

# Impact of preoperative change in physical function on postoperative recovery: Argument supporting prehabilitation for colorectal surgery

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**Background.** Abdominal surgery represents a physiologic stress and is associated with a period of recovery during which functional capacity is often diminished. "Prehabilitation" is a program to increase functional capacity in anticipation of an upcoming stressor. We reported recently the results of a randomized trial comparing 2 prehabilitation programs before colorectal surgery (stationary cycling plus weight training versus a recommendation to increase walking coupled with breathing exercises); however, adherence to the programs was low. The objectives of this study were to estimate: (1) the extent to which physical function could be improved with either prehabilitation program and identify variables associated with response; and (2) the impact of change in preoperative function on postoperative recovery.

**Methods.** This study involved a reanalysis of data arising from a randomized trial. The primary outcome measure was functional walking capacity measured by the Six-Minute Walk Test; secondary outcomes were anxiety, depression, health-related quality of life, and complications (Clavien classification). Multiple linear regression was used to estimate the extent to which key variables predicted change in functional walking capacity over the prehabilitation and follow-up periods.

**Results.** We included 95 people who completed the prehabilitation phase (median, 38 days; interquartile range, 22–60), and 75 who were also evaluated postoperatively (mean, 9 weeks). During prehabilitation, 33% improved their physical function, 38% stayed within 20 m of their baseline score, and 29% deteriorated. Among those who improved, mental health, vitality, self-perceived health, and peak exercise capacity also increased significantly. Women were less likely to improve; low baseline walking capacity, anxiety, and the belief that fitness aids recovery were associated with improvements during prehabilitation. In the postoperative phase, the patients who had improved during prehabilitation were also more likely to have recovered to their baseline walking capacity than those with no change or deterioration (77% vs 59% and 32%;  $P = .0007$ ). Patients who deteriorated were at greater risk of complications requiring reoperation and/or intensive care management. Significant predictors of poorer recovery included deterioration during prehabilitation, age > 75 years, high anxiety, complications requiring intervention, and timing of follow-up assessment.

**Conclusion.** In a group of patients undergoing scheduled colorectal surgery, meaningful changes in functional capacity can be achieved over several weeks of prehabilitation. Patients and those who care for them, especially those with poor physical capacity, should consider a prehabilitation regimen to enhance functional exercise capacity before colectomy. (Surgery 2011;150:505-14.)

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DESPITE ADVANCES IN SURGICAL CARE, the incidence of postoperative complications following colorectal surgery remains high, ranging from 25% to 60%.<sup>1,2</sup> Even in the absence of complications, major surgery is associated with a 20–40% reduction in physiologic and functional capacity when measured by energy expenditure, endurance time, workload, and heart rate during maximum exercise.<sup>3</sup> This reduction in physiologic reserve is experienced as a greater level of fatigue 6–8 weeks after hospital discharge.<sup>4</sup> Fatigue is manifested by muscular weakness, increased need for sleep, and decreased ability to concentrate. It is correlated with preoperative health status, preoperative fatigue, weight, grip strength, degree of operative trauma, intensity of metabolic response, and postoperative deterioration.<sup>5</sup> The elderly and others with limited metabolic protein reserve are the most susceptible to the negative effects of operative stress. Furthermore, many colorectal cancer patients undergo adjuvant chemotherapy and radiotherapy, which, together with operation, have prolonged physical, functional, nutritional, and psychological effects.

The process of enhancing functional capacity of the individual to enable him or her to withstand an incoming stressor has been termed *prehabilitation*.<sup>6,7</sup> Although education has been used to prepare patients for procedures,<sup>8</sup> little has been developed to enhance systematically functional capacity with exercise before operation. Poor baseline physical performance capacity increases the risk of complications after major noncardiac surgery<sup>9,10</sup> and prolongs recovery after abdominal surgery.<sup>3</sup> Although the effects of physical activity are highly beneficial in medical conditions such as diabetes, hypertension, and some forms of cancer, very little has been published in surgical patients. In addition, exercise has benefits beyond the physical, and in the face of the health threat faced by patients requiring colorectal surgery, active participation in the preparation process may have benefits beyond the physical and alleviate some of the emotional distress surrounding the anticipation of abdominal surgery and the recovery process.

Based on the notion that preoperative exercise would have an impact on recovery of functional capacity after colorectal surgery, we reported recently the results of a randomized trial<sup>11</sup> comparing 2 prehabilitation interventions. This trial compared 2 exercise programs (stationary cycling plus weight training versus a recommendation to increase walking coupled with breathing exercises) for several weeks before colorectal surgery. Surprisingly, the results of this trial revealed that a greater proportion

of people assigned to the walk plus breathing intervention recovered functional walking capacity postoperatively, our measure of outcome, than those assigned to the more demanding regimen.

This trial, however, proved challenging, because this was a heterogeneous group of patients with different health states, needs and expectations for recovery, and adherence. There was variation in the degree to which the prehabilitation program was effective in improving or maintaining the physical reserve of patients awaiting colorectal surgery. This finding indicates that, regardless of the prehabilitation group, there were people who could be considered “responders,” whose functional capacity improved with either prehabilitation intervention, whereas others had no response or actually declined during the program. To understand more completely the benefits and risks of a preoperative prehabilitation program, an understanding of who responds to this intervention and the effect of prehabilitation response on postoperative recovery is warranted. The specific objectives of this reanalysis of the trial data were to estimate: (1) the extent to which physical function could be improved with either prehabilitation intervention and identify variables associated with a positive response; and (2) the impact of change in preoperative function on postoperative recovery and other outcomes.

## METHODS

The results of the original trial have been reported previously.<sup>11</sup> In brief, adults persons scheduled for resection of benign or malignant colorectal lesions or for colon reconstruction of nonactive inflammatory bowel disease were eligible unless they had compromised health status (American Society of Anesthesiologists [ASA] class 4–5) or comorbid medical conditions interfering with the ability to perform exercise at home or to complete the testing procedures. Following enrollment, persons were assessed. The primary outcome measure was the 6-minute walk test (6MWT), a measure of functional walking capacity<sup>12–15</sup> that evaluates the capacity of a person to maintain a moderate level of walking for a period of time, reflective of activities of daily living.<sup>16</sup> Percentages of age- and gender-specific norms are calculated from the predicted distance using the following formula: predicted distance (m) = 868 – (age\*2.9) – (female\*74.7); where age is in years and the value “1” is assigned for women.<sup>15</sup> A recent paper supports the validity of the 6MWT as a measure of postoperative recovery.<sup>17</sup>

To prescribe the intensity of the prehabilitation exercise program, a  $\text{VO}_{2\text{peak}}$  test was administered on an electronically braked cycle ergometer using

a standard protocol. Subjects began at a very low workload (approximately 5–20 Watts) and the workload was increased by 1 Watt every 2–5 seconds until volitional exhaustion.

Health-related quality of life was assessed using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36),<sup>18</sup> a reliable and valid generic index of perceived health status.<sup>18–20</sup> It incorporates behavioral functioning, subjective well-being, and perceptions of health by assessing 8 health concepts on a 0–100 scale: (1) physical function, limitations in physical activities owing to health problems; (2) role physical, limitations in role activities owing to physical health problems; (3) role emotional (RE), limitations in usual role activities due to emotional problems; (4) social functioning, limitations in social activities owing to health problems; (5) bodily pain, pain; (6) general health, general health perceptions; (7) vitality, energy and fatigue; and (8) mental health, general mental health.<sup>18</sup> Two summary scores have been developed: The Physical Component Summary and the Mental Component Summary have been standardized to have a mean of 50 and a standard deviation of 10.<sup>18</sup> A greater score on the SF-36 subscales or component summary measures indicates a better quality of life. A change of as little as 2 units on the Physical Component Summary has been shown to be the minimum clinically meaningful change; 5 points is often targeted by medical intervention studies, although operative interventions can have an impact as great as 10 points.<sup>18</sup> Norms for the Canadian population are available.<sup>21</sup>

Subjects were also asked to evaluate their health using the EuroQuol EQ-5D<sup>22,23</sup>; clinically meaningful change has been estimated at approximately 10 points.<sup>25</sup> Emotional health was measured using the Hospital Anxiety and Depression Scale (HADS)<sup>26,27</sup>; values of  $\geq 8$  are sensitive for detecting depression. Persons were also asked to rate their level of physical fitness on a scale from 0 (“worst possible fitness”) to 10 (“best possible fitness”) and to indicate the degree to which they felt their level of fitness before surgery was a factor affecting recovery (likely/unlikely).

Both groups were instructed to follow their assigned program daily, were visited at home at least once to verify the exercise program, and were telephoned weekly until operation. During the week before the scheduled date of operation, a second appointment was made to reassess participants on all measures. The reassessment postoperatively was scheduled to coincide with participants surgical follow-up visit between 2 and 4 months postoperatively.

**Statistical methods.** There were 2 parts to this study: (1) the prehabilitation phase and (2) the follow-up phase, looking at the impact of changes during the prehabilitation phase, on recovery after operation. Analyses for the prehabilitation phase were restricted to people with either a 6MWT or a 2-minute walk test (2MWT) at baseline and at operation. To evaluate the postoperative follow-up phase, analyses were restricted to persons who completed the prehabilitation phase and who had either a 6MWT or a 2MWT at least once within 6 months postoperatively.

Persons who completed the prehabilitation phase were compared with those who did not using the *t*, chi-square, or Fischer exact tests, depending on the measurement scale of the variable under study and the sample distribution. Change in the 6MWT over the prehabilitation period and at follow-up was calculated and categorized as improved (gain of  $\geq 20$  m), no change (within 20 m of baseline), or deteriorated (loss of 20 m). Changes in key variables over the prehabilitation phase were calculated for each of the 3 prehabilitation change groups and evaluated using paired *t* tests.

Change in 6MWT scored as a percent of baseline was also calculated for each person and, because it was normally distributed, it was treated as a continuous variable. Multiple linear regression was used to estimate the extent to which key explanatory variables predicted change in functional walking capacity over the prehabilitation phase. Regression coefficients from this model are interpreted as the effect on the percent change from baseline associated with each level or unit of the variable under study. All estimates were adjusted for age, gender, body mass index, diagnosis, baseline 6MWT, and time to operation as well as all other variables given in the table. Similar analyses were done for the follow-up phase.

To minimize potential bias arising from missing data, multiple imputation was performed<sup>28,29</sup> on the longitudinal data. Imputation was based on the data arising from key measured variables including 6MWT and 2MWT,  $VO_{2peak}$ , age, gender, weight, diagnosis, and values on the health questionnaires. Imputation for the main outcome variable, the 6MWT, was only performed if there were data on the 2MWT; the 6MWT at the preoperative visit was imputed for 4 subjects. Multiple imputation provides estimates of the value on a missing variable that would have been recorded if the person had been assessed. The estimated values incorporate the data that are available, cross-sectionally and over time, as well as variation in the multivariate distribution of this existing data. Although data from a

single imputation are presented in data tables for ease of comprehension, analyses were performed using 20 multiply imputed datasets in order to incorporate error both within and between imputed data sets so that the model error term includes the usual sources of error as well as error arising from imputation, to avoid the *P* value being underestimated and more likely to cross the conventional threshold for significance.<sup>28,29</sup>

All analyses were done using SAS version 9 (SAS, Inc., Cary, NC)<sup>30</sup>; analyses using multiply imputed data were done through the SAS procedure, *proc mianalyse*.

## RESULTS

In the original trial, 167 persons were assessed for eligibility, 26 refused entry, and 8 were not randomized, leaving 133 persons. Of this trial sample, 95 persons (80%) completed the prehabilitation phase; the median duration of the prehabilitation period was 38 days (interquartile range, 22–60). Another 20 persons did not attend for the follow-up assessment within a reasonable time postoperatively. The average time (mean  $\pm$  standard deviation) to postoperative visit was  $9 \pm 2.2$  weeks postoperatively (range, 4–17). Those who completed the baseline assessment ( $n = 95$ ) and returned for a preoperative assessment were compared with those who did not ( $n = 38$ ) on all baseline variables. Of the 28 variables available for comparison, significant differences were observed for 2 subscales of the SF-36, Physical Function and Social Function. For both variables, noncompleters had poorer function (data not shown).

One or more postoperative complication occurred within 30 days of operation in 35 of the 95 subjects (37%).<sup>31</sup> Clavien grade I complications (bedside treatment) occurred in 9 patients, grade II (operative or radiologic intervention) in 17 patients, and grade III in 6 patients. Grade III complications included deep surgical site infections in 3 patients, perineal infection requiring skin graft in 1, and anastomotic leak requiring reoperation in 2; 2 patients had grade IV complications (requiring intensive care unit admission), 1 for a gastrointestinal bleed from esophagitis and 1 with a non-ST-elevation myocardial infarction. One patient with metastatic disease died many months postoperatively without ever being discharged after a prolonged course including myocardial infarction, intra-abdominal sepsis, fistula, and respiratory failure.

Baseline variables for the 95 subjects completing the prehabilitation phase are presented in Table I. The most common indications for operation were neoplasm (62%), inflammatory bowel disease

(15%), and diverticular disease (23%). Health-related quality of life was less than population norms for most subscales. The operative procedures included segmental colon resection (47%), anterior rectal resection (31%), and proctocolectomy with or without pouch (12%). Operations were performed by colorectal specialists. A laparoscopic approach was used in 25%, and 28% of patients had a stoma.

Table II shows that over the prehabilitation phase, functional walking capacity improved in 33% of subjects, did not change in 38%, and deteriorated in 29% (using the criterion of  $\pm 20$  m). A comparison is made for key variables at baseline and after completing prehabilitation for patients in whom walking capacity improved, remained the same or deteriorated. Also presented is the change from baseline. Of note, is that missing data was rare (1–8 persons) for many measures;  $VO_{2peak}$  was missing in 22 patients at the preoperative visit; 10 and 12 persons did not complete the HADS at the 2 preoperative assessments.

On average, those who improved did so by 46.6 m. (approximately 9% of baseline), and those who deteriorated did so by approximately the same amount ( $-48.9$  m). Those who improved in functional walking capacity over the prehabilitation phase had significant improvements in mental health, vitality, self-perceived health (EQ-VAS), and  $VO_{2peak}$ . There was no association between ASA class at baseline and degree of change over prehabilitation period.

Variables associated with change in functional walking capacity over the prehabilitation period (“response to prehabilitation”) are shown in Table III. Women showed, on average, 6.3% less improvement than men. Baseline functional walking capacity was also predictive, with those in the lowest quartile showing the most improvement from baseline (7.2%), probably because there was more room for improvement. High and moderate anxiety levels were also associated with improvement from baseline (10.2% and 5.6%, respectively), as was the belief that fitness level affected recovery (5.3%). Using the regression weights for each level of each variable in Table III, it is possible to estimate a predicted value for percent change. For example, men aged 50–74 with cancer who are fit (6MWT above the median), have no anxiety, and a short wait to operation would have a predicted change of near 0%.

Clinical outcomes during hospitalization were compared between patients who improved, stayed the same, or deteriorated during the prehabilitation program. The median duration of hospital stay was 5 days in each group. There was no difference in



**Table I.** Characteristics and baseline values on measures of physical and mental function and health of the 95 persons completing the prehabilitation phase

		Completers (n = 95*), mean (SD) or %
Age (yr)		60 (16)
<65 years		54%
Men		60%
Body mass index		28 (5)
Belief that fitness aids recovery		75%
ASA 1/2/3		6%/71%/23%
Neoplasm/inflammatory bowel disease/diverticular†		62%/15%/23%
Bike + strengthening/walk + breathing		52%/48%
Physical function		
Self-rated physical fitness (0–10)		5 (2)
6MWT (m)		489 (103)
% Predicted		102 (17)
2MWT (m)		166 (33)
VO <sub>2</sub> max (mL/min)		1435 (541)
VO <sub>2</sub> max (mL/kg/min)		18.6 (6.5)
Health and mental status		
EQ-5D utility		76.0 (11.0)
EQ-5D VAS		67.4 (17.7)
HADS‡: anxiety (0–21)		5.8 (4.2)
HADS‡: depression (0–21)		3.5 (3.2)
SF-36 subscales (0–100) [Norm 55–64 yr]		
Physical function	[82.3]	81.1 (21.8)
Role physical	[81.3]	64.3 (43.7)
Role emotional	[87.8]	74.5 (40.2)
Social function	[88.1]	78.9 (25.3)
Bodily pain	[74.9]	69.7 (26.0)
General health perception	[74.8]	65.3 (18.2)
Vitality	[68.3]	58.0 (22.6)
Mental health index	[79.5]	71.7 (19.4)
Physical health (Physical Component Summary)§	[49.0]	46.8 (9.3)
Mental health (Mental Component Summary)§	[53.7]	48.7 (10.5)

\*Owing to missing data, the number of persons with data ranged from 84 to 95.

†From pathology.

‡Each subscale is scored 0–21; higher values indicate more anxiety or depression.

§Measures are standardized to have a mean of 50 and a standard deviation of 10.

Percent predicted 6MWT calculated from the regression equation using age and gender provided by Gibbons et al.<sup>24</sup>

SD, Standard deviation.

the overall rate of complications across the 3 groups; however, patients who deteriorated during prehabilitation had a greater rate of complications requiring reoperation and/or intensive care (ie, grade IIIb or greater) compared with patients who improved or stayed the same (5/28 [18%] vs 1/66 [2%];  $P = .008$ ).

In the postoperative follow-up phase, the impact of the response to the prehabilitation intervention on postoperative recovery was evaluated as the primary outcome. Of the 95 people completing the prehabilitation phase, 20 did not return for postoperative assessment. Of the >20 variables examined, there was a difference between completers and drop-outs on only HADS depression at baseline (3.0 for completers vs 5.5 for drop-outs;

$P \leq .02$ ), although drop-outs were also more impaired ( $P < .10$ ) than completers on the SF-36 mental health subscale (65 for drop-outs vs 73 for completers at baseline and preoperatively). There were no significant differences in clinical variables, including postoperative complications, duration of stay, presence of a stoma, laparoscopic approach, or rectal anastomosis, to account for differences in follow-up.

Using the same criteria to define change over the follow-up period as for the prehabilitation period (20 m), 57% would be considered recovered (within 20 m of baseline 6MWT value) at follow-up. Table IV presents the association between prehabilitation change and recovery using this classification. Of those persons who improved

**Table II.** Prehabilitation period: Outcomes according to prehabilitation change in functional walking capacity (imputed data for  $n = 95$ )

	Change in 6MWT during prehabilitation			All* (n = 95), mean (SD)[n]
	Improved (n = 31; 33%), mean (SD)	No change (n = 36; 38%), mean (SD)	Deteriorated (n = 28; 29%), mean (SD)	
6MWT (m)				
Baseline	499 (112)	487 (100)	482 (100)	489 (103) [95]
Preoperatively	545 (112)	485 (103)	433 (109)	489 (116) [91]
Change	46.6 (25.0)	-1.7 (11.4)	-48.9 (26.0)	0.2 (43.3) [91]
SF-36†: improvements in mental health				
Baseline	65.9 (18.8)	71.4 (18.6)	78.5 (18.9)	71.7 (19.2) [93]
Preoperatively	71.5 (18.2)	74.3 (16.7)	75.5 (19.1)	73.7 (17.8) [94]
Change	5.6† (15.2)	2.9 (14.4)	-3.0 (15.4)	2.1 (15.2) [93]
SF-36†: vitality				
Baseline	55.3 (20.0)	55.1 (23.5)	62.4 (25.2)	57.3 (22.9) [93]
Preoperatively	64.5 (19.3)	59.2 (19.9)	58.1 (22.7)	60.6 (20.5) [94]
Change	9.2† (20.3)	4.0 (19.4)	-4.2 (17.9)	3.3 (19.8) [93]
SF-36†: PFI				
Baseline	84.9 (19.2)	80.4 (21.7)	77.2 (24.8)	81.0 (21.9) [93]
Preoperatively	89.4 (13.2)	82.8 (24.6)	74.6 (29.4)	82.5 (23.7) [95]
Change	4.5 (17.8)	2.4 (18.1)	-2.6 (26.7)	1.6 (20.9) [93]
SF-36†: bodily pain				
Baseline	68.2 (27.9)	72.9 (23.8)	68.5 (27.2)	70.1 (26.0) [94]
Preoperatively	76.7 (26.5)	78.1 (21.7)	73.3 (30.3)	76.2 (25.8) [94]
Change	8.5 (31.2)	5.3 (24.0)	4.8 (23.2)	6.2† (26.1) [93]
EQ-VAS				
Baseline	67.3 (19.0)	68.4 (17.6)	69.5 (18.1)	68.3 (18.1) [87]
Preoperatively	76.9 (11.6)	75.1 (12.4)	69.3 (15.9)	74.0 (13.5) [89]
Change	9.6† (19.6)	6.7† (17.5)	-0.2 (14.9)	5.6† (17.8) [85]
VO <sub>2peak</sub> /mL/kg/min				
Baseline	19.9 (7.0)	17.7 (6.8)	18.3 (5.7)	18.6 (6.5)
Preoperatively	22.3 (7.3)	19.4 (6.5)	18.9 (6.8)	20.2 (7.0)
Change	2.4† (3.6)	1.7† (3.2)	0.6 (3.8)	1.6† (3.6)
VO <sub>2peak</sub> /mL/min				
Baseline	1505 (583)	1397 (522)	1405 (528)	1434 (541) [95]
Preoperatively	1682 (595)	1535 (523)	1462 (611)	1562 (575) [73]
Change	177† (282)	138† (221)	57 (295)	127† (266) [73]
HADS§: anxiety				
Baseline	6.2 (4.2)	6.2 (4.6)	3.7 (2.9)	5.5 (4.2) [85]
Preoperatively	6.0 (3.6)	6.0 (4.8)	3.4 (3.2)	5.3 (4.2) [83]
Change	-0.2 (3.1)	-0.2 (3.3)	-0.3 (3.1)	-0.2 (3.1) [78]
HADS§: depression				
Baseline	3.5 (3.2)	3.8 (2.8)	3.2 (3.7)	3.5 (3.2) [85]
Preoperatively	2.8 (2.7)	3.5 (3.5)	3.1 (3.9)	3.2 (3.3) [83]
Change	-0.7 (3.3)	-0.3 (2.9)	-0.1 (2.3)	-0.4 (2.9) [78]

\*Based on observed data.

† $P < .05$  (with both single and multiple imputation) for within group comparison; paired  $t$  test for change from baseline to preoperatively (6MWT not included as it is used to define groups).

‡SF-36 subscales are scored from 0 to 100 with higher values indicating better health.

§Each subscale is scored 0–21; higher values indicate more anxiety or depression.

PFI, Physical function index; SD, standard deviation (based on  $n = 95$  from a single imputation).

over the prehabilitation phase ( $n = 26$ ), 77% (23% + 54%) would be considered as recovered (within 20 m of baseline). These proportions for people who did not change or deteriorated during prehabilitation were 59% and 32%, respectively ( $P = .0007$ ).

Table V indicates the predictors of recovery in the postoperative follow-up period. Compared with people who improved during the prehabilitation phase, those who deteriorated had significantly less follow-up 6MWT scores, on average 13.8% less than their baseline; those with no change ( $\pm 20$  m)

**Table III.** Prehabilitation phase: Predictors of change (% of baseline) in functional walking capacity

	Estimate ( $\beta$ )	SE	Probability
Women (40%) vs. men (60%)	-6.3	2.3	.006
Age, yr (50–74 years is the referent)			
18–49 (23%)	-4.6	2.8	.097
$\geq 75$ (22%)	-5.0	3.2	.119
Baseline 6MWT (above median, 489–749 m is the referent)			
Lowest quartile (24%): 154–419 m	7.2	3.3	.032
Second quartile (25%): 420–488 m	3.5	2.6	.183
ASA (2 is the referent)			
ASA 1 (6%)	6.8	4.1	.095
ASA 3 (23%)	-4.7	2.6	.065
HADS anxiety (<5 is the referent)			
5–7 (25%)	5.6	2.7	.042
$\geq 8$ (28%)	10.2	2.8	<.001
Belief that fitness affects recovery			
Yes (75%) vs no (25%)	5.3	2.3	.022

SE, Standard error.

Estimates are adjusted for all other variables in the tables as well as nonsignificant prognostic variables: Diagnosis (referent = neoplasm; inflammatory bowel disease 15%,  $\beta = 3.8$ ,  $se_{\beta} = 3.6$ ; other 23%,  $\beta = 2.2$ ,  $se_{\beta} = 2.6$ ), body mass index categories (referent = <25; overweight 28%,  $\beta = 2.5$ ,  $se_{\beta} = 2.6$ ; obese 34%,  $\beta = -2.9$ ,  $se_{\beta} = 2.7$ ), time to surgery ( $\beta$  per week = 0.05,  $se_{\beta} = 0.18$ ). Estimates are interpreted as the effect on the percent change from baseline value achieved during the prehabilitation phase associated with each level or unit of the variable.  $\beta$ /SE is equivalent to a *t* test. Based on multiply imputed data.

**Table IV.** Association between recovery and change over prehabilitation period

Follow-up prehabilitation	Recovery to baseline			N
	Below	Equal*	Greater	
Deteriorated	15 (68%)	4 (18%)	3 (14%)	22
No change*	11 (41%)	13 (48%)	3 (11%)	27
Improved	6 (23%)	6 (23%)	14 (54%)	26
	32	23	20	75

\* $\pm 20$  m.

Data from a single imputation ( $P = .0003$ ).  $P \leq .0007$  on each of the 20 multiple imputations.

during prehabilitation showed a decrease of 7.6% at follow-up compared with their baseline 6MWT ( $P = .066$ ). Given the average baseline 6MWT was 491 m ( $n = 75$ ), these differences translate into decreases of a 68 and 37 m, respectively, values that are meaningful clinically.<sup>13,14,32</sup>

Age was a significant predictor of recovery with the oldest age group, those  $\geq 75$  years of age, falling short of their baseline by 12%. Postoperative complications of grade II or greater also significantly delayed recovery, as did higher anxiety at baseline. Finally, people with early follow-up had a significantly greater degree of recovery, suggesting that patients with poorer recovery took longer to present for follow-up assessment.

## DISCUSSION

Of 95 people who completed a prehabilitation program while awaiting scheduled colorectal surgery,

**Table V.** Follow-up period: Significant predictors of recovery to baseline functional walking capacity (imputed data)

Preoperative factor	Estimate ( $\beta$ )	SE	P value
Change in 6MWT during prehabilitation			
Improved (referent)			
Deteriorated	-13.8	4.2	.001
No change	-7.6	4.1	.066
Age, yr (<50 is referent)			
50–74	-7.6	4.4	.088
$\geq 75$	-12.4	5.2	.018
Clavien score 2–4 vs 0 or 1	-12.2	3.9	.002
HADS anxiety (<3 is the referent)			
3–4	-2.3	5.0	.644
5–7	-9.7	4.9	.050
$\geq 8$	-14.1	6.6	.033
Weeks to follow-up (9–11 is referent)			
<6	12.8	5.6	.023
6–9	-2.1	3.7	.573
>11	-5.5	4.4	.214

Estimates are interpreted as the effect on the percent of baseline value achieved postoperatively of each level or unit of the variable. All estimates are adjusted for all other variables in the table as well as nonsignificant prognostic variables: Gender, baseline 6MWT, baseline depression as measured by the HADS, prehabilitation time, ASA, diagnosis, and high-risk surgery.  $\beta$ /SE is equivalent to a *t* test.

33% improved their physical function, 38% stayed the same, and 29% deteriorated. Patients randomized to the walking plus breathing intervention were more likely to improve compared with the bike plus strengthening program.<sup>11</sup> At postoperative follow-up,

those who improved during prehabilitation were more likely to have recovered to baseline functional walking capacity compared with those who did not change or deteriorated (77% vs. 59% and 32%;  $P = .0007$ ). Additionally, patients who deteriorated while waiting for operation were at particular risk for more serious operative complications. Although recovery is a complex outcome influenced by multiple factors, improved preoperative functional capacity remained a predictor of recovery after adjusting for multiple other prognostic variables including age, diagnosis, rectal resection, complications, baseline physical capacity, and follow-up time. This analysis suggests that a prehabilitation intervention lasting several weeks and based on walking and breathing exercises can improve functional exercise capacity in patients awaiting colorectal surgery, and this improvement is associated with improved postoperative recovery.

The proportion of drop outs was high, with only 95 of 133 enrolled patients completing the prehabilitation phase (71%) and 75 completing follow-up (56%). This proportion of drop outs is similar to a study of preoperative training for people scheduled for lung cancer surgery with reported prehabilitation completion and follow-up rates of 72% and 52%, respectively, in a sample of only 13 persons.<sup>33</sup> We performed a detailed, statistical comparison of completers and noncompleters for both the prehabilitation program and the follow-up phase, which showed very few differences between these groups. Although we restricted our sample to those with outcomes data, a strength of the analysis was appropriate handling of missing covariate data using multiple imputation.<sup>28,29</sup> Excluding observations with missing data not only decreases statistical power, it results in biased estimates of effect and error, resulting in  $P$  values that are too small and leading to false conclusions about relationships studied.

The results of this study provide insight as to who is most likely to benefit from a prehabilitation and who will be difficult to engage in such a program. People who did not complete the program had poor physical and social function, the latter variable an indicator of social support. Women showed less improvement over the prehabilitation period. People with a lesser walking capacity at baseline were more likely to improve, most likely because they have more room for improvement. Interestingly, the belief that fitness aids recovery was a strong predictor of improvement during prehabilitation, as was anxiety. A question that arises from these observations is whether these 2 constructs are modifiable. For the belief variable, educational material

on the benefits of fitness could be provided to the patient to reinforce this message. High anxiety at baseline was also associated with improvement during prehabilitation. This observation at first glance might seem paradoxical, but participants who were anxious were so because of anticipation and fear of the operation (state anxiety) and participating in the exercise program may have been a way of offsetting their anxiety. Anxiety at baseline, however, was also associated with poorer recovery. Anxiety has been shown consistently to affect pain and mood postoperatively, but less consistently physical recovery.<sup>34</sup>

Not surprisingly, other factors associated with poorer recovery were advanced age and postoperative complications. Factors associated with better recovery were change in 6MWT distance over the prehabilitation period and prompt attendance for follow-up. There was a positive, significant, independent effect of prehabilitation change on recovery, with those who deteriorated having a recovery score (percent return to baseline) 13.8% less than those who improved ( $P = .001$ ), whereas those who made no change scored 7.6% less ( $P = .066$ ). The impact of the prehabilitation period can be appreciated by considering that those who deteriorated were still, on average, 10.4% less than their baseline 6MWT at 9 weeks postoperatively, whereas those who improved were 3.0% greater than their baseline value. This 13.4% difference is equivalent to a between-group separation of 68 m on the 6MWT at follow-up, given the baseline 6MWT for the group seen at follow-up ( $n = 75$ ) was on average 491 m. The minimal important difference for 6MWT distance in patients recovering from operation is not known, but is approximately 25 m in patients with chronic respiratory disease.<sup>35</sup> The minimal important difference is defined as “the smallest difference in score in the outcome of interest that informed patients... perceive as important and which would lead the patient or clinician to consider a change in management.”<sup>36</sup> The magnitude of the changes in functional walking capacity in the prehabilitation period are likely clinically relevant since patients who improved (by an average of 45 m) also reported improvements in mental health, vitality, and self-perceived health status and had improved cardiorespiratory fitness as measured by the gold standard  $VO_{2peak}$ .

Recovery is a complex outcome with multiple contributing factors. There is no standard definition or measure to estimate this construct. Although its face validity may not be obvious to clinicians, we used the 6MWT as the measure of recovery because it is a functional test of walking



capacity, an outcome needed for all activities of daily living, including self-care, community mobility, and return to usual roles. The 6MWT integrates all components of functional walking capacity such as balance, speed, and endurance in 1 measure. It is easily obtainable on everyone because it is easy to administer with minimum training and space. It does not rely on self-report of symptoms or activities by patients, constructs that have been shown to be affected by response shift.<sup>37,38</sup> When postoperative values are compared with preoperative values in surgical populations who are not undergoing operation for improvement in functional status, it is a true measure of recovery. This test has been used previously to evaluate recovery in surgical populations.<sup>17,33</sup> To put its values in context, a person needs to achieve a 6MWT distance of >288 meters to be able to cross a single lane intersection during the time the traffic light remains green (equivalent to a gait speed of 0.8 m/s)<sup>39</sup>; a person needs to achieve a 6MWT distance of >432 meters to be able to cross 4 lanes of traffic with the green light (1.2 m/s).<sup>39</sup> If these distances are not achieved, it is unlikely that the person would be resuming usual community activities such as shopping or returning to work and, hence, he or she could not be considered to have recovered.

The 6MWT was also used by Jones et al<sup>33</sup> in their study of preoperative training before pulmonary resection, and they showed that lung cancer patients gained on average 49 m on the 6MWT over the course of a 4-week program of supervised aerobic training. Adherence to the intervention was 73% (range, 0–100%). Because the “per protocol” sample size in this study was small ( $n = 13$ ), the 95% confidence interval was very wide (12–85 m). Of the 95 people in the prehabilitation program, almost equal proportions of people improved, stayed the same, or deteriorated over the prehabilitation period.

Deterioration while waiting for the scheduled operation was associated with serious complications and prolonged recovery. Older patients were at risk, but other reasons for deterioration were not clear. These might include progression of the disease process itself, the effect of medical treatments, or lack of physical activity. The cohort included a wide range of disease states, ranging from rectal cancer requiring neoadjuvant therapies to cecal polyps to active inflammatory bowel disease to elective resection for diverticular disease. Patients with cancer did not have a greater risk of deterioration and there were no differences in the proportion of patients with rectal cancer who may have received neoadjuvant therapy. The

ASA classification was similar in the 3 groups. Nutritional data and information about symptom status were not collected, however. The median duration of the prehabilitation period was 38 days (interquartile range, 22–60), and was not different across the 3 groups. The group who deteriorated had less of a belief in the benefits of fitness at baseline. They also had a tendency to deteriorate in mental health and fatigue. Deterioration preoperatively is a strong argument for either a lesser waiting time or for developing prehabilitation strategies to combat deterioration. There is a growing literature on mind–body interventions that use mindfulness-based stress reduction to decrease anxiety and sleep disturbances.<sup>40</sup> Our prehabilitation program was very physically oriented and incorporating mental strategies to attenuate stress response may be of added value.

The present reanalysis suggests that, no matter how walking capacity was improved, those who improved over the preoperative waiting period had a better postoperative recovery. Additionally, those whose functional walking capacity deteriorated were at risk for clinically important postoperative complications. Colectomy accounts for a disproportionate share of complications in general surgery<sup>41</sup> and complications may be related more to patient factors than quality of care.<sup>42</sup> Accordingly, a prehabilitation program to improve or at least maintain functional capacity preoperatively may play a role in decreasing rates of complications after colorectal surgery.

In conclusion, this study supports that prehabilitation in patients undergoing scheduled colorectal surgery is feasible and meaningful changes in functional capacity can be achieved during a period of 3–8 weeks, which in turn have a positive impact on postoperative recovery. Patients, especially those with poor physical capacity, should consider a prehabilitation regimen to enhance functional exercise capacity before preplanned, elective surgery.

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