Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery

A Randomized Blinded Controlled Trial

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Objective: The aim of this study was to assess the impact of personalized prehabilitation on postoperative complications in high-risk patients undergoing elective major abdominal surgery.

Summary Background Data: Prehabilitation, including endurance exercise training and promotion of physical activity, in patients undergoing major abdominal surgery has been postulated as an effective preventive intervention to reduce postoperative complications. However, the existing studies provide controversial results and show a clear bias toward low-risk patients.

Methods: This was a randomized blinded controlled trial. Eligible candidates accepting to participate were blindly randomized (1:1 ratio) to control (standard care) or intervention (standard care + prehabilitation) groups. Inclusion criteria were: i) age >70 years; and/or, ii) American Society of Anesthesiologists score III/IV. Prehabilitation covered 3 actions: i) motivational interview; ii) high-intensity endurance training; and promotion of physical activity. The main study outcome was the proportion of patients suffering postoperative complications. Secondary outcomes included the endurance time (ET) during cycle-ergometer exercise.

Results: We randomized 71 patients to the control arm and 73 to intervention. After excluding 19 patients because of changes in the surgical plan, 63 controls and 62 intervention patients were included in the intention-to-treat analysis. The intervention group enhanced aerobic capacity [ΔET 135 (218) %; $P < 0.001$), reduced the number of patients with postoperative complications by 51% (relative risk 0.5; 95% confidence interval, 0.3–0.8; $P = 0.001$) and the rate of complications [1.4 (1.6) and 0.5 (1.0) ($P = 0.001$)] as compared with controls.

Conclusion: Prehabilitation enhanced postoperative clinical outcomes in high-risk candidates for elective major abdominal surgery, which can be explained by the increased aerobic capacity.

Keywords: aerobic capacity, aerobic exercise, exercise training, major abdominal surgery, major surgery, perioperative complications, physical activity, postoperative complications, prehabilitation, preoperative optimization

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Major abdominal surgery is associated with high rate of postoperative complications.[1] Moreover, a transient but marked postoperative reduction of functional capacity is observed in these patients, even in the absence of complications.[2]

Individual aerobic capacity determines preoperative functional reserve which, in turn, is negatively associated with postoperative morbi-mortality.[3,4] Accordingly, it can be hypothesized that preoperative interventions aiming at enhancing maximum oxygen uptake and increasing physical activity, such as prehabilitation, may contribute to reduce postoperative complications.

Prehabilitation is defined as a preparatory intervention aiming at reducing perioperative complications wherein both enhanced aerobic capacity, through supervised endurance exercise training, and promotion of physical activity play central roles.[5]

A comprehensive systematic review on elective intracavity surgery[6] acknowledges positive effects of prehabilitation on patients' fitness, but indicates limited evidence of impact on postoperative clinical outcomes in candidates for elective cardiac, abdominal and pulmonary surgical procedures. Moreover, available studies are clearly biased toward assessment of low-risk candidates for surgery and their methodological heterogeneity[7,8] results in limited comparability. Therefore, there is a clear need for randomized control trials (RCT) to assess the effects of prehabilitation in candidates for major surgery showing high risk for perioperative complications.

The present research relies on the assumption that elderly patients with multimorbidities are prone for perioperative complications and, consequently, they are the most likely to benefit from

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We Anael Barberan-Garcia and Josep Roca, the corresponding authors of this manuscript, certify that we have listed everyone who contributed significantly to the work.

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prehabilitation programs. Accordingly, the aim of the present investigation was to evaluate the impact of a personalized preoperative holistic intervention having high-intensity endurance exercise training and promotion of physical activity as key actionable factors to prevent postoperative complications in high-risk patients undergoing elective major abdominal surgery.

METHODS

Study Design

The research was designed as a randomized blinded controlled trial carried out at *Hospital Clínic de Barcelona*. The *Ethics Committee for Clinical Research of Hospital Clínic de Barcelona* approved the study (CEIC 2013/8579). The informed consent was understood, accepted, and signed by all subjects included in the trial. The study protocol is displayed at https://clinicaltrials.gov/ct2/show/NCT02024776.

Subjects

A consecutive sample of high-risk candidates for elective major abdominal surgery was recruited from the outpatient's clinics of *Hospital Clínic de Barcelona*. All eligible patients fulfiled the following inclusion criteria: i) candidate to elective major abdominal surgery; ii) high risk for surgical complications defined by: age > 70 years and/or American Society of Anesthesiologists score III/IV[9]; iii) duke Activity Status Index score ≤ 46[10]; and iv) preoperative schedule allowing for at least 4 weeks for the prehabilitation intervention. Exclusion criteria encompassed: i) nonelective surgery; ii) unstable cardiac or respiratory disease; iii) locomotor limitations precluding exercise training; and iv) cognitive deterioration impeding adherence to the program.

Randomization and Masking

Following the routine practice in our institution, candidates for elective major abdominal surgery were scheduled for a preoperative assessment with an anesthesiologist. During the visit, eligible candidates were randomized and invited to participate in the study and those who agreed were enrolled in the trial after signature of the informed consent. For oncologic patients, this visit was just after confirmation of cancer diagnosis even when the study of cancer stage was not yet completed.

Patients were blindly randomized to the 2 study arms using a 1:1 ratio: i) standard preoperative care (control group) or ii) standard preoperative care + prehabilitation (intervention group). Assignment to group allocation was carried out by means of a computer-generated random number through a web-based centralized procedure with an https security protocol hosted by the Biostatistics and Data Management Platform from our Institution. The randomization was done by means of the SAS Proc Plan System procedure (version 9.1.3 Service Pack 3 or superior). The collaborating anesthesiologists and surgeons who attended and followed the patients to register perioperative incidents by daily chart review were blinded to the patients' group allocation.

Procedures

Baseline assessment of the patients was done within 1 week after the preoperative assessment visit. Prehabilitation was initiated in the intervention group immediately after baseline assessment. Moreover, all participants were reassessed the week before the surgical procedure.

Standard care consisted of physical activity recommendation, nutritional counseling, and advices on smoking cessation and reduction of alcohol intake. Moreover, patients suffering from iron-deficiency anemia received intravenous iron and in those at high-risk of malnutrition (Malnutrition Universal Screening Tool ≥ 2[11]) nutritional intervention was done by a registered dietician.

The intervention group underwent a personalized prehabilitation program based on their health conditions and social circumstances.[12] The program was mostly performed in the community setting. Accordingly, the prehabilitation intervention encompassed 3 major steps: i) motivational interview to assess patient's adherence profile and to codesign the characteristics of the physical activity program with the patient; ii) personalized program to promote daily physical activity; and iii) supervised high-intensity endurance exercise training program. The intervention was tailored to each patient by a specialized physiotherapist taking into account several characteristics of the patient, namely clinical complexity (primary disease and co-morbidities), fitness, logistics (proximity to the hospital, facilitators and barriers for physical activity including degree of patient's dependence, among others) and adherence profile of the candidate assessed through the motivational interview. An additional aim of the interview was to reinforce patients' motivation and to raise the compromise with the behavior change regarding the program objectives. In a constructive atmosphere, the physiotherapist shaped the interview with the goal to optimize the patient's potential to drive the change toward a more active lifestyle. The interview was done according to the following rules: i) avoid the passive speech format, imperative forms, discussions, and situations generating resistance; ii) allow the subject to expose his/her fears, barriers, and doubts and empathize to understand his/her situation and therefore facilitate accomplishment of the specific needs; and iii) generate summaries of the information obtained while highlighting the positive aspects and fostering self-efficacy. Additional patient empowerment was reinforced during the supervised training sessions described below.

The nonsupervised program promoting physical activity was mainly focused on 2 objectives: i) increasing patient's steps per day, measured by a pedometer (Walking style X; Omron; Kyoto, Japan); and/or ii) optimization of walking intensity, assessed by the Borg scale.[13] International recommendations on step-based physical activity[14,15] were used as a theoretical frame to set up the objectives. Moreover, patients with severely reduced aerobic capacity and/or physical activity were empowered on home-based functional exercises (ie, sit-to-stand exercise, stairs climbing, elastic bands, indoor walking, among others) to decrease sedentary behavior at home. Patients were asked to report in a diary on a daily basis the number of steps per day, the intensity of non-supervised walks and/or home-based functional exercises during the entire prehabilitation period. The information was reviewed out and registered by the physiotherapist during the outpatient training sessions described below.

The supervised program consisted of a high-intensity endurance training performed on the cycle-ergometer stationary bicycle (Jaeger ER 550; Wüerzburg, Germany). The program was 1 to 3 sessions per week and personalized to the subject. Each session included 5 minutes of warm-up cycling at 30% of the peak work-rate achieved in a standard cardiopulmonary exercise testing (WR), 37 minutes of interval training, and 5 minutes of cool-down pedaling at 20% of peak WR. The interval training combined 2 minutes of high-intensity pedaling and 3 minutes of active rest. Work-rate progress during the prehabilitation period was tailored on individual basis, according to subjects' symptoms, to maximize the training effect. During the first 2 weeks, high-intensity pedaling interval was at least 70% of peak WR and the active rest interval was at least 40% of peak WR. Thereafter, work-rate was increased by approximately 5% every week up to a maximum of 85% of peak WR during the last week for the high-intensity period and 50% of peak WR for the active rest. The cycling rate during the sessions was maintained at 60 to 70 rpm. Pulseoximetry (Konica-Minolta; Pulsox-300; Osaka, Japan) and levels of self-perceived exertion[13] were monitored during the

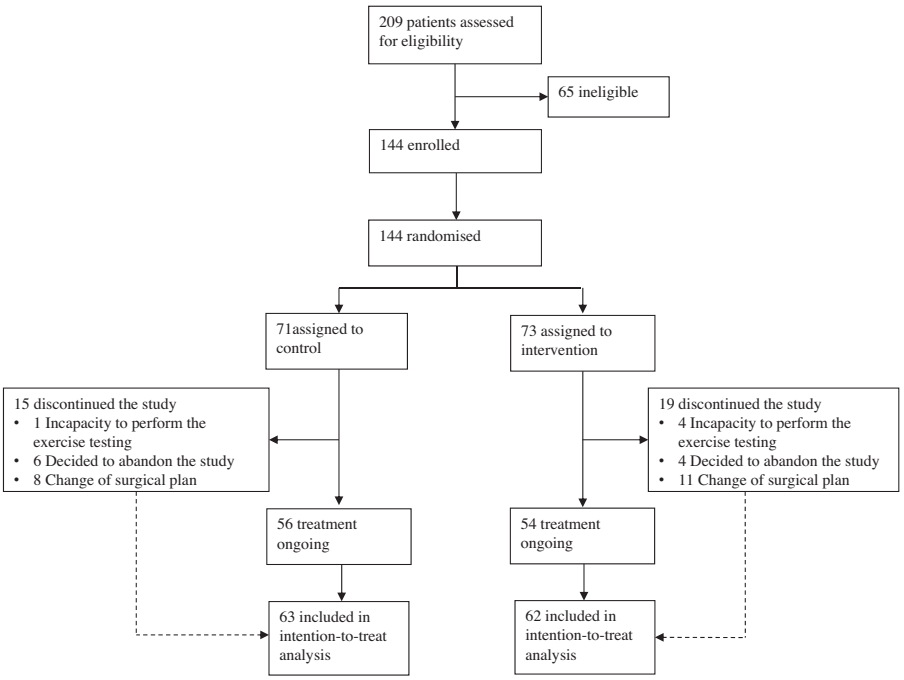

FIGURE 1. Flow-chart of the study.

sessions. As described above, the supervised training sessions were also used to reinforce the personalized objectives codesigned in the motivational interview. Those objectives were revisited and modified, if necessary, to optimize patient's performance.

Outcomes

The primary outcome variable of the study was the number of patients with postoperative complications defined as any deviation from the normal postoperative course and classified following the standards of the European Society of Anaesthesiology and European Society of intensive Care Medicine.[16] Secondary outcome variables were: i) number and severity of postoperative complications using Dindo-Clavien classification[17]; and ii) hospital and intensive care unit (ICU) days of stay. Other outcome variables included: i) endurance time (ET) measured by a cycling constant work-rate exercise testing at 80% of peak oxygen uptake[18] (Ergocard Professional; Medisoft; Sorinnes, Belgium); ii) distance covered in the 6-minute walking test[19]; iii) physical activity by the Yale physical activity survey (YPAS)[20]; iv) self-perceived health status by the Short Form (36) health survey (SF-36)[21]; and v) psychological status by the Hospital Anxiety and Depression scale.[22] In addition to clinical history and physical examination, the following descriptive tests were also included: i) standard cardiopulmonary exercise testing on cycle-ergometer[23] (Ergocard Professional); and ii) Resting pulmonary function testing (BodyBox Plethysmography; Medisoft; Sorinnes, Belgium).

Statistical Analysis

The calculation of the sample size was done using nQuery 7.0 and taking the reduction of the rate of patients with postoperative complications as main outcome. Taking data of a similar group of patients underwent colorectal surgery in our hospital in whom the complication rate was of 30%, and accepting an α-risk of 0.05 and β-risk of 0.20 in a 2-sided test, anticipating 20% of drop-outs, indicated the need of including 70 participants per group to detect a reduction of the percentage of patients with complications in the intervention group compared with the control group $\geq$20%. Results are presented as mean (SD) or n (%) when indicated. Comparisons were done using chi-square or Fisher exact tests for categorical variables, and Student' or Wilcoxon tests, depending on the distribution of the variables, for numerical variables.

Role of Funding Source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Baseline Characteristics of the Study Group

Between February 3rd, 2013, and June 13th, 2016, we assessed for eligibility a total of 209 candidates to be included in the research, as displayed in the study flow (Fig. 1). From the initial sample of patients, 65 were considered as ineligible because they did not meet inclusion criteria. Therefore, 144 high-risk patients (69%) were subsequently randomized, 71 allocated to the control group and 73 to the intervention. Nineteen of the 144 patients did not receive an operation and thus were excluded from all analysis. Baseline characteristics of participants, including complexity and duration of the surgical approach, in the intention-to-treat population were balanced across the 2 study groups (Table 1).

Prehabilitation Intervention

The mean duration of the prehabilitation program was 6 (2) weeks and during this period patients attended 12 (5) supervised exercise training sessions. No intervention patient reported any relevant incidence during the prehabilitation period. At program discharge, patients in the intervention group showed an improvement of 135 (218) % in ET ($P < 0.001$) and 37 (16) points in the YPAS ($P < 0.001$) but not in quality of life or psychological status. However, baseline values of all variables remained unchanged in the control group (Table 2).

Impact of the Intervention

Intraoperative parameters were equivalent in the 2 groups. Nevertheless, the intervention group showed a trend toward lower

TABLE 1. Baseline Characteristics of the Intention-to-treat Population

	Control (n = 63)	Intervention (n = 62)
Sex		
Male	51 (80%)	43 (68%)
Female	12 (20%)	19 (32%)
Age, y	71 (10)	71 (11)
BMI, kg/m^2	22 (7)	21 (7)
FEV_1 (%)	84 (25)	79 (24)
DLco (%)	71 (18)	69 (19)
Smoking status		
Never smoker	4 (6%)	6 (10%)
Former smoker	40 (63%)	37 (60%)
Current smoker	20 (31%)	20 (32%)
Chronic drug therapy*	25 (39%)	20 (32%)
ASA index		
II	24 (38%)	19 (30%)
III	36 (56%)	43 (68%)
IV	4 (6%)	1 (2%)
Adjusted Charlson index	7 (8)	7 (9)
Oncologic surgery	48 (75%)	48 (76%)
Type and complexity of surgery		
High surgical aggression		
Esophagectomy	5 (8%)	8 (13%)
Pancreaticodoudenectomy	1 (2%)	3 (5%)
Total gastrectomy	5 (8%)	0 (0%)
Intermediate surgical aggression		
Gastric bypass	6 (10%)	3 (5%)
Total colectomy	1 (2%)	3 (5%)
Rectal resection	10 (16%)	7 (11%)
Major liver resection	1 (2%)	2 (3%)
Pancreas resection	1 (2%)	2 (3%)
Minor surgical aggression		
Partial gastrectomy	2 (3%)	1 (2%)
Sleeve gastrectomy	4 (6%)	5 (8%)
Segmental colon resection	26 (41%)	28 (45%)
Minor liver resection	1 (2%)	0 (0%)

Data are n (%) or mean (SD). BMI indicates body mass index; ASA, American Society of Anesthesiologists; FEV_1, forced expiratory volume in the first second; DLco, diffusion capacity of the lung for carbon monoxide.

*≥5 Drugs.

requirement of vasoactive drugs during surgery, as compared with the control group ($P = 0.053$) (Table 3).

The incidence of complications in the overall sample of patients was 46%. When stratifying by groups, the intervention group showed a lower rate of complications, 31% versus 62%, than the control group ($P = 0.001$). Accordingly, the estimated relative risk (RR) for complications demonstrated that prehabilitation intervention has a protective role for postoperative complications: RR 0.5, 95% confidence interval (CI), 0.3–0.8 (Table 4).

Among the secondary outcomes, the intervention group showed lower mean number of complications per patient: lower rate of cardiovascular complications (RR 0.1, 95% CI, 0.1–1.0), less infection of uncertain source (not possible to calculate RR), and lower rate of paralytic ileus (not possible to calculate RR) when compared with control group (Table 4). Moreover, the intervention significantly reduced the length of stay in the ICU, as showed in the sensitivity analysis including only those patients admitted in the ICU [(n = 44) 3 (2) vs 12 (20) days for intervention and control group respectively; $P = 0.046$].

The sensitivity analysis restricted to patients with complications showed a protective role of prehabilitation for having >1 complication (n = 58; RR 0.6; 95% CI, 0.3–1.1). Nevertheless, no effects on severity of complications were observed using the Clavien-Dindo classification.

Likewise, similar results for primary outcomes were achieved in by-protocol analysis (110 (88%) of 125 patients in the intention-to-treat population).

DISCUSSION

This is the first randomized blinded controlled trial assessing the impact of a prehabilitation intervention on perioperative complications in high-risk patients undergoing major abdominal surgery. The main finding of the study showed that prehabilitation was a protective factor for postoperative complications in high-risk candidates for elective major abdominal surgery. Moreover, the sensitivity analysis reinforced the role of prehabilitation preventing >1 complication and reducing the days of ICU stay. Our investigation demonstrated that high-intensity endurance exercise training is feasible and safe in elderly and/or multimorbid candidates to major abdominal surgery.

Available reports on prehabilitation programs for candidates to elective surgery show heterogeneous designs in terms of duration of the intervention and modalities of exercise training. The duration of the prehabilitation program is dependent upon the interval of time before surgical date, which, in turn, is highly modulated by organizational aspects of healthcare providers, as well as by type of surgical intervention. Reported lengths of the prehabilitation programs range from 3 to 6 weeks in cancer abdominal surgery[8] and from 2 to 10 weeks in cardiac surgery.[7,24]

Regarding the modalities of exercise training carried out in prehabilitation programs, the reports include endurance exercise training, resistance training, inspiratory muscle training, or a combination of all these approaches.[7,8,24–27] In a recent systematic review, Katsura et al[24] concluded that preoperative inspiratory muscle training seems to be effective to reduce pulmonary complications and length of hospital stay in patients undergoing cardiac or major abdominal surgery. However, the impact of enhanced aerobic capacity on undesirable postoperative clinical events has been poorly documented.[6] To our knowledge, there is only 1 robust RCT[7] including endurance training as part of the prehabilitation program. In this trial, O'Doherty et al[7] assessed the impact of enhanced aerobic capacity in low-risk patients undergoing coronary artery bypass graft surgery showing positive effects on both hospital and ICU length of stay; however, the rate of complications did not differ between the groups. However, in major intra-abdominal surgery, the trials assessing the effect of enhanced aerobic capacity on postoperative complications failed to find differences between control and prehabilitation groups probably because of methodological weaknesses like poor statistical power and/or low-to-moderate intensity of exercise training.[8] The methodological strengths of the present study overcome limitations observed in previous reports and provides evidence to support a relationship between enhanced aerobic capacity (increased ET) and reduction of surgical complications induced by prehabilitation (Tables 2 and 4). The sensitivity analysis performed in the present study showed prehabilitation as a protective intervention for having >1 complication (n = 58; RR 0.6; 95% CI, 0.3–1.1) and reducing ICU days of stay [n = 44; 12 (20) vs 3 (2) days; $P = 0.046$]. It is of note that the intervention had no detectable effects on quality of life and psychological status (Table 2). It could be argued that the short duration of the program [mean 6 (2) weeks] and the absence of specific psychological intervention may explain the lack of impact of the program on both quality of life and psychological status.

The present study encompasses a wide spectrum of major abdominal surgeries representative of the palette of conditions attended in a digestive surgery department. The study design

TABLE 2. Impact of the Intervention on Aerobic Capacity, Quality of Life, Psychological Status and Physical Activity (Data Only Available From the By-protocol Population)

	Control (n = 56)			Intervention (n = 54)		
	Baseline	**Presurgery**	***P***	**Baseline**	**Presurgery**	***P***
Aerobic capacity						
Endurance time, s	323 (168)	362 (215)	0.118	325 (151)	765 (395)	<0.001
6MWT, min	471 (95)	469 (109)	0.804	472 (94)	473 (91)	0.953
Quality of life						
SF-36 physical functioning	46 (9)	46 (9)	0.807	45 (9)	46 (10)	0.379
SF-36 physical role	47 (12)	48 (10)	0.453	46 (12)	49 (10)	0.206
SF-36 bodily pain	50 (13)	49 (12)	0.518	48 (11)	49 (10)	0.621
SF-36 general health	43 (10)	43 (9)	0.907	41 (8)	42 (8)	0.496
SF-36 vitality	51 (12)	53 (12)	0.210	47 (9)	50 (8)	0.078
SF-36 social functioning	47 (13)	47 (13)	0.657	45 (13)	48 (11)	0.178
SF-36 emotional role	47 (13)	47 (12)	0.932	44 (15)	47 (12)	0.107
SF-36 mental health	47 (14)	47 (13)	0.789	41 (14)	43 (12)	0.227
SF-36 PCS	45 (11)	45 (11)	0.938	45 (9)	45 (9)	0.536
SF-36 MCS	48 (13)	48 (13)	0.659	44 (13)	46 (12)	0.146
Psychological status						
HAD anxiety	6 (5)	6 (5)	0.734	8 (4)	8 (3)	0.939
HAD depression	4 (4)	4 (3)	0.818	5 (4)	5 (3)	0.949
HAD total score	10 (8)	10 (8)	0.834	12 (7)	12 (6)	0.937
Physical activity						
YPAS index	41 (16)	39 (19)	0.403	34 (17)	71 (19)	<0.001

Data are mean (standard deviation). 6MWT indicated 6-minute walking test; HAD, Hospital Anxiety and Depression scale; MCS, mental component summary; PCS, physical component summary; SF-36, Short Form (36) Health Survey.

provides valuable information about the real impact that a prehabilitation service could represent being implemented in the clinical practice. Moreover, the recruitment of consecutive patients in a prospective manner reinforces external validity of the results. It is important to highlight that the robustness of our findings is warranted as the by-protocol analyses are consistent with those from the intention-to-treat approach and there were no missing data in the complications register (main study outcome). Furthermore, in the current trial, the sample size was powered for postoperative complications, there was a blinded evaluation, and there was no contamination among study groups. Furthermore, this study provides a thorough characterization of the patients with a detailed analysis of perioperative aspects, which further facilitates the interpretation of the results and enhances comparability with other studies.

Nevertheless, the current investigation shows a design limitation. The trial is not double-blinded but a randomized trial that cannot be double-blinded because of the type of intervention. However, while acknowledging this fact, there was no contamination among groups as we used 2 different informed consents and, therefore, each group did not know about the existence of the other. It is important to highlight that clinicians collecting perioperative outcomes were blinded to group status.

Lately, information and communication technologies (ICTs) have been postulated as enabling tools for the integrated healthcare model enhancing patient's management within programs and providing prospective follow-up.[28,29] The rather low use of technology in the present study suggests that the role of ICT as enabler of enhanced efficiencies in the integrated assessment of surgical risk and perioperative strategies should be further explored.

TABLE 3. Intraoperative Parameters of the Intention-to-treat Population

	Control (n = 63)	Intervention (n =62)	***P***
Laparoscopy	56 (89%)	48 (79%)	0.147
Duration of the surgery, min	168 (94)	159 (89)	0.608
Planned postoperative ICU stay	16 (25%)	22 (36%)	0.247
Intraoperative monitoring			
Invasive blood pressure	28 (44%)	26 (42%)	0.858
Central venous catheter	38 (60%)	32 (52%)	0.469
Noninvasive cardiac output	6 (10%)	4 (7%)	0.744
Transfusion requirements			
Blood red cells	1 (2%)	2 (3%)	0.616
Fresh frozen plasma	0 (0%)	1 (2%)	0.492
Platelets	0 (0%)	2 (3%)	0.240
Intraoperative remarkable events			
Vasoactive drugs	19 (30%)	9 (15%)	0.053
Hypoxemia	3 (5%)	1 (2%)	0.619
Arrhythmia	4 (6%)	1 (2%)	0.365
Deferred tracheal extubation	2 (3%)	1 (2%)	1.000

Data are n (%) or mean (standard deviation).

TABLE 4. Postoperative Outcomes of the Intention-to-treat Population

	Control (n = 63)	Intervention (n = 62)	*P*
Hospital days of stay	13 (20)	8 (8)	0.078
ICU days of stay	4 (13)	1 (2)	0.078
Surgical reintervention	6 (10%)	2 (3%)	0.273
In-hospital mortality	1 (2)	1 (2)	1.000
Patients suffering postoperative complications	39 (62%)	19 (31%)	0.001
Number of complications per patient	1.4 (1.6)	0.5 (1.0)	0.001
Medical complications	0.9 (1.2)	0.2 (0.6)	<0.001
Surgical complications	0.5 (0.6)	0.3 (0.7)	0.119
Type of complication			
Medical			
Cardiovascular	8 (13%)	1 (2%)	0.033
Respiratory	10 (16%)	4 (7%)	0.155
Neurological	5 (8%)	2 (3%)	0.440
Acute kidney injury	4 (6%)	0 (0%)	0.119
Nausea/vomiting	6 (10%)	3 (5%)	0.491
Deep venous thrombosis	1 (2%)	0 (0%)	1.000
Urinary tract infection	4 (6%)	3 (5%)	1.000
Bloodstream infection (lab confirmed)	4 (6%)	1 (2%)	0.365
Infection of uncertain source	7 (11%)	0 (0%)	0.013
Others*	13 (21%)	6 (10%)	0.134
Surgical			
Postoperative hemorrhage	6 (10%)	4 (7%)	0.744
Anastomotic breakdown	3 (5%)	3 (5%)	1.000
Paralytic ileus	10 (16%)	0 (0%)	0.001
Surgical site infection (superficial and deep)	1 (2%)	1 (2%)	1.000
Surgical site infection (organ and space)	1 (2%)	1 (2%)	1.000
Mechanical ileus	0 (0%)	1 (2%)	0.496

Data are n (%) or mean (standard deviation).
*Liver insufficiency, diabetic decompensation, acute urinary retention. ICU, Intensive Care Unit.

This investigation provides encouraging findings which are supposed to have a positive impact on the healthcare value chain; however, large-scale adoption of the service requires studies proving cost-effectiveness, introducing reimbursement strategies and specific business models allowing sustainability.

We strongly believe that the present work should prompt a major consideration of prehabilitation as a core intervention to carry out in the preoperative setting in high-risk patients undergoing major elective surgery.

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