Impact of six weeks trimodal prehabilitation program on short-term functional recovery for elderly patients undergoing colorectal cancer surgery

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Abstract

Background and objectives

The impact of prehabilitation on physical fitness and postoperative course after colorectal cancer surgery for elderly patients is unknown. The aim of this study was to assess whether a 6-week trimodal prehabilitation program (exercise, nutritional supplementation, and counseling on relaxation techniques) is sufficient to modify physical fitness, nutritional status, and postoperative outcomes of patients undergoing colorectal cancer surgery for elderly patients.

Materials and methods

From January 2018 to October 2021, the clinical data of patients undergoing cancer surgery in our department were collected. Patients were assigned to either a prehabilitation (n=26) or matched time control group (n=26). Patients before the introduction of prehabilitation were included as historical control subjects for 1:1 propensity score-matching (control group). Over the 6-week period prior to surgery, patients in prehabilitation group participated in a trimodal prehabilitation program. Patients in control group received the same program but only postoperatively. The 6-min walk test (6MWT) was used for assessment of functional walking capacity. Hospital anxiety and depression scale (HADS) score was recorded before intervention and before operation. The recovery of intestinal function, postoperative complications, the length of hospital stay were compared between the two groups.

Results

Over the preoperative period, serum albumin levels were significantly deteriorated in the control group, whereas this index did not deteriorate or even improved in the prehabilitation group. By performing prehabilitation, prehabilitation group significantly increased the amount of moderate and vigorous intensity physical activities that they performed. Prehabilitation group patients also demonstrated a greater improvement in 6MWT compared to Control group during the prehabilitation period. Although the overall incidence of postoperative complications did not differ between the two groups, the postoperative hospital stay and recovery of intestinal function was shorter in the prehabilitation group than in the control group.

Conclusions

These findings highlight that the positive effects of a trimodal prehabilitation program can significantly improve the perioperative physical function, psychological status and nutritional status of patients on elderly colorectal cancer patients within the 6-week prehabilitation period are an achievable goal and could have a significant effect on the cancer care continuum.

Introduction

Colorectal cancer (CRC) is the third most frequent cancer worldwide in both men and women. Worldwide, 10% of the new cases of cancer account for CRC[1]. As the ageing population grows, the incidence of CRC will also rise and it will become an ever more significant health burden[2].Surgery remains the cornerstone of treatment in patients with CRC. Elderly people have a higher risk of postoperative complications, which leads to higher mortality rates, a longer hospital stay, and a higher risk of institutionalization and readmission[3–6].

Physical function and nutritional status are often compromised in older patients[7–9] and are aggravated by cancer (treatment) that can cause fatigue, loss of appetite, nausea, and pain, leading to unintentional weight loss and loss of muscle mass[10].In the preoperative period approximately half of elderly patients with CRC suffer from sarcopenia, half lose weight, and 1 in 5 are malnourished[11, 12].Recent studies have found that compromised nutritional status and sarcopenia predict adverse outcomes such as postoperative complications and mortality in older patients after CRC surgery[13]. Elderly patients, particularly if frail, could potentially benefit from prehabilitation.

In recent years, much focus has been placed on the importance of prehabilitation, an optimization of physical fitness before surgery, with the intent of improving postoperative outcomes[10] Previous reviews indicated that preoperative prehabilitation interventions for patients undergoing elective colorectal resection for cancer is feasible, safe [14]. However, the impact of preoperative physical exercise on physical fitness, postoperative complications, and hospital stay after highly surgeries for elderly CRC patients is unknown.Moreover, the benefit of trimodal prehabilitation intervention has not been well evaluated in elderly CRC patients.

Accordingly, this study aimed to investigate the effectiveness of preoperative trimodal prehabilitation therapies on physical fitness, nutritional status, postoperative complications, and hospital stay during the waiting period for elderly patients undergoing CRC surgery.

Patients And Methods

Study design

This study was based on a reanalysis of preoperative data that assessed the effectiveness of a trimodal prehabilitation intervention for elderly CRC patients undergoing colorectal resection[15]. Eligible patients were assigned in a 1:1 ratio to either prehabilitation or a control group. All patients were required to visit the lab for baseline (6 weeks prior to surgery) and before surgery (within 1 week of surgery) measurements, which included a 3-day dietary recall assessment, a 6-min walk test (6MWT) to measure functional walking capacity (Figure 1).

Data Collection

Demographic data including age, sex, height, body weight, body mass index, diagnosis, cancer stage, functional capacity, and other comorbidities were recorded(Table 1).The waiting period for surgery was determined as the term between the date of hospitalization for examination of cancer (first hospitalization) and the date of re-hospitalization for surgery (second hospitalization). Intraoperative data such as operative procedure, operation time and intraoperative blood loss also were recorded. The severity of postoperative complications was classified using the Clavien-Dindo classification system[16]. A major complication was defined as a complication with a Clavien-Dindo grade of 3 or higher. Postoperative infectious complications included intra-abdominal abscess, bacteremia, surgical-site infection, and pneumonia. The discharge criteria were constant throughout the study period. Discharge from the hospital was allowed when patients were estimated without any drainage tube and with stable oral intake.

Prehabilitation programme

Trimodal prehabilitation interventions

The trimodal prehabilitation interventions of both studies included exercise, nutrition, and anxiety-reduction components that began approximately 6 weeks before surgery. Each patient received a baseline appointment with a kinesiologist, dietitian, and an expert trained in psychology all of whom assessed the patient and provided personalized instructions. Prehabilitation group patients received a personalized,supervised,and home-based multimodal program prescribed by a kinesiologist, a nutritionist, and a psychology-trained nurse. The program started after the baseline visit and continued for 6 weeks before surgery.Participation in the prehabilitation program had no effect on surgical waiting time. The program did not continue after surgery.

Exercise Intervention

The home-based exercise regimen involved a prescription of unsupervised total-body exercise of up to 50 min for at least 3 days per week, alternating between aerobic and resistance training. During these sessions, patients performed 30 minutes of moderate aerobic exercise (including a 5-minute warm-up) on a recumbent stepper, 25 minutes of resistance exercises using an elastic band, and 5 minutes of stretching. In addition to the supervised exercise sessions, participants were prescribed a personalized home-based program of aerobic activities (walk daily for a total of 30 minutes as moderate-intensity aerobic activity) and resistance training (elastic band routine 3 times per week) in the hospital once per week before surgery.

Nutrition Intervention

All participants had their nutritional status assessed by a registered dietitian. At baseline,participants were asked to complete a 3-day food diary from which macronutrients were estimated using food exchange lists and compositiontables. Nutritional status was evaluated using the NRS 2002 score and frailty index[16,17]. Patients were advised on how to improve their own daily dietary intake based on the

balanced plate concept. Target protein intake was 1.5g/kg of body weight (or adjusted body weight in obese patients) as per the European Society for Clinical Nutrition and Metabolism recommendation for patients with cancer[18]. If the patient did not Meet the protein requirement by diet alone, they were provided with whey protein supplementation. Patients were instructed to use the supplements within 1 hour of their exercise training to maximize muscle protein synthesis[19].Further nutritional counseling included caloric balance, bowel movement regularity.

Psychological Intervention

The study participants had an assessment by a psychology trained nurse. Potential causes of perioperative fatigue, anxiety, and depression were discussed. Study participants were provided with personalized coping strategies and received a compact disc with an audio track containing the instructions to help them perform the exercises at home 3 times a week. The intervention also included counseling regarding smoking and alcohol cessation. The use of nicotine replacement therapy was decided through shared decision-making. A trained psychologist provided patients with relaxation and breathing exercises to reduce anxiety. Patients practiced with the psychologist during the initial visit, after which they were provided with an instructional compact disk for performing these exercises at home.In order to facilitate adherence to the intervention program, all patients in prehabilitation received a standardized instructional booklet, written in easily comprehensible language with pictures and figures, describing all elements of the program in detail. The booklet also contained a diary for patients to document all physical activities performed. For ethical reasons, the control group was provided with an intervention program, similar to prehabilitation. During the preoperative period, patients were given a hospital booklet informing patients on how to prepare for surgery.

Statistical analysis

Data analysis was performed by comparing the prehabilitation group to the control group using SPSS Statistics software. All continuous variables were analyzed using a t-test from independent samples. All categories were described as percentages and were compared using a chi-squared test or Fisher’s exact test, p values<0.05 were considered signifcant.

Results

Participants

The prehabilitation group consisted of 32 patients scheduled to undergo CRC resection. Of these patients, 4 declined to participate, 2 did not record their history of exercise and nutritional therapies. Thus, 26 patients finally were analyzed as the prehabilitation group. As historical control subjects, a backward consecutive series of 26 patients who underwent highly invasive surgeries for CRC surgery without prehabilitation was selected (control group). After one-to-one propensity score matching, 26 patients in each group finally were analyzed (Figure 1).

Baseline Characteristics

Gender, age, height, body weight, body mass index, diagnosis, cancer stage, Charlson comorbidity index, did not differ significantly between the two groups. The median waiting period before surgery (the interval between the first and second hospitalizations) was 7 days in the control group and 8 days in the prehabilitation group (Table 1)..

Intra- and Postoperative Characteristics

The proportion of surgical procedures did not differ between the two groups. Among the patients who underwent major hepatectomy, 18 of 26 patients in the control group and 15 of 26 patients in the prehabilitation group underwent combined CRC resection. Intraoperative variables including operation time, blood loss, and rate of allogeneic blood transfusion also did not differ between the two groups.

No patients died within 90 days after surgery in either of the two groups. Although the overall morbidity rate, as indicated by a Clavien-Dindo grade of 3 or higher, did not differ between the two groups, the incidence of clinically significant leakage was significantly lower in the prehabilitation group than in the control group. Additionally, the postoperative hospital stay in the prehabilitation group was significantly shorter than in the control group (Table 2).

Nutritional Status

During the waiting period, the indexes for nutritional status (body weight, body mass index, and serum albumin) all were significantly deteriorated in the control group. However, the levels of serum albumin did not deteriorate or even increased during the waiting period in the prehabilitation group. The level of serum albumin tended to decrease in the control group. In sharp contrast, the level of serum albumin improved significantly during the waiting period in the prehabilitation group.

Changes in the body weight, serum albumin, and serum albumin were compared between the control and prehabilitation groups according to the length of the waiting period before surgery. In the control group, the decrease in body weight was greater depending on the length of the waiting period before surgery. The decrement in body weight of the patients who waited more than 6 weeks was significantly greater than that of the patients who waited less than 3 weeks. However, this change was attenuated in the prehabilitation group. Although serum albumin level decreased during the waiting period in the control group, these indexes of nutritional status did not deteriorate or even improved in the prehabilitation group (Figure 2).

Alteration of physical fitness status

For the patients with prehabilitation, the 6MWT at the second hospital stay was significantly longer than at the first hospital stay for both the males and females. Although the difference was not statistically significant, total skeletal muscle mass measured at the second hospital stay was greater than at the first hospital stay for both the males and females. In contrast, the total fat mass for both the males and

females at second hospital stay was significantly less than at the first hospital stay. Interestingly, the levels of serum albumin and the 6MWT showed a significant positive correlation in the prehabilitation group((Figure 3).

Psychological status

The means and standard deviations of the scores obtained in HADS-Anxiety and HADS-Depression are shown in Table3.In the anxiety sphere (HADS-Anxiety), it was found that patients had a pathological score at diagnosis, increasing at the time of surgery. During the postoperative period, these figures decreased.In the depression sphere (HADS-Depression), patients had a probably pathological score at diagnosis. These values remained stable at the time of surgery and during the different postoperative measurements. It was found that patients in our sample were chronically taking some type of anxiolytic or anti-depressant treatment before diagnosis. These same patients had higher HADS-Anxiety scores at both at diagnosis and on the day of surgery. Higher scores were also seen in the HADS-Depression questionnaire at follow-up.

Discussion

The goal of prehabilitation is to enhance the functional capacity of patients during the waiting period for surgery[20]. In the current study, a trimodal prehabilitation program consisting of moderate-intensity physical exercise supported with nutritional supplementation and anxiety reduction techniques resulted in significantly improved functional walking capacity in the intervention group. The main finding of this study indicates that 6 weeks of prehabilitation in elderly CRC patients is sufficient to modify exercise behavior, specifically increasing levels of moderate and vigorous activities, during the preoperative period. Participating in prehabilitation resulted in a greater proportion of patients meeting current exercise recommendations for cancer prevention and healthy living in a similarly aged population. This adjustment in activity level subsequently improved functional walking capacity, as indicated by 6MWT results. This is important to highlight as the prehabilitation period, when compared to traditional training programs, is relatively short due to the time frame between diagnosis and surgery. Given that the postoperative period may not be the most optimal for patient adherence, it is imperative to better understand the potential of the preoperative period for effective intervention. Furthermore, prehabilitation has been demonstrated to enhance postoperative outcomes and decrease postoperative morbidity for some surgical procedures[21].

There is a strong relationship between poor preoperative physical status and risk of complications after major surgery. Even in the absence of complications, there is often a 20–40% reduction in physiologic and functional capacity after major surgery[22]. One of the goals of prehabilitation is therefore to safely increase physical activity levels and functional capacity in surgical patients during the preoperative period in order to enhance physiological reserve, thus enabling patients to better withstand the stress of surgery, and ultimately, to facilitate postoperative recovery and faster return to baseline functions. Previous studies reported that patients who had undergone prehabilitation were able to increase their

preoperative 6MWT by up 6–10%, but the specific exercise behavior changes through which functional improvement is obtained are unclear[23].In the present study, we evaluated the different intensity of activities performed by our elderly CRC patients. We found that patients in the prehabilitation group exhibited a significant increase in levels of predominantly moderate intensity physical activity that respected current guidelines during the 6 weeks preoperative period[24]. Along with the increase in moderate-intensity exercise, the prehabilitation group also exhibited an increase in 6MWT distance. A systematic review of epidemiologic cancer studies showed that moderate-intensity physical activity provides greater primary protective effect than light-intensity activities[25]. Together, the data suggests that moderate-intensity activity is a feasible target in this population and can contribute to improved functional walking capacity in the elderly CRC patients[26]. Future studies should aim to understand the frequency and type of activity that is most beneficial for this patient population in order to provide clinicians with sufficient evidence to effectively prescribe prehabilitation exercise programs. In the trimodal approach used in this study, exercise remained the primary component, but the impact of psychological and nutritional interventions should not be discounted. Alterations in bowel function are common in colorectal cancer patients and may increase protein catabolism. In fact, up to 50% of patients awaiting surgery experience weight loss, and up to one in five is malnourished[27]. For this reason, we adjusted the supplemented protein intake to ensure that all patients in the prehabilitation group received 1.5g/kg of protein per day as recommended by the ESPEN guidelines[28]. This strategy is supported by a recent RCT of CRC resection patients demonstrating improved functional walking capacity in patients receiving whey protein supplementation[29]. Similarly, anxiety symptoms are common in cancer patients and associated with reduced quality of life as well as increased incidence of postoperative morbidity. Evidence suggests that psychological prehabilitation interventions may be effective in improving postoperative psychological outcomes(anxiety and depression), quality of life, and somatic symptoms[30]. The direct impact of preoperative psychological intervention or anxiety reduction on exercise behavior is unclear, but the relationship between physical and psychological health is well established. In an era of holistic, multidisciplinary, and patient-centered cancer care, the importance of psychological wellbeing cannot be understated[31].Given the feasibility of altering exercise behaviors and improving functional capacity within a short period of time, as demonstrated in this study, prehabilitation programs should be widely implemented for the elderly CRC patients scheduled for surgery. A particular strength of our prehabilitation program is that it is a home-based program.

A few limitations are present in our study design and analysis. First, the study was not a randomized controlled trial but compared the data of patients before and after the introduction of prehabilitation. Ideally, the exact effects of prehabilitation should be elucidated through a randomized controlled trial. However, in reality, a randomized controlled trial was diffificult to perform because most of the patients eligible for enrollment desired to perform prehabilitation when the investigators explained this study. Therefore, the method of comparing the patients with historical control subjects using propensity score-matching was selected. Second, there was variability among the patients during the waiting period. Because the number of surgeries that can be performed at a single institution is limited, it was unrealistic to set a uniform waiting period for all the patients. These patients generally have a long waiting period

before surgery. The impact of prehabilitation on these patients should be elucidated in a future study. Third, the study was not originally designed to compare physical activity of different intensities, the intensity of home-based exercise may potentially have differed among the patients because they were unsupervised at home. Thus, we could not compare the direct effects of prescribing patients with physical activity programs of varying intensity, the physical activity levels were self-reported and thus subject to recall bias.

In conclusion, In elderly patients undergoing resection of CRC, a prehabilitation program involving exercise, nutritional, and psychological interventions did not appear to affect postoperative complications. Exercise successfully increased total physical activity levels in elderly patients scheduled for CRC resection, primarily through increases in moderate-intensity activity. These changes in activity translated into improvements in functional walking capacity. A better understanding of which aspects of prehabilitation influence surgical outcomes and functional recovery. Alternative strategies should be considered to prepare elderly CRC patients for surgery.

Declarations

Data Availability The datasets used in the current study are available from the corresponding author on reasonable request.

Authors' contributions Bin Liu and Yousheng Li designed the study. Bin Liu and Lei Zheng analyzed the data and prepared the figures. Bin Liu drafted the initial manuscript. All authors read and approved the final manuscript.

Ethical Approval This study was approved by the Institutional Review Board of Shanghai Ninth People's Hospital.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication The patients were informed that the data obtained during the study could be used for publications in scientific journals.

Conflicts of Interest The authors have no conflicts of interest to declare.

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Tables

Table 1 Baseline characteristics and clinical data of patients in prehabilitation and control groups

	Prehabilitation（n=26）	Control（n=26）	*P* value
Age (years)	78.3±3.5	75.3±2.1	0.083
Gender（Male/Female）	26（14/12）	26（15/11）	0.061
BMI（kg/m^2）	20.4±1.5	21.1±1.9	0.077
NRS 2002 score			0.729
1-2	12	13	0.514
3-4	14	13	0.884
ASA physical status			
I	2	3	
II	17	15	
III	7	8	
IV	0	0	
V	0	0	
6MWT distance (m)	348.3±15.5	328.5±11.3	0.018*
Neoadjuvant therapy(%)	20 (77)	15 (60)	
Type of resection(n)			
Colon	14	13	0.647
Rectum	12	13	0.563
TNM cancer stage(n)			
I	3	5	
II	17	15	
III	6	6	
IV	0	0	
Frailty Index(n)			
2	1	0	
3	4	3	
4	15	18	
5	6	5	
Comorbidities, No. (n)			

Diabetes type 2	4	3	
Hypertension	2	3	
Cardiovascular diseases	1	2	
Asthma	2	2	
Atrial fibrillation	1	2	
Minimally invasive (%)	25 (96%)	23 (92%)	0.571

BMI: body mass index, ASA: American Society of Anesthesiologists,6-MWT:6-min walk test.

Table 2 Comparison of perioperative observation indexes between two groups

	Prehabilitation（n=26）	**Control（n=26）**	**P value**
Duration of surgery（min）	127.3±18.2	116.3±30.5	0.075
Length of stay(LOS)	9.1±2.4	12.2±1.8	0.038*
Clavien-Dindo (n)			
I	5	4	
II	2	7	
III	1	4	
IV	0	1	
V	0	0	
Readmission, n (%)	2（7.6%）	3（11.5%）	0.151
90-day mortality, n (%)	0	0	

Table 3 Comparison of change trend of psychological state baseline status and after prehabilitation ($\bar{x} \pm s$)

	Prehabilitation（n=26）	Control（n=26）	*P* value
Baesline HADS-Anxiety	7.3±1.9	7.6±1.3	0.614
Before surgery HADS-Anxiety	4.9±1.2*	6.9±2.3	0.024*
Baesline HADS-Depression	7.3±1.2	7.8±1.5	0.805
Before surgery HADS-Depression	4.5±1.4*	6.7±1.1	0.031*

HADS:Hospital anxiety and depression scale.

Figures

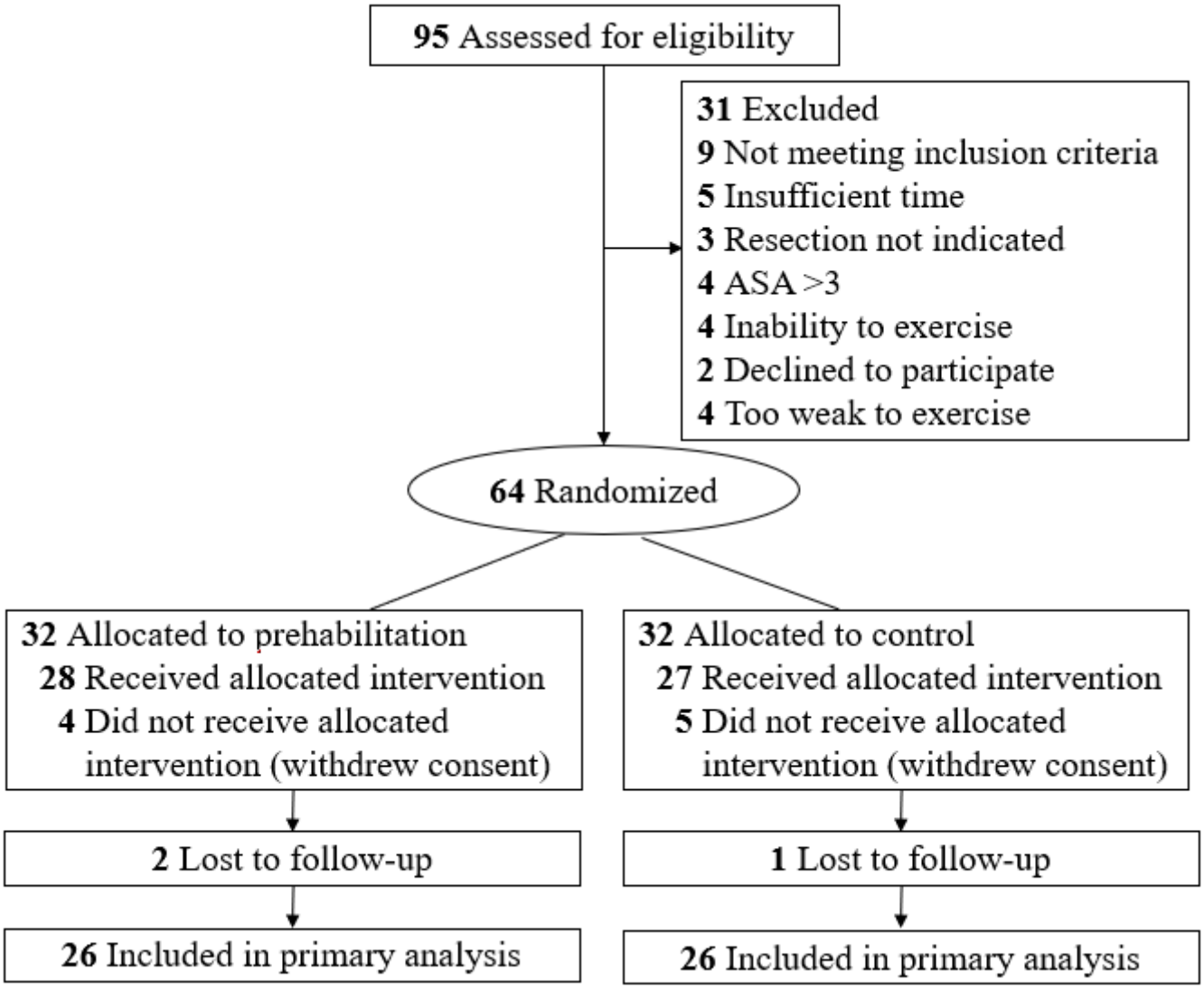

Figure 1

Consort diagram for the study

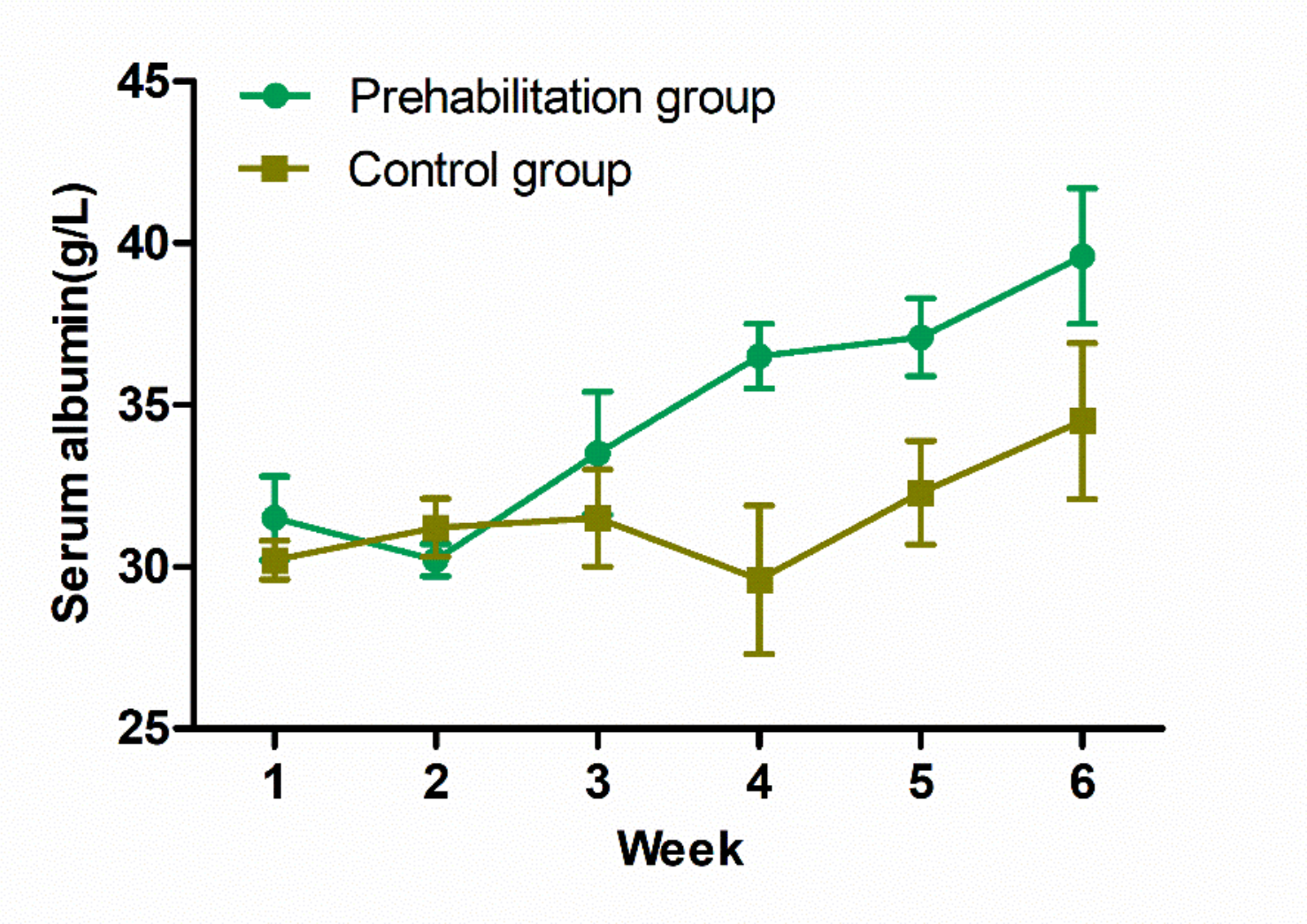

Figure 2

Change of serum albumin in the perioperative Period

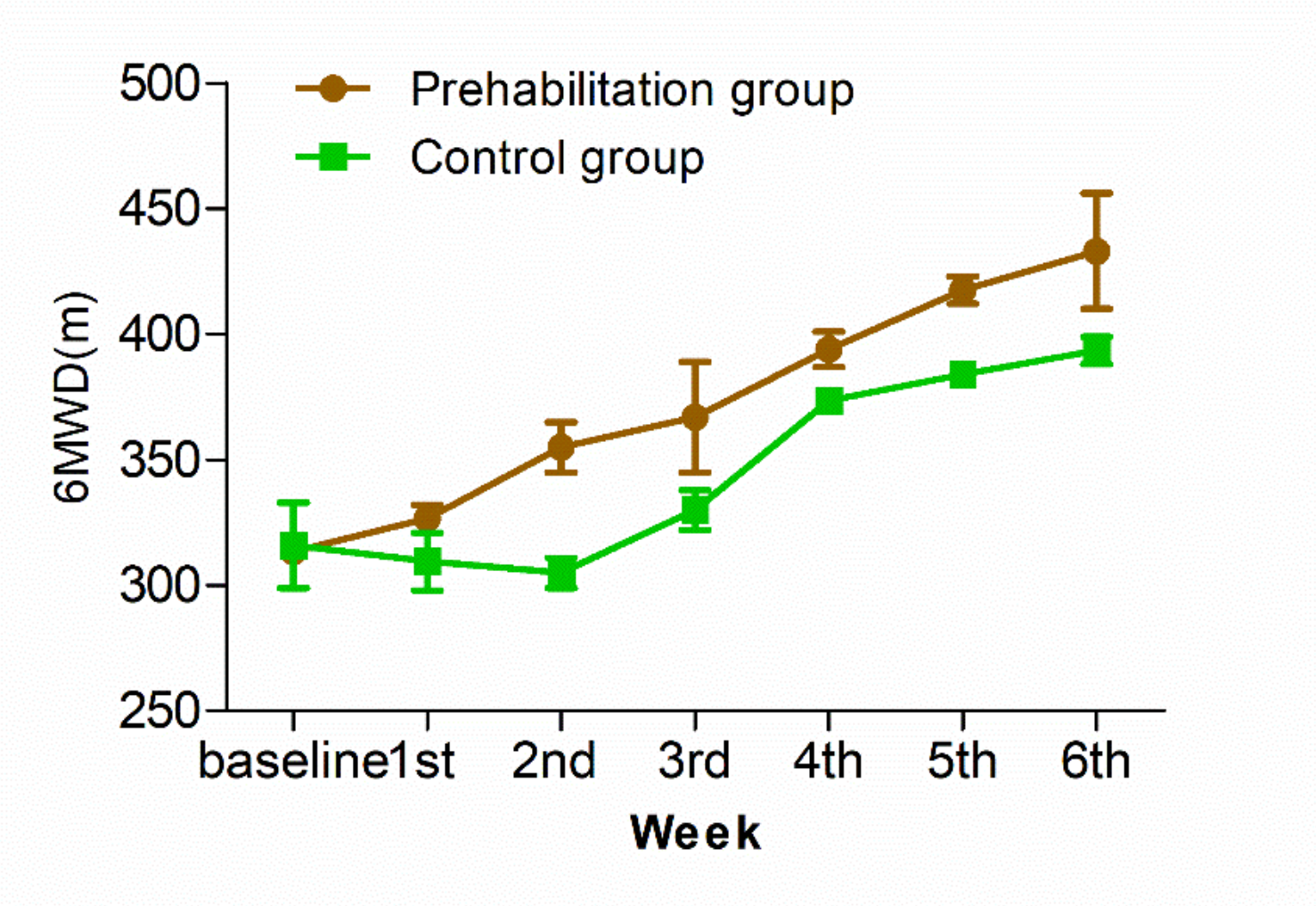

Figure 3

Change in functional capacity in the perioperative Period