

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods 1. Fried Frailty Scoring Index

1. Shrinking (weight loss)
Shrinking was defined through self-report as an unintentional weight loss of >10 pounds in the last year.
2. Decreased grip strength (weakness)
Weakness was assessed by grip strength, and was measured directly with a hand-held JAMAR dynamometer (Sammons Preston Rolyan). Three serial tests of maximum grip strength with the dominant hand were performed, and a mean of the 3 values were adjusted by gender and body mass index (BMI). Weakness was defined as an adjusted grip strength in the lowest 20th percentile of a community-dwelling population of adults 65 years of age and older. <ul style="list-style-type: none">– Men met the criteria for weakness if their BMI and grip strength were ≤ 24 kg/m² and ≤ 29 kg; 24.1–26 kg/m² and ≤ 30 kg; 26.1–28 kg/m² and ≤ 31 kg; >28 kg/m² and ≤ 32 kg, respectively.– Women met the criteria for weakness if their BMI and grip strength were ≤ 23 kg/m² and ≤ 17 kg; 23.1–26 kg/m² and ≤ 17.3 kg; 26.1–29 kg/m² and ≤ 18 kg; and >29 kg/m² and ≤ 21kg, respectively.
3. Exhaustion
Exhaustion was measured by responses to the following 2 statements from the modified 10-item Center for Epidemiological Studies-Depression scale. (1)“I felt that everything I did was an effort” and (2) “I could not get going.” Subjects were asked, “How often in the last week did you feel this way?” Potential responses were: 0=rarely or none of the time (<1 day); 1=some or a little of the time (1–2 days); 2=a moderate amount of the time (3–4 days); and 3=most of the time. Subjects answering either statement with response 2 or 3 met the criteria for exhaustion.
4. Low activity
Physical activities were ascertained for the 2 weeks before this assessment using the short version of the Minnesota Leisure Time Activities Questionnaire, and included frequency and duration. Weekly tasks were converted to equivalent kilocalories of expenditure, and individuals reporting a weekly kilocalorie expenditure in the lowest 20th percentile for their gender (men, <383 kcal/week; women, <270 kcal/week) were classified as having low physical activity.
5. Slowed walking speed
Slowness was measured by averaging 3 trials of walking 15 feet at a normal pace. Individuals with a walking speed in the lowest 20th percentile, adjusted for gender and height, were scored as having slow walking speed. <ul style="list-style-type: none">– Men met criteria if height and walk time were ≤ 173 cm and ≥ 7 seconds, or >173 cm and ≥ 6 seconds, respectively.– Women met criteria if height and walk time were ≤ 159 cm and ≥ 7 seconds, or >159 cm and ≥ 6 seconds, respectively.

Each criterion is scored with a 0 or 1.

Score 1 = Non-frail

Score 2-3 = Intermediately frail

Score 4-5 = Frail

eMethods 2. Definition of Complications

<p>MEDICAL</p> <p>Cardiovascular</p> <ul style="list-style-type: none"> – <i>Heart failure</i>: clinical or radiological signs of congestive heart failure and specific treatment initiated.¹ – <i>Acute myocardial infarction</i>: increase in cardiac biomarker values or characteristic ECG changes or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.² – <i>Cardiac arrhythmia</i>: ECG diagnosis of new arrhythmia requiring at least a pharmacologic intervention.³ – <i>Cardiac arrest</i>: cardiopulmonary resuscitation performed. – <i>Deep vein thrombosis</i>: radiological confirmation of deep vein thrombosis or anticoagulation started due to clinical findings. – <i>Pulmonary embolism</i>: radiological evidence of pulmonary embolism. – <i>Cerebrovascular accident</i>: new focal or global neurologic deficit of cerebrovascular cause that persists beyond 24 h or is interrupted by death within 24 h.⁴ <p>Respiratory</p> <ul style="list-style-type: none"> – <i>Pneumonia</i>: Hospital acquired pneumonia, defined as presence of lung infiltrate at chest x-ray accompanied with signs of infection and initiation of antibiotic treatment.⁵ – <i>Lobar atelectasis</i>: radiological finding of at least one lobar collapse.³ – <i>Pleural fluid</i>: pleural effusion requiring drainage of the pleural cavity. – <i>Respiratory failure</i>: delayed extubation > 24 hours after primary surgery, or reintubation at any time for ventilatory support.³ – <i>Pulmonary edema</i>: clinical signs and radiological confirmation.⁶ <p>Other medical</p> <ul style="list-style-type: none"> – <i>Acute Kidney Injury</i>: increase in serum creatinine $\times 2$ from baseline or reduction of glomerular filtration rate greater than 50%.⁷ – <i>Urinary retention</i>: Reinsertion of indwelling urinary catheter after removal attempt or patient discharged with urinary drainage (excluding patients with permanent indwelling urinary catheter). – <i>Anemia</i>: low serum hemoglobin requiring transfusion of PRBC, unrelated to any identified source of bleeding. – <i>Hepatic dysfunction</i>: Increased serum bilirubin concentration > 34 $\mu\text{mol/l}$ (2 mg/dl) compared to preoperative value AND elevated liver enzymes AND has NOT undergone a pancreaticobiliary procedure.³ – <i>Acute Pancreatitis</i>: diagnosis requires 2 of the following: upper abdominal pain of acute onset often radiating through to the back; increase in serum amylase or lipase ($\times 3$ normal value); cross-sectional abdominal imaging consistent with acute pancreatitis.⁸ – <i>Other gastrointestinal complications</i>: any other complication of the gastrointestinal tract requiring treatment (e.g. blood per rectum, diarrhea, high stoma output). – <i>Neurological complications</i>: any neurological complication excluding cerebrovascular events or anesthesia-related injuries (e.g. epileptic seizure) – <i>Psychiatric complications</i>: new psychiatric symptoms including delirium and depression, requiring pharmacological treatment. <p>INFECTIOUS</p>

- *Urinary Tract Infection*: upper or lower urinary symptoms and urine culture with no more than two species of organisms, at least one of which is a bacteria of $\geq 10^5$ CFU/ml.⁹
- *Wound infection*: Purulent drainage, with or without positive culture, from the superficial incision or any sign or symptom of infection (e.g. pain, tenderness, localized swelling and/or redness) and superficial incision is deliberately opened by the surgeon or attending physician. Not included if part of intra-peritoneal abscess.¹⁰
- *Intra- or retroperitoneal abscess*: Radiologic finding of deep collection of pus associated with systemic signs of infection or finding during reoperation.
- *Sepsis*: at least two SIRS criteria positive and a documented or suspected infection. SIRS criteria are the following: Temperature < 36 or > 38 °C; heart rate > 90 beats per minute, respiratory frequency > 20 breath per minute, leukocytosis (WBC > 12) or leukopenia (WBC < 4) AND documented or suspected infection.¹¹
- *Other infectious complications*: any other documented infectious complication (e.g. *Clostridium difficile* colitis).

SURGICAL

- *Anastomotic leak*: documentation at reoperation OR documentation by imaging technique (e.g. radiologically or endoscopically) of leakage from the surgical connection between the two bowel ends into the abdomen or pelvis with either spillage and/or fluid collection around the anastomotic site or extravasation through a wound, drain site, or anus.¹² In the case of rectal surgery, a pelvic abscess close to the anastomosis is also considered as anastomotic leakage.¹³
- *Bowel perforation*: documentation at reoperation OR radiologically of perforation of small or large bowel.⁶
- *Mechanical bowel obstruction*: documentation at reoperation OR radiological documentation of mechanical small or large bowel obstruction.
- *Wound dehiscence*: separation of the abdominal wall muscle fascia large enough to necessitate operative closure of the wound OR incisional hernia diagnosed after primary discharge.⁶
- *Bleeding*: any postoperative bleeding (e.g. intra-abdominal, gastrointestinal) requiring transfusion of at least 2 PRBC after surgery.¹⁴
- *Ileus (primary postoperative ileus)*: abdominal distention OR vomiting associated with intolerance of solid food intake or inability to pass gas or stool beyond POD3 (target day for discharge), unrelated to any other ongoing complication.
- *Other surgical complications*: any other surgical complication necessitating treatment or delaying discharge (e.g. abdominal wall hematoma).

eMethods 3. Statistical Analysis Plan

Variable	Type	Time point(s)	Planned analysis	Adjustment variables included in the model	Multiple imputation model
30-day Comprehensive Complication Index (CCI)	Continuous	30 days	Linear regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI and Fried score (2-3 vs. 4-5).	There was no missing data for the outcome CCI. Imputation conducted for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
30-day Overall complications	Dichotomous	30 days	Logistic regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI and Fried score (2-3 vs. 4-5).	There was no missing data for the outcome overall complications. Imputation conducted for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
30-day Severe complications	Dichotomous	30 days	Logistic regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI and Fried score (2-3 vs. 4-5).	There was no missing data for the outcome severe complications. Imputation conducted for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
Primary length of stay, days	Continuous	Not applicable	Linear regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI and Fried score (2-3 vs. 4-5).	There was no missing data for the outcome primary length of stay. Imputation conducted for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
30-day total length of stay, days	Continuous	30 days	Linear regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI and Fried score (2-3 vs. 4-5).	There was no missing data for the outcome total length of stay. Imputation conducted for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). Imputation conducted for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
30-day Emergency room visit	Dichotomous	30 days	Logistic regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI and Fried score (2-3 vs. 4-5).	There was no missing data for the outcome emergency room visit. Imputation conducted for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
30-day Hospital readmission	Dichotomous	30 days	Logistic regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI and Fried score (2-3 vs. 4-5).	There was no missing data for the outcome hospital readmission. Imputation conducted for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
Walking capacity: six-minute walking distance (6MWD)	Continuous	Baseline Preoperative 4-weeks after surgery	Linear regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery,	Imputation conducted for the outcomes preoperative 6MWD (missing n=25) and postoperative 6MWD (missing n=45) and for the adjustment variables baseline 6MWD (missing n=1) and BMI (missing n=1). The

				baseline 6MWD (in deciles), BMI and Fried score (2-3 vs. 4-5).	multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
SF-36 Total Physical SF-36 Total Mental	Continuous	Baseline Preoperative 4-weeks after surgery	Linear regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI, Fried score (2-3 vs. 4-5), baseline Total Physical (in deciles) and baseline Total Mental (in deciles).	Imputation conducted for the outcomes preoperative Total Physical (missing n=35), preoperative Total Mental (missing n=35), postoperative Total Physical (missing n=42) and postoperative Total Mental (missing n=42) and for the adjustment variables baseline Total Physical (missing n=5), baseline Total Mental (missing n=5), baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
HADS anxiety HADS anxiety	Continuous	Baseline Preoperative 4-weeks after surgery	Linear regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI, Fried score (2-3 vs. 4-5), baseline HADS anxiety (in deciles) and baseline HADS depression (in deciles).	Imputation conducted for the outcomes preoperative HADS anxiety (missing n=36), preoperative HADS depression (missing n=36), postoperative HADS anxiety (missing n=43) and postoperative HADS depression (missing n=43) and for the adjustment variables baseline HADS anxiety (missing n=5), baseline HADS depression (missing n=5) baseline HADS anxiety (missing n=5), baseline HADS depression (missing n=5), baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.
Energy Expenditure: CHAMPS questionnaire	Continuous	Baseline Preoperative 4-weeks after surgery	Linear regression model	Recruitment site (fixed-effect), age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI, Fried score (2-3 vs. 4-5), baseline light energy expenditure (in deciles), baseline moderate-vigorous energy expenditure (in deciles)	Imputation conducted for the preoperative light energy expenditure (missing n=33), preoperative moderate-vigorous energy expenditure (missing n=33), postoperative light energy expenditure (missing n=42) and postoperative moderate-vigorous energy expenditure (missing n=42) and for the adjustment variables baseline light energy expenditure (missing n=5), baseline moderate-vigorous energy expenditure (missing n=5), baseline 6MWD (missing n=1) and BMI (missing n=1). The multiple imputation model included: CCI, recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery and Fried score.

eTable 1. Detailed Description of Postoperative Complications in the Prehabilitation vs Rehabilitation Groups

		Prehabilitation		Rehabilitation
	n		n	
Medical Complications				
Cardiovascular	55	4 (7%)	55	3(5%)
Heart failure	55	3(5%)	55	0
Arrhythmias	55	1(2%)	55	2(4%)
Deep vein thrombosis	55	1(2%)	55	2(4%)
Respiratory	55	9(16%)	55	9(16%)
Pneumonia	54	5(9%)	55	5(9%)
Lobar atelectasis	55	3(5%)	55	1(2%)
Pleural fluid	55	1(2%)	55	0
Respiratory failure	55	3(5%)	55	3(5%)
Infectious	55	6(11%)	55	7(13%)
Urinary tract infection	55	1(2%)	55	2(4%)
Wound infection	55	2(4%)	55	1(2%)
Intra- or retro-peritoneal infection	55	2(4%)	55	1(2%)
Sepsis	55	2(4%)	55	0
Other	55	0	55	3(5%)
Other medical	55	12(22%)	55	13(24%)
Acute kidney injury	55	6(11%)	54	4(7%)
Urinary retention	55	1(2%)	55	3(5%)
Anemia	55	4(7%)	55	0
Other GI ^a	55	5(9%)	55	6(11%)
Psychiatric complications	55	3(5%)	55	1(2%)
Surgical complications	55	14(25%)	55	14(25%)
Anastomotic leak	55	2(4%)	55	3(6%)
Bowel perforation	55	0	55	1(2%)
Ileus	55	12(22%)	55	7(13%)
Wound dehiscence	55	2(4%)	55	1(2%)
Bleeding	55	2(4%)	55	5(9%)
Other	55	0	55	1(2%)

Data are presented as n (%)

^a Gastrointestinal

eTable 2. Intention to Treat Unadjusted Postoperative Outcomes in the Prehabilitation vs Rehabilitation Groups

	Prehabilitation n=55	Rehabilitation n=55	Unadjusted estimate (95% CI)^a	P Value
30-day Comprehensive Complication Index	12.7 (21.5) 0 [0-12.2]	15.7(25.3) 0 [0-29.6]	MD -3.1(-11.9 to 5.8)	0.49
30-day Overall complications	25(45%)	25(45%)	OR 1.0(0.47 to 2.1)	1.00
30-day Severe complications	7(13%)	11(20%)	OR 0.58(0.21 to 1.6)	0.31
Primary length of stay, days	4[3-8]	4[3-8]	HR 0.95(0.65 to 1.4)	0.79
30-day Total Length of stay, days	4[3-8]	5[3-9]	MD -3.9(-14.8 to 7.0)	0.48
30-day Emergency room visit	3(5%)	6(11%)	OR 0.47(0.11 to 2.0)	0.31
30-day Hospital readmission	2(4%)	5(9%)	OR 0.38(0.07 to 2.0)	0.26

Data are presented as mean (SD), median [IQR], or n (%)

MD: Mean difference; OR: Odds ratio; HR: Hazard ratio

^a Coefficients derived with imputation of missing data and no adjustment for confounders. There was no missing data for the variables described in this table, so imputation was conducted only for adjustment variables. Details about the multiple imputation model is described in eMethods 3.

eTable 3. Intention to Treat Unadjusted Walking Capacity in the Prehabilitation vs Rehabilitation Groups

	Prehabilitation		Rehabilitation		Unadjusted estimate (95% CI) ^a	P Value
	n		n			
Baseline 6MWD, m	55	325.3(114.3)	54	304.0(107.3)		
Preoperative 6MWD, m	47	346.1(117.8)	38	315.8(107.5)	MD 39.2(-5.2 to 83.6)	0.08
6MWD improved preoperatively ^b	47	26(55%)	38	10(26%)	OR 2.0(0.86 to 4.8)	0.10
Postoperative (4 weeks) 6MWD, m	38	336.4(121.8)	30	286.1(105.1)	MD 39.2(-8.2 to 86.6)	0.10
6MWD recovered at 4 weeks ^c	38	26(68%)	30	16(53%)	OR 1.4(0.58 to 3.5)	0.45

Data presented as mean (SD), or n(%)

^a Coefficients derived with imputation of missing data and no adjustment for confounders. Details about the multiple imputation model is described in eMethods 3.

^b improvement of 6MWD above 20m in comparison to baseline; ^c recovered to 6MWD within 20 meters of the baseline value or above.

eTable 4. Intention to Treat Unadjusted Patient-Reported Outcome Measures in the Prehabilitation vs Rehabilitation Groups

	Prehabilitation		Rehabilitation		Unadjusted estimate (95% CI) ^a	P Value
	n		n			
SF-36 Subscales						
Total Physical						
Baseline	53	49.4(21.2)	52	52.9(18.7)		
Before Surgery	42	57.1(19.3)	33	58.7(19.4)	MD -1.3(-9.1 to 6.5)	0.73
4 weeks after surgery	38	49.7(20.2)	30	51.1(14.7)	MD -1.4(-8.0 to 5.1)	0.66
Total Mental						
Baseline	53	54.2(23.1)	52	58.8(20.2)		
Before surgery	42	59.2(20.8)	33	66.0(19.4)	MD -4.8(-13.0 to 3.4)	0.24
4 weeks after Surgery	38	55.3(22.6)	30	63.6(15.3)	MD -5.2(-12.5 to 2.2)	0.17
HADS anxiety						
Baseline	52	6[4-8]	53	5[2-8]		
Before surgery	41	6[4-8]	33	4[1-7]	MD 1.3(-0.29 to 2.8)	0.11
4 weeks after surgery	37	5[2-7]	31	4[1-8]	MD -1.6(-6.7 to 3.5)	0.53
HADS Depression						
Baseline	52	5[3-7.5]	53	4[3-9]		
Before surgery	41	4[2-6]	33	4[2-7]	MD -0.09(-1.6 to 1.4)	0.90
4 weeks after surgery	37	4[2-5]	31	4[1-7]	MD -0.04(-1.6 to 1.5)	0.96
Energy Expenditure						
Baseline						
Light energy expenditure	52	20.8[9-51]	53	16[1-65]		
Moderate-vigorous energy expenditure	52	4[0-21]	53	0[0-3.5]		
Before Surgery						
Light energy expenditure	44	23.8[8.5-58.3]	33	15[6.5-42]		
Moderate-vigorous energy expenditure	44	17.6[10.2-33]	33	3[0-13]	MD 13.4(-2.4 to 29.2)	0.10
4 weeks						
Light physical energy expenditure	38	20[5-37.5]	30	16.9[5-35]		
Moderate-vigorous energy expenditure	38	12[0-31.3]	30	13.5[0-36]	MD -2.9(-21.0 to 15.3)	0.75

Data presented as mean (SD), or n(%)

^a Coefficients derived with imputation of missing data and no adjustment for confounders. Details about the multiple imputation model is described in eMethods 3.

SF-36: 36-Item Short Form Health Survey. Range 0–100. Higher values represent better scores; HADS: Hospital Anxiety and Depression Scale. Range 0–21. Higher values represent worse scores.

eTable 5. Per Protocol Baseline and Operative Characteristics in the Prehabilitation vs Rehabilitation Groups

	Prehabilitation				Rehabilitation	
	n	<75% compliance	n	≥75% compliance	n	
Age, years	22	74.5[72-82]	33	78[72.5-84.5]	55	82[75-84]
≥75 years old	22	11(50%)	33	21(64%)	55	42(76%)
Male Sex	22	11(50%)	33	18(55%)	55	23(42%)
Body Composition						
Weight, kg	22	67.3[56.3-73.5]	33	65.5[61.8-86.2]	54	71.6[57-79.7]
Lean Body Mass, kg	22	46.5 (7.8)	33	47.1(10.0)	54	46.2(10.2)
Fat, %	22	29.7[18.5-39.1]	33	34.3[29.3-38.9]	54	35.9[25.4-41.1]
BMI, kg/m ²	22	23.5[21.3-29.2]	33	26.0[24.0-30.7]	54	26.4[23.8-30.6]
≥30	22	5(23%)	33	9(27%)	54	16(30%)
Baseline 6MWD, m		366.3 (118.1)		297.9(104.8)	54	304.0 (107.3)
% predicted	22	66.4 [56.1 – 73.8]	33	54.8[34.6-61.0]	54	52.7[40.5-63.6]
< 400m	22	13(59%)	33	27(82%)	54	44(81%)
Grip Strength	22	24.9(7.8)	33	21.3(8.4)	55	21.0(6.7)
Frailty Score						
2	22	11(50%)	33	14(42%)	55	17(31%)
3	22	8(36%)	33	8(24%)	55	22(40%)
4	22	1(5%)	33	6(18%)	55	10(18%)
5	22	2(9%)	33	5(15%)	55	6(11%)
Comorbidities						
Diabetes Mellitus	22	7(32%)	33	12(36%)	55	21(38%)
Hypertension	22	9(41%)	33	20(61%)	55	42(76%)
Cardiovascular diseases	22	5(23%)	33	11(33%)	55	19(35%)
Atrial Fibrillation	22	2(9%)	33	7(21%)	55	5(9%)
OSA	22	0	33	5(15%)	55	5(9%)
COPD	22	2(9%)	33	6(18%)	55	3(5%)
Arthritis/connective tissue disease	21	5(24%)	33	10(30%)	54	23(43%)
Dyslipidemia	22	9(41%)	33	18(55%)	54	26(48%)
Hypothyroidism	22	4(18%)	33	8(24%)	55	11(20%)
Asthma	22	0	33	7(21%)	55	1(2%)
Charlson Index	22	3[2-4.3]	33	3[2-4]	55	4[3-5]
ASA status						
2	22	9(41%)	33	10(30%)	55	9(16%)
3	22	11(50%)	33	22(67%)	55	43(78%)
4	22	2(9%)	33	1(3%)	55	3(5%)
Metabolic status						
CRP, mg/L	19	6.3[1.5-22.9]	31	6.0[2.3-24.2]	47	4.5[1.7-14.5]
Albumin, g/L	20	38.7 (4.4)	33	39.1(5.0)	52	38.3 (4.0)

HbA1C, %	19	5.9(0.60)	28	6.4(0.97)	49	6.3 (1.4)
Hemoglobin, g/L	21	118.3 (18.5)	33	115.5(21.1)	51	111.6 (19.4)
Energy Expenditure, kcal/kg/week	20	36.4[10.6-80.3]	32	38.4[15.3-80.4]	53	23.0 [5-68.5]
Subjective Global Assessment						
A	21	6(29%)	33	10(30%)	45	20(44%)
B	21	9(43%)	33	18(55%)	45	12(27%)
C	21	6(29%)	33	5(15%)	45	13(29%)
Oncology						
Rectal Cancer Site	22	9(41%)	33	9(27%)	55	13(24%)
Neoadjuvant chemotherapy	22	5(23%)	33	2(6%)	54	6(11%)
Tumor stage						
TNM stage 0-I	22	6(27%)	33	12(36%)	53	15(28%)
TNM stage II	22	5(23%)	33	10(30%)	53	18(34%)
TNM stage III	22	10(45%)	33	9(27%)	53	16(30%)
TNM stage IV	22	1(5%)	33	2(6%)	53	4(8%)
Surgical approach						
Open	22	8(36%)	33	5(15%)	55	10(18%)
Minimally Invasive	22	14(64%)	33	28(85%)	55	45(82%)
Type of surgery						
Ileocecal resection	22	1(5%)	33	1(3%)	55	1(2%)
Right hemicolectomy	22	8(36%)	33	15(45%)	55	23(42%)
Left hemicolectomy	22	2(9%)	33	3(9%)	55	8(15%)
Subtotal colectomy	22	0	33	2(6%)	55	1(2%)
Anterior/sigmoid resection	22	2(9%)	33	4(12%)	55	9(16%)
Transverse colectomy	22	0	33	1(3%)	55	1(2%)
Low anterior resection	22	4(18%)	33	6(18%)	55	7(13%)
Abdominoperineal resection	22	3(14%)	33	1(3%)	55	4(7%)
Other bowel surgery	22	2(9%)	33	0	55	1(2%)
Surgery						
Stoma creation	22	10(45%)	33	5(15%)	55	9(16%)
Duration of surgery, minutes	22	180[110-338.8]	33	195[122.5-280.0]	55	180[130-300]
Intraoperative blood loss, mL	22	100[68.8-312.5]	33	100[50-200]	55	100[50-200]

Data are presented as mean (SD), median [IQR], or n (%)

BMI: body mass index; 6MWD: 6-minute walk distance; OSA: obstructive sleep apnea; COPD: chronic obstructive pulmonary disease; ASA: American Society of Anesthesiologists; CRP: C-reactive protein; HbA1C: glycated hemoglobin; Minimally Invasive: Laparoscopic or Transanal minimally invasive surgery (TAMIS); TNM = tumor–node–metastasis.

eTable 6. Per Protocol Adjusted postoperative outcomes in the Prehabilitation vs Rehabilitation Groups

	Prehabilitation (≥75% compliance) n=33	Rehabilitation n=55	Adjusted estimate (95% CI)^a	P Value
	11.1(22.6)	15.7(25.3)	MD:-4.3(-14.5 to 6.0)	0.41
30- day CCI	0 [0-8.7]	0 [0-29.6]		
Overall complications rate	15(45%)	25(45%)	OR:0.84 (0.30 to 2.3)	0.74
Severe complications rate	3(9%)	11(20%)	OR:0.35(0.07 to 1.70)	0.19
Primary length of stay, days	5[3-7]	4[3-8]	HR:21.4(-2.4 to 1.9)	0.85
Total Length of stay, days	5[3-7]	5[3-9]	MD:-6.9[-21.7 to 7.9]	0.35
Emergency room visit rate	2(6%)	6(11%)	OR:0.22(0.03 to 2.0)	0.18
Hospital readmission rate	1(3%)	5(9%)	OR:0.07(0.004 to 1.26)	0.07

Data are presented as mean (SD), median [IQR], or n (%)

MD: Mean difference; OR: Odds ratio; HR: Hazard ratio

^a Coefficients derived with imputation of missing data and adjustment for confounders, including recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI and Fried score (2-3 vs. 4-5). There was no missing data for the variables described in this table, so imputation was conducted only for adjustment variables. Details about the multiple imputation model is described in eMethods 3.

eTable 7. Per Protocol Adjusted Walking Capacity in the Prehabilitation vs Rehabilitation Groups

	Prehabilitation (≥75% compliance)		Rehabilitation		Adjusted estimate (95%CI) ^a	P Value
	n		n			
Baseline 6MWD, m	33	297.9(104.8)	54	304.0 (107.3)		
Preoperative 6MWD, m	32	340.4(109.6)	38	315.8(107.5)	MD 29.1(2.6 to 55.6)	0.03
6MWD improved preoperatively ^b	32	20(63%)	38	10(26%)	OR 3.8(1.3 to 11.1)	0.02
Postoperative (4 weeks) 6MWD,m	27	335.7(122.5)	30	286.1(105.1)	MD 38.4(-3.1 to 80.0)	0.07
6MWD recovered at 4 weeks ^c	27	20(74%)	30	16(53%)	OR 3.1(0.81 to 11.7)	0.10

Data presented as mean (SD), or n(%)

^a Coefficients derived with imputation of missing data and adjustment for confounders, including recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD (in deciles), BMI and Fried score (2-3 vs. 4-5). Details about the multiple imputation model is described in eMethods 3.

^b improvement of 6MWD above 20m in comparison to baseline; ^c recovered to 6MWD within 20 meters of the baseline value or above

eTable 8. Per Protocol Adjusted Patient-Reported Outcome Measures in the Prehabilitation vs Rehabilitation Groups

	Prehabilitation (≥75% compliance)		Rehabilitation		Adjusted estimate (95%CI) ^a	P Value
	n		n			
SF-36 Subscales						
Total Physical						
Baseline	32	49.1(20.9)	52	52.9(18.7)		
Before Surgery	31	57.8(19.0)	33	58.7(19.4)	MD 2.4(-4.6 to 9.5)	0.49
4 weeks after surgery	27	51.3(22.0)	30	51.1(14.7)	MD 1.5(-6.2 to 9.1)	0.70
Total Mental						
Baseline	32	52.8(22.0)	52	58.8(20.2)		
Before surgery	31	61.4(20.0)	33	66.0(19.4)	MD 1.0(-7.4 to 9.5)	0.81
4 weeks after Surgery	27	58.7(22.3)	30	63.6(15.3)	MD 1.1(-6.8 to 9.0)	0.79
HADS anxiety						
Baseline	32	6[4-7.5]	53	5[2-8]		
Before surgery	31	6[3-9]	33	4[1-7]	MD 1.0(-0.46 to 2.5)	0.17
4 weeks after surgery	26	4.5[2-7]	31	4[1-8]	MD -2.0(-7.9 to 3.9)	0.50
HADS Depression						
Baseline	32	5.5[3-7.5]	53	4[3-9]		
Before surgery	31	4[1-6]	33	4[2-7]	MD -0.64(-1.9 to 0.64)	0.32
4 weeks after surgery	26	3[1-5]	31	4[1-7]	MD -0.71(-2.4 to 0.94)	0.39
Energy Expenditure						
Baseline						
Light energy expenditure	32	26[9.3-53]	53	16[1-65]		
Moderate-vigorous energy expenditure	32	4[0-19]	53	0[0-3.5]		
Before Surgery						
Light energy expenditure	31	35[12.5-64]	33	15[6.5-42]		
Moderate-vigorous energy expenditure	31	17.5[10.5-31]	33	3[0-13]	MD 5.2(-9.8 to 20.2)	0.49
4 weeks						
Light energy expenditure	27	21.3[5-38.5]	30	16.9[5-35]		
Moderate-vigorous energy expenditure	27	18[0-33.2]	30	13.5[0-36]	MD -1.9(-23.6 to 19.9)	0.86

Data presented as mean (SD), or n(%)

^a Coefficients derived with imputation of missing data and adjustment for confounders, including recruitment site, age, gender, ASA score, colon vs. rectal surgery, minimally invasive vs. open surgery, baseline 6MWD, BMI, Fried score (2-3 vs. 4-5) and baseline scores of the respective measures (in deciles). Details about the multiple imputation model is described in eMethods 3.

SF-36: 36-Item Short Form Health Survey. Range 0–100. Higher values represent better scores; HADS: Hospital Anxiety and Depression Scale. Range 0–21. Higher values represent worse scores.

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