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Short-term high-intensity interval training improves fitness before surgery: A randomized clinical trial

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Purpose: Improving cardiopulmonary reserve, or peak oxygen consumption($\dot{V}O_{2peak}$), may reduce postoperative complications; however, this may be difficult to achieve between diagnosis and surgery. Our primary aim was to assess the efficacy of an approximate 14-session, preoperative high-intensity interval training(HIIT) program to increase $\dot{V}O_{2peak}$ by a clinically relevant 2 $ml \cdot kg^{-1} \cdot min^{-1}$. Our secondary aim was to document clinical outcomes.

Methodology: In this prospective study, participants aged 45–85 undergoing major abdominal surgery were randomized to standard care or 14 sessions of HIIT over 4 weeks. HIIT sessions involved approximately 30 min of stationary cycling. Interval training alternated 1 min of high (with the goal of reaching 90% max heart rate at least once during the session) and low/moderate-intensity cycling. Cardiopulmonary exercise testing(CPET) measured the change in $\dot{V}O_{2peak}$ from baseline to surgery. Clinical outcomes included postoperative complications, length of stay(LOS), and Short Form 36 quality of life questionnaire(SF-36).

Results: Of 63 participants, 46 completed both CPETs and 50 completed clinical follow-up. There was a significant improvement in the HIIT group's mean ± SD $\dot{V}O_{2peak}$ (HIIT 2.87 ± 1.94 $ml \cdot kg^{1} \cdot min^{-1}$ vs standard care 0.15 ± 1.93, with an overall difference of 2.73 $ml \cdot kg^{1} \cdot min^{-1}$ 95%CI [1.53, 3.93] $p < 0.001$). There were no statistically significant differences between groups for clinical outcomes, although the observed differences consistently favored the exercise group. This was most notable for total number of complications (0.64 v 1.16 per patient, $p = 0.07$), SF-36 physical component score ($p = 0.06$), and LOS (mean 5.5 v 7.4 days, $p = 0.07$).

Conclusions: There was a significant improvement in $\dot{V}O_{2peak}$ with a four-week preoperative HIIT program. Further appropriately powered work is required to explore the impact of preoperative HIIT on postoperative clinical outcomes.

KEYWORDS
clinical outcomes, peak oxygen consumption, prehabilitation, preoperative exercise

1 | INTRODUCTION

Postoperative complications are common after major abdominal surgery, occurring in up to 40% of patients.[1,2] Unfortunately, important risk factors, such as the number of pre-existing comorbidities, the extent of the underlying pathology, and the magnitude of the required operation, cannot be changed prior to surgery. Most modifiable risk factors, such as smoking cessation[3] and optimizing specific medical problems, will improve the outcome in only a subset of patients. Cardiopulmonary fitness is the one modifiable risk factor that it may be possible to improve in a larger proportion of patients, by the introduction of preoperative aerobic exercise training. A peak oxygen consumption ($\dot{V}\,O_{2peak}$) below 18.6 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ [4] or an anaerobic threshold (AT) of <10–11 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$ [4–6] is associated with significantly higher rates of postoperative complications. High-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) are the most common methods of improving cardiopulmonary fitness. Studies in clinical populations have shown that HIIT results in substantial[5] and rapid[6,7] improvement in $\dot{V}\,O_{2peak}$ and is safe in those with coronary artery disease and cardiac failure.[7] HIIT is also appealing for preoperative patients because rapid improvement is important where there is a limited period of time between diagnosis and surgery.

There is an increasing body of evidence indicating that preoperative aerobic exercise can improve peak oxygen consumption. We identified eleven studies that document the impact of preoperative aerobic exercise on either peak oxygen consumption or AT in a four to six-week period before surgery.[8–18] All studies were conducted in patients undergoing major abdominal or thoracic procedures. All except two[14,16] demonstrated an improvement in oxygen consumption. All but one[18] had a small sample size, with 26 or fewer patients being exercised. Only four studies were randomized,[10,11,16,18] and only one was designed to prospectively assess postoperative complications.[18] Of the three studies that based their exercise program around the principles of HIIT,[8,11,16] two showed a significant improvement in $\dot{V}\,O_{2peak}$ of at least 2.0 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$,[8,11] while one showed no change in $\dot{V}\,O_{2peak}$.[16] In this context, we believe that further well-designed randomized studies are required to confirm the extent of the impact of preoperative HIIT on oxygen consumption and the volume of HIIT required to increase $\dot{V}\,O_{2peak}$. An important practical question is whether HIIT can be used to benefit the large number of major abdominal surgery patients whose time between diagnosis and surgery is brief (e.g., 4 weeks).

In terms of complications, although we know that fitter patients do better,[4,19,20] there are conflicting results in the literature when assessing the impact that improving preoperative cardiopulmonary fitness has on postoperative complications.[21] While some studies suggest that prehabilitation could reduce hospital stay[22,23] and the risk of specific complications such as chest infection,[22] the results of most reviews have been equivocal.[24] However, two recent randomized controlled trials (RCTs),[18,25] powered to assess complications, have demonstrated a statistically significant and clinically important reduction of complications after 6 weeks preoperative exercise. While these strengthen the evidence for prehabilitation to reduce complications, patients often have less than 6 weeks between diagnosis and surgery due to the urgency of required surgery.

In an effort to understand whether a short course of exercise "prehabilitation" can provide the benefits demonstrated in longer exercise interventions, this RCT compares a 4 weeks exercise program using HIIT against standard preoperative care for patients undergoing major abdominal surgery. The overarching objective of this study was to examine the impact of a focused, individualized HIIT exercise program over a 4 week period on both cardiopulmonary fitness and postoperative clinical outcomes. The primary hypothesis was that an individualized and supervised preoperative HIIT program would result in a clinically relevant increase in $\dot{V}\,O_{2peak}$ of 2 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ when compared to standard care.[8,11] The secondary hypothesis was that a HIIT program that delivers a clinically significant increase in cardiopulmonary fitness would also result in an improvement in clinical outcomes.

2 | METHODS

We performed a single center, two arm, parallel, prospective RCT comparing an exercise program using HIIT against standard preoperative care for patients undergoing major abdominal surgery. The study was approved by the Southern Health and Disability Ethics Committee (reference number 15/STH/116) and was registered with the Australasian Clinical Trials Registry (ACTRN12617000587303). An overview of the study design is presented in Figure 1 and in our protocol paper.[26] The inclusion criteria were patients aged 45–85 undergoing major abdominal surgery, who lived close enough to the hospital to attend multiple exercise sessions. Major abdominal surgery included a procedure expected to last two hours, or with an anticipated blood loss of greater than 500ml.[27] This included gastrointestinal resections, liver surgery, large abdominal wall hernia repair, abdominal aortic aneurysm repair, hysterectomy, radical prostatectomy, cystectomy, and nephrectomy. The exclusion criteria were as follows: (A) Inability to perform a CPET or a contraindication to exercise found on CPET, such as

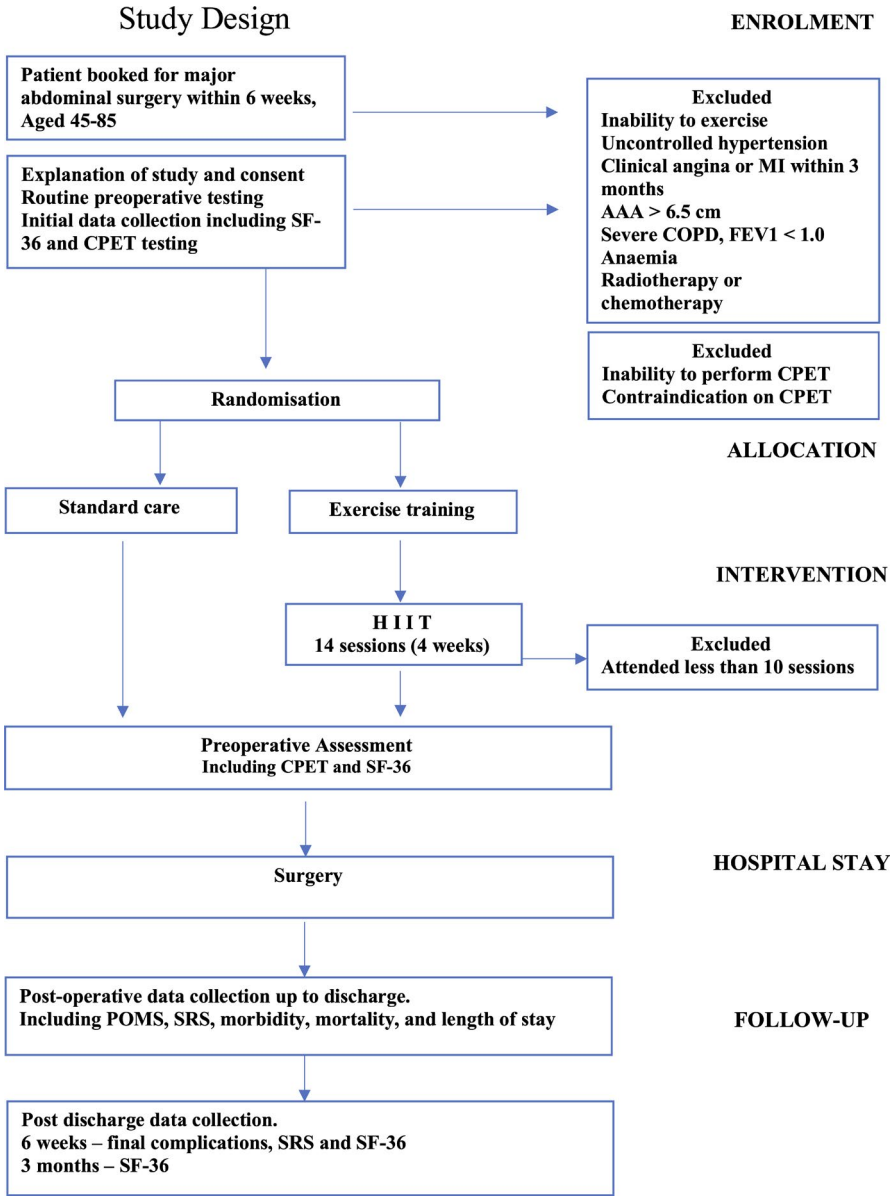

FIGURE 1 Study Design. AAA, aortic abdominal aneurysm, COPD, chronic obstructive pulmonary disorder; CPET, cardiopulmonary exercise testing; FEV, forced expiratory volume; HIIT, high-intensity interval training; SF-36, Short Form 36 quality of life questionnaire; POMS, Postoperative morbidity survey; SRS, Surgical Recovery Score

an arrhythmia or ST segment changes. (B) Medical conditions where exercise may contribute to adverse events. These included symptomatic angina, a myocardial infarction in the last three months, and uncontrolled cardiac arrhythmia. Patients with a history of ischemic heart disease with no symptomatic angina or with successful revascularization were included. Other medical contraindications included uncontrolled hypertension (BP>180/100), aortic aneurysm >6.5 cm, and severe obstructive pulmonary disease with a FEV1<1.0 liters. (C) Receiving medical therapy which could change oxygen consumption at the same time as the proposed exercise program. This included treatment of anemia and receiving neoadjuvant chemotherapy and/or radiotherapy. (D) Inability to follow instructions or to provide consent.

Potentially eligible patients were interviewed by a research nurse and assessed by the study anesthetist. After consent, CPET was performed on a stationary cycle ergometer (Quark Ergoline). The CPET protocol has been previously published.[26] Tests were terminated when the participant achieved a maximal effort or for medical reasons.[28] Evidence of a maximal effort test included a respiratory exchange ratio (RER) of ≥1.1 or a plateau in the $\dot{V}O_2$ with increasing workload. $\dot{V}O_{2peak}$, resting and maximal heart rate (HRmax), maximal workload in Watts, and the workload required to elicit 60% and 90% HRmax were recorded. A cardiologist checked the electrocardiogram results. Randomization was performed using a computer-generated sequence of numbers kept in sealed envelopes that were sequentially opened. The randomization ratio was 1:1 for the first 40 participants. This was changed to 2 for standard care and 1 for HIIT for the remainder of the study (due to lack of adherence in attending the second CPET in the control group).[26]

For those randomized to exercise, the protocol included 14 sessions of HIIT over 4 weeks. Each session included approximately 30 min of stationary cycling on a cycle ergometer (Monark Ergomedic 828E) under the supervision of an exercise physiologist. The session began with 5 min of warm-up cycling, followed by 20 min of interval training and 5 min of pedaling against a light load. The interval training was based around ten 1 min intervals of high-intensity cycling against a high resistance with the objective of reaching 90% HRmax (determined via CPET) at least once during the session. Intense intervals were alternated with 1 min intervals of active rest, defined as cycling against minimal resistance at ≥60% HRmax. The duration of intense training did not exceed 10 min. Once 90% HRmax was achieved, we aimed to achieve this target in as many intense intervals as possible, and in sustaining this for a longer proportion of the interval. Individualization of the protocol included increasing the training load or the duration of intense intervals, with the aim of achieving five 2 min intervals followed by 1–2 min of lower intensity cycling. Individualization also included the ability to start with shorter periods of intense exercise in those with medical comorbidities. Participants on beta blockers had pulse and level of perceived exertion monitored using the 6–20 Borg scale.[29] Patient heart rate was recorded using Polar heart rate monitors. Standard care for all participants included anesthetic preassessment, hospital orientation to enhanced recovery after surgery (ERAS) targets,[30] treatment of identified medical problems, advice on stopping smoking and reducing alcohol consumption, and advice on healthy living, including diet and being encouraged to exercise more before surgery. An independent safety monitoring committee, including an anesthetist, surgeon, and cardiologist, independently reviewed the study protocols and any adverse events.

The primary outcome was change in $\dot{V}\,O_{2peak}$, defined as the highest oxygen consumption measured over a 20 s interval during the CPET.[31] Secondary physiological outcomes included peak work rate and AT. Adherence was determined by the number of HIIT sessions attended, and the number of sessions where a target HR of >90% HR_{max} was reached. As we were unable to perform a study large enough to use complications as our primary outcome, we included a range of clinical outcomes as secondary endpoints to assess their relationship to HIIT training. Length of stay was the number of postoperative days in hospital, with day zero being the day of surgery. Postoperative complications, using standard definitions,[32,33] were documented in hospital and up to 6 weeks after discharge. In-hospital complications were prospectively identified in the ward, and a validated questionnaire[34] was sent 6 weeks later to identify complications that developed after discharge from hospital. We also collected data using three postoperative surveys. The postoperative morbidity survey (POMS), which assesses postoperative adverse events in nine different domains according to predefined criteria,[35] was performed on postoperative day 5. The surgical recovery scale (SRS), which assesses 13 items including energy levels, feeling of fatigue, and a number of practical physical activities[36] was performed on postoperative day five and 6 weeks after surgery. Quality of life (QoL) was measured using the Short Form 36 Health Survey (SF-36).[37] This documented the impact of HIIT on the patients' QoL and enabled us to assess differences in physical function (PCS score) after surgery. QoL was documented on four occasions: at randomization, before surgery, 6 weeks after surgery, and 12 weeks after surgery. With respect to blinding, although the exercise physiologist was not blinded, two researchers always performed the CPET. The assessor of the clinical endpoints was blinded to the group the participant was in.

For patient demographics, mean and standard deviation were used for normally distributed continuous variables, median and interquartile range for other continuous variables. Differences in changes of $\dot{V}\,O_{2peak}$ between groups were compared using linear mixed model analysis and the Student's t-test. For secondary endpoints, differences in the number of postoperative complications and in the number of POMS events per person were compared using the Wilcoxon rank-sum tests. Differences in the number of patients with a postoperative complication and an identified POMS event were compared using Pearson's chi-squared tests. Differences in the length of stay were compared using the Student's *t*-test. Differences between groups were also compared using appropriate models depending on the categorical or continuous nature of the endpoint and the distribution of the data. These adjusted for age, operative severity, and ASA score. For endpoints recorded on more than one occasion (the SF-36 and the surgical recovery scale scores), linear mixed models were used to give an overall comparison between groups. An analysis was also performed for individual time points, comparing the change in score from baseline between groups with the Student's *t*-test using Bonferroni corrections. Both per-protocol (PP) and intention-to-treat (ITT) analyses were performed, with PP being the main planned analysis.[26] Statistical analysis was performed using R 4.0.2,[38] and significance was determined by two-sided $p < 0.05$. In order to provide 80% power to detect a difference of 2 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$ in the change in $\dot{V}\,O_{2peak}$ between groups, using a two-sided test at the 0.05 level, a sample size of 20 participants per group was required. Based on a dropout rate of 1 in 3, we aimed to enroll 60 patients. Additional details about the statistical methods, statistical modeling, regression analyses, sample size calculation,

and our ITT results are presented in the Supplemental Digital Content.

3 | RESULTS

Sixty-three patients were enrolled between September 2015 and February 2019. This included 30% of those contacted. Reasons for non-enrollment are outlined in the Supplemental Digital Content p1, Patient Recruitment. Participants randomized into the exercise and control groups were not different with respect to age, sex, smoking status, ASA score, medical comorbidities, medications, and the type of surgery performed (Table 1). Drop out after randomization (Table 2) ranged from 19% to 32% for different endpoints. Of those randomized to exercise, 75% (21/28) completed the exercise program. Reasons for withdrawal included acute respiratory infection, chest pain in the initial exercise session, anxiety, discomfort sitting on a bike seat because of previous surgery, and competing time commitments. In the control group, five patients did not attend their second CPET, two withdrew as "there was no point being in the study if they were not exercised," and three patients set up their own well-designed aerobic exercise programs. These three patients were included in the ITT, but not the PP analysis. Two adverse events were documented: a new arrhythmia diagnosed during the initial CPET and an episode of chest pain during HIIT. Both events resolved on stopping the intervention without additional sequel.

For those who completed the exercise program, adherence for attending exercise sessions was 85% (on average participants completed 12 of their 14 sessions). The main reason for not completing 14 sessions was limited time before surgery. Adherence to reaching 90% HR max at least once during an exercise session was 97.5%. On average, participants trained 3.7 times a week and performed 8 min of intense exercise per session, resulting in approximately 100 min of intense exercise throughout the exercise program.

The results for the primary endpoint, change in $\dot{V}O_{2peak}$, are summarized in Table 3. The difference in the mean improvement of $\dot{V}O_{2peak}$ between groups was 2.73 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, 95% CI [1.53–3.93], $p < 0.001$. Comparable changes in $\dot{V}O_{2peak}$ were found for the ITT analysis (Table S3, Supplemental Digital Content p5). Improvements in $\dot{V}O_{2peak}$ were seen in both average and high-risk patients (Table S7, Supplemental Digital Content p8). The peak work rate during CPET increased significantly in the exercise group in comparison with the control group ($p = 0.037$ PP, $p = 0.05$ ITT analysis).

The results for complications, POMS, and LOS are presented in Table 4. Although there were no significant differences for these clinical outcomes, the observed training-induced reductions in total number of complications (0.64 v 1.16 per patient, $p = 0.072$) and in the LOS (median 4 v 5 days, and mean 5.5 v 7.4 days, $p = 0.067$ when adjusting for age, ASA, and operative severity)

TABLE 1 Comparison of demographics and risk factors for enrolled participants

	Exercise	Control
Number enrolled	28	35
Sex		
Male	20 (71)	18 (51)
Female	8 (29)	17(49)
Age median (IQR)	66.5 (13.5)	66.0 (15.0)
Smoking status		
Never	16 (57)	22 (65)
Former	11 (39)	12 (35)
Current	1 (4)	0 (0.0)
Missing		1
ASA		
1,2	22 (79)	31 (89)
3	6 (21)	4 (11)
Comorbidities		
Cardiovascular	19 (68)	25 (71)
Renal	3 (11)	1 (3)
Respiratory	2 (7)	4 (11)
Diabetes	5 (18)	6 (17)
Morbid Obesity	2 (7)	5 (14)
None	4 (14)	5 (14)
Type of surgery		
Colonic resection	7 (25)	9 (26)
Rectal surgery	3 (11)	6 (17)
Major esophageal, pancreatic	2 (7)	2 (6)
Large ventral hernia	1 (4)	1 (3)
Urology	14 (50)	10(29)
Hysterectomy	1 (4)	5 (14)
Canceled	0	2 (6)
Medications		
Statin	16 (47)	15 (54)
Beta blocker	6 (21)	5 (14)
Metformin	5 (18)	4 (14)
Calcium Channel blocker	6 (18)	6 (21)
Digoxin	0	1 (3)
Ace Inhibitor/Angiotensin receptor blocker	11 (39)	17 (49)

Note: Results are number (%) unless otherwise stated.

Abbreviation: IQR, interquartile range.

provide evidence that supports further and larger studies on the effect of preoperative HIIT on clinical outcomes. These effects were not different between average and high-risk participants (Table S8, Supplemental Digital Content p9).

The PCS scores at baseline, after HIIT, 6 weeks after surgery, and 12 weeks after surgery are presented in Table 5, Table S2 Supplemental Digital Content p4, and illustrated in Figure 2. The overall difference in PCS for all time periods combined, when adjusting for repeated measures, age, ASA, and operative severity was not significantly different ($p = 0.057$). Although after HIIT there was an improvement in PCS, the difference was greatest 6 weeks after surgery ($p = 0.015$, see supplemental digital content Table S2) due to the decrease in PCS being greater in the control group than in the exercise group. By three months after surgery, both groups were similar to their baseline.

Further results for clinical outcomes are presented in the supplement. Tables S1–S2 pp 3–4 present the PP results, and Tables S3–S5 Supplemental Digital Content pp5–7 the ITT results.

TABLE 2 Patient enrollments and attrition after randomization

	Exercise	Control
Enrolled	28	35
Change in $\dot{V}$ O_{2peak} (PP)	21	22
Change in $\dot{V}$ O_{2peak} (ITT)	21	25
Complication data (PP)	22	25
Complication data (ITT)	22	28
Reasons for drop out from the primary endpoint (PP measurement of $\dot{V}$ O_{2peak})		
Air leak on CPET	1	1
Did not attend second CPET	0	5
Change in operation	0	2
Medical withdrawal	2	0
Patient withdrawal	4	2
Initiation of own exercise program	0	3

Abbreviations: CPET, Cardiopulmonary exercise test; ITT, Intention to Treat; PP, Per protocol.

4 | DISCUSSION

This RCT confirms that preoperative HIIT increases aerobic capacity. Novel findings are that these benefits are realized after a brief training program (average 12 sessions) that can be achieved in the short time period (average 3.7 sessions a week) before surgery. This study was not powered to detect changes in postoperative outcomes; however, the observed differences in several outcomes, including length of stay and the number of complications, were numerically lower in the exercise groups ($p < 0.1$). If these findings are substantiated in larger RCTs, it would suggest that a brief, intense period of preoperative exercise, aimed at improving patient outcomes, should be considered as an addition to standard preoperative care before major abdominal surgery.

Our 2.7 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ improvement in aerobic capacity with HIIT involved approximately 100 min of intense exercise. Participants were supervised and attained the target heart rate of 90% HRmax in >95% of the attended exercise sessions. This improvement is comparable with

TABLE 3 Physiological outcomes compared between patients undergoing exercise or standard care, Per-protocol analysis

Time	Exercise ($n = 21$)	Standard care ($n = 22$)	Difference in change	p
VO_{2peak} (mL·kg−1·min−1)[a]				
Pre	20.34 ± 5.21	21.83 ± 6.45	2.7 (−1.53,3.93)	**<0.001**
Post	23.21 ± 5.61	21.98 ± 5.83		
Peak Work Rate (W)[b]				
Pre	125 (75, 175)	125 (50, 250)	25 (0, 25)	**0.037**
Post	150 (75, 175)	125 (50, 250)		
Anaerobic Threshold[a]				
Pre	10.89 ± 2.97	10.97 ± 2.96	0.68 (−0.57, 1.92)	0.280
Post	12.28 ± 3.20	11.69 ± 2.87		
RER				
Pre	1.23 (1.1, 1.4)	1.20 (1.1, 1.4)	- 0.05 (−0.07, 0.03)	0.404
Post	1.18 (1.1, 1.4)	1.20 (1.2, 1.4)		

*Significantly different change (post-pre) between groups, $p < 0.05$.

[a]Mean±SD.

[b]Median (IQR).

TABLE 4 Comparison of Clinical Outcomes (Per-protocol analysis)

Outcome	Exercise ($n = 22$)	Standard care ($n = 25$)	p
Total Complications	14	29	
Complications per person[a]	0.64 ± 0.95	1.16 ± 1.11	0.072
Patients with complications[b]	10 (45%)	17 (68%)	0.206
Wound infection	4	5	
Wound other	1	1	
Space Surgical Site Infection	2	3	
Ileus	0	5	
Urinary Tract Infection	2	5	
Urinary retention	0	1	
Chest (atelectasis)	2	2	
Cardiac (AF)	1	2	
Neurological (TIA)	0	1	
Other	2	4	
POMS value[a]	0.50 ± 0.80)	0.88 ± 1.13	0.266
Patients with POMS[b]	8 (36%)	12 (48%)	0.610
Length of stay[c]	4 (2.8)	5 (6.0)	0.313

Abbreviation: TIA, Transient ischemic attack.

[a]Mean ± SD.

[b]n (%).

[c]Median (IQR).

TABLE 5 Per-Protocol Regression Analysis of Quality of life and Surgical Recovery Scale questionnaire results

Unadjusted			Adjusted for Age, ASA, and Operative Severity		
Exercise ($n = 22$)	Control ($n = 25$)	p	Exercise ($n = 22$)	Control ($n = 25$)	p
PCS					
47.66 ± 9.65	44.1 ± 9.81	0.193	50.1 ± 11.36	48.6 ± 12.98	0.059
43.46 ± 9.39	35.92 ± 9.40		46.5 ± 11.22	36.2 ± 12.49	
45.93 ± 9.85	45.54 ± 9.62		50.1 ± 12.10	47.5 ± 12.49	
MCS					
42.71 ± 12.87	47.24 ± 13.12	0.778	44.7 ± 17.36	45.5 ± 19.4	0.823
44.80 ± 12.55	45.63 ± 12.54		43.5 ± 17.13	45.0 ± 17.13	
46.37 ± 13.19	48.78 ± 12.84		44.2 ± 18.37	58.6 ± 18.52	
SRS					
35.59 ± 9.89	34.45 ± 10.07	0.234	38.52 ± 13.41	35.13 ± 14.50	0.948
55.45 ± 9.89	51.63 ± 10.07		56.69 ± 13.41	52.68 ± 14.50	

Note: Estimated Marginal Means ± SD.

Abbreviations: ASA, American Society of Anaesthesiologists Score; PCS, Physical Component Score of the Short Form 36 Quality of Life Questionnaire, measured at three time points; MCS, Mental Component Score of the Short Form 36 Quality of Life Questionnaire, measured at three time points; SRS, Surgical Recovery Score, measured at two time points.

the findings of West et al.[8] who administered 18 sessions of HIIT over 6 weeks between chemoradiotherapy and rectal cancer surgery in 22 patients, resulting in a 2.65 mL·kg^{-1}·min^{-1} improvement in $\dot{V}$ O_{2peak}. Similarly, in a RCT by Dunne et al.,[11] 12 sessions of HIIT resulted in a 2.0 ml·kg^{-1}·min^{-1} improvement in $\dot{V}$ O_{2peak} in 19 patients before liver surgery. In contrast, Boereboom et al.[16] found that eight sessions of HIIT performed over 2 weeks,

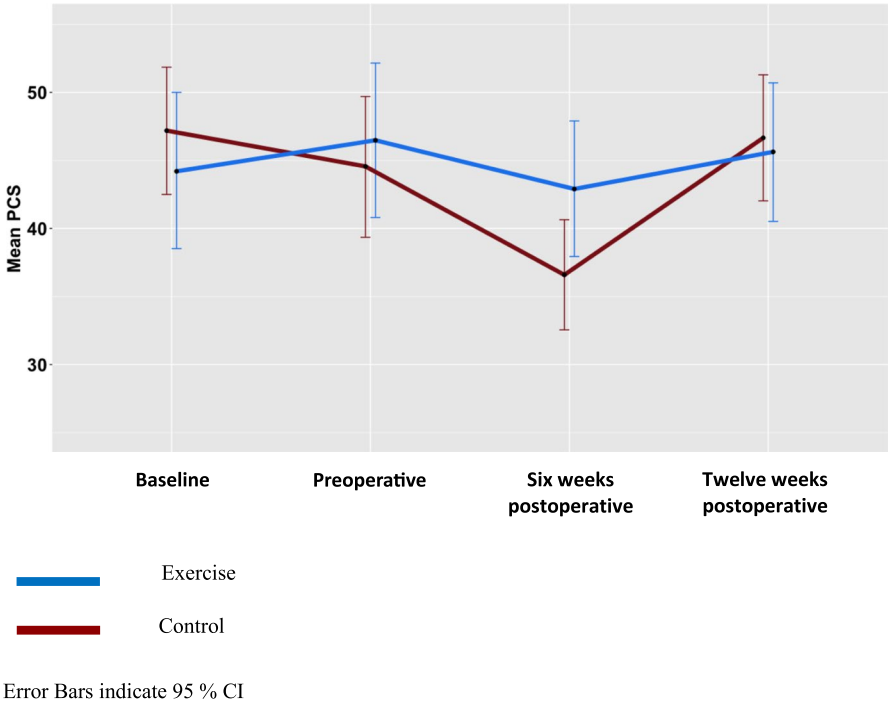

FIGURE 2 Changes in SF-36 Physical Component Score over time. Error bars indicate 95% confidence intervals. PCS, Physical Component Summary Score; SF-36, Short Form 36 quality of life survey

with a total of 40 min of intense exercise, did not change $\dot{V}$ O_{2peak}. As many cancer patients do not have 6 weeks between diagnosis and surgery, we needed to achieve a high-intensity training volume comparable to West et al.[8] in a shorter period of time. Achieving approximately 100 min of high-intensity activity during their training period required our participants to train an average of 3.7 times per week, rather than three sessions per week as described by others.[4] An obvious criticism is that this exceeds, in an already compromised cohort, the ACSM recommendation of three days per week of vigorous activity.[39] We would note, however, that the program was well attended and tolerated by participants with minimal adverse events.

We believe the observed differences in postoperative clinical outcomes between study groups should be interpreted carefully. Our study was not powered to compare differences in clinical outcomes or their association with changes in $\dot{V}$ O_{2peak}. In this context, three observations can be made. Firstly, for all clinical endpoints, preoperative HIIT was consistently associated with fewer adverse outcomes in the exercise group. Secondly, some of the non-significant differences were of a sufficient size, with p values <0.10, and of sufficient clinical relevance, to warrant further investigation. These include the impact of HIIT on postoperative complications, quality of life, and length of stay. Finally, some of these improvements have recently been confirmed in two RCTs, which were appropriately powered to identify differences in postoperative complications. A RCT of 124 patients undergoing abdominal aneurysm surgery demonstrated that a multi-modal moderate-intensity aerobic exercise program resulted in fewer patients with complications (41.9% v 22.6% ($p = 0.021$)) and a reduced median hospital stay from 8 to 7 days ($p = 0.025$).[18] Similarly, a RCT of 144 patients undergoing major abdominal surgery demonstrated that a multi-modal HIIT program resulted in fewer patients with complications (62% v 31% ($p = 0.001$)) and a reduced mean hospital stay from 13 to 8 days ($p = 0.078$).[25] These results are consistent with the 45% mean reduction in the number of complications, and the one-day median reduction of hospital stay in our study.

While overall there was no significant difference in the PCS of the SF-36 for all time periods combined, we were interested in assessing changes at individual time points because of their clinical relevance. The PCS score includes questions examining what you can physically do (Physical Function), your ability to accomplish different tasks (Physical Role), and your assessment of your health (General Health). When measured postoperatively, it therefore provides a good measurement of physical recovery from surgery. Our results at 6 weeks after surgery suggest that participants in the HIIT group recovered more rapidly. The ability of prehabilitation to improve the speed of physical recovery after surgery is an important clinical observation, both for patients and healthcare providers, which needs to be further assessed.

Challenges in performing this RCT have been discussed previously.[26] There were difficulties randomizing patients to standard care. As most patients enrolled because their imminent surgery and the study provided motivation to exercise, randomization to standard care came as a disappointment. This contributed to

withdrawals, poor protocol adherence, and not attending the second CPET. For example, three participants initiated preoperative aerobic exercise programs that included (but were not limited to) training at a gymnasium or walking daily up a steep hill. This is the reason for the smaller difference between groups in the ITT analysis. We would recommend that future studies provide alternative preoperative programs for the control group, such as strength and balance classes, walking programs, or breathing exercises.

Limitations include the inability to blind patients. It is therefore possible that the psychological effect of being included in the exercise group contributed to differences in the quality of life scores. Another limitation is that our data do *not* provide a basis for how preoperative HIIT can be best applied to a complete surgical cohort, including less motivated and non-adherent patients. We did, however, perform an analysis assessing if all enrolled patients, or a subset of surgical patients would benefit from HIIT. This found no evidence against the hypothesis that the benefits of preoperative HIIT are shared by both average and high-risk patients.

5 | PERSPECTIVE

We demonstrated that a brief-duration, high-frequency program of HIIT resulted in a significant improvement in $\dot{V}\,O_{2peak}$. Though underpowered, our study identified clinically important, but statistically insignificant improvements in postoperative outcomes. Differences in some of these clinical outcomes have subsequently been identified by others.[18,25] Based on these findings, a lack of adverse events, and minimal cost, we believe preoperative HIIT training should be encouraged for patients receiving major abdominal surgery. Larger RCTs powered to detect clinical outcomes, including complications, LOS, and recovery of physical function after surgery, should be performed.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

AUTHOR CONTRIBUTIONS

Woodfield involved in conceptualization, methodology, recruitment, investigation, supervision, and writing (original and review). Clifford involved in data visualization, data analysis, and writing (original and review). Wilson involved in HIIT training and data collection. Munro involved in co-ordination of study, recruitment, and data collection. Baldi involved in conceptualization, methodology, investigation, HIIT supervision, and writing (original and review).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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