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Effect of Exercise and Nutrition Prehabilitation on Functional Capacity in Esophagogastric Cancer Surgery
A Randomized Clinical Trial

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IMPORTANCE Preserving functional capacity is a key element in the care continuum for patients with esophagogastric cancer. Prehabilitation, a preoperative conditioning intervention aiming to optimize physical status, has not been tested in upper gastrointestinal surgery to date.

OBJECTIVE To investigate whether prehabilitation is effective in improving functional status in patients undergoing esophagogastric cancer resection.

DESIGN, SETTING, AND PARTICIPANTS A randomized clinical trial (available-case analysis based on completed assessments) was conducted at McGill University Health Centre (Montreal, Quebec, Canada) comparing prehabilitation with a control group. Intervention consisted of preoperative exercise and nutrition optimization. Participants were adults awaiting elective esophagogastric resection for cancer. The study dates were February 13, 2013, to February 10, 2017.

MAIN OUTCOMES AND MEASURES The primary outcome was change in functional capacity, measured with absolute change in 6-minute walk distance (6MWD). Preoperative (end of the prehabilitation period) and postoperative (from 4 to 8 weeks after surgery) data were compared between groups.

RESULTS Sixty-eight patients were randomized, and 51 were included in the primary analysis. The control group were a mean (SD) age, 68.0 (11.6) years and 20 (80%) men. Patients in the prehabilitation group were a mean (SD) age, 67.3 (7.4) years and 18 (69%) men. Compared with the control group, the prehabilitation group had improved functional capacity both before surgery (mean [SD] 6MWD change, 36.9 [51.4] vs −22.8 [52.5] m; $P < .001$) and after surgery (mean [SD] 6MWD change, 15.4 [65.6] vs −81.8 [87.0] m; $P < .001$).

CONCLUSIONS AND RELEVANCE Prehabilitation improves perioperative functional capacity in esophagogastric surgery. Keeping patients from physical and nutritional status decline could have a significant effect on the cancer care continuum.

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Invited Commentary
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Supplemental content

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Esophageal and gastric cancers are lethal tumors, with an estimated 43 300 new cases and 26 400 deaths in the United States per year.[1] Surgery, the cornerstone of curative intent treatment for localized or locally advanced esophagogastric cancers, is associated with important adverse events.[2,3] Current best surgical practice involves the Enhanced Recovery After Surgery (ERAS) program, which has been shown to have a positive association in terms of length of hospital stay, resource use, and complications.[4,5]

Despite these advances, esophagogastric surgery is still associated with short-term and long-term adverse effects, including high rates of postoperative complications and mortality, decreased muscle strength and cardiorespiratory fitness, fatigue, depression, emotional distress, anxiety, and poor quality of life.[6-9] As a result of surgical complications or impaired nutritional, physical, and performance status, most patients are not able to receive the complete sequence of neoadjuvant or adjuvant therapy.[10,11] Surgery alone is inadequate for locoregional control in patients with locally advanced disease,[12] and overall 5-year survival remains poor.[13] Therefore, optimizing perioperative functional capacity is a compelling aim in these patients.

The process of enhancing physical fitness before an operation to enable the patient to withstand the stress of surgery has been termed *prehabilitation*.[14] The main elements are preoperative exercise and nutrition optimization. Increasing evidence indicates that prehabilitation improves perioperative physical function in major abdominal surgery.[15-19] Nevertheless, upper gastrointestinal surgery presents unique challenges in clinical management because of the high-risk population and treatments, and there have been few trials in this field.[20,21] However, because physical and nutritional status are key potentially modifiable factors in esophagogastric cancer,[22,23] prehabilitation is a notable intervention in these patients.

Therefore, the objective of this randomized clinical trial was to investigate the effectiveness of prehabilitation in preventing physical decline in upper gastrointestinal surgery. We hypothesized that prehabilitation could improve functional capacity throughout the perioperative period in adults undergoing esophagogastric cancer surgery.

Key Points

Question What is the effect of a structured preoperative exercise and nutrition conditioning program (prehabilitation) on functional capacity after esophagogastric surgery?

Findings In this randomized clinical trial (26 prehabilitation participants vs 25 control participants), prehabilitation significantly improved functional capacity before and after surgery.

Meaning Prehabilitation may be considered for optimizing physical fitness during esophagogastric cancer care.

Methods

Trial Design

This study was a parallel-group, randomized, single-blind, pragmatic clinical trial conducted at McGill University Health Centre (Montreal, Quebec, Canada). The trial protocol (Supplement) was approved by the McGill University Health Centre Research Ethics Board, and written informed consent was obtained from each patient before randomization. Due to administrative error and oversight on the part of the principal investigator (FC), the Research Ethics Board inadvertently terminated this project in September 2016 without our notice following failure to request renewal. We had recruited most patients by then, but 6 patients were recruited after that time until February 2017. We have confirmation from the chair of the Research Ethics Board that our study was conducted according to ethical standards and we have received retroactive renewed approval through September 2017. The study was completed in July 2017.

Study Participants

Patients were assessed for eligibility at their first visit to a regional upper gastrointestinal cancer referral center within the Division of Thoracic Surgery at McGill University Health Centre. Patients were eligible for participation if they were 18 years or older and were referred electively for management of nonmetastatic esophagogastric cancer. Exclusion criteria were the following: comorbid medical, physical, and mental conditions that contraindicate exercise or oral nutrition, acute or unstable cardiac conditions (eg, unstable angina or symptomatic severe aortic stenosis), American Society of Anesthesiologists physical status classes 4 and 5, disabling orthopedic and neuromuscular disease, psychosis, dementia, cardiac failure (New York Heart Association functional classes III and IV), severe chronic obstructive pulmonary disease (forced expiratory volume in the first second of expiration <50% predicted), end-stage kidney or liver disease, anemia (symptomatic or hematocrit <30%), inability to swallow, or the presence of feeding gastrostomy or jejunostomy. Patients with poor English or French comprehension were also excluded, as were patients residing more than 50 km from Montreal General Hospital.

Study Design

Eligible patients were assigned in a 1:1 ratio to either prehabilitation or a control group. Participants were randomized using computer-generated blocks of 4, and group assignments were placed in sequentially numbered opaque envelopes. The main investigator (F.C.), assessor (R.A.), and statistician (A.V.R.) were unaware of the group assignments. Because of the nature of the intervention, it was not possible to mask participants or health care professionals, such as kinesiologists or nutritionists (S.-E.L. and other nonauthors).

Prehabilitation

Prehabilitation is a preoperative intervention aiming to enhance perioperative functional capacity to enable a patient to withstand the upcoming surgical stress.[14] The main elements are exercise and nutrition. This multidisciplinary strategy has

also been termed *multimodal prehabilitation*, unlike a *unimodal* approach that includes only exercise.[24]

Exercise Program

At baseline, all patients had an evaluation of their fitness level and functional ability in terms of walking and endurance, strength, joint mobility, and posture. A physician (E.M.M.) prescribed an individualized, home-based exercise training program 4 times per week according to guidelines provided by the American College of Sports Medicine.[25] Participants received an individual session with a kinesiologist, who demonstrated the complete training program and provided corrective feedback as necessary.[26] Aerobic exercise consisted of 30 minutes (including 5-minute warm-up and 5-minute cooldown) of moderate continuous training 3 days per week. Exercise modalities were brisk walk, jogging, or cycling depending on personal physical level and attitude. Patients were instructed by the kinesiologist to self-select the intensity to reach 12 to 13 on rated perceived exertion (range, 6-20 on the Borg Rating of Perceived Exertion Scale).[27,28] Strengthening activity, prescribed 1 day per week, consisted of 30 minutes (including 5-minute flexibility and 5-minute stretching) of 3 sets of 8 to 12 repetitions for 8 muscle groups using an elastic band as resistance (TheraBand). Resistance level was selected by the kinesiologist to reach a moderate-intensity effort, rated as 5 to 6 on a 10-point scale.[29] Participants were provided with a logbook to record all activities. The kinesiologist monitored the adherence and addressed issues or doubts by weekly telephone calls.

Nutrition Program

At the time of enrollment, participants completed a 3-day estimated food record of 2 weekdays and 1 weekend day. A dietitian (S.-E.L.) assessed dietary habits and anthropometric data to create a comprehensive status evaluation and to estimate the required amount and relative proportion of macronutrients.[30] Metabolic requirement was adjusted to meet the increased nutritional demand due to the stress associated with their upcoming surgery.[31,32] Food-based dietary advice was given, and whey protein supplement (Immunocal; Immunotec Inc) was prescribed to guarantee a daily protein intake of 1.2 to 1.5 g/kg of ideal body weight (or approximately 20% of total energy requirements).[33] These supplements, if needed, were consumed every morning after breakfast or immediately after exercise during training days. Nutrition therapy was given to all participants in the intervention group, even in the absence of malnutrition.[34] Participants were provided with a logbook, and the nutritionist monitored the adherence and addressed issues or doubts by weekly telephone calls.

Usual Care

All participants received standardized perioperative care according to the ERAS Society Guideline protocol,[4,5] which is based on a clinical program implemented at our institution since 2008. The main elements include a minimally invasive surgical approach when feasible, epidural analgesia, limited use and duration of drains, minimized blood loss and perioperative fluid administration, avoidance of preoperative overnight fasting, early oral nutrition, respiratory physiotherapy, and early mobilization. The standard preoperative pathway at our institution includes risk assessment, medication management, perioperative blood management, and smoking cessation.

At the time of initial visit to the upper gastrointestinal cancer referral center, all patients received nutritional counseling to plan adequate caloric provision and address specific nutritional or dysphagic disorders. Neoadjuvant chemotherapy with a docetaxel-based triplet was the preferred approach for locally advanced adenocarcinoma (cT3 or N+) based on the results of a local institutional phase 2 trial.[35] Patients with locally advanced squamous cell carcinoma tended to be offered neoadjuvant chemoradiotherapy. A multidisciplinary tumor board (L.E.F. and other nonauthors) defined personalized oncologic treatment, establishing specific indication, timing, regimen, and strategy according to patient performance status and tumor characteristics. Patients were referred for psychosocial counseling, if needed.

The control group was treated according to conventional care. They received no specific intervention before surgery.

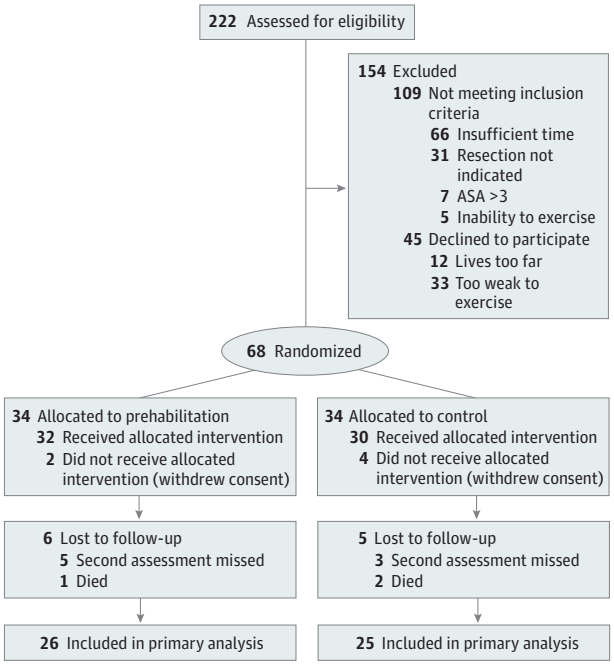
Outcomes

Measurements were recorded at 3 times in all participants. These included at baseline (beginning of the prehabilitation period for the intervention group), immediately before surgery (end of the prehabilitation period for the intervention group), and after surgery (4-8 weeks after surgery).

The primary outcome was change in functional capacity over time, measured as the difference in absolute change in 6-minute walk distance (6MWD) between baseline and the preoperative visit (primary analysis) and between baseline and the postoperative visit. A significant change was defined as an improvement or a deterioration of 20 m from baseline.[36] Participants, who were advised to wear comfortable shoes, were instructed to walk back and forth in a 20-m stretch of hallway for 6 minutes at a pace that would make them tired by the end of the walk. A masked assessor (R.A.) supervised all tests, following a standardized procedure to minimize potential sources of error due to bias or different levels of encouragement.[37] Walk tests are commonly used in a wide variety of clinical settings to provide a reliable and valid measure of exercise capacity and functional ability to withstand household and community activities.[38-40] When used as an outcome measure, change in walk test distance reflects change in aerobic capacity due to a specific intervention.[41] Moreover, walk tests are particularly advantageous for patients who have low exercise tolerance because the intensity and the posture control are completely controlled by the patient, and rest intervals can be taken, if needed. Furthermore, these tests are inexpensive to administer because they require minimal equipment, facility space, expertise, and time.

Secondary outcomes were postoperative morbidity at 30 days (according to the Clavien-Dindo classification[42] and the Comprehensive Complication Index[43,44]), length of hospital stay, 30-day hospital visits, readmission rate, death, and full adherence to the planned neoadjuvant chemotherapy. Compliance was evaluated, integrating both exercise (number of

Figure 1. CONSORT Diagram of Enrollment and Follow-up



ASA indicates American Society of Anesthesiologists physical status class.

weekly training sessions completed) and nutrition (adherence to the prescribed protein supplementation).

Statistical Analysis

Because there were no data on the effect of prehabilitation for upper gastrointestinal surgery, we used an estimation based on previous trials in colorectal cancer.[45,46] According to these data, patients who were randomly assigned to the control group were expected to decrease their 6MWD by a mean (SD) of 15 (66) m below baseline after surgery. In the intervention group, patients were expected to increase a mean (SD) of 37 (68) m. Therefore, to detect a difference of 53 m (with a pooled SD of 68.5) and an effect size of 0.77, the present trial would need to enroll 56 participants (28 patients per group) to have 80% power at a 2-sided significance level of .05. Because of differences between esophageal and colon surgery populations, a conservative estimate to avoid underpowering would be an effect size of 0.70, yielding a total sample size of up to 68 (34 per group).

Baseline characteristics were compared between groups with the use of independent-samples *t* test or Mann-Whitney test for continuous variables, and data are presented as the mean (SD) or the median (interquartile range [IQR], 25-75) according to the distribution. χ^2 Test or Fisher exact test was used for categorical variables, and data are presented as the number (percentage). Analyses of the primary outcome were performed among all patients who had complete follow-up, defined as the presence of a preoperative assessment. The trial was an available-case analysis based on completed assessments. For the primary outcome, we analyzed differences between groups at all follow-up times (baseline, preoperative, and postoperative) using a mixed-model analysis of variance for repeated measurement. Secondary outcomes were compared using standard 2-sample *t* tests. All tests were 2 sided, and the level of significance was $P = .05$, unlike for repeated-measures analysis, in which a Bonferroni-corrected level of significance was applied. We used a software program (SPSS, version 23.0; IBM) for all statistical analyses.

Results

Patient Characteristics

Between February 13, 2013, and February 10, 2017, a total of 222 consecutive patients referred with esophagogastric cancer to the upper gastrointestinal cancer referral center at our institution were assessed for eligibility. Sixty-eight patients (31%) provided informed consent, and 51 patients (23%) were included in the primary analysis (**Figure 1**).

Baseline characteristics and surgical variables were broadly similar between the 2 groups (**Table 1**). Eleven participants (22%) missed the postoperative assessment (3 in the prehabilitation group and 8 in the control group): among the 11 patients, 3 (2 prehabilitation and 1 control) had severe complications (length of hospital stay >30 days), 2 (both control) died (1 of intraoperative cardiac arrest and 1 of chyle leak), and 6 (1 prehabilitation and 5 control) failed to attend the postoperative assessment (because of weakness).

The median length of prehabilitation was 36 days (IQR, 17-73 days), and the median length of the preoperative period in the control group was 51 days (IQR, 12-71 days) ($P = .88$). Twenty participants (77%) had prehabilitation during neoadjuvant chemotherapy, 11 of whom (55%) started prehabilitation before medical treatment. Overall compliance with prehabilitation was 63%, and no exercise-related adverse events were reported.

Primary Outcome

A statistically significant difference in walking distance change was observed between groups both at the preoperative assessment (mean [SD], 36.9 [51.4] m in the prehabilitation group vs −22.8 [52.5] m in the control group; $P < .001$) and after surgery (mean [SD], 15.4 [65.6] m in the prehabilitation group vs −81.8 [87.0] m in the control group; $P < .001$) (**Figure 2**). A significant difference was also observed in the total 6MWD covered over time and in the proportion of patients who experienced a significant change in functional capacity (**Table 2**).

Secondary Outcomes

Two patients included in the primary analysis had their surgery canceled and are represented as missing data for surgical outcomes. There were no statistically significant differences between groups in terms of number and severity of complications, length of hospital stay, emergency department visits, or readmission rates (**Table 3**). Two patients in each group did not receive the full planned neoadjuvant chemotherapy (8% in the prehabilitation group vs 8% in the control group, $P > .99$).

Table 1. Characteristics of Patients

Variable	Prehabilitation (n = 26)	Control (n = 25)
Demographics and Anthropometrics		
Age, mean (SD), y	67.3 (7.4)	68.0 (11.6)
Male, No. (%)	18 (69)	20 (80)
BMI, mean (SD)	26.1 (4.8)	25.7 (4.7)
Fat mass, mean (SD), kg	27.1 (10.0)	27.3 (10.4)
Comorbidity		
ASA physical status class, No. (%)		
II	13 (50)	12 (48)
III	13 (50)	13 (52)
Charlson Comorbidity Index, No. (%)		
2	7 (27)	10 (40)
3-4	17 (65)	10 (40)
5-6	2 (8)	5 (20)
Current smoker, No. (%)	2 (8)	2 (8)
Medically treated type 2 diabetes, No. (%)	7 (27)	4 (16)
Serum laboratory values, mean (SD)		
Albumin, g/dL	3.8 (0.5)	3.8 (0.4)
Hemoglobin, g/dL	11.3 (1.9)	12.3 (1.9)
Glycated hemoglobin, %	6.0 (0.6)	6.2 (0.9)
C-reactive protein, mg/L	5.7 (6.7)	10.0 (15.8)
Nutritional Characteristics, No. (%)		
PG-SGA score		
Not at nutrition risk, 0-8	17 (65)	14 (56)
At nutrition risk, ≥9	9 (35)	11 (44)
NRS 2002 score		
1-2	22 (85)	21 (84)
3-4	4 (15)	4 (16)
Pathological Characteristics, No. (%)		
Tumor site		
Esophagus	20 (77)	21 (84)
Gastric	6 (23)	4 (16)
Tumor histology		
Squamous cell carcinoma	7 (27)	7 (28)
Adenocarcinoma	19 (73)	18 (72)
AJCC pathologic tumor stage[a]		
I	6 (25)	5 (20)
II	0	2 (8)
III	18 (75)	18 (72)
Treatment Characteristics		
Neoadjuvant therapy, No. (%)	20 (77)	15 (60)
Surgical procedure, No. (%)[a]		
Esophagectomy	18 (75)	21 (84)
Partial gastrectomy	4 (17)	2 (8)
Total gastrectomy	2 (8)	2 (8)
Minimally invasive approach, No. (%)[a]	10 (42)	11 (44)
Duration of surgery, median (IQR), min[a]	195 (170.0-225.5)	226 (179.0-315.0)

Abbreviations: AJCC, American Joint Committee on Cancer; ASA, American Society of Anesthesiologists physical status class; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range; NRS 2002, Nutrition Risk Screening 2002; PG-SGA, Patient-Generated Subjective Global Assessment. SI conversion factors: To convert albumin level and hemoglobin level to grams per liter, multiply by 10.0; glycated hemoglobin level to proportion of total hemoglobin, multiply by 0.01; and C-reactive protein level to nanograms per liter, multiply by 9.524.

[a] Missing data for 2 patients (both prehabilitation) who did not have surgery.

Discussion

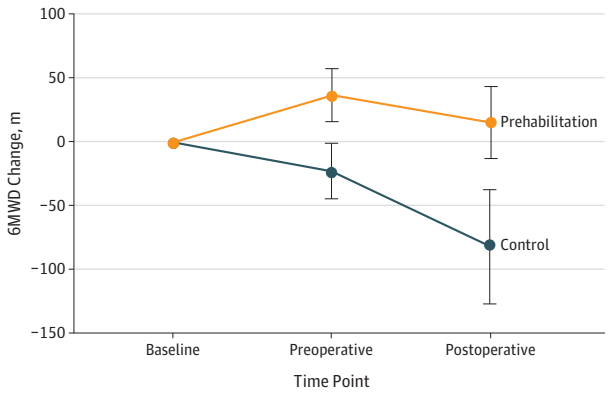
The main finding of this randomized clinical trial is that prehabilitation resulted in perioperative functional improvement of patients undergoing esophagogastric surgery for cancer. Poor physical fitness and malnutrition are prevailing adverse effects of esophagogastric cancer and its treatment, with negative consequences for quality of life and care adherence. Therefore, experts have highlighted the urgent need for randomized clinical trials

of multidisciplinary interventions aiming to optimize cardiorespiratory fitness in this field.[47,48] Most studies have investigated the safety and efficacy of exercise therapy after the completion of cancer therapy.[49] Once detrimental effects of a treatment have been experienced, patients generally will need an intervention to restore the pretreatment physical status or obtain a faster recovery. The concept of rehabilitation in oncologic surgery is applied to the postoperative period. Unlike this traditional approach, the purpose of prehabilitation is to prevent, rather than cure, functional consequences of cancer therapy by addressing modifiable risk factors, such as fitness and nutrition. Aiming to increase the quality of perioperative care by accelerating recovery, prehabilitation is mandated in the ERAS pathway and represents its clinical and scientific development.[26]

To our knowledge, this is the first demonstration that a structured preoperative conditioning intervention is feasible, safe, and efficacious for preventing functional impairment before and after surgical treatment for upper gastrointestinal cancer. Sixty-two percent (16 of 26) of the patients herein improved before surgery, and the positive effect was maintained after surgery in more than half of the population. Conversely, as shown in a previous study,[6] patients assigned to a control group had a decline in cardiopulmonary fitness that did not reverse and further deteriorated in the recovery period after surgery. No exercise-related adverse events were reported in the present randomized clinical trial, and the adherence rate was comparable to that in a previous study.[50] Compliance is an arduous outcome of behavioral interventions in patients with cancer and is a unique challenge in esophagogastric cancer care. Plausible explanations may be the low physical fitness of this particular population, their comorbidities, and the high rate of neoadjuvant therapy (77% [20 of 26] in the intervention group), carrying significant functional impairment. Owing to the pragmatic nature of our trial, there were no restrictions on the duration of the program, and we used the entire period from referral to surgery. Because our randomized clinical trial is the first study to date to our knowledge on prehabilitation in this population, evidence of effectiveness was lacking; therefore, we decided not to alter timing or modality of cancer treatment planned by the multidisciplinary tumor board. Nonetheless, the median length of prehabilitation was 36 days, a reasonable training period compared with other surgical settings.[51] The present trial was not powered to determine whether the difference in physical fitness was associated with fewer complications, and the morbidity rate and length of hospital stay were comparable to local and international reports at other high-volume centers.[52]

Because cancer and its treatments frequently lead to disability and financial burden,[24] our findings may have several implications. Treatment-related fatigue is a common adverse effect, affecting up to 90% of patients undergoing radiotherapy and up to 80% of patients receiving chemotherapy.[53,54] Surgical-related decline in physical fitness is one of the most distressing symptoms reported by patients with cancer and directly affects their ability to function in terms of activities of daily living and quality of life.[55] Because survivorship is improving, there is a growing interest in strategies aimed to ameliorate the quality of life in cancer survivors. Also problematic is physical status deterioration, with any impairment in a patient's ability to function being

Figure 2. Trajectory of Change in Functional Capacity in the Perioperative Period



Data are means (95% CIs). 6MWD indicates 6-minute walking distance.

Table 2. Functional Outcomes

Variable	Prehabilitation (n = 26)	Control (n = 25)	*P* Value
6MWD, Mean (SD), m			
Baseline	452.1 (83.4)	449.2 (83.9)	.43
Preoperative	489.0 (73.5)	426.4 (102.7)	.02
Postoperative[a]	481.5 (81.5)	379.8 (106.0)	<.001
6MWD Change From Baseline, Mean (SD), m			
Preoperative	36.9 (51.4)	−22.8 (52.5)	<.001
Postoperative[a]	15.4 (65.6)	−81.8 (87.0)	<.001
Preoperative 6MWD Change, No. (%)			
Deterioration	2 (8)	8 (32)	<.001
Back to baseline	8 (31)	16 (64)	
Improvement	16 (62)	1 (4)	
Postoperative 6MWD Change, No. (%)[a]			
Deterioration	4 (17)	14 (82)	<.001
Back to baseline	7 (30)	2 (12)	
Improvement	12 (52)	1 (6)	

Abbreviation: 6MWD, 6-minute walking distance.

[a] Missing data for 11 patients (3 prehabilitation and 8 control).

Table 3. Thirty-Day Surgical Outcomes

Variable	Prehabilitation (n = 24)	Control (n = 25)	*P* Value
Patients with no complications, No. (%)	10 (42)	7 (28)	.24
Clavien-Dindo classification of complication severity, No. (%)			
I	2 (8)	0	.23
II	6 (25)	8 (32)	
IIIa	3 (13)	7 (28)	
IVa	2 (8)	1 (4)	
IVb	1 (4)	0	
V	0	2 (8)	
CCI of complication severity, median (IQR)	14.8 (0.0-28.8)	20.9 (20.9-36.2)	.17
In-hospital mortality, No. (%)	0	2 (8)	.26
Length of hospital stay, median (IQR), d	8.0 (5.75-11.75)	7.0 (5.5-12.5)	.44
Emergency department visit, No. (%)	5 (21)	7 (28)	.40
Readmission rate, No. (%)	1 (4)	2 (8)	.60

Abbreviations: CCI, Comprehensive Complication Index; IQR, interquartile range.

a potential limitation to his or her ability to withstand cancer care interventions. Evidence has shown that receiving the full cancer treatment is strongly related to good physical and nutritional status,[10,11] and 60% to 70% of patients with esophageal cancer do not receive the planned treatment.[56] Considering the importance of receiving the complete treatment relative to survivorship,[10] there is a compelling need to include functional outcome as a core perioperative outcome. By attenuating functional impairment, prehabilitation in cancer treatment pathways could be of considerable value.

Limitations

This study has several limitations. As previously mentioned, the variability of neoadjuvant treatment in terms of duration and regimen may limit the consistency, generalizability, and applicability of our findings. In addition, the exclusion of patients who were not willing to start a physical intervention could represent a potential selection bias. The small sample size is another limitation (222 patients were assessed to recruit 68 participants), which precluded testing of secondary outcomes. The tightness of the inclusion criteria, the need for a reasonable time to intervene before surgery, and the individual commitment to exercise are possible explanations for this high rate of exclusions. Furthermore, 17% (4 of 23) of the study population experienced deterioration after surgery. Therefore, further work is required to explore in detail the optimal type, intensity, and timing of physical and nutritional intervention. Other considerations include the introduction of a supervised training session, a consistent duration of the intervention, better integration into the medical treatment, and a larger sample size.

Conclusions

This randomized clinical trial demonstrated prehabilitation-induced significant improvement in physical status among patients undergoing surgery for malignant gastroesophageal lesions. Further investigation is required to determine the optimal modality of the intervention and its effect on overall oncologic outcomes.

ARTICLE INFORMATION

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Concept and design: Minnella, Awasthi, Ferri, Carli.
Acquisition, analysis, or interpretation of data: Minnella, Loiselle, Agnihotram, Carli.
Drafting of the manuscript: Minnella, Carli.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Minnella, Agnihotram.
Administrative, technical, or material support: Awasthi, Loiselle, Carli.
Supervision: Minnella, Awasthi, Loiselle, Ferri.

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Invited Commentary

Moving Toward Every Patient Training for Surgery

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Prehabilitation aims to enhance functional status before surgery. Through multimodal approaches, including structured exercise, nutritional counseling, and patient empowerment, prehabilitation programs can improve the patient's preoperative functional status, reduce postoperative complications and length of stay, and lower costs of care.[1-5]

In this issue of *JAMA Surgery*, Minnella and coauthors[6] report their findings from a randomized clinical trial analyzing 51 patients undergoing esophagogastric cancer resection. Prehabilitation was associated with improved preoperative and postoperative functional capacity. One notable limitation of their trial is that frail and at-risk patients were excluded. While exclusion was done to facilitate rigor of the trial, frail and at-risk patients are the patients for whom surgical care carries the greatest risk and presumably who may benefit the most. Furthermore, like most prehabilitation clinical trials, this study was not powered to detect improvements in traditional surgical outcomes, such as complication rates, length of stay, or readmissions.

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This group at McGill University Health Centre (Montreal, Quebec, Canada) leads the scientific investigation of prehabilitation and has convinced many clinicians that prehabilitation benefits patients. Their present trial demonstrates that a prehabilitation program can mitigate the expected functional decline from comprehensive esophagogastric cancer care.[6] Unfortunately, the rigorous science translates poorly into the clinical realities of day-to-day care. In other words, patients are not randomized in standard practice, and physicians may intuitively prescribe prehabilitation for those patients whom they believe stand to benefit the most. In addition, it is often unrealistic to delay a patient's medical care to undergo a prehabilitation program, especially for patients with time-sensitive, surgically amenable conditions. Diverse patients, diverse stakeholders, and diverse financing strategies contribute to a complex milieu for care and impede the acceptance and implementation of prehabilitation. More pragmatic, population-based studies of prehabilitation are essential to prove its effect and drive care transformation.

As the science behind prehabilitation moves forward, it is also imperative to prove the business case for prehabilitation to surgeons, payers, and hospitals. A strong business case will jump-start widespread implementation and facilitate multiinstitutional collaboration to further advance the nuanced science behind prehabilitation.

The evidence demonstrates that, at worst, prehabilitation does no harm, and it can be a transformative clinical pathway to facilitate a better life for some patients. Over the next decade, more excellent research, such as this study by Minnella and coauthors,[6] will convince us that every patient should train for surgery.

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