Impact of Facilitation of Early Mobilization on Postoperative Pulmonary Outcomes After Colorectal Surgery

A Randomized Controlled Trial

Saba Balvardi, MD,† Nicolò Pecorelli, MD,*† Tanya Castelino, MD,*† Petru Niculiseanu, MD,‡ Mohsen Alhashemi, MD,*† Alexander Sender Liberman, MD,* Patrick Charlebois, MD,* Barry Stein, MD,* Franco Carli, PhD,§ Nancy E. Mayo, PhD,¶ Liane S. Feldman, MD,*†‡ and Julio F. Fiore Jr., PhD*†‡✉*

Objective: To estimate the extent to which staff-directed facilitation of early mobilization impacts recovery of pulmonary function and 30-day postoperative pulmonary complications (PPCs) after colorectal surgery.

Summary Background Data: Early mobilization after surgery is believed to improve pulmonary function and prevent PPCs; however, adherence is low. The value of allocating resources (eg, staff time) to increase early mobilization is unknown.

Methods: This study involved the analysis of a priori secondary outcomes of a pragmatic, observer-blind, randomized trial. Consecutive patients undergoing colorectal surgery were randomized 1:1 to usual care (preoperative education) or facilitated mobilization (staff dedicated to assist transfers and walking during hospital stay). Forced vital capacity, forced expiratory volume in 1 second (FEV1), and peak cough flow were measured preoperatively and at 1, 2, 3 days and 4 weeks after surgery. PPCs were defined according to the European Perioperative Clinical Outcome Taskforce.

Results: Ninety-nine patients (57% male, 80% laparoscopic, median age 63, and predicted FEV1 97%) were included in the intention-to-treat analysis (usual care 49, facilitated mobilization 50). There was no between-group difference in recovery of forced vital capacity [adjusted difference in slopes 0.002 L/d (95% CI −0.01 to 0.01)], FEV1 [−0.002 L/d (−0.01 to 0.01)] or peak cough flow [−0.002 L/min/d (−0.02 to 0.02)]. Thirty-day PPCs were also not different between groups [adjusted odds ratio 0.67 (0.23–1.99)].

Conclusions: In this randomized controlled trial, staff-directed facilitation of early mobilization did not improve postoperative pulmonary function or reduce PPCs within an enhanced recovery pathway for colorectal surgery.

Trial Registration: ClinicalTrials.gov Identifier: NCT02131844.

Keywords: colorectal surgery, early mobilization, enhanced recovery pathways, outcome research, pulmonary outcomes

From the *Department of Surgery, McGill University, Montreal, QC, Canada; †Steinberg-Bernstein Centre for Minimally Invasive Surgery and Innovation, McGill University Health Centre, Montreal, QC, Canada; ‡Centre for Outcomes Research and Evaluation (CORE), Research Institute of the McGill University Health Centre, Montreal, QC, Canada; §Department of Anesthesia, McGill University, Montreal, QC, Canada; and ¶Division of Clinical Epidemiology, McGill University, Montreal, QC, Canada.

✉julio.fiorejunior@mcgill.ca.

This study was supported by a MITACS Elevate Postdoctoral Fellowship (Ref. IT02887) awarded to J.F.F. J.F.F. receives an investigator salary award from the Fonds de recherche du Québec-Santé. The Steinberg-Bernstein Centre for Minimally Invasive Surgery (McGill University Health Centre, Montreal, Canada) is supported in part by Medtronic. The study funders had no role in collection, analysis, interpretation of data, writing of the report, or decision to submit the article for publication.

The authors report no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.annalsofsurgery.com).

ISSN: 0003-4932/20/27305-0868

DOI: 10.1097/SLA.0000000000003919

(*Ann Surg* 2021;273:868–875)

Abdominal surgery has evolved in recent years with the widespread use of laparoscopy and standardization of perioperative care using enhanced recovery pathways (ERPs).[1,2] The evidence for the benefit of these interventions is particularly strong in patients undergoing colorectal surgery, with meta-analyses supporting a marked reduction in hospital length of stay, and overall morbidity.[3,4] However, despite these innovations, postoperative pulmonary complications (PPCs) are still relatively common and, therefore, remain a target for quality improvement.[5,6] The pathophysiology of PPCs after major abdominal surgery is related to postoperative changes in respiratory drive and muscle function, reduction in pulmonary volumes, and development of atelectasis; which increase risk of pulmonary infections and acute respiratory failure.[7] The reported incidence of PPCs after colorectal surgery varies from 8% to 20%[5,6,8] and accounts for over 60% postoperative in-hospital deaths.[5] The incremental costs of PPCs after colorectal surgery are also considerable, reaching over 25 thousand dollars per patient in comparison with those without complications.[5]

Findings from a recent meta-analysis support that ERPs are beneficial in reducing PPCs[9]; however, evidence regarding the role of individual ERP components in improving PPCs is lacking.[6] Prolonged bed rest after surgery is considered an important risk factor for PPCs as it favors reduction of pulmonary volumes and atelectasis.[10–12] For this reason, early mobilization (ie, starting out-of-bed activities from the day of surgery) is recommended by guidelines as a strategy to prevent PPCs.[13–16] Although studies suggest an association between early mobilization and better pulmonary outcomes within colorectal ERPs,[6] there is no evidence that this relationship is causal.[17] Also, despite guideline recommendations, studies suggest that adherence to early mobilization after colorectal surgery remains very low.[18–20] A potential solution to increase adherence to early mobilization and improve postoperative pulmonary outcomes is dedicating specific staff time to facilitate out-of-bed activities after surgery; however, this approach is resource-intensive and not evidence-based.[17]

The overall aim of this study was to contribute evidence regarding the impact of postoperative facilitation of early mobilization on pulmonary outcomes after colorectal surgery in the context of an ERP. The study addressed the following research question: In comparison to usual care, to what extent does staff-directed facilitation of early mobilization impact recovery of pulmonary function and 30-day PPCs after colorectal surgery?

METHODS

Study Design and Patients

This study involved analysis of secondary outcomes of a pragmatic, observer-blind, parallel-group randomized trial. Hypotheses

regarding the impact of facilitated early mobilization on pulmonary outcomes were set a priori and were addressed in our study protocol (ClinicalTrials.gov Identifier: NCT02131844). The study protocol and list of amendments after initial ethics approval are available in Supplement 1, http://links.lww.com/SLA/C127. Analysis and reporting of this study follow the CONSORT checklist.[21] The study was approved by our institutional review board (MUHC Research Ethics Board ref. 13–329-SDR) and all patients provided informed consent.

The primary trial was powered to examine the impact of staff-directed facilitation of early mobilization on proportion of patients returning to preoperative functional walking capacity (6-min walk test) at 4 weeks after surgery. The full description of the study methods, baseline sample characteristics, and trial results are reported elsewhere.[22] We considered for inclusion adult patients (>18 yrs) planned for colorectal resection in a tertiary university hospital in Montreal. Criteria for exclusion were: metastatic disease, inability to fully mobilize preoperatively (eg, neurological or musculoskeletal diseases), inability to understand English or French and planned admission to ICU immediately after surgery. All patients were treated within an ERP according to Enhanced Recovery After Surgery Society recommendations.[13] Details about our ERP program have been previously described.[23]

Interventions

Patients included in the trial were randomly assigned (1:1) to receive usual care (perioperative education) or facilitated postoperative mobilization.[22]

Usual Postoperative Care

Participants randomized to this group participated in an education session with a surgery nurse at the Preoperative Clinic, approximately 1 week before the surgery. In this session, they received instructions about postoperative early mobilization verbally and in writing (via a postoperative care booklet). The mobilization instructions were set according to recommendations by Enhanced Recovery After Surgery Society Guidelines[13,24] and included: sitting in a chair for at least 2 hours on the day of surgery and staying out of bed (sitting and/or walking) for at least 6 hours from postoperative day (POD) 1 until discharge. Patients in this group received assistance from nursing staff when getting out of bed for the first time. Subsequent mobilization was not routinely assisted unless deemed necessary by the ward team or requested by the patient. Patients were referred to a physiotherapist if they had difficulty mobilizing. As part of usual care, patients also received an incentive spirometer and were instructed to conduct breathing exercises (10 repetitions hourly, while awake) until hospital discharge.

Facilitated Postoperative Mobilization

Participants randomized to this group, in addition to usual care (as outlined above), had early mobilization facilitated by a trained health professional (eg, physiotherapist or graduate trainee). The health professional: 1) visited the participant on the day of surgery (after admission to the ward) to reinforce mobilization goals and assisted with transfer to a chair and 2) visited the participant 3 times per day starting from POD1 to reinforce mobilization goals and walk with the participant. The targeted walking distance during each session was at least the length of the hallway (approximately 200 m) with progressive increase according to the participant's tolerance. The use of incentive spirometry was as per usual care.

Randomization and Blinding

Patients were randomized in random permuted blocks (2, 4, or 6) using an independent web-based randomization service (www.sealedenvelope.com). Intervention staff conducted all randomizations via a secured website and allocation was concealed until patients arrived at the Post-Anesthesia Care Unit after the surgery. Outcome assessors were blinded to group assignment. To ensure blinding during PFT assessments performed at the surgical ward, a schedule was set so that assessment times did not coincide with interventions. Any inadvertent unblinding was reported and another assessor was assigned. As reported elsewhere, these blinding procedures were deemed effective as the rate of inadvertent unblinding was low (n = 5) and outcome assessors did not guess patients' treatment allocation more than expected by chance.[22] Due to the nature of the intervention, it was not possible to blind patients or ward staff to group assignment. To minimize performance bias, ward staff were informed that we were conducting a study on activity monitoring but were not given specific information about the specific interventions being tested.

Outcome Assessment

Pulmonary function testing was undertaken preoperatively (approximately 1 week before surgery at the patient's visit to the Preoperative Clinic), during hospital stay (POD 1, 2, and 3) and at 4 weeks after surgery. Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) were measured using a portable spirometer (Spirobank, Medical International Research, Rome, Italy) according to American Thoracic Society standards.[25] The same spirometer was also connected to a facemask and used to assess peak cough flow (PCF), which is a measure of cough efficacy.[26] Each test was repeated at least 3 times to ensure consistency and accuracy, and the best result was recorded for analysis. Parameter values were recorded in liters (FVC and FEV1) and liters per minute (PCF).

Postoperative pulmonary complications (PPCs) up to 30 days after surgery were recorded by a blinded assessor via chart review. According to recommendation by the European Perioperative Clinical Outcome (EPCO) Taskforce,[27] the presence of PPC was defined in the presence of 1 or more of the following criteria: respiratory infection, atelectasis, respiratory failure, pleural effusion, pneumothorax, bronchospasm, or aspiration pneumonitis. The specific definition of each criterion is presented in Table 1.

Other outcome measures assessed in the trial were detailed in our previous publication.[22] These included: in-hospital mobilization (assessed up to POD 3 via an activity monitor and self-report), recovery of functional walking capacity (measured using the 6-min walk test), recovery of gastrointestinal function, time to achieve discharge criteria, 30-day overall complications, and patient-reported outcome measures.

Statistical Analysis

This trial was originally powered with a sample of 100 patients based on potential between-group differences in recovery of walking capacity (6-min walk distance) at 4 weeks after surgery.[22] This sample provides 80% power to detect a 15% difference in postoperative FVC between groups accounting for a standard deviation of 1.0 (estimated from the previous literature[28]) and alpha of 0.05. Although no previous research has reported minimal important differences in postoperative pulmonary function in surgical patients, a 15% difference in the FVC has been shown to be detectable and deemed clinically relevant in the previous colorectal surgery literature.[28]

The impact of facilitated early mobilization on pulmonary function measures (FVC, FEV1, and PCF) was analyzed using mixed model analysis. Comparison of PPC rates was conducted using logistic regression. To improve the precision of estimates and compensate for potential between-group imbalances, all analyses were adjusted for potential prognostic factors for poor postoperative pulmonary outcomes including: sex, age, surgical approach (laparoscopic vs open), disease (benign vs malign), ASA score, surgery

TABLE 1. Definitions of Postoperative Pulmonary Complications by the European Perioperative Clinical Outcome (EPCO) Taskforce

Respiratory infection	Patient has received antibiotics for a suspected respiratory infection and met 1 or more of the following criteria: new or changed sputum, new or changed lung opacities, fever, white blood cell count $>12\times10^9$/L
Respiratory failure	Postoperative PaO2 < 8 kPa (60 mm Hg) on room air, a PaO2:FI02 ratio <40 kPa (300 mm Hg) or arterial oxyhemoglobin saturation measured with pulse oximetry < 90% and requiring oxygen therapy
Pleural effusion	Chest radiograph demonstrating blunting of the costophrenic angle, loss of sharp silhouette of the ipsilateral hemidiaphragm in upright position, evidence of displacement of adjacent anatomical structures or (in supine position) a hazy opacity in 1 hemithorax with preserved vascular shadows
Atelectasis	Lung opacification with a shift of the mediastinum, hilum or hemidiaphragm toward the affected area, and compensatory over-inflation in the contralateral lung
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura
Bronchospasm	Newly detected expiratory wheezing treated with bronchodilators
Aspiration pneumonitis	Acute lung injury after the inhalation of regurgitated gastric contents

Adapted from Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. *Eur J Anaesthesiol.* 2015;32(2):88–105.

duration, smoking status, and body mass index.[29–32] We followed an intention-to-treat principle analyzing all participants in the groups to which they had been allocated. To test the robustness of our statistical approach, post hoc sensitivity analyses were conducted 1) with no adjustment for prognostic factors and 2) with adjustment only for prognostic factors that seemed to differ between study arms. To minimize potential bias arising from missing data from incomplete assessments or losses to follow-up, multiple imputation was carried out using chained equations and predictive mean matching. Estimates from 20 imputed datasets were combined using Rubin rules.[33] Statistical analyses were performed using STATA version 14.2 (StataCorp, College Station, TX).

RESULTS

Patients were recruited between July 2014 and July 2015; the last follow-up assessment was in August 2015. One hundred seventy-one patients were screened for eligibility, 24 met the exclusion criteria, 47 eligible patients were excluded due to lack of consent (n = 41), participation in another simultaneous study involving exercise (n = 4), and unavailability of intervention staff after surgery (n = 2) (Fig. 1). One hundred patients were randomized but one was excluded after randomization due to protocol violation; consequently, 99 patients (49 in usual care and 50 in facilitated mobilization) were included in the intention-to-treat analysis (Fig. 1). As reported in our previous publication, the proportion of patients with low physical status (ASA$\geq$ 3) was higher among patients who did not consent to participation in comparison with those who participated in the study (34% vs 15%; $P = 0.008$), but other demographic characteristics such as mean age, sex, ASA score, surgical procedure, and type of anesthesia were similar.[22] Rates of missing data that were subsequently imputed are reported in Figure 1. The highest missing data rate occurred on POD 3, likely due to hospital discharges.

Patients in each randomized group had similar preoperative characteristics, except for sex ratio (57% female in usual care vs 30% female in facilitated mobilization) and surgery duration (mean 205 ± 10 min in usual care vs 226 ± 14 min in in facilitated mobilization) (Table 2). Both patient groups had a mean age of 60 years. Patients had similar preoperative PFTs (FVC 3.5 ± 1.3 L in usual care vs 3.7 ± 1.2 L in facilitated mobilization, FEV1 2.7 ± 0.9 L in usual care vs 2.9 ± 0.9 L in facilitated mobilization, PCF 5.8 ± 2.1 L/min in usual care vs 6.4 ± 2.3 L/min in facilitated mobilization). In both groups, rates of laparoscopic surgery were high (80% in usual care and 82% in facilitated mobilization) and the majority of patients had high preoperative physical status (ASA I–II; 84% in usual care and 86% in facilitated mobilization) (Table 2). Postoperatively, 4 patients (4%) received a physical therapy referral during hospital stay in addition to the trial intervention (2 in usual care and 2 in facilitated mobilization).

The trajectory of pulmonary function variables (FVC, FEV1, and PCF) postoperatively was similar between patients randomized to facilitated mobilization or usual care (Fig. 2). This trajectory involved a rapid drop in all pulmonary function variables immediately after surgery followed by a gradual recovery toward preoperative values. There was no between-group difference in recovery of FVC [adjusted difference in slopes 0.002 L/d (95% CI −0.01 to 0.01)], FEV1 [−0.002 L/d (−0.01 to 0.01)], or PCF [−0.002 L/min/d (−0.02 to 0.02)] (Table 3).

Thirty-day PPCs occurred in 18% of patients in the facilitated mobilization group versus 24% in the usual care group [adjusted odds ratio 0.67 (0.23–1.99)] (Table 4). The PPCs most commonly identified were: respiratory failure (facilitated mobilization 10% vs usual care 20%), atelectasis (12% vs 10%), and pleural effusion (10% vs 6%). Only 5% of PPCs were diagnosed in isolation, whereas the majority (95%) were diagnosed in conjunction with other postoperative complications (ie, ileus, urinary retention, surgical site infections). Median time to PPC diagnosis was 2 days in usual care (IQR 1.5–5) and 1 day in facilitated mobilization (IQR 1–3).

Results of the post hoc sensitivity analyses with no adjustment for prognostic factors and with adjustment for prognostic factors that seemed to differ between study arms (sex and surgery duration) were consistent with the primary analysis (Supplement 2, http://links.lww.com/SLA/C128).

DISCUSSION

In this randomized controlled trial, staff-directed facilitation of early mobilization did not improve postoperative pulmonary function or reduce PPCs within an ERP for colorectal surgery. Hence, our results do not support the need to allocate extra resources (staff time) to increase early mobilization targeting improvement of pulmonary outcomes in this context of care.

The lack of intervention effect occurred despite high adherence to mobilization sessions and a considerable increase in out-of-bed activities during hospital stay. As reported in our previous publication,[22] adherence to the mobilization sessions proposed for the intervention group was >80%. In-hospital mobilization was significantly greater in the intervention group in comparison with usual care: rate of patients out-of-bed on the day of surgery (72% facilitated mobilization vs 36% usual care), mobilization $\geq$ 6 hours

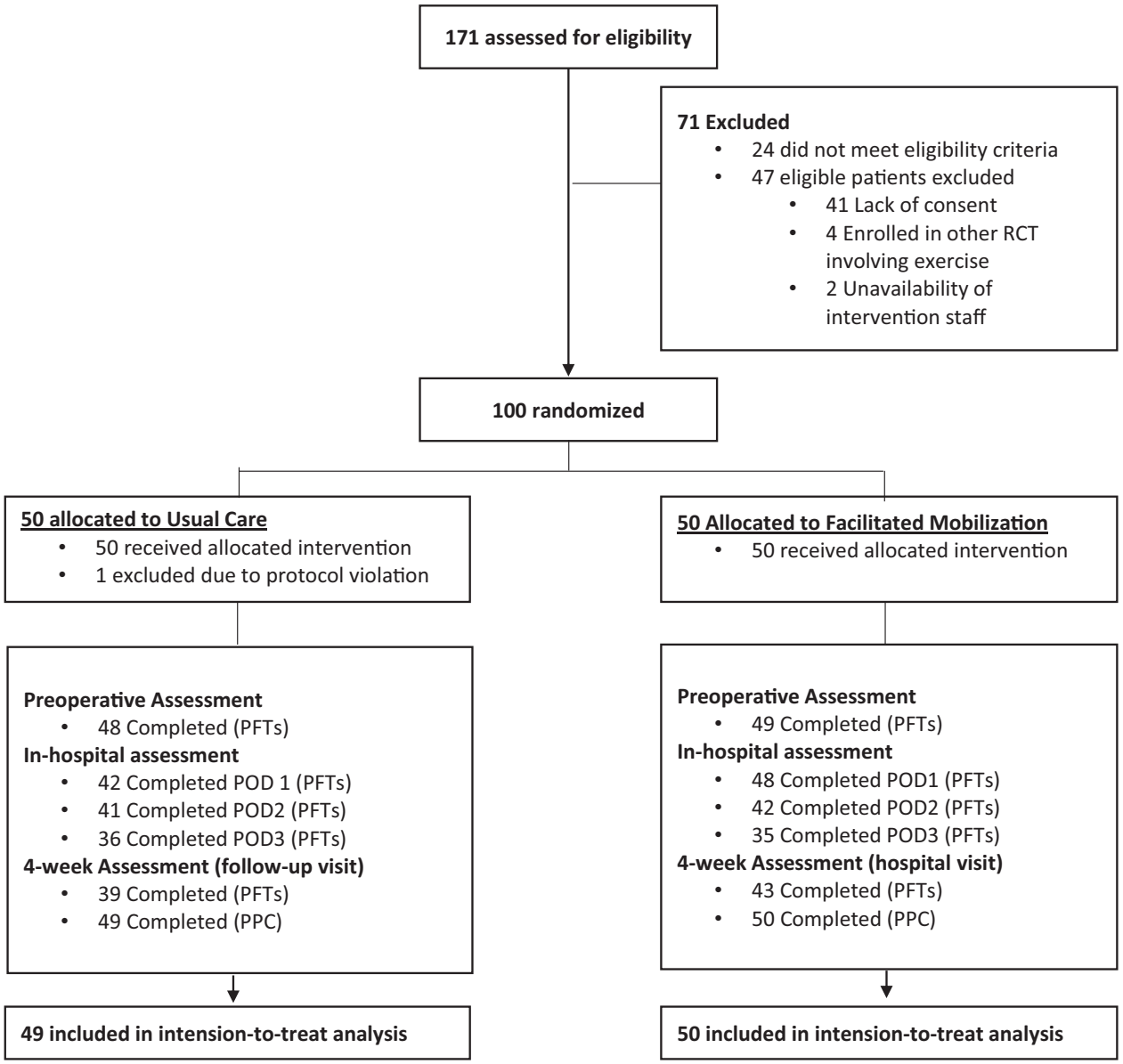


FIGURE 1. Consort diagram. PFT indicates pulmonary function test; POD, post-operative day; PPC, postoperative pulmonary complication.

(62% vs 24% on POD1, 63% vs 42% on POD2) and step count (542 vs 250 on POD 1, 1021 vs 483 on POD2).[22] The intervention did not impact other outcome measures such as recovery of functional walking capacity at 4 weeks, recovery of gastrointestinal function, time to achieve discharge criteria, 30-day overall complications, and patient-reported outcome measures.[22] Median hospital length of stay was 3 days in the usual care group and 4 days in the facilitated mobilization group.[22] The only adverse event attributable to early mobilization was orthostatic intolerance, but rates were not different between groups (26% facilitated mobilization vs 20% usual care).[22]

Although many ERP guidelines recommended early mobilization as a strategy to prevent PPCs after colorectal surgery,[13–16,34] a recent systematic review identified that RCTs supporting this recommendation are lacking.[17] To our knowledge, the present study is the first randomized trial investigating the impact of enhancing early mobilization on postoperative pulmonary outcomes. A major strength of our study was its methodological rigor in minimizing risk of selection bias (robust randomization and concealment of allocation), detection bias (blinding outcome assessors and indication of blinding effectiveness), attrition bias (intention-to-treat analysis with multiple imputation of missing data), and selective reporting (key protocol information registered a priori). Another major strength is the use of activity monitors to confirm that the intervention was effectively delivered.[22] As the definition of PPCs has greatly varied in the literature, our study used the definition criteria set by the EPCO Taskforce[27] to ensure standardization and comparability with studies using similar criteria. Due to these methodological strengths, we believe that our results contribute important evidence about the impact of staff-directed early mobilization on postoperative pulmonary outcomes after colorectal surgery.

TABLE 2. Baseline and Operative Characteristics

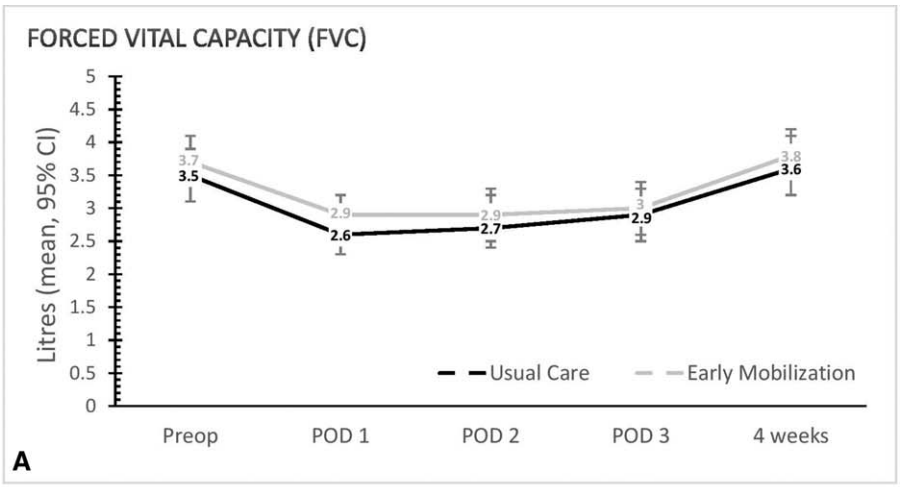
Patient Characteristics	Usual Care (n = 49)	Facilitated Mobilization (n = 50)
Age, years	60.2 ± 14.6	60.6 ± 15
75+ yrs old	7 (14)	9 (18)
Female	28 (57)	15 (30)
Body mass index, kg/m^2	26.6 ± 5.8	26.2 ± 4.0
Current smoker	6 (12)	5 (10)
Neoadjuvant chemotherapy	5 (10)	6 (12)
Physical status (ASA score)		
Higher (score I–II)	41 (84)	43 (86)
Lower (score III–IV)	8 (16)	7 (14)
Comorbidity (Charlson Comorbidity Index)	2 (0–2)	2 (0–2)
Diagnosis		
Malignancy	28 (57)	30 (60)
Inflammatory bowel disease	8 (16)	11 (22)
Benign polyps	6 (12)	6 (12)
Diverticular disease	6 (12)	2 (4)
Other benign disease	1 (2)	1 (2)
6MWD, m	478.6 ± 105.1	477.6 ± 120
Preoperative pulmonary function tests		
Forced vital capacity, L	3.5 ± 1.3	3.7 ± 1.2
Forced expiratory volume in 1 s, L	2.7 ± 0.9	2.9 ± 0.9
Peak cough flow, L/min	5.8 ± 2.1	6.4 ± 2.3
Procedures performed		
Right hemicolectomy/ileocecal resection	14 (29)	21 (42)
Left hemicolectomy	3 (6)	3 (6)
Total/subtotal colectomy	1 (2)	2 (4)
Sigmoid resection	4 (8)	2 (4)
Anterior resection	17 (35)	15 (30)
Abdominoperineal resection	2 (4)	1 (2)
Total proctocolectomy and IPAA	3 (6)	4 (8)
Other colorectal procedures	5 (10)	2 (4)
Surgical approach		
Laparoscopic	39 (80)	41 (82)
Open/converted	10 (20)	9 (18)
Surgery duration, min	205.4 ± 10.34	226.2 ± 14.4
Type of analgesia		
Epidural	25 (51)	24 (48)
Intravenous patient controlled analgesia	24 (49)	26 (52)

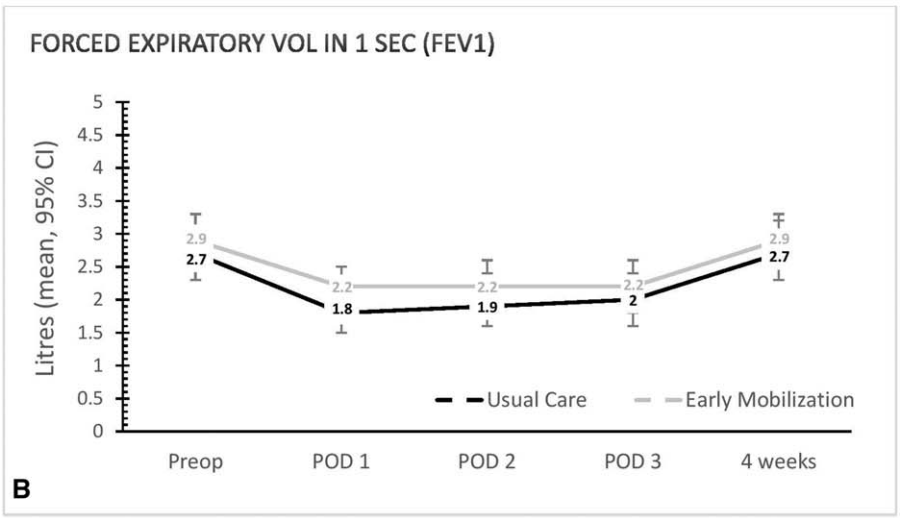
Data are n (%), mean ± SD or median (IQR).
BMI indicates body mass index; ASA, American Society of Anesthesiologists; 6MWD, 6-min walk distance.

Findings from this trial corroborate previous literature supporting that, even in the context of minimally invasive colorectal surgery, patients are subject to a rapid decline in pulmonary function postoperatively, which is followed by a gradual return toward preoperative values. In our sample including over 80% of patients undergoing laparoscopic procedures, the observed decline in FVC and FEV1 on POD1 was in accordance with results observed in similar surgical populations (20%–30% decline).[28] Our patients regained more than 80% of their preoperative FVC by POD3, which is also consistent with results from previous studies.[28,35]

Our results do not provide evidence that assisted early mobilization reduces PPCs; however, the 95% confidence interval was wide indicating a large degree of uncertainty. The overall rate of PPCs in our study, defined according to composite criteria set by the EPCO Taskforce,[27] was 21%. This is in agreement with the incidence reported in the previous abdominal surgery literature using similar criteria.[36,37] A potential criticism to the EPCO composite definition of PPCs is that the composite includes outcomes of doubtful clinical relevance such as ''respiratory failure'' (defined in the presence of desaturation > 90% requiring oxygen therapy), radiological diagnosis of pleural effusion (even when minor, ie, with no need for drainage), and radiological diagnosis of atelectasis (even in the absence of clinical signs and symptoms). A newly proposed consensus-based definition of PPCs, which accounts for both the presence and severity of complications (none, mild, moderate, and severe), should be considered for use in future research.[38] According to this definition, 19 of the 21 PPCs diagnosed in our sample were of ''none'' or ''mild'' severity (ie, no therapeutic supplemental oxygen required or $FiO_2 < 0.6$), while only 2 were ''severe'' (ie, required mechanical ventilation: 1 in facilitated mobilization, 1 in usual care). None of the PPCs identified were ''moderate'' (ie, required $FiO_2 \geq 0.6$, high-flow nasal oxygen, or both). Given the low rate of clinically meaningful PPCs observed in our study, we expect that the prophylactic impact of early mobilization on such events, if any, can only be detected through large-scale multicenter trials or meta-analyses. Nonetheless, the number-needed-to-treat may be too large to justify recommending staff-directed mobilization as standard practice.

Results of this trial must be interpreted keeping in mind that our study was conducted in the context of a well-established ERP and involved predominantly laparoscopic cases. Our ERP program already includes several interventions that aim to improve postoperative pulmonary outcomes, including multimodal anesthesia with short-acting neuromuscular blocking agents, opioid-sparing postoperative analgesia techniques, avoidance of postoperative nasogastric tubes, and incentive spirometry.[13,39] The previous literature also supports that laparoscopic colorectal surgery is associated with a





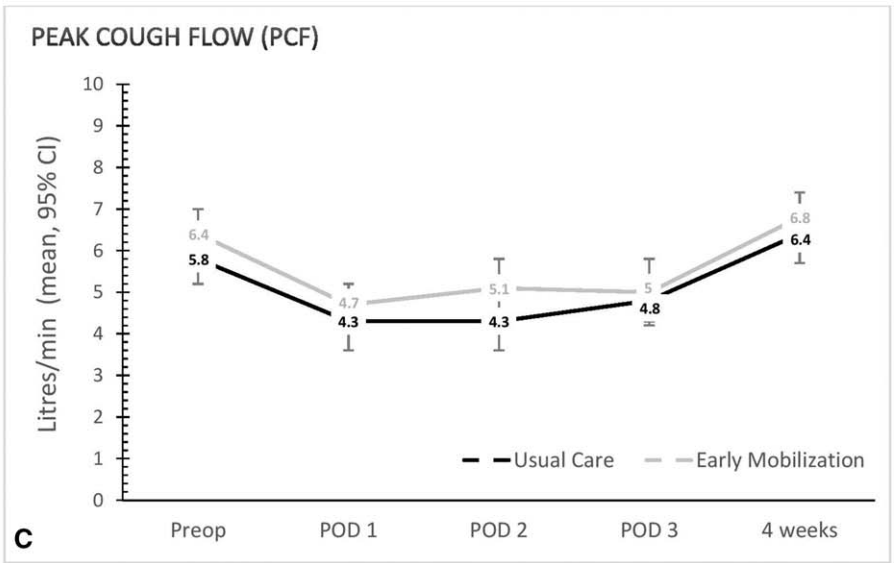


FIGURE 2. Preoperative and postoperative pulmonary function.

TABLE 3. Between-group Difference in Postoperative Pulmonary Function Tests

	Usual Care Mean (SD)				Facilitated Mobilization Mean (SD)					
	POD1	POD2	POD3	POW4	POD1	POD2	POD3	POW4	Difference in Slopes (95% CI)*	*P* Value
FVC, L/d	2.58 (1.32)	2.67 (1.25)	2.88 (1.17)	3.57 (1.3)	2.92 (1.00)	2.92 (1.23)	3.04 (1.21)	3.81 (1.20)	0.002 (−0.01 to 0.01)	0.75
FEV1, L/d	1.85 (0.88)	1.87 (0.82)	2.00 (0.82)	2.73 (1.00)	2.19 (0.12)	2.16 (0.99)	2.26 (0.96)	2.95 (0.94)	−0.002 (−0.01 to 0.01)	0.70
PCF, L/min/d	4.34 (2.07)	4.34 (2.08)	4.77 (1.82)	6.40 (2.02)	4.75 (1.82)	5.07 (2.00)	4.97 (2.09)	6.78 (1.98)	−0.002 (−0.02 to 0.02)	0.86

*Coefficients derived with adjustment for sex, age, surgical approach (laparoscopic vs open), disease (benign vs malign), ASA score, surgery duration, smoking status, body mass index, and preoperative results of the specific test (in deciles).

POW indicates postoperative week.

TABLE 4. Between-group Difference in Postoperative Pulmonary Complications

Variable	Usual Care (n = 49)	Facilitated Mobilization (n = 50)	Adjusted Odds Ratio (95% CI)*	*P* Value
Postoperative pulmonary complications	12 (24.5%)	9 (18%)	0.67 (0.23–1.99)	0.47
Respiratory infection	1 (2%)	1 (2%)		
Respiratory failure	10 (20.4%)	5 (10%)		
Pleural effusion	5 (10.2%)	3 (6%)		
Atelectasis	5 (10.2%)	6 (12%)		
Pneumothorax	0 (0%)	0 (0%)		
Bronchospasm	0 (0%)	0 (0%)		
Aspiration pneumonitis	1 (2%)	0 (0%)		

Data are expressed as n (%), unless otherwise stated.

*Coefficient derived with adjustment for sex, age, surgical approach (laparoscopic vs open), disease (benign vs malign), ASA score, surgery duration, smoking status, and body mass index.

more rapid recovery of pulmonary function and reduced the risk of PPCs in comparison with open procedures.[40,41] Our results support that, in the aforementioned context of care (ERP + laparoscopic surgery), patients may be already ''optimized'' to mobilize as tolerated to avoid the negative effects of prolonged bed rest on pulmonary outcomes. However, we cannot exclude that patients may benefit from staff-directed early mobilization in settings where there is a greater prevalence of open surgery and patients receive traditional perioperative care (ie, in non-ERP settings).

A limitation of this study is that it involved the analyses of secondary outcomes of an RCT. This raises concerns regarding the likelihood of finding a statistically significant result by chance alone due to multiple comparisons.[42] The analysis reported in this paper, however, was preplanned and, despite the potential for type I error (with bias against the ''null hypothesis''), no statistical differences were found between groups. Results from further post hoc sensitivity analyses were consistent with the primary analysis. We did not find evidence that facilitated early mobilization reduces PPCs; however, we cannot exclude that our trial was underpowered to detect between-group differences in this outcome. To move this field forward, our RCT provides a rich data source for future confirmatory meta-analyses assessing the impact of early mobilization on PPCs. Another potential limitation of this RCT is the risk of performance bias as patients and staff were not blinded to the interventions being compared. However, any bias attributed to lack of blinding, would likely have favored patients who received the intervention and we found no differences between groups. Patients with difficulty mobilizing at baseline (neurological or musculoskeletal disease) were not eligible for this RCT and patients with lower physical status were less likely to consent participation; hence, we cannot exclude that these patients, usually carrying a higher baseline risk for PPCs, may benefit from the intervention. As this study was a single-center trial, the external validity of our results should be interpreted with caution.

In conclusion, this RCT did not find evidence that allocating extra resources (staff time) to enhance early mobilization improves pulmonary outcomes within an ERP for colorectal surgery. In this context of care, allowing patients to mobilize at will (ie, as tolerated) after giving instructions may be enough to avoid the negative effects of prolonged bed rest on pulmonary function and risk of postoperative pulmonary complications.

REFERENCES

1. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152:292–298.
2. Lee L, Feldman LS. Improving surgical value and culture through enhanced recovery programs. *JAMA Surg*. 2017;152:299–300.
3. Zhuang CL, Huang DD, Chen FF, et al. Laparoscopic versus open colorectal surgery within enhanced recovery after surgery programs: a systematic review and meta-analysis of randomized controlled trials. *Surg Endosc*. 2015;29:2091–2100.
4. Nicholson A, Lowe MC, Parker J, et al. Systematic review and meta-analysis of enhanced recovery programmes in surgical patients. *Br J Surg*. 2014;101:172–188.
5. Fleisher LA, Linde-Zwirble WT. Incidence, outcome, and attributable resource use associated with pulmonary and cardiac complications after major small and large bowel procedures. *Perioper Med (Lond)*. 2014;3:7.
6. Jurt J, Hubner M, Pache B, et al. Respiratory complications after colorectal surgery: avoidable or fate? *World J Surg*. 2018;42:2708–2714.
7. Warner DO. Preventing postoperative pulmonary complications: the role of the anesthesiologist. *Anesthesiology*. 2000;92:1467–1472.
8. ERAS Compliance Group. The impact of enhanced recovery protocol compliance on elective colorectal cancer resection: results from an international registry. *Ann Surg*. 2015;261:1153–1159.
9. Greco M, Capretti G, Beretta L, et al. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. *World J Surg*. 2014;38:1531–1541.
10. Killewich LA. Strategies to minimize postoperative deconditioning in elderly surgical patients. *J Am Coll Surg*. 2006;203:735–745.
11. Allen C, Glasziou P, Del Mar C. Bed rest: a potentially harmful treatment needing more careful evaluation. *Lancet*. 1999;354:1229–1233.
12. Brower RG. Consequences of bed rest. *Crit Care Med*. 2009;37(10 suppl):S422–428.
13. Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS(®)) Society recommendations. *World J Surg*. 2013;37:259–284.

14. Khan S, Gatt M, Horgan A, et al. The Association of Surgeons of Great Britain and Ireland. Guidelines for implementation of enhanced recovery protocols. Available at: https://pdfs.semanticscholar.org/7960/2827d47ea07452ec326b4448304dc1bc8714.pdf. Published December 2009. Accessed June 1, 2016.
15. McLeod RS, Aarts MA, Chung F, et al. Development of an enhanced recovery after surgery guideline and implementation strategy based on the knowledge-to-action cycle. *Ann Surg*. 2015;262:1016–1025.
16. SAGES SMART task force. SAGES SMART enhanced recovery program. Available at: https://www.sages.org/smart-enhanced-recovery-program/. Accessed July 8, 2016.
17. Castelino T, Fiore JF Jr, Niculiseanu P, et al. The effect of early mobilization protocols on postoperative outcomes following abdominal and thoracic surgery: a systematic review. *Surgery*. 2016;159:991–1003.
18. Gustafsson UO, Hausel J, Thorell A, et al. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Arch Surg*. 2011;146:571–577.
19. Bergman S, Deban M, Martelli V, et al. Association between quality of care and complications after abdominal surgery. *Surgery*. 2014;156:632–639.
20. Vlug MS, Bartels SA, Wind J, et al. Which fast track elements predict early recovery after colon cancer surgery? *Colorectal Dis*. 2012;14:1001–1008.
21. Schulz KF, Altman DG, Moher D, et al. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c332.
22. Fiore JF Jr, Castelino T, Pecorelli N, et al. Ensuring early mobilization within an enhanced recovery program for colorectal surgery: a randomized controlled trial. *Ann Surg*. 2017;266:223–231.
23. Pecorelli N, Hershorn O, Baldini G, et al. Impact of adherence to care pathway interventions on recovery following bowel resection within an established enhanced recovery program. *Surg Endosc*. 2017;31:1760–1771.
24. Lassen K, Soop M, Nygren J, et al. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Arch Surg*. 2009;144:961–969.
25. Miller MR, Crapo R, Hankinson J, et al. General considerations for lung function testing. *Eur Respir J*. 2005;26:153–161.
26. Fiore JF Jr, Chiavegato LD, Denehy L, et al. Do directed cough maneuvers improve cough effectiveness in the early period after open heart surgery? Effect of thoracic support and maximal inspiration on cough peak expiratory flow, cough expiratory volume, and thoracic pain. *Respir Care*. 2008;53:1027–1034.
27. Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. *Eur J Anaesthesiol*. 2015;32:88–105.
28. Schwenk W, Bohm B, Witt C, et al. Pulmonary function following laparoscopic or conventional colorectal resection: a randomized controlled evaluation. *Arch Surg*. 1999;134:6–12.
29. McAlister FA, Bertsch K, Man J, et al. Incidence of and risk factors for pulmonary complications after nonthoracic surgery. *Am J Respir Crit Care Med*. 2005;171:514–517.
30. Brooks-Brunn JA. Predictors of postoperative pulmonary complications following abdominal surgery. *Chest*. 1997;111:564–571.
31. Miskovic A, Lumb AB. Postoperative pulmonary complications. *Br J Anaesth*. 2017;118:317–334.
32. Canet J, Gallart L, Gomar C, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology*. 2010;113:1338–1350.
33. Li P, Stuart EA, Allison DB. Multiple imputation: a flexible tool for handling missing data. *JAMA*. 2015;314:1966–1967.
34. Mackay MR, Ellis E, Johnston C. Randomised clinical trial of physiotherapy after open abdominal surgery in high risk patients. *Aust J Physiother*. 2005;51:151–159.
35. Milsom JW, Bohm B, Hammerhofer KA, et al. A prospective, randomized trial comparing laparoscopic versus conventional techniques in colorectal cancer surgery: a preliminary report. *J Am Coll Surg*. 1998;187:46–54.
36. Spadaro S, Caramori G, Rizzuto C, et al. Expiratory flow limitation as a risk factor for pulmonary complications after Major abdominal surgery. *Anesth Analg*. 2017;124:524–530.
37. Moore J, Conway D, Thomas N, et al. Impact of a peri-operative quality improvement programme on postoperative pulmonary complications. *Anaesthesia*. 2017;72:317–327.
38. Abbott TEF, Fowler AJ, Pelosi P, et al. A systematic review and consensus definitions for standardised end-points in perioperative medicine: pulmonary complications. *Br J Anaesth*. 2018;120:1066–1079.
39. Lawrence VA, Cornell JE, Smetana GW. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians. *Ann Intern Med*. 2006;144:596–608.
40. Schwenk W, Haase O, Neudecker J, et al. Short term benefits for laparoscopic colorectal resection. *Cochrane Database Syst Rev*. 2005;CD003145.
41. Lee CZ, Kao LT, Lin HC, et al. Comparison of clinical outcome between laparoscopic and open right hemicolectomy: a nationwide study. *World J Surg Oncol*. 2015;13:250.
42. Freemantle N. Interpreting the results of secondary end points and subgroup analyses in clinical trials: should we lock the crazy aunt in the attic? *BMJ*. 2001;322:989–991.