

Original Article



Feasibility and Effects of a Postoperative Recovery Exercise Program Developed Specifically for Gastric Cancer Patients (PREP-GC) Undergoing Minimally Invasive Gastrectomy

In Cho^{1,2,*}, Younsun Son^{3,*}, Sejong Song³, Yoon Jung Bae⁴, Youn Nam Kim⁵,
Hyong-Il Kim^{6,7}, Dae Taek Lee^{3,8}, Woo Jin Hyung^{1,6,7,9}

OPEN ACCESS

Received: Feb 19, 2018

Revised: Apr 16, 2018

Accepted: Apr 17, 2018

Correspondence to

Woo Jin Hyung

Department of Surgery, Yonsei University
College of Medicine, 50-1 Yonsei-ro,
Seodaemun-gu, Seoul 03722, Korea.
E-mail: wjhyung@yuhs.ac

*In Cho and Younsun Son contributed equally
to this work.

Copyright © 2018. Korean Gastric Cancer
Association

This is an Open Access article distributed
under the terms of the Creative Commons
Attribution Non-Commercial License ([https://
creativecommons.org/licenses/by-nc/4.0](https://creativecommons.org/licenses/by-nc/4.0))
which permits unrestricted noncommercial
use, distribution, and reproduction in any
medium, provided the original work is properly
cited.

ORCID iDs

Woo Jin Hyung
<https://orcid.org/0000-0002-8593-9214>

Funding

This work was supported by the technology
commercialization R&D program of the Small &
Medium Business Administration (S2078437).

Author Contributions

Conceptualization: C.I., S.Y., H.W.J.; Data
curation: C.I., S.Y., S.S., B.Y.J.; Formal analysis:
K.Y.N., K.H., L.D.T.; Funding acquisition:
B.Y.J., L.D.T., H.W.J.; Investigation: H.W.J.;
Methodology: C.I., S.Y., L.D.T., H.W.J.;

¹Department of Surgery, Graduate School, Yonsei University College of Medicine, Seoul, Korea

²Department of Surgery, Soonchunhyang University College of Medicine, Bucheon, Korea

³Exercise Physiology Laboratory, Kookmin University, Seoul, Korea

⁴Medi Plus Solution, Seoul, Korea

⁵Department of Biostatistics, Yonsei University College of Medicine, Seoul, Korea

⁶Department of Surgery, Yonsei University College of Medicine, Seoul, Korea

⁷Gastric Cancer Center, Yonsei Cancer Center, Yonsei University Health System, Seoul, Korea

⁸Sports, Health, and Rehabilitation Major, Kookmin University, Seoul, Korea

⁹Robot and MIS Center, Severance Hospital, Yonsei University Health System, Seoul, Korea

ABSTRACT

Purpose: Exercise intervention after surgery has been found to improve physical fitness and quality of life (QOL). The purpose of this study was to investigate the feasibility and effects of a postoperative recovery exercise program developed specifically for gastric cancer patients (PREP-GC) undergoing minimally invasive gastrectomy.

Materials and Methods: Twenty-four patients treated surgically for early gastric cancer were enrolled in the PREP-GC. The exercise program comprised sessions of In-hospital Exercise (1 week), Home Exercise (1 week), and Fitness Improvement Exercise (8 weeks). Adherence and compliance to PREP-GC were evaluated. In addition, body composition, physical fitness, and QOL were assessed during the preoperative period, after the postoperative recovery (2 weeks after surgery), and upon completing the PREP-GC (10 weeks after surgery).

Results: Of the 24 enrolled patients, 20 completed the study without any adverse events related to the PREP-GC. Adherence and compliance rates to the Fitness Improvement Exercise were 79.4% and 99.4%, respectively. Upon completing the PREP-GC, patients also exhibited restored cardiopulmonary function and muscular strength, with improved muscular endurance and flexibility ($P < 0.05$). Compared to those in the preoperative period, no differences were found in symptom scale scores measured using the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30) and Quality of Life Questionnaire-Stomach Cancer-Specific Module (QLQ-STO22); however, higher scores for global health status and emotional functioning were observed after completing the PREP-GC ($P < 0.05$).

Conclusions: In gastric cancer patients undergoing minimally invasive gastrectomy, PREP-GC was found to be feasible and safe, with high adherence and compliance. Although randomized studies evaluating the benefits of exercise intervention during postoperative recovery are

Project administration: B.Y.J., L.D.T, H.W.J.;
Resources: C.I., S.Y., S.S.; Software: C.I., S.Y.,
S.S.; Supervision: K.H., B.Y.J., L.D.T, H.W.J.;
Validation: K.Y.N., B.Y.J., L.D.T, H.W.J.;
Visualization: C.I. S.Y.; Writing - original draft:
C.I., S.Y., S.S., B.Y.J., K.Y.N., K.H., L.D.T., H.W.J.;
Writing - review & editing: C.I., S.Y., S.S., B.Y.J.,
K.Y.N., K.H., L.D.T., H.W.J.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

This study was presented at the American College of Sports Medicine (ACSM)'s 61st Annual Meeting and the 5th World Congress on Exercise in Medicine® in Indianapolis, Indiana, USA on May 28–29, 2014.

needed, surgeons should encourage patients to participate in systematic exercise intervention programs in the early postoperative period (Registered at the ClinicalTrials.gov, NCT01751880).

Keywords: Exercise; Gastric cancer; Recovery; Minimally invasive surgery

INTRODUCTION

While early detection and advances in cancer treatment have facilitated steady increases in the survival of gastric cancer patients, improvement in the quality of life (QOL) after surgery continues to be pursued, even in the early postoperative period. Accordingly, minimally invasive surgery (MIS) to treat gastric cancer has garnered increasing popularity owing to more rapid recovery and shorter hospital stays after surgery than those after open surgery [1,2]. Apart from advances in surgical techniques, dedicated management tools such as exercise and dietary programs during the postoperative recovery can also be helpful in improving the QOL after surgery.

Exercise intervention after surgery has been found to improve physical fitness and QOL and to reduce treatment-related side effects in several organ cancers, such as breast, colorectal, prostate, and hematological malignancies [3-8]. However, most studies have only assessed exercise intervention that is conducted after full recovery from surgery or on completion of treatment. No exercise program has been devised for use during the postoperative recovery, especially after MIS for gastric cancer. Thus, evidence is still lacking regarding the feasibility of applying exercise intervention to patients undergoing MIS for gastric cancer during the early postoperative period.

Accordingly, we developed a postoperative recovery exercise program developed specifically for gastric cancer patients (PREP-GC) after minimally invasive gastrectomy. This study investigated the safety and feasibility of the PREP-GC in gastric cancer patients who underwent MIS. Moreover, we evaluated and compared body composition, physical status, and QOL before surgery and after completing the PREP-GC.

MATERIALS AND METHODS

Study design

This study was designed as a prospective, single-arm, interventional study to assess the feasibility and effects of PREP-GC in gastric cancer patients after minimally invasive gastrectomy. PREP-GC consisted of sessions of In-hospital Exercise (1 week), Home Exercise (1 week), and Fitness Improvement Exercise (8 weeks). All patients were assessed preoperatively, after postoperative recovery (2 weeks after surgery), and upon completion of the PREP-GC (10 weeks after surgery). This study was reviewed and approved by the Institutional Review Board of Severance Hospital, Yonsei University College of Medicine (4-2012-0221) and registered with ClinicalTrials.gov (NCT01751880).

Patients

Patients were recruited between August 2012 and August 2013. **Fig. 1** shows the flow of patient enrollment. The following criteria for patient inclusion were applied: 1) pathologically proven gastric adenocarcinoma, 2) age between 20–70 years, 3) preoperative diagnosis

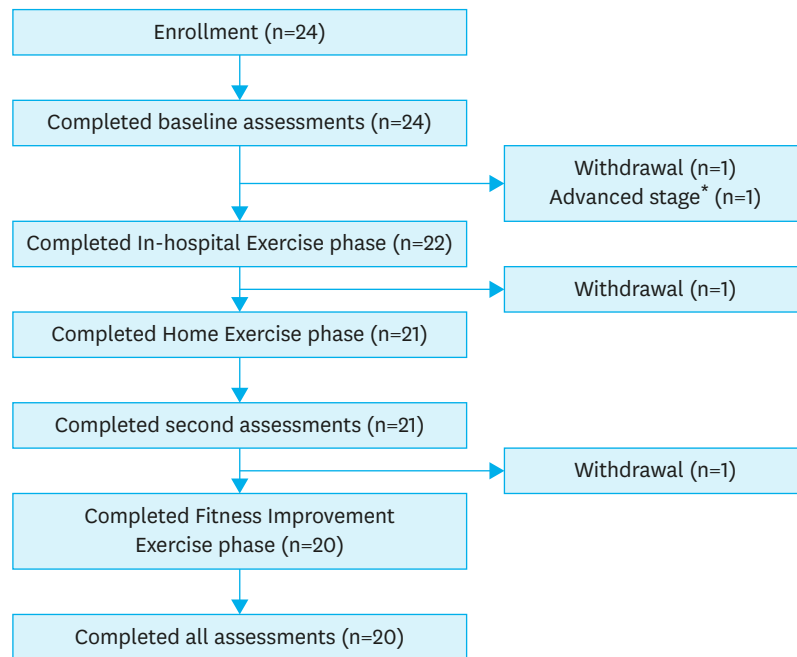


Fig. 1. CONSORT flow diagram.
 CONSORT = CONSolidated Standards Of Reporting Trials.
 *Excluded since postoperative chemotherapy was required.

of early gastric cancer, 4) consent to undergo MIS (laparoscopic or robotic), 5) Eastern Cooperative Oncology Group score of 0 to 1, 6) no regular exercise during the previous 6 months, and 7) submission of signed informed consent to participate in the study. The following criteria were used for patient exclusion: 1) pregnancy or plans to become pregnant, 2) cognitive disabilities, 3) history of other primary cancer, 4) history of major abdominal surgery, or 5) presence of cardiopulmonary medical comorbidities. All patients were freely permitted to withdraw from the study at any time.

Surgery

All patients underwent laparoscopic or robotic gastrectomy. Five trocars were utilized for surgery, with a 10-mm trocar placed just below the umbilicus for a camera port and an additional 4 trocars for working ports. Standard radical subtotal or total gastrectomy with partial omentectomy and D1+ or more extended lymphadenectomy was performed on the basis of Japanese gastric cancer treatment guidelines [9]. After gastric resection, gastroduodenostomy, loop gastrojejunostomy, or Roux-en-Y esophagojejunostomy was performed intracorporeally. Resected specimens were retrieved through extension of an umbilical incision up to 3 cm.

Postoperative management

Following the operation, all patients with no serious comorbidities were sent to the general ward. A Foley catheter was indwelled after general anesthesia in the operating room and was removed on postoperative day 1. No nasogastric tube was inserted in any patient and a drain was inserted for selected patients. Postoperative pain control was achieved with intravenous patient-controlled anesthesia over the first 2 postoperative days. After these 2 days, intravenous painkillers were administered when required. When tolerated, water was given from postoperative day 2, a liquid diet was started on postoperative day 3, and a soft diet was started on postoperative day 4. Patients were discharged after 1 day of soft diet with no complications.

PREP-GC after minimally invasive gastrectomy

The exercise program was divided into 3 phases: In-hospital Exercise, Home Exercise, and Fitness Improvement Exercise (Fig. 2). In-hospital Exercise was conducted during hospitalization for 5 to 7 days. The exercises were chosen to facilitate anatomical adaptation and to help increase range of motion after minimally invasive gastrectomy. Patients were asked to perform each exercise for 5–10 seconds and were encouraged to perform a minimum of 2 sets of all exercises under the supervision of exercise specialists (SY and SS). Walking without supervision was encouraged as much as possible. The 1-week Home Exercise was designed to improve the range of motion after discharge from the hospital, without supervision. Patients were provided a handout illustrating the Home Exercise regimen, which exercise specialists used to educate patients. The patients were encouraged to complete the Home Exercise regimen more than once per day and to report their daily activity using an exercise log. By mainly focusing on resistance exercises, the Fitness Improvement Exercise was designed to improve reduction in muscle volume and function resulting from surgery. Patients were instructed to exercise 3 times a week at an appointed place and time with a small group of 1 to 2 patients under the supervision of accredited exercise specialists. Each session comprised a warm-up, a resistance exercise, and a cool-down phase. Patients were instructed to warm-up and cool-down for 10 minutes via low-level aerobic exercise and stretching before and after performing the resistance exercises. The 8 weeks of resistance exercise were divided into four 2-week periods, during which patients were to complete 4 different regimens of increasing strenuousness on the abdominal area. The resistance exercises included weight-bearing exercises, along with some upper-body work with

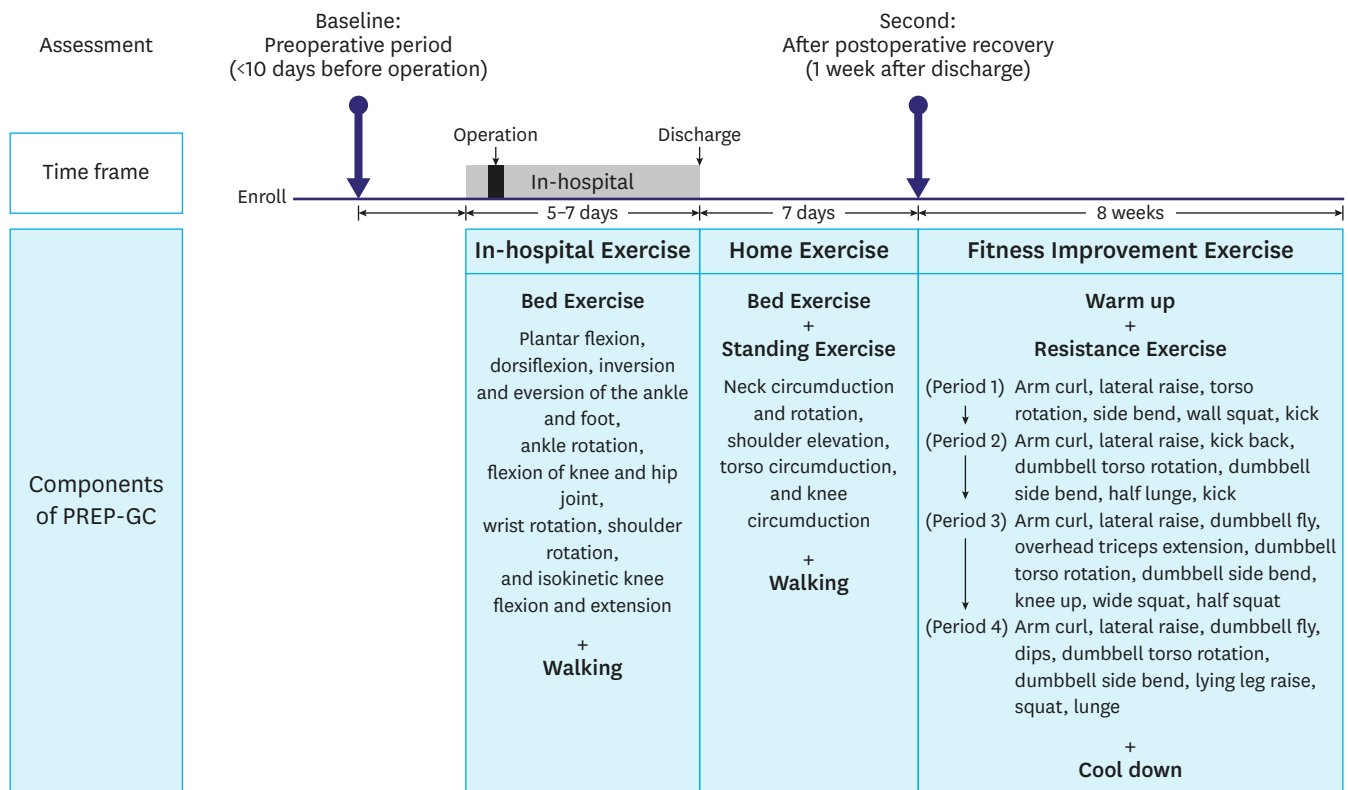


Fig. 2. Study scheme. PREP-GC = postoperative recovery exercise program for gastric cancer patients.

dumbbells or elastic bands. During the Fitness Improvement Exercise phase, exercise specialists led patients to exercise at a perceived exertion of 12 to 14 (somewhat hard) on the Borg Scale [10].

Primary outcome measures

The safety of PREP-GC was assessed as the incidence of adverse events (AEs, any clinical symptoms and signs) on exercise. The feasibility of In-hospital Exercise was evaluated according to adherence to and completion of the planned exercise regimen. The feasibility of Home Exercise was determined by reviewing the patients' self-reports listing their daily performance and adherence to the prescribed exercise program. The feasibility of the Fitness Improvement Exercise was evaluated in terms of adherence and compliance to the exercise regimen. Adherence was defined as the number of completed sessions relative to the number of scheduled sessions with the exercise specialist. Compliance to each component was defined as the completion of exercises for the prescribed duration, frequency, and intensity as assessed by the exercise specialists. Any modification to the duration, frequency, or intensity of any exercise was considered as non-compliance.

Secondary outcome measures

Anthropometric parameters

All anthropometric parameters were measured by the same individual. Height and weight were measured to the nearest one decimal point. Circumference was measured according to the procedures outlined by the American College of Sports Medicine (ACSM) at the following 7 sites: abdomen, waist, upper arm, lower arm, hips, thigh, and calf. Subcutaneous fat thickness was measured at the following 7 sites: chest/pectoral, midaxillary, abdominal, suprailiac, subscapular, triceps, and thigh muscles. The technical error of all measurements was less than 0.3 mm [11]. The percent body fat was calculated using the 7-site Jackson Pollock skinfold equation [12].

Fat and muscle volume measurement using computed tomography (CT)

To determine standard CT values for muscle and fat volume, muscle CT cross-sectional areas of whole muscular components at each section and fatty CT cross-sectional areas of visceral and subcutaneous fat were obtained (**Fig. 3**). Regions of interest were drawn at a pre-specified level, including the whole muscle, to generate region of interest values. Data were acquired with a Multi-Detector Row CT scanner (Somatom Sensation 64 and 128, Siemens Medical System, Erlangen, Germany; Light Speed VCT 64 or Discovery 750-HD 64, General Electric Medical Systems, Milwaukee, WI, USA). Cross-sectional areas were measured at the levels of T11-12, L2-3, L3-4, and L4-5. CT imaging was performed with a 512×512 matrix and a tube

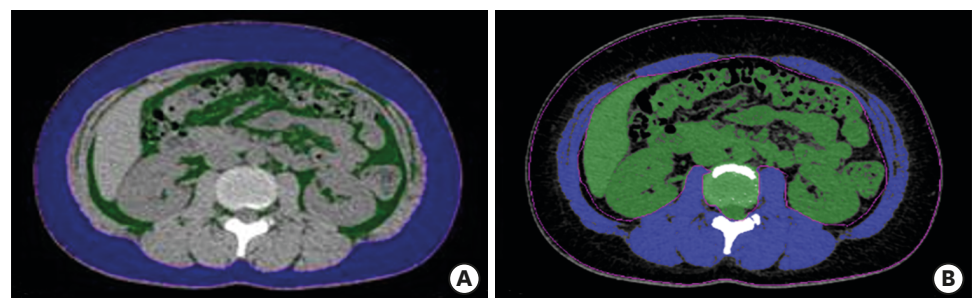


Fig. 3. Computed tomography-based calculation of muscle and fat volume. (A) Intervertebral subcutaneous (blue) and visceral (green) fat volume measurements. (B) Intervertebral muscle volume measurement (blue).

voltage of 120 kV. CT values were transferred to commercial three-dimensional software (Aquarius iNtuition, version 4.4.11, TeraRecon, California, CA, USA) and analyzed.

Physical fitness measurement (cardiopulmonary function and muscular endurance, strength, and flexibility)

To measure cardiopulmonary function, a cardiopulmonary exercise test using a modified Bruce protocol was utilized [13]. Prior to testing, the resting heart rate, blood pressure, and electrocardiograms (ECG) were recorded. After the beginning the exercise session, 12-lead ECG, heart rate, blood pressure, and rating of perceived exertion (Borg 6 to 20 scale) assessments were taken at 3-minute intervals. Patients were instructed to perform each test for as long as possible to ensure a true maximal attempt. Standard ACSM test termination criteria were monitored and followed throughout each test [11]. Breath-by-breath data were collected using a K4B2 Metabolic Measurement System (Cosmed, Rome, Italy) using real-time analysis.

To measure muscular endurance, a chair stand test and wall half squat test were used. The chair stand test was conducted to assess leg strength and endurance and measured the number of times a person could rise from a chair in 30 seconds [14]. The wall half squat test was administered to assess leg strength, targeting the quadriceps muscle. To perform the exercise, the participant assumed a sitting position with their back against a wall, feet flat on the ground, at a 90° angle at the hips and knees for as long as possible [15].

Muscular strength was measured by grip strength. To test grip strength, patients stood with their upper limbs relaxed down to the sides of their body and with their palms toward the torso. The elbow was extended without any flexion. The patients were then encouraged to exert their maximal grip [16]. The maximum force in kilograms was taken after 2 consecutive attempts in each hand using a dynamometer (TTM, Tokyo, Japan).

To measure flexibility, a back-stretch exercise and a sit-and-reach exercise were used. The back-stretch exercise measured upper arm and shoulder girdle flexibility, whereas the sit-and-reach test measured lower flexibility.

QOL

QOL was assessed using validated Korean versions of the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Stomach Cancer-Specific Module (EORTC QLQ-STO22) [17,18]. All scales and single item measures ranged in score from 0 to 100. Missing values were processed as recommended in the EORTC QLQ-C30 scoring manual [19].

Statistical analysis

Data are expressed as mean±standard deviation (SD) or frequency (percent). Data were evaluated using repeated-measures analysis of variance (ANOVA) to assess differences in study outcomes at the 3 assessment points (preoperative period, 1 week after discharge, and after completing PREP-GC). Outcomes for which only 2-time points were available were analyzed using Student's t-test. A P-value less than 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics, version 20 (SPSS Inc., Chicago, IL, USA).

RESULTS

Patients

Initially, 24 patients agreed to participate in the study and underwent baseline assessment. Of these, 4 patients dropped out of the study: 3 patients withdrew due to difficulty with traveling to the place of exercise intervention after baseline assessment, during the Home Exercise program, and after the follow-up assessment at 1 week after discharge, respectively; the other patient was excluded due to advanced disease requiring adjuvant chemotherapy. Finally, 20 patients completed the PREP-GC and were included in the analyses of body composition, physical fitness, and QOL (Table 1).

The patients who completed PREP-GC (n=20) were aged 30–64 years (mean, 45.9 years). Eleven patients were male (55%) and 9 were female (45%). The mean body mass index (BMI) was 24.0±3.2, and most patients (70%) were overweight or obese (BMI >25 kg/m²). The majority of patients underwent robotic surgery (60%), subtotal gastrectomy (95%), or gastroduodenostomy (60%). Because all of the patients were diagnosed with early gastric cancer preoperatively, D1+ lymphadenectomy was primarily performed (95%). There were no complications higher than grade III according to the Clavien-Dindo classification [20] and no deaths reported.

Safety and feasibility

None of the patients who participated in PREP-GC experienced any AEs related to the exercise program. During the In-hospital Exercise phase, all patients (n=22) participated in and finished the planned exercise program without modification (adherence and compliance rates of 100%). During the Home Exercise phase (n=21), 16 patients completed the prescribed exercise program; 4 patients completed the exercise program with modification; and one did not perform any of the exercises (adherence and compliance rates of 95.2%

Table 1. Patient demographics and clinicopathological features

Variables	Values
No. of patients	20
Age (yr)	45.90±10.31 (30–64)
Sex	
Male	11 (55)
Female	9 (45)
BMI (kg/m ²)	24.0±3.2 (17.6–30.6)
Operation method	
Laparoscopic	8 (40)
Robotic	12 (60)
Operation extent	
Subtotal	19 (95)
Total	1 (5)
Reconstruction	
Gastroduodenostomy	12 (60)
Loop gastrojejunostomy	7 (35)
Roux-en-Y esophagojejunostomy	1 (5)
Lymph node dissection	
D1+	19 (95)
D2	1 (5)
Pathologic stage	
Stage Ia	15 (75)
Stage Ib	5 (25)

Data shown are number (%) or mean±standard deviation (range).
BMI = body mass index.

and 80%, respectively). During the Fitness Improvement Exercise (n=20), 14 patients (70%) participated in over 20 of the 24 scheduled exercise sessions (mean±SD, 22.4±1.3). The adherence to the Fitness Improvement Exercise was 79.4%±23.9%. An adherence greater than 80% was recorded for 14 patients, while adherence of 60%–79%, 40%–59%, and <40% was recorded for one, three, and 2 patients, respectively. Six patients recorded below-average attendance with a mean adherence rate of 45% for different reasons: having gout (n=1), not interested in the program (n=1), planned a long-term overseas trip (n=1), and had an early return to work (n=3). With the exception of these 6 patients, 14 patients attended 93.5% of the exercise sessions.

Nine patients completed the Fitness Improvement Exercise regimen without any modification, whereas 11 patients completed it with modifications. Only 17 (0.6%) of the total 2,908 exercise components performed were modified during the Fitness Improvement Exercise phase. Compliance during the Fitness Improvement Exercise was 99.4%. Three modifications were recorded for a single patient, while 2 modifications and a single modification were observed for 4 and 6 patients, respectively. Major reasons for modification were incision site pain caused by “side bend” and dizziness. Nevertheless, the patients continued to follow the Fitness Improvement Exercise without exacerbation of symptoms. Other reasons for modification included pre-existing medical conditions before surgery, such as intermittent arthralgia.

Changes in body composition and physical fitness

Body weight decreased significantly during postoperative recovery (61.6±10.2 kg) and after completing the PREP-GC (60.6±9.9 kg) compared to the preoperative period (65.1±11.8 kg) (P<0.001). Skinfolds and circumferences at all sites were also significantly reduced after completion of the PREP-GC (P<0.05), except for the circumference of the lower arm. Thigh circumference measurement was significantly higher after completion of the PREP-GC than during postoperative recovery (2.61%±5.4%, P<0.05), although it was still significantly less than that in the preoperative period (4.56%±5.5%, P<0.001) (Fig. 4).

Both visceral fat and subcutaneous fat volumes on CT images decreased at all measured levels upon completion of the PREP-GC compared to the preoperative period. In particular, statistically significant decreases were observed for visceral fat and subcutaneous fat at level L4–5 and subcutaneous fat at level L3–4 (P=0.011, 0.029, and 0.034, respectively).

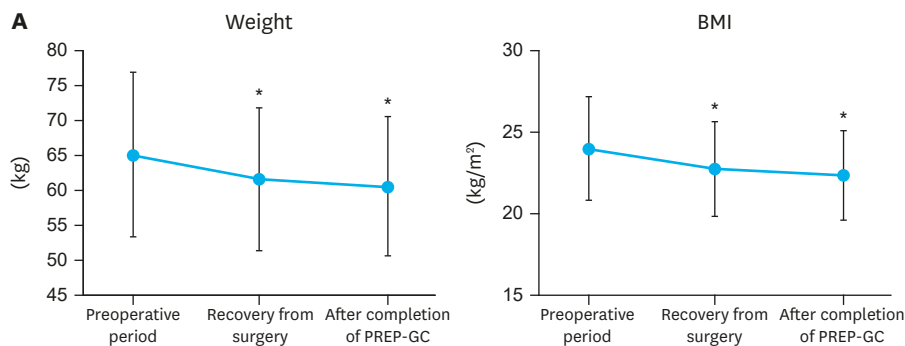


Fig. 4. Changes in body composition and physical fitness. (A) Body weight and BMI. (B) Fat and muscle volume based on CT. (C) Circumference measurements at each site. (D) Skinfold measurements at each site. BMI = body mass index; CT = computed tomography; PREP-GC = postoperative recovery exercise program developed specifically for gastric cancer patients. *P<0.05 versus preoperative period; †P<0.05 versus after postoperative recovery. (continued to the next page)

Exercise Program after Gastrectomy

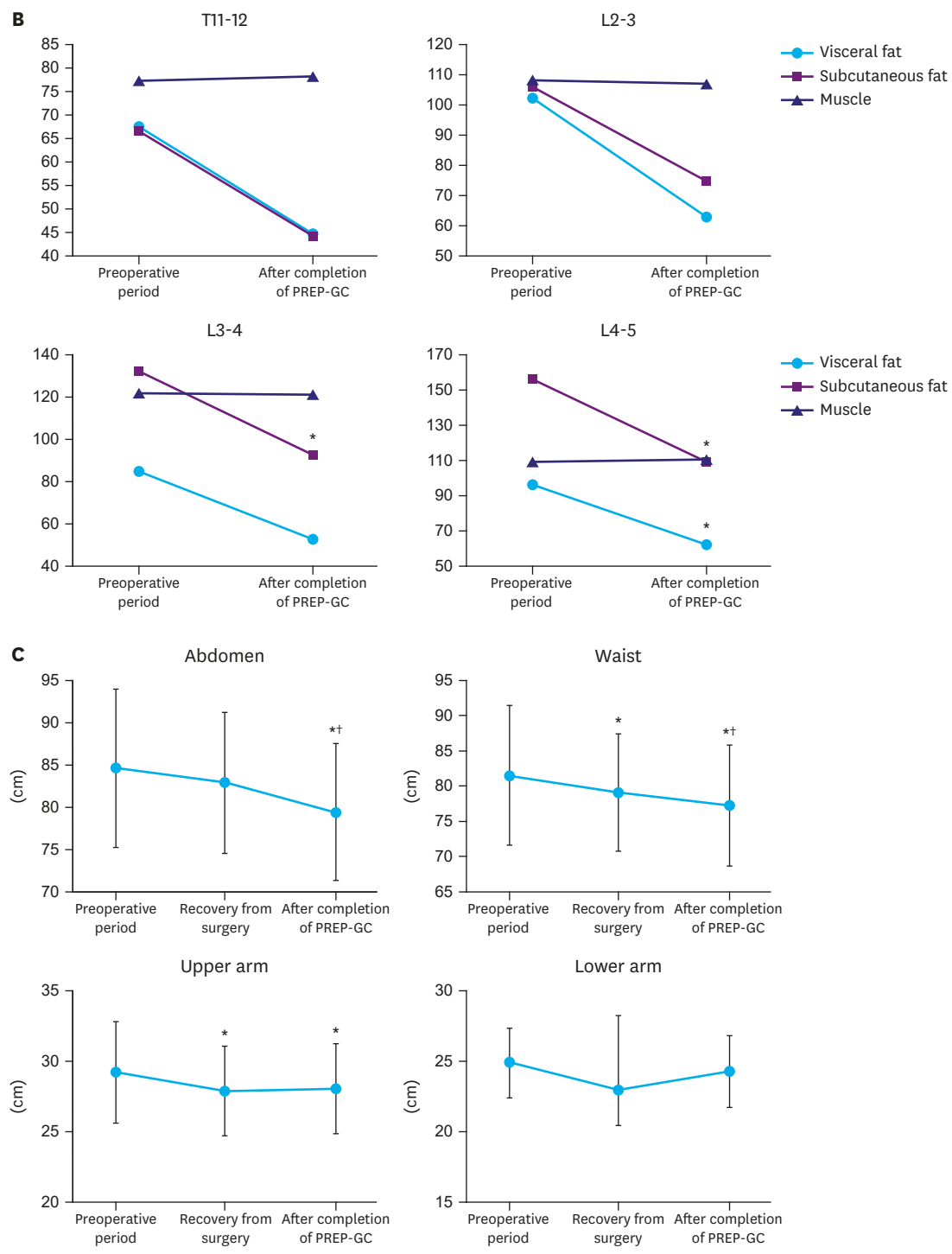


Fig. 4. (Continued) Changes in body composition and physical fitness. (A) Body weight and BMI. (B) Fat and muscle volume based on CT. (C) Circumference measurements at each site. (D) Skinfold measurements at each site. BMI = body mass index; CT = computed tomography; PREP-GC = postoperative recovery exercise program developed specifically for gastric cancer patients. *P<0.05 versus preoperative period; †P<0.05 versus after postoperative recovery. (continued to the next page)

Exercise Program after Gastrectomy

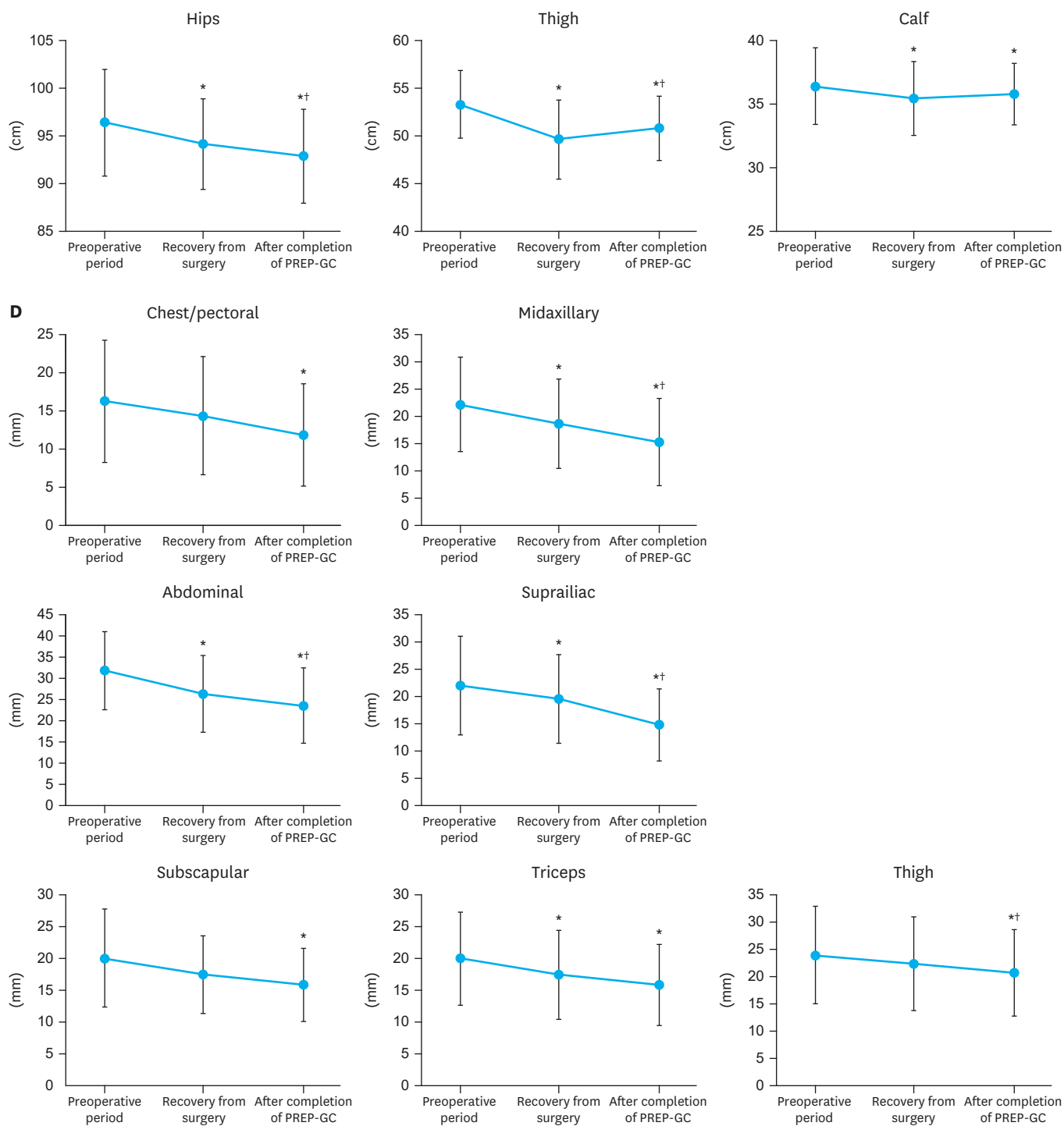


Fig. 4. (Continued) Changes in body composition and physical fitness. (A) Body weight and BMI. (B) Fat and muscle volume based on CT. (C) Circumference measurements at each site. (D) Skinfold measurements at each site. BMI = body mass index; CT = computed tomography; PREP-GC = postoperative recovery exercise program developed specifically for gastric cancer patients. * $P < 0.05$ versus preoperative period; † $P < 0.05$ versus after postoperative recovery.

Table 2. Effects of the PREP-GC on physical fitness

Effects	Preoperative period (n=20)	After postoperative recovery (n=20)	Completion of PREP-GC (n=20)	P-value
Cardiorespiratory endurance				
Relative VO ₂ peak (mL/kg/min)	35.1±6.5	29.3±5.5*	35.8±6.3 [†]	<0.001
Absolute VO ₂ peak (mL/min)	2,268.5±618.1	1,801.1±437.7*	2,164.0±505.2 [†]	<0.001
Muscular endurance				
Chair stand (unit/30 sec)	24.3±5.2	22.2±5.4*	28.8±5.3* [†]	<0.001
Wall half squat (sec)	39.2±16.5	25.4±12.6*	71.2±32.7* [†]	<0.001
Muscular strength				
Grip strength (kg)	30.1±8.1	28.5±8.4	30.0±8.3 [†]	0.046
Flexibility				
Back stretch (cm)	-6.9±9.5	-7.4±9.8	-5.4±9.2* [†]	0.006
Sit and reach (cm)	6.9±11.0	4.6±12.5*	9.3±10.4* [†]	<0.001

The P-values indicate analysis of variance results.

PREP-GC = postoperative recovery exercise program developed specifically for gastric cancer patients; VO₂ peak = peak oxygen consumption.

*P<0.05 versus preoperative period; [†]P<0.05 versus after postoperative recovery.

Meanwhile, no significant differences in muscle volumes were recorded between the preoperative period and upon completion of the PREP-GC at any measured level.

All parameters related to physical fitness changed significantly upon completion of the PREP-GC. Compared to that during the preoperative period, the peak oxygen consumption (VO₂ peak) significantly decreased during postoperative recovery and then increased to the preoperative level upon completing the PREP-GC. The chair stand, wall half squat, and sit and reach measurements significantly decreased in the postoperative recovery period and significantly increased upon completion of the PREP-GC, compared to baseline measurements (**Table 2**).

Changes in QOL

Global health status reduced significantly during the postoperative recovery period and improved upon completion of the PREP-GC when compared to the preoperative period (**Fig. 5**). Emotional functioning improved significantly upon completing the PREP-GC compared to the preoperative and postoperative recovery periods. The other functional measures all declined after postoperative recovery, but recovered upon completing the PREP-GC. Fatigue, nausea and vomiting, pain, and dyspnea scores on symptoms scales were highest after the postoperative recovery period but recovered to scores similar to those in the preoperative period upon completing the PREP-GC. Appetite loss scores were significantly lower upon completing the PREP-GC than those after postoperative recovery; there were no differences between appetite loss scores during the preoperative period and after completing the PREP-GC. Moreover, scores for dysphagia, abdominal pain, and disorders of taste increased significantly after postoperative recovery compared to the preoperative period, although they recovered upon completing the PREP-GC.

DISCUSSION

In the present study, we found that PREP-GC was safe and feasible for use in gastric cancer patients who underwent minimally invasive gastrectomy, with a high adherence and compliance rate and no AEs. Compared to preoperative measurements, anthropometric parameters, and muscle volumes were well preserved with the PREP-GC, whereas fat volumes significantly decreased. Moreover, completion of the PREP-GC recovered and improved physical fitness status and QOL.

Exercise Program after Gastrectomy

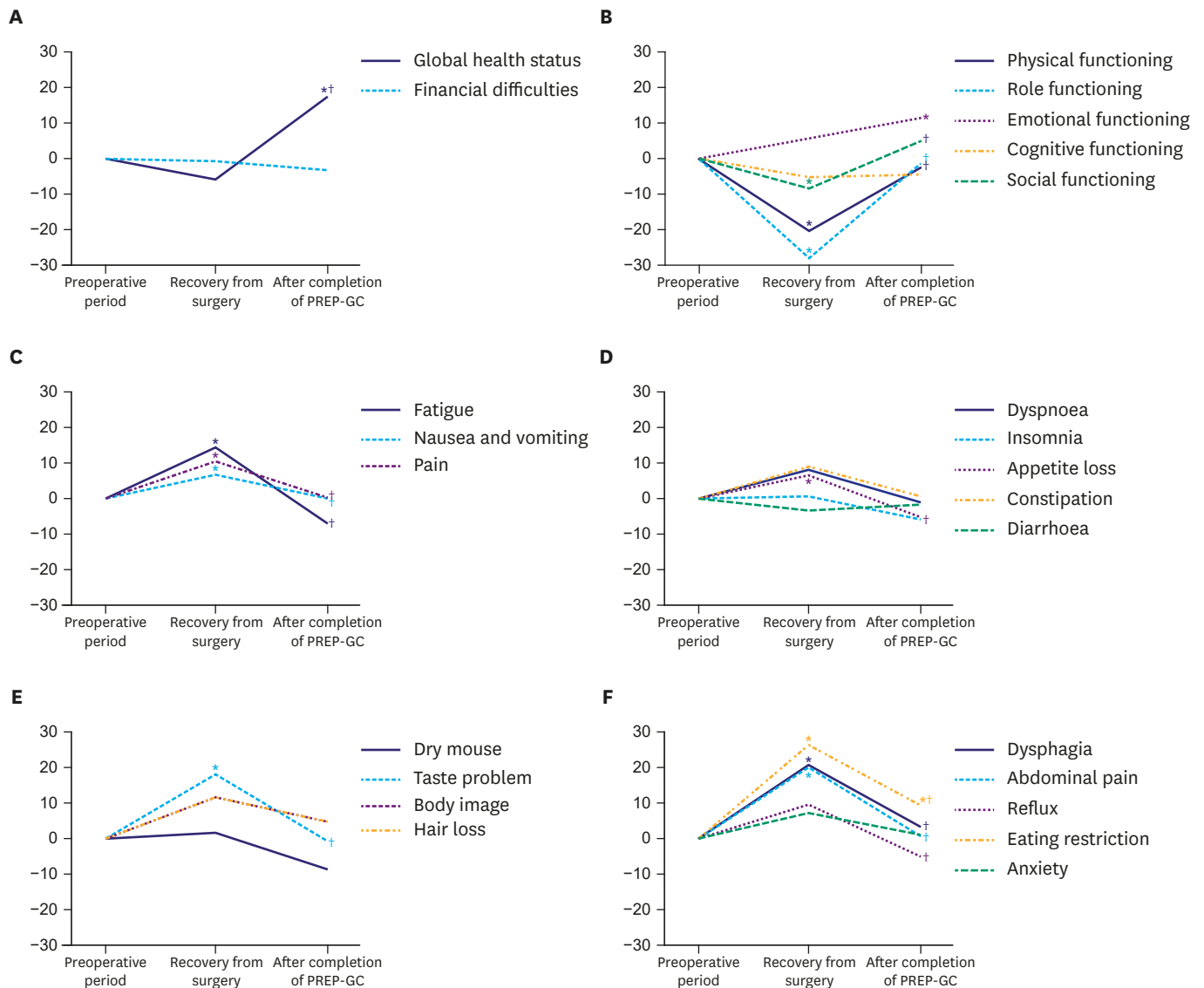


Fig. 5. Changes in QOL. (A, B) Mean changes in QOL score by EORTC QLQ-C30. (C-F) Mean changes in EORTC QLQ-STO22. QOL = quality of life; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire; EORTC QLQ-STO22 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Stomach Cancer-Specific Module. *P<0.05 versus preoperative period; †P<0.05 versus after postoperative recovery.

Adherence and compliance rates to the PREP-GC were high and similar to those reported in previous studies on patients undergoing abdominal surgery [4,21,22] and to the rates derived from a systematic review on the health effects of exercise during cancer rehabilitation [23]. Notwithstanding, the subjects in these previous studies were all cancer survivors who had completed treatment. The high adherence in our study is important as the exercise intervention was conducted beginning from the early postoperative period. Achieving high adherence was possible owing to the advantages of MIS, tailoring the exercise program specifically for gastric cancer patients, and the supervision by an exercise specialist of the program. MIS facilitates reduced postoperative pain and early functional recovery [24], making early exercise intervention feasible. The specialized exercise program, comprising tension-free motion at the upper abdomen and maintenance of erect movements to prevent esophageal regurgitation, allowed participants to complete the exercise regimen without

any AEs. Additionally, the exercise specialists ensured proper physical form and provided emotional support throughout the program. Nevertheless, we found that side bend caused some incision site pain, which reduced compliance and might have resulted in potential adverse effects. Therefore, we suggest that the side bend motion be limited and applied carefully during the early postoperative period after upper abdominal surgery.

In this study, we found that the relative VO_2 peak and the absolute VO_2 peak values decreased by approximately 15% and 20%, respectively, during postoperative recovery. Studies have established that exercise training can improve these values by about 15%–20% in healthy middle-aged individuals [25]. Upon completing the PREP-GC, we also observed improvements of about 23% in relative VO_2 peak and 21% in absolute VO_2 peak. Therefore, we suggest that early gastric cancer patients subjected to MIS can experience improvements in cardiopulmonary function similar to those in healthy individuals. Another unique finding of this study was that the PREP-GC led to clinically important improvements in muscular endurance. Of particular note, patients in this study not only showed recovery of their physical fitness with a return to baseline levels but also exhibited improvements above their preoperative measurements, despite body weight loss.

In this study, muscle volumes measured on CT scans were well preserved after completing the PREP-GC, even though the patient's total body weight decreased as also observed in most studies [26–28]. Muscle mass reportedly decreases significantly in the early postoperative period, failing to recover to baseline levels at 6 months after a gastrectomy [26]. In the present study, the mean weight loss was 4.59 kg (7.2%), which is similar to that in previous reports. However, muscle volumes at 10 weeks after surgery completely recovered to their preoperative level. This finding suggests that early postoperative exercise could prevent muscle volume consumption, thereby maintaining muscular strength, endurance, and function.

According to a comparative study on QOL after gastrectomy, most function and symptom scales do not recover until 6 months after surgery [29,30]. Moreover, a randomized controlled study on QOL after gastrectomy showed a better QOL is achieved for patients undergoing laparoscopy-assisted gastrectomy compared to open surgery; nevertheless, most QOL parameters still did not return to their baseline levels at 90 days after surgery [27]. Our newly developed systemic postoperative exercise program, however, provided full recovery of baseline QOL within 10 weeks after MIS. Accordingly, we suggest that exercise starting from the early postoperative period could facilitate faster recovery of QOL after minimally invasive gastrectomy.

At present, we believe this study to be the first prospective interventional study to validate the safety and feasibility of an exercise intervention program designed specifically for gastric cancer patients undergoing gastrectomy using a comprehensive assessment of anthropometric parameters, body composition using CT scan, physical fitness, and QOL. As a distinctive feature of our study, we enrolled patients who underwent MIS of the upper abdomen in exercise intervention from the very early postoperative period (postoperative day 1). Despite the positive findings, this study has several limitations. Because this was a single-arm, non-comparative study, we could not evaluate the benefits of PREP-GC in comparison to no exercise intervention. Currently, we are carrying out a randomized controlled study (NCT01637909) to address this limitation. Furthermore, we only included patients undergoing MIS without any scheduled chemotherapy. Additionally, the majority of the enrolled patients were young, well-educated, and lived in a large city, which limits the

generalizability of our results. A study with expanded inclusion criteria for patients, such as older age, conventional open surgery, and receiving chemotherapy, should be performed in the future. Additionally, diet and routine physical activity were not measured and controlled for in this study. Future studies addressing these issues will provide more precise evaluation of the effects of PREP-GC after surgery.

In conclusion, we found our newly developed postoperative exercise program, PREP-GC, to be feasible and safe, facilitating the recovery and improvement of physical fitness and QOL after MIS for gastric cancer patients. For improved care of gastric cancer patients after minimally invasive gastrectomy, surgeons should encourage gastric cancer patients to participate in systematic exercise intervention programs in the early postoperative period. Meanwhile, results from randomized studies evaluating the benefits of exercise intervention during postoperative recovery are needed.

ACKNOWLEDGMENTS

We would like to thank Anthony Milliken for his help with editing the manuscript. We acknowledge the assistance of BioScience Writers, LLC (Houston, TX, USA) in copyediting of the manuscript and corrections of English language usage.

REFERENCES

1. Lee JH, Kim KM, Cheong JH, Noh SH. Current management and future strategies of gastric cancer. *Yonsei Med J* 2012;53:248-257.
[PUBMED](#) | [CROSSREF](#)
2. Akoh JA, Macintyre IM. Improving survival in gastric cancer: review of 5-year survival rates in English language publications from 1970. *Br J Surg* 1992;79:293-299.
[PUBMED](#) | [CROSSREF](#)
3. Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. *J Clin Oncol* 2003;21:1660-1668.
[PUBMED](#) | [CROSSREF](#)
4. Sellar CM, Bell GJ, Haennel RG, Au HJ, Chua N, Courneya KS. Feasibility and efficacy of a 12-week supervised exercise intervention for colorectal cancer survivors. *Appl Physiol Nutr Metab* 2014;39:715-723.
[PUBMED](#) | [CROSSREF](#)
5. Zopf EM, Bloch W, Machtens S, Zumbe J, Rubben H, Marschner S, et al. Effects of a 15-month supervised exercise program on physical and psychological outcomes in prostate cancer patients following prostatectomy: the prorehab study. *Integr Cancer Ther* 2015;14:409-418.
[PUBMED](#) | [CROSSREF](#)
6. Streckmann F, Kneis S, Leifert JA, Baumann FT, Kleber M, Ihorst G, et al. Exercise program improves therapy-related side-effects and quality of life in lymphoma patients undergoing therapy. *Ann Oncol* 2014;25:493-499.
[PUBMED](#) | [CROSSREF](#)
7. van Waart H, Stuiver MM, van Harten WH, Geleijn E, Kieffer JM, Buffart LM, et al. Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the PACES randomized clinical trial. *J Clin Oncol* 2015;33:1918-1927.
[PUBMED](#) | [CROSSREF](#)
8. Broderick JM, Guinan E, Kennedy MJ, Hollywood D, Courneya KS, Culos-Reed SN, et al. Feasibility and efficacy of a supervised exercise intervention in de-conditioned cancer survivors during the early survivorship phase: the PEACH trial. *J Cancer Surviv* 2013;7:551-562.
[PUBMED](#) | [CROSSREF](#)

9. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma. *Gastric Cancer* 2011;14:101-112.
[PUBMED](#) | [CROSSREF](#)
10. O'Sullivan SB. Perceived exertion. A review. *Phys Ther* 1984;64:343-346.
[PUBMED](#) | [CROSSREF](#)
11. Thompson WR, Gordon NF, Pescatello LS; American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription. 8th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2010.
12. Jackson AS, Pollock ML, Gettman LR. Intertester reliability of selected skinfold and circumference measurements and percent fat estimates. *Res Q* 1978;49:546-551.
[PUBMED](#)
13. American College of Sports Medicine. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 2009;41:687-708.
[PUBMED](#) | [CROSSREF](#)
14. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport* 1999;70:113-119.
[PUBMED](#) | [CROSSREF](#)
15. Escamilla RF, Zheng N, Imamura R, Macleod TD, Edwards WB, Hreljac A, et al. Cruciate ligament force during the wall squat and the one-leg squat. *Med Sci Sports Exerc* 2009;41:408-417.
[PUBMED](#) | [CROSSREF](#)
16. Chen CH, Ho C, Huang YZ, Hung TT. Hand-grip strength is a simple and effective outcome predictor in esophageal cancer following esophagectomy with reconstruction: a prospective study. *J Cardiothorac Surg* 2011;6:98.
[PUBMED](#) | [CROSSREF](#)
17. Fayers P, Bottomley AEORC Quality of Life GroupQuality of Life Unit. Quality of life research within the EORTC-the EORTC QLQ-C30. European Organisation for Research and Treatment of Cancer. *Eur J Cancer* 2002;38 Suppl 4:S125-S133.
[PUBMED](#) | [CROSSREF](#)
18. Yun YH, Park YS, Lee ES, Bang SM, Heo DS, Park SY, et al. Validation of the Korean version of the EORTC QLQ-C30. *Qual Life Res* 2004;13:863-868.
[PUBMED](#) | [CROSSREF](#)
19. Fayers PM, Aronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A. EORTC QLQ-C30 scoring manual. 3rd ed. Brussels: European Organisation for Research and Treatment of Cancer; 2001.
20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-213.
[PUBMED](#) | [CROSSREF](#)
21. Campo RA, Agarwal N, LaStayo PC, O'Connor K, Pappas L, Boucher KM, et al. Levels of fatigue and distress in senior prostate cancer survivors enrolled in a 12-week randomized controlled trial of Qigong. *J Cancer Surviv* 2014;8:60-69.
[PUBMED](#) | [CROSSREF](#)
22. Jensen W, Baumann FT, Stein A, Bloch W, Bokemeyer C, de Wit M, et al. Exercise training in patients with advanced gastrointestinal cancer undergoing palliative chemotherapy: a pilot study. *Support Care Cancer* 2014;22:1797-1806.
[PUBMED](#) | [CROSSREF](#)
23. Spence RR, Heesch KC, Brown WJ. Exercise and cancer rehabilitation: a systematic review. *Cancer Treat Rev* 2010;36:185-194.
[PUBMED](#) | [CROSSREF](#)
24. Son T, Kwon IG, Hyung WJ. Minimally invasive surgery for gastric cancer treatment: current status and future perspectives. *Gut Liver* 2014;8:229-236.
[PUBMED](#) | [CROSSREF](#)
25. Blair SN, Kohl HW 3rd, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. *JAMA* 1989;262:2395-2401.
[PUBMED](#) | [CROSSREF](#)
26. Abdiev S, Kodera Y, Fujiwara M, Koike M, Nakayama G, Ohashi N, et al. Nutritional recovery after open and laparoscopic gastrectomies. *Gastric Cancer* 2011;14:144-149.
[PUBMED](#) | [CROSSREF](#)
27. Kim YW, Baik YH, Yun YH, Nam BH, Kim DH, Choi JJ, et al. Improved quality of life outcomes after laparoscopy-assisted distal gastrectomy for early gastric cancer: results of a prospective randomized clinical trial. *Ann Surg* 2008;248:721-727.
[PUBMED](#) | [CROSSREF](#)

28. Aoyama T, Kawabe T, Hirohito F, Hayashi T, Yamada T, Tsuchida K, et al. Body composition analysis within 1 month after gastrectomy for gastric cancer. *Gastric Cancer* 2016;19:645-650.
[PUBMED](#) | [CROSSREF](#)
29. Misawa K, Fujiwara M, Ando M, Ito S, Mochizuki Y, Ito Y, et al. Long-term quality of life after laparoscopic distal gastrectomy for early gastric cancer: results of a prospective multi-institutional comparative trial. *Gastric Cancer* 2015;18:417-425.
[PUBMED](#) | [CROSSREF](#)
30. Kim AR, Cho J, Hsu YJ, Choi MG, Noh JH, Sohn TS, et al. Changes of quality of life in gastric cancer patients after curative resection: a longitudinal cohort study in Korea. *Ann Surg* 2012;256:1008-1013.
[PUBMED](#) | [CROSSREF](#)