of Cancer Therapy – Colorectal® FACT-C (34)**
Data compilazione ___/___/____; preop □; dimissione □; tardivo □

*Sotto abbiamo elencato delle affermazioni ritenute importanti da persone con la sua stessa malattia.* ***La preghiamo di cerchiare o contrassegnare un solo numero per riga per indicare la sua risposta in riferimento agli ultimi 7 giorni.***

| BENESSERE FISICO | | Per Niente | Un po | Abbastanza | Molto | Moltissimo |
|---|---|---|---|---|---|---|
| GP1 | Mi manca l'energia | 0 | 1 | 2 | 3 | 4 |
| GP2 | Ho nausea | 0 | 1 | 2 | 3 | 4 |
| GP3 | Ho difficoltà ad occuparmi delle necessità della mia famiglia a causa delle mie condizioni fisiche | 0 | 1 | 2 | 3 | 4 |
| GP4 | Ho dolori | 0 | 1 | 2 | 3 | 4 |
| GP5 | Mi danno fastidio gli effetti collaterali della cura | 0 | 1 | 2 | 3 | 4 |
| GP6 | Mi sento male | 0 | 1 | 2 | 3 | 4 |
| GP7 | Sono costretto a trascorrere del tempo a letto | 0 | 1 | 2 | 3 | 4 |

| BENESSERE SOCIALE/FAMILIARE | | Per Niente | Un po | Abbastanza | Molto | Moltissimo |
|---|---|---|---|---|---|---|
| GS1 | Mi sento vicino ai miei amici | 0 | 1 | 2 | 3 | 4 |
| GS2 | La mia famiglia mi sostiene moralmente | 0 | 1 | 2 | 3 | 4 |
| GS3 | Ho appoggio morale dai miei amici | 0 | 1 | 2 | 3 | 4 |
| GS4 | La mia famiglia ha accettato la mia malattia | 0 | 1 | 2 | 3 | 4 |
| GS5 | Sono soddisfatto della comunicazione a proposito della malattia nella mia famiglia | 0 | 1 | 2 | 3 | 4 |
| GS6 | Mi sento vicino al mio compagno/a | 0 | 1 | 2 | 3 | 4 |
| *Q1 * Se preferisce non rispondere alla domanda successiva barri la seguente casella* □ | | | | | | |
| GS7* | Sono sodisfatto della mia attività sessuale | 0 | 1 | 2 | 3 | 4 % |

| BENESSERE EMOTIVO | | Per Niente | Un po | Abbastanza | Molto | Moltissimo |
|---|---|---|---|---|---|---|
| GE1 | Mi sento triste | 0 | 1 | 2 | 3 | 4 |
| GE2 | Sono soddisfatto/a di come sto affrontando la mia malattia | 0 | 1 | 2 | 3 | 4 |
| GE3 | Sto perdendo la speranza nella lotta contro la mia malattia | 0 | 1 | 2 | 3 | 4 |
| GE4 | Sono nervoso | 0 | 1 | 2 | 3 | 4 |
| GE5 | Mi preoccupo al pensiero della morte | 0 | 1 | 2 | 3 | 4 |
| GE6 | Mi preoccupo che le mie condizioni possano peggiorare | 0 | 1 | 2 | 3 | 4 |

| BENESSERE FUNZIONALE | | Per Niente | Un po | Abbastanza | Molto | Moltissimo |
|---|---|---|---|---|---|---|
| GF1 | Sono in grado di lavorare (si intende anche il lavoro a casa) | 0 | 1 | 2 | 3 | 4 |
| GF2 | Il mio lavoro (si intende anche il lavoro a casa) mi gratifica | 0 | 1 | 2 | 3 | 4 |
| GF3 | Riesco a godermi la vita | 0 | 1 | 2 | 3 | 4 |
| GF4 | Ho accettato la mia malattia | 0 | 1 | 2 | 3 | 4 |
| GF5 | Dormo bene | 0 | 1 | 2 | 3 | 4 |
| GF6 | Provo ancora piacere nel dedicarmi ad attività di tempo libero | 0 | 1 | 2 | 3 | 4 |
| GF7 | Al momento, sono soddisfatto/a della qualità della mia vita | 0 | 1 | 2 | 3 | 4 |

| ULTERIORI PROBLEMI | | Per Niente | Un po | Abbastanza | Molto | Moltissimo |
|---|---|---|---|---|---|---|
| C1 | Ho gonfiore o crampi nella zona dello Stomaco | 0 | 1 | 2 | 3 | 4 |
| C2 | Sto dimagrendo | 0 | 1 | 2 | 3 | 4 |
| C3 | Riesco a controllare le mie funzioni Intestinali | 0 | 1 | 2 | 3 | 4 |
| | | Per Niente | Un po | Abbastanza | Molto | Moltissimo |
| C4 | Digerisco bene ciò che mangio | 0 | 1 | 2 | 3 | 4 |
| C5 | Soffro di diarrea | 0 | 1 | 2 | 3 | 4 |
| C6 | Il mio appetito è buono | 0 | 1 | 2 | 3 | 4 |
| C7 | Sono soddisfatto/a del mio aspetto fisico | 0 | 1 | 2 | 3 | 4 |
| *Q2* | *Deve portare un sistema per pazienti che hanno subito stomia addominale?* | | | | | |
| | □ ***No (ignori le domande successive;*** | □ ***SI (risponda alle domande successive)*** | | | | |
| C8 | Mi imbarazza dover portare il sistema a seguito della stomia addominale | 0 | 1 | 2 | 3 | 4 |
| C9 | Mi riesce difficile prendermi cura del sistema che devo usare per la stomia | 0 | 1 | 2 | 3 | 4 |

## Appendix 7 **Coordinating Investigators**

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## Appendix 8 **Edmonton Frail Scale (39)**

| Data gg/mm/aaaa | 0 punti | 1 punto | 2 punti |
|---|---|---|---|
| Metta le braccia ad indicare le 11:10 come sul quarante di un orologio | No errori □; | impreciso□; | errori □; |
| Nell'ultimo anno, quante volte è stato ricoverato in ospedale? | Mai □; | 1-2 volte □; | > 2 volte □; |
| Indipendenza funzionale In generale, come descriverebbe la sua salute? | Buona □; | Discreta □; | Scarsa □; |
| Per quante attività ha bisogno di aiuto (cucinare, shopping, mobilità, telefonare, faccende domestiche, lavanderia, gestione del denaro, assumere la terapia) | 0-1 □; | 2-4 □; | > 4 □; |
| Quando ha bisogno di aiuto, può contare su qualcuno disponibile e in grado di risolvere il suo bisogno? | Sempre □; | Talvolta □; | Mai □; |
| Assumi 5 o più farmaci al giorno? | No □; | Si □; | |
| Recentemente hai perso peso tanto che i vestiti ti vanno larghi? | No □; | Si □; | |
| Ti senti spesso infelice o depresso? | No □; | Si □; | |
| Hai problemi nel controllo delle urine? | No □; | Si □; | |
| Seduto a riposo su una sedia; al VIA, si alzi e cammini con calma per 3 metri E, quindi, torni a sedersi rilassato (durata in secondi) | 0-10s □; | 11-20s □; | >20s ko □; |

Punteggio (somma; 0-17): _____