Taking Control of Your Surgery: Impact of a Prehabilitation Program on Major Abdominal Surgery

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BACKGROUND: Surgery is a major physiologic stress comparable to intense exercise. Diminished cardiopulmonary reserve is a major predictor of poor outcomes. Current preoperative workup focuses mainly on identifying risk factors; however, little attention is devoted to improving cardiopulmonary reserve beyond counseling. We propose that patients could be optimized for a "surgical marathon" similar to the preparation of an athlete.

STUDY DESIGN: The Michigan Surgical and Health Optimization Program (MSHOP) is a formal prehabilitation program that engages patients in 4 activities before surgery: physical activity, pulmonary rehabilitation, nutritional optimization, and stress reduction. We prospectively collected demographic, intraoperative (first hour), and postoperative data for patients enrolled in MSHOP undergoing major abdominal surgery. Statistical analysis was performed using 2:1 propensity score matching to compare the MSHOP group (n = 40) to emergency (n = 40) and elective, non-MSHOP (n = 76) patients.

RESULTS: Overall, 70% of MSHOP patients complied with the program. Age, sex, American Society of Anesthesiologists (ASA) classification, and BMI did not differ significantly between groups. One hour intraoperatively, MSHOP patients showed improved systolic and diastolic blood pressures and lower heart rate (Figure). There was a significant reduction in Clavien-Dindo class 3 to 4 complications in the MSHOP group (30%) compared with the nonprehabilitation (38%) and emergency (48%) groups ($p = 0.05$). This translated to total hospital charges averaging $75,494 for the MSHOP group, $97,440 for the nonprehabilitation group, and $166,085 for the emergency group ($p < 0.001$).

CONCLUSIONS: Patients undergoing prehabilitation before colectomy showed positive physiologic effects and experienced fewer complications. The average savings of $21,946 per patient represents a significant cost offset for a prehabilitation program, and should be considered for all patients undergoing surgery. (J Am Coll Surg 2019;228:72−80. © 2018 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Surgery is a significant physiologic stress comparable to intense exercise.[1] It causes increased metabolism and catabolism, increased oxygen uptake, stress hormone production, and release of inflammatory cytokines.[2,3] Although this stressor affects all patients undergoing surgery, frail patients with poor cardiopulmonary reserve and overall physical deconditioning do worse in response to this major stressor. Frail patients are less able to

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Abbreviations and Acronyms

ASA = American Society of Anesthesiologists
DBP = diastolic blood pressure
HR = heart rate
MAP = mean arterial pressure
MSHOP = Michigan Surgical and Health Optimization Program
SBP = systolic blood pressure

compensate for these increased metabolic demands, resulting in physiologic dysregulation.[4] Consequently, frail patients have an increased rate of postoperative complications.[5] Frailty has also been shown to be associated with increased mortality, morbidity, and poor outcomes overall.[6,7] This results in increased hospital costs and greater resource use for frail patients compared with nonfrail patients.[8,9] Prehabilitation—or "training for surgery"—can improve a patient's functional status before this major stressor, and therefore, has the potential to improve outcomes.[10]

To date, data are mixed on the effects of prehabilitation. It is generally accepted that prehabilitation before surgery results in a more rapid return to baseline functional capacity after surgery.[11-13] Prehabilitation has also been shown to reduce postoperative complications, but studies that have investigated mortality outcomes have had equivocal results.[14] Although there has been a large focus on postoperative outcomes in patients undergoing prehabilitation, few studies have addressed the specific physiologic effects that prehabilitation has on patients undergoing surgery. Moreover, less is known about the potential cost savings associated with prehabilitation. Because prehabilitation is first and foremost a form of physiologic conditioning for patients about to undergo the "marathon" of surgery, further study is needed of the physiologic changes that result.

Within this context, we sought to analyze the physiologic effects and outcomes of prehabilitation on patients undergoing major abdominal surgery. Our goal was to compare these differences in patients undergoing major abdominal surgery after they participated in a formal prehabilitation program. These patients were compared with a similar cohort of patients who underwent abdominal surgery without participating in prehabilitation, as well as a cohort of patients who underwent emergent abdominal surgery. Understanding the physiologic, clinical, and financial effects of surgical prehabilitation may further assist clinicians in targeting high-risk patients who may benefit from this type of intervention.

METHODS

This study was approved by the Institutional Review Board. A retrospective chart review was conducted to identify adult patients who underwent major abdominal surgery between 2012 and 2017 at a single academic health system. Procedures primarily included open and laparoscopic colectomy, hemicolectomy, and ostomy takedown. Patients were included if they participated in our institution's formalized surgical prehabilitation program before their surgery. We then selected a random sample of patients who underwent elective and emergency abdominal surgery during the same time period for comparison via propensity score matching.

Propensity score matching

Patients undergoing prehabilitation were propensity score matched to patients undergoing elective abdominal surgery and patients undergoing emergency abdominal surgery. A 2-to-1 propensity score match was performed for prehabilitation and elective surgery patients. A 1-to-1 propensity score match was performed for patients undergoing emergency surgery. Patients were matched on age, sex, BMI, American Society of Anesthesiologists (ASA) classification, cancer diagnosis, and smoking status, as well as surgical procedure and characteristics related to their procedure (operative time, laparoscopic vs open procedure).

Frailty was compared between groups by calculating total psoas muscle size for each patient, a method described elsewhere. In brief, cross-sectional imaging was used to measure the total psoas muscle size in each patient with available imaging. The areas of the left and right psoas muscles were outlined at the inferior border of the fourth lumbar vertebral body and summed to compute the total psoas muscle area (cm^2).[15,16] This was then normalized across patients by calculating a frailty index for each patient as total psoas muscle area (cm^2)/total body surface area (m^2).[17,18] Total body surface area (TBSA) was computed using the Du Bois formula as TBSA = ([weight $(kg)^{0.425}$ × height $(m)^{0.725}$] × 0.007184).[19] Sarcopenia was defined as a frailty index less than the median for all patients. Values were calculated independently between males and females, then for each group using sex as a covariate.

Michigan Surgical and Health Optimization Program

The Michigan Surgical and Health Optimization Program (MSHOP) is a structured prehabilitation program available to select patients before surgery at our institution.[20,21] It is offered to patients undergoing major

abdominal or thoracic surgery, with at least 2 weeks between enrollment and surgery. There are no discrete inclusion criteria, and referral to the program is made at the surgeon's discretion. The MSHOP engages patients in 4 domains: walking (patients receive a pedometer to track steps); breathing (patients receive an incentive spirometer); nutrition and stress management; and smoking cessation, as appropriate. Patients receive a DVD and brochure with instructions and resources for each domain, as well as a way to log their participation. Lastly, during their involvement in the program, they receive emails, phone messages, and text message-based reminders to continue.

Variables and outcomes

Demographic data included age, sex, BMI, ASA classification, cancer diagnosis, and smoking status. Procedure characteristics included length of surgery, laparoscopic vs open surgery, estimated blood loss, use of blood products, and postoperative admission to an ICU. Because prehabilitation has been shown to improve physiologic reserve during a major stressor such as surgery, intraoperative physiologic data were collected.[22] Physiologic variables included systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). These variables were recorded at induction of anesthesia and again at 1 hour into surgery. The difference between these 2 points was calculated to represent physiologic variability during this time. Within this hour, SBP, DBP, and HR were recorded at 5-minute intervals. Physiologic variability was further calculated by measuring a continuous line between these points for SBP, DBP, and HR. We also calculated the number of times there was a >20-point change over a 5-minute interval for SBP and DBP in mmHg, and for HR in beats per minute.

Complications were represented on the Clavien-Dindo Classification scale from I to V.[23] They were grouped as none, minor complications (class I to II), major complications (class III to IV), and death (class V).

The primary financial outcomes included hospital charges, professional charges, and total charges for each patient. All financial data were obtained from billing records at our institution. The cost of the MSHOP program is not included in hospital charges; however, we have previously reported that the program costs roughly $100 per patient.

Statistical analysis

All continuous primary outcomes variables were compared between the 3 groups using 1-way analysis of variance (ANOVA). Where a significant difference was found, Bonferroni post-hoc analysis was conducted to specifically compare the prehabilitation group with the elective surgery group. For analysis of hospital charges, linear regression was conducted to control for open vs laparoscopic surgery and length of stay. Categorical variables were compared between groups using chi-square test. Two-sided significance tests were used for all analyses, and significance was set at $p \leq 0.05$. All analyses were conducted using Stata 15 (StataCorp).

RESULTS

Demographics

After propensity score matching, the following groups were included for analysis: 40 patients enrolled in MSHOP who underwent abdominal surgery, 76 patients who underwent elective abdominal surgery, and 40 patients who underwent emergency abdominal surgery. Demographic data for the 3 groups are presented in Table 1. There was a significant difference in ASA classification between groups, with an increased frequency of ASA IV to V patients in the emergency surgery group. There was no significant difference in the incidence of smoking between groups ($p = 0.142$); however, 3 of 4 smokers in the prehabilitation group reported cessation before surgery. There was a higher incidence of cancer in the elective surgery group. Lastly, there was a significant difference in the use of laparoscopy between patients in the MSHOP, elective, and emergency groups (70% vs 53% vs 3%, $p < 0.001$). Comparison of the MSHOP and elective groups revealed a nonsignificant difference between laparoscopic and open surgery ($p = 0.08$). There was no difference in operative time between groups.

A total of 19 different surgeons performed the operations. There was no significant difference in surgeon distribution between the MSHOP and elective groups ($p = 0.465$) or between the MSHOP and emergency groups ($p = 0.175$). The MSHOP referrals were made by 12 of the 19 surgeons. A total of 46 anesthesiologists provided anesthesia for the operations. There was no significant difference in anesthesiologist distribution between the MSHOP and elective groups ($p = 0.334$) or between the MSHOP and emergency groups ($p = 0.208$).

Cross-sectional imaging was available for 32 patients in the MSHOP group, 76 patients in the elective group, and 38 patients in the emergency group (Table 2). Total psoas muscle area was significantly different between groups for males ($p = 0.008$) but not for females ($p = 0.431$). However, after normalizing for total body surface area, there was a significant difference in frailty index between groups for both males and females ($p = 0.002$, $p = 0.045$,

Table 1. Demographic and Procedural Characteristics

Demographic or characteristic	MSHOP (n = 40)	Elective (n = 76)	Emergency (n = 40)	p Value
Age, y, mean (SD)	59.3 (10.8)	58.3 (13.2)	54.5 (17.8)	0.252
Female sex, %	48	50	45	0.874
BMI, kg/m^2, mean (SD)	30.2 (7.7)	29.9 (7.2)	28.5 (9.6)	0.601
ASA classification, %				
I	0	0	3	0.005
II–III	98	96	77	
IV–V	3	4	20	
Current smoker, %	10	26	18	0.142
Cancer diagnosis, %	35	53	27	0.02
Laparoscopic procedure, %	70	53	3	<0.001
Operative time, min, mean (SD)	241.4 (114.2)	226.7 (98.4)	220.1 (87.1)	0.614

There is no significant difference between MSHOP and elective groups.
ASA, American Society of Anesthesiologists; MSHOP, Michigan Surgical and Health Optimization Program.

respectively). Sex-adjusted total psoas muscle size and frailty index were significantly different between groups (p = 0.004). Post-hoc analysis revealed that patients enrolled in MSHOP had significantly smaller psoas muscle size compared with non-MSHOP patients undergoing elective surgery (21.98 ± 7.75 vs 25.27 ± 8.38, p = 0.002). Overall, sarcopenia was more common in patients in the MSHOP group compared with the elective surgery and emergency surgery groups (73% vs 42% vs 45%, p = 0.01).

Physiologic

There were significant differences in physiologic variables between the 3 groups. At the start of the operation, MSHOP patients had significantly lower SBP than non-MSHOP and emergency patients (Table 3). At 1 hour into the operation, MSHOP patients had an increase in SBP compared with non-MSHOP and emergency groups, both of which had a decrease in SBP at 1 hour (Fig. 1A). There was no significant difference in DBP between groups at the start of the operation. At 1 hour, MSHOP patients had a significant increase in DBP compared with the other groups (Fig. 1B). Mean arterial pressure (MAP) was significantly lower in MSHOP patients at the start of the operation. At 1 hour, MSHOP patients had a significant increase in MAP compared with both elective and emergency groups, which had a decrease in MAP at 1 hour.

There was a significant difference in heart rate between groups at the start of the operation (p = 0.015). However, post hoc analysis revealed that the difference between MSHOP and elective groups was not significant (p = 0.978).

Physiologic variability during the first hour of surgery was different between groups (Table 3). The length of a continuous line charting SBP was significantly different between groups (p = 0.008), with post-hoc analysis revealing that this was greater in the MSHOP group

Table 2. Frailty Data Compared Between Groups

Group	MSHOP	Elective	Emergency	p Value
Male, n	16	38	20	
Total psoas muscle area, cm^2, mean (SD)	24.90 (7.99)*	31.43 (5.93)	29.30 (7.27)	0.008
Frailty index, mean (SD)	11.64 (4.57)*	14.67 (1.94)	14.91 (3.34)	0.002
Sarcopenia, %	75	37	45	0.036
Female, n	16	38	18	
Total psoas muscle area, cm^2, mean (SD)	17.29 (5.42)	19.10 (5.37)	17.65 (5.06)	0.431
Frailty index, mean (SD)	8.57 (3.05)*	10.65 (2.82)	10.34 (2.66)	0.045
Sarcopenia, %	65	45	44	0.350
All patients, n	32	76	38	
Sex-adjusted total psoas muscle area, cm^2, mean (SD)	21.09 (7.75)*	25.27 (8.38)	23.78 (8.58)	0.006
Sex-adjusted frailty index, mean (SD)	10.11 (4.13)*	12.66 (3.14)	12.75 (3.79)	<0.001
Sarcopenia, %	73	42	45	0.010

*Significant difference between MSHOP and elective groups (p < 0.05).
MSHOP, Michigan Surgical and Health Optimization Program.

Table 3. Physiologic Characteristics and Variability

Characteristic	MSHOP (n = 40)	Elective (n = 76)	Emergency (n = 40)	p Value
SBP, mmHg, mean (SD)				
Start	106 (19)*	121 (21)	123 (28)	0.001
1-hour	114 (20)	116 (17)	120 (25)	0.373
Change	8 (25)†	−6 (23)	−7 (33)	0.016
DBP, mmHg, mean (SD)				
Start	61 (11)	66 (13)	65 (16)	0.146
1-hour	68 (11)	66 (12)	65 (15)	0.613
Change	7 (13)†	0 (13)	0 (17)	0.031
Mean arterial pressure, mmHg, mean (SD)				
Start	76 (13)†	85 (15)	84 (18)	0.014
1-hour	83 (13)	82 (13)	83 (16)	0.918
Change	7 (16)†	−2 (16)	−1 (21)	0.024
HR, beats per min, mean (SD)				
Start	76 (14)	79 (15)	86 (22)	0.015
1-hour	74 (14)	75 (12)	84 (20)	0.008
Change	−2 (12)	−4 (14)	−3 (23)	0.803
Length, mean (SD)				
SBP	3.56 (1.10)	3.20 (0.98)	2.83 (0.98)	0.008
DBP	2.18 (0.53)	2.13 (0.51)	1.92 (0.64)	0.081
HR	1.82 (0.68)	1.71 (0.55)	1.73 (0.82)	0.703
Frequency change, >20 mmHg, mean (SD)				
SBP	9.26 (2.99)*	7.00 (2.75)	7.56 (3.91)	0.002
DBP	5.74 (2.97)	4.97 (2.43)	3.79 (2.69)	0.006
HR	3.47 (2.93)	2.97 (3.87)	2.59 (3.24)	0.430

*Significant difference between MSHOP and elective groups ($p < 0.001$).
†Significant difference between MSHOP and elective groups ($p < 0.05$).
DBP, diastolic blood pressure; HR, heart rate; MSHOP, Michigan Surgical and Health Optimization Program; SBP, systolic blood pressure.

compared with the emergency group ($p = 0.005$). Compared with both elective and emergency groups, patients in the MSHOP group had more variability in systolic and diastolic blood pressure ($p = 0.002$, $p = 0.006$, respectively), as measured by the number of 5-minute variations > 20 points.

Outcomes and complications

There was no significant difference in length of hospital stay between the MSHOP and elective groups ($p = 1.0$). However, the emergency group had a significantly longer length of stay by roughly 4 days compared with the other groups ($p = 0.003$). Rate of hospital readmission within 30 days was similar between groups ($p = 0.737$).

The MSHOP patients were less likely to be admitted to an ICU after surgery and less likely to require transfusion of blood products during surgery (Table 4). The MSHOP patients experienced fewer complications compared with patients undergoing elective and emergency surgery ($p = 0.05$) (Table 4). As shown in the table, MSHOP patients had the highest rate of no complication (70% vs 61% vs 53%) and the lowest rates of minor complication (18% vs 21% vs 23%) (Fig. 2). Rate of major complication was lower in MSHOP patients compared to non-MSHOP elective patients (10% vs 16%), but not compared to emergency patients (10% vs 10%). Deaths were most common in patients undergoing emergency surgery (15%).

Financial outcomes

Mean total hospital charges for patients enrolled in MSHOP were $75,493.97 ± $55,151.21, compared with $97,439.88 ± $100,377.06 for elective patients and $166,085.44 ± $124,394.84 for emergency patients ($p < 0.001$) (Table 4). Post hoc analysis revealed that although the total charges for MSHOP patients are lower than in both groups, this difference is significant only between MSHOP and emergency groups ($p < 0.001$) (Fig. 3).

Patients undergoing laparoscopic surgery also had increased hospital charges of $138,158.60 ± $125,337.06 compared with $73,171.11 ± $46,910.44 for patients undergoing open surgery ($p < 0.001$).

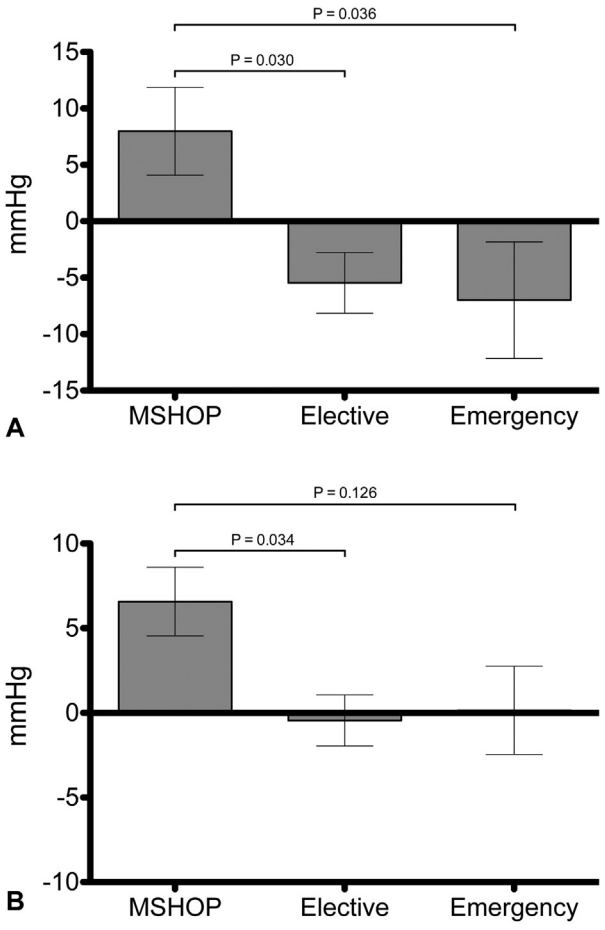

Figure 1. (A) Change in systolic blood pressure (SBP) and (B) diastolic blood pressure (DBP) after the first hour of surgery. Patients who participated in the Michigan Surgical and Health Optimization Program (MSHOP) had significantly increased SBP and DBP 1 hour into surgery compared with both elective and emergency surgery patients.

Hospital length of stay also contributed to hospital charges, with a \$11,173.67 ± \$852.51 increase for every hospital day ($p < 0.001$). Importantly, however, after controlling for both of these factors, total charges were still significantly less for the prehabilitation group compared with both elective and emergency surgery groups. Specifically, this model revealed that hospital charges for the prehabilitation group were \$25,785.96 ± \$6,417.83 less compared to the elective surgery group ($p < 0.001$) and \$65,039.31 ± \$17,856.68 less compared to the emergency surgery group ($p < 0.001$).

DISCUSSION

The major finding of this study is that surgical prehabilitation may convey a variety of multifactorial benefits to patients undergoing major abdominal surgery. Specifically, patients who completed prehabilitation through our institution's MSHOP program had better physiologic characteristics during surgery, fewer complications, and may derive a moderate hospital savings compared with other patients.

These findings reinforce a number of the benefits of prehabilitation that have been demonstrated in earlier studies. Frail patients are physiologically deconditioned at baseline, and therefore are expected to experience more complications compared with otherwise healthy patients undergoing elective surgery. Prehabilitation has been shown to reduce this rate of complications.[24] Although referral to our institution's prehabilitation program was not based on explicit inclusion criteria, psoas muscle size analysis revealed that there was a higher incidence of frailty in patients who were referred to MSHOP. As a result, these patients should be expected to do worse. This study demonstrates that surgical

Table 4. Clinical Outcomes and Cost

Outcome	MSHOP (n = 40)	Elective (n = 76)	Emergency (n = 40)	p Value
ICU admission, %	0	2.70	47.50	<0.001
Blood product administration, %	0	1.30	15.00	0.001
Length of stay, d, mean (SD)	7.6 (5.5)	7.6 (7.2)	11.9 (6.8)	0.003
Readmission, %	23	18	22	0.737
Complication, %				
None	70.0	61.3	52.5	0.050
Minor	17.5	21.3	22.5	
Major	10.0	16.0	10.0	
Death	2.5	1.3	15.0	
Mortality	2.5	1.3	15.0	0.005
Total charge, \$, mean (SD)	75,493.97 (55,151.21)	97,439.88 (100,377.06)	166,085.44 (124,394.84)	0.001
System charge, \$, mean (SD)	67,083.97 (50,409.17)	82,198.04 (93,538.02)	144,858.53 (113,169.23)	<0.001
Professional charge, \$, mean (SD)	11,038.12 (5,861.32)	15,249.84 (9,238.38)	21,226.89 (12,552.24)	<0.001

MSHOP, Michigan Surgical and Health Optimization Program.

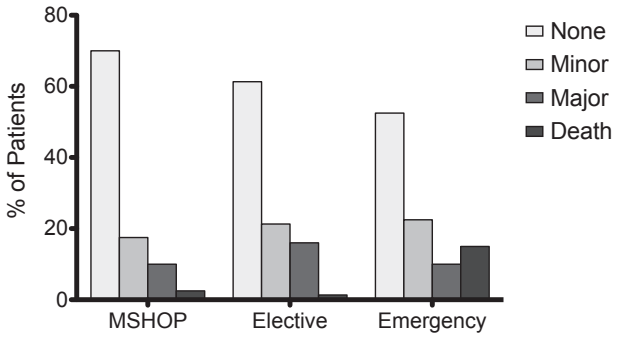

Figure 2. Comparison of postoperative complications between groups. MSHOP, Michigan Surgical and Health Optimization Program.

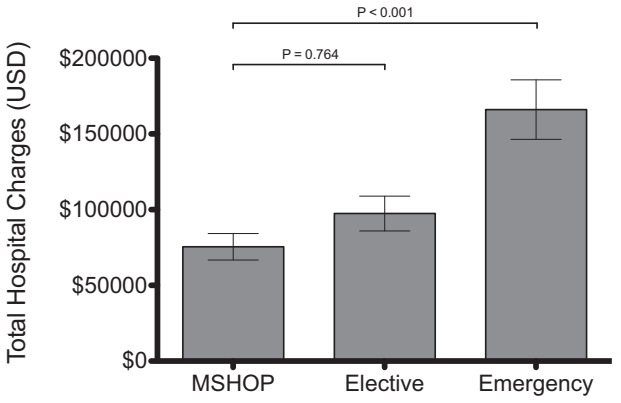

Figure 3. Differences in total hospital charges between 3 groups. Total costs were significantly lower for the Michigan Surgical and Health Optimization Program (MSHOP) group compared with the emergency surgery group; however, this decreased cost was not significantly different compared with the elective surgery group's cost.

prehabilitation is beneficial in that these patients do not have the inferior outcomes that they are expected to have. Moreover, patients who completed prehabilitation had superior outcomes in some cases. When they experienced complications, for example, these complications were more likely to be minor compared with those in both elective and emergency surgery groups. Prehabilitation patients also did not have higher rates of hospital readmission compared with the other groups. It is worth noting, however, that the readmission rate of roughly 20% across all patients is high compared to the reported average of 10% to 15% after colorectal surgery.[25] As a quaternary referral center, it may be the case that patient complexity drives this increased readmission rate. Currently, however, our data preclude further analysis of readmission diagnosis and treatment. Future work should examine the role that prehabilitation plays in hospital readmission.

It is well established that frail patients have a reduced physiologic reserve, and prehabilitation can optimize this prior to surgery.[26] Simple exercise before surgery improves lung capacity and overall cardiopulmonary function.[27,28] A unique finding of this study is that this benefit translates to improved physiologic reserve during surgery itself. Patients who have diminished physiologic reserve are less able to respond to stressors, which translates to less variability in parameters such as blood pressure and heart rate.[29] For example, lower preoperative heart rate variability has been associated with greater risk of hypotension after anesthesia induction, as well as postoperative cardiac events.[30,31] Although patients who underwent prehabilitation did have nonsignificantly increased heart rate variability, they demonstrated significantly increased variability in blood pressure, with an overall increase in systolic and diastolic blood pressure an hour into surgery compared with both other groups. This suggests that the improvements in physiologic reserve resulting from prehabilitation may translate into improved ability to respond to intraoperative stressors, whereas patients who do not undergo prehabilitation are more likely to be at their "physiologic maximum" throughout surgery.

Our analysis revealed that there is a significant savings when comparing total charges between the prehabilitation group and patients undergoing emergency surgery. This is unsurprising given that emergent status imparts significant risk and increased resource use compared with elective surgery.[32] The lack of a significant difference in charges between prehabilitation and elective patients, however, is not necessarily a negative finding. Given the finding of increased frailty in these patients, these patients should be reasonably expected to result in increased health system resource use, as reflected by higher charges. Therefore, this study demonstrates that at the very least, the anticipated increased expenditures are offset by participating in prehabilitation. Further study is needed to determine what drove these financial differences.

This study is not without its limitations. First, we only investigated the effects of a single institution's prehabilitation program (MSHOP). Given the practical and logistical challenges of implementing a functional prehabilitation program, there are, no doubt, considerable differences in these programs between institutions. Therefore, prehabilitation at other health systems may have different effects, limiting the generalizability of our results. Another limitation is the difference in laparoscopic vs open surgery between groups. As expected, the emergency surgery group underwent almost exclusively open procedures, which likely plays a role in patient outcomes. Additionally, surgeons were at their discretion

to enroll patients in MSHOP before surgery. This detracts from the homogeneity of the group, although this aspect may be more representative of a "real world" prehabilitation cohort because the definition of frailty is unclear. Nevertheless, this limitation was addressed by retrospectively comparing frailty data between groups to determine that there was a higher incidence of frailty in the MSHOP group.

Developing a more robust prehabilitation program in the future may rely on objective prospective criteria to target patients who may derive the most benefit from prehabilitation before surgery. Another limitation is the lack of preoperative data regarding the effects of prehabilitation before surgery. These data reflect intraoperative physiologic function after prehabilitation; however, it is also important to capture the effects of prehabilitation before surgery (such as changes in baseline vital signs, cardiopulmonary function, and protein intake). This would be similar to reporting the incidence of smoking cessation, as mentioned previously.

CONCLUSIONS

Patients who complete surgical prehabilitation experience a number of benefits compared with patients who undergo elective abdominal surgery without prehabilitation and patients undergoing emergency abdominal surgery. These benefits include improved physiologic characteristics during surgery, reduced rate of complications, and lower charges. Further studies are needed to determine whether it is these physiologic benefits that drive the reduction in complications and financial variation.

Author Contributions

Study conception and design: Machado-Aranda
Acquisition of data: Yin, McCandless, Machado-Aranda
Analysis and interpretation of data: Howard, Machado-Aranda
Drafting of manuscript: Howard, Machado-Aranda
Critical revision: Howard, Wang, Englesbe, Machado-Aranda

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