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ORIGINAL ARTICLE

A 31-day time to surgery compliant exercise training programme improves aerobic health in the elderly

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Abstract
Background Over 41,000 people were diagnosed with colorectal cancer (CRC) in the UK in 2011. The incidence of CRC increases with age. Many elderly patients undergo surgery for CRC, the only curative treatment. Such patients are exposed to risks, which increase with age and reduced physical fitness. Endurance-based exercise training programmes can improve physical fitness, but such programmes do not comply with the UK, National Cancer Action Team 31-day time-to-treatment target. High-intensity interval training (HIT) can improve physical performance within 2–4 weeks, but few studies have shown HIT to be effective in elderly individuals, and those who do employ programmes longer than 31 days. Therefore, we investigated whether HIT could improve cardiorespiratory fitness in elderly volunteers, age-matched to a CRC population, within 31 days.
Methods This observational cohort study recruited 21 healthy elderly participants (8 male and 13 female; age 67 years (range 62–73 years)) who undertook cardiopulmonary exercise testing before and after completing 12 sessions of HIT within a 31-day period.
Results Peak oxygen consumption (VO_2 peak) (23.9 ± 4.7 vs. 26.2 ± 5.4 ml/kg/min, $p = 0.0014$) and oxygen consumption at anaerobic threshold (17.86 ± 4.45 vs. 20.21 ± 4.11 ml/kg/min, $p = 0.008$) increased after HIT.
Conclusions It is possible to improve cardiorespiratory fitness in 31 days in individuals of comparable age to those presenting for CRC surgery.

Keywords Colorectal cancer · Exercise · Surgery · Fitness · Elderly · Preoperative

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Introduction

In 2010, 10 million people in the UK were over 65 years old, a number that will increase to 19 million by 2050 [1]. As such there is an increase in the prevalence of age-related diseases, including most cancers. Bowel cancer is common with 41,581 new cases in the UK in 2011. It is also strongly related to age with incidence increasing sharply after the age of 50 [2]. Due to increased longevity [1], the age of patients operated on for cancer is also rising [3]; major resections for colorectal cancer most frequently occur in the 65- to 74-year age group [4].

Surgery places profound metabolic and cardiorespiratory stresses on the body [5, 6]. The risk of dying within 30 days of a major colorectal resection is 2.9 %. Cardiovascular fitness has been shown to be an independent risk factor for post-operative complications including death [7, 8]. Despite this knowledge, there are few interventions designed to improve cardiovascular fitness before surgery.

In the UK, the National Cancer Action Team specifies that treatment (including surgery) should start within 31 days of the decision to treat CRC [9]. Methods of improving fitness in cancer patients, prior to surgery, must therefore be acceptable to patients and be effective within 31 days. Traditional endurance exercise training fails to improve cardiorespiratory fitness in healthy older individuals and cancer patients within this time, taking at least 8 weeks to show improvements in parameters such as maximum oxygen consumption (VO_2 max) [10]. In contrast, high-intensity interval training (HIT) has the potential to rapidly improve cardiorespiratory fitness [11, 12], making it an attractive intervention in the time available before operation.

HIT is a well-established method of exercise training characterized by brief intervals of high-effort exercise interspersed with periods of active recovery or rest. In healthy individuals, it can produce equivalent improvements in cardiorespiratory fitness to longer-term endurance training programmes within 2–4 weeks [13, 14]. HIT is purported to improve fitness via both central and peripheral pathways [15]. Proposed mechanisms include: more efficient myoglobin reloading of oxygen improving efficiency of respiration [16], up-regulation of glycolytic and oxidative enzyme pathways, and increased mitochondrial biogenesis [17]. Changes in cardiovascular dynamics have also been reported, with increases in plasma volume [18, 19], left ventricular ejection fraction, stroke volume, and ejection velocity [20]. Improved vascular endothelial function and arterial distensibility are also documented following HIT [21].

There is some evidence supporting the use of HIT in older individuals, although these studies commonly report on a training duration longer than 31 days. One recent study demonstrated significant improvements in cardiovascular fitness in healthy subjects with a mean age of 68 years after 8 weeks of HIT [22], with additional work in both sedentary and active men with mean ages of 63 and 61 years, respectively, showing improvements after 13 weeks of HIT [23]. In healthy, older volunteers, Ahmaidi et al. [24] showed an increase in anaerobic threshold (AT) after 12 weeks of HIT using a training intensity set just below AT. An increase in VO_2 max after 14 weeks of HIT has also been reported [25] in older individuals, as has an increased peak oxygen consumption (VO_2 peak) after 9 weeks of training [26]. In frail, elderly individuals (mean age 83 years) with no specific co-morbidities, significant improvements in VO_2 max using a combination of endurance training and HIT have been shown over a 9-month period [27]. Similarly, Wisløff et al. showed an increase in VO_2 max in elderly heart failure patients (mean age 76 years) after 12 weeks of HIT [20].

In addition, HIT has also been shown to have benefit in both the post-operative setting and in patients with specific conditions. Following coronary artery bypass grafting, HIT produced a significant improvement in VO_2 max, which persisted for at least 6 months [11]. Similarly, a study of patients 1–8 years after cardiac transplantation showed HIT to be both safe and effective for producing significant increases in VO_2 peak [28]. In patients with chronic obstructive airway disease, HIT produced a 25 % increase in peak work rate and 14 % increase in AT and improved quality of life scores [29]. Despite these reported benefits, HIT remains infrequently used in clinical practice.

Beyond optimizing modifiable risk factors such as medication and smoking cessation, there is currently little attempt to improve patient fitness in the pre-operative period. HIT has the potential to improve fitness before major surgery. However, before HIT can be evaluated in a pre-operative setting, it must be shown to be effective and acceptable in an elderly population within 31 days.

This prospective, observational cohort study aimed to explore whether it is possible and feasible, within 31 days, to significantly improve the cardiorespiratory fitness of older healthy volunteers, age-matched to a CRC patient population, by an intervention acceptable to subjects. The purpose of this preliminary study was to ensure that the mechanics of the intervention (the laboratory setting, the time spent exercising etc.) were acceptable to a group similar to CRC patients. It was also important to assess whether it was possible to improve VO_2 peak specifically in a short time frame, mimicking the time to a CRC operation. With this information, we could then plan a study assessing HIT as a methods for improving the fitness of CRC patients before surgery.

Materials and methods

Participants

Participants (male and female, between 60 and 75 years old) were recruited by demographically targeted postal invitation (Royal Mail, UK) and local advertising. The study was approved by the University of Nottingham Medical School Ethics Committee, and informed consent was obtained from all participants. Medical screening was performed before the study which included: a cardiorespiratory examination, blood sampling for routine haematology and biochemistry profiles, an electrocardiogram (ECG), and blood pressure measurement. In line with the British Society of Cardiology and American Thoracic Society (ATS) Cardiopulmonary Exercise Test (CPET) Guidelines [30], participants were excluded if they displayed evidence of uncontrolled hypertension (blood pressure >140/100 mmHg (Stage 1 Hypertension NICE guidelines CG127 [31]), significant cardiorespiratory disease, or had taken part in another research study in the previous 3 months. Participant characteristics are displayed in Table 1. The study was registered with

Table 1 Participant characteristics

Characteristic	
Age (range)	66.6 (62–73) years
Gender	8 male; 13 female
Previous exercise episodes/week (±SD)	1.5 ± 1.4 episodes
Body mass index (±SD)	26.1 ± 2.9 kg/m^2
Comorbidities (number of participants affected)	Asthma (2)
	Hypothyroidism (3)
	Hypercholesterolaemia (4)
	Musculoskeletal disorders (3)
	Hypertension (5)
Medication (number of participants affected)	Inhaled bronchodilators (2)
	Thyroxine (3)
	Statins (4)
	Antihypertensives (5):
	Calcium channel blocker (1)
	Diuretics (3)
	Beta blocker (1)
	Angiotensin II receptor antagonist (1)
	Angiotensin-converting enzyme inhibitor (1)

SD standard deviation

ClinicalTrials.gov (NCT02188342) and complied with the 1964 Declaration of Helsinki.

Experimental design

For this observational cohort study, participants underwent baseline testing consisting of a cardiopulmonary exercise test (CPET) using a 15 W/min ramp protocol (outlined below). Other measurements taken included a whole-body dual-energy X-ray absorptiometry (DXA) scan and ultrasound scan (US) of the *M. vastus lateralis*. Participants then completed 12 fully supervised HIT sessions within a 31-day period (~3 sessions per week), with intensity determined from the baseline CPET and by performing an initial assessment session with 1-min intervals at 90, 95, 100, 105, and 110 % Watt max derived from the CPET. Participants trained at the load of the highest interval completed during their assessment session. Baseline testing was repeated after the 12 HIT sessions. A questionnaire investigating the acceptability of the training programme was also completed.

Cardiopulmonary exercise testing

CPET was performed with a Lode Corival cycle ergometer (Lode Corival, Lode, Groningen) and inline gas analysis system (ZAN 680, nSpire Health, Colorado, USA), using a standard 15 W/min ramp protocol [30]. Following a 2-min period of unloaded cycling, participants were instructed to maintain a cadence of 50–60 revolutions per minute (rpm) and were verbally encouraged to exercise to 85 % or more of predicted maximal heart rate and to a respiratory exchange ratio (VCO_2/VO_2) above one. The test was complete when the participant indicated that they had reached their maximum possible effort, with the time to failure recorded. During all CPET and HIT sessions, participants were monitored with a 12-lead ECG, non-invasive blood pressure monitoring, and pulse oximetry. All sessions were supervised by an advanced life support-trained clinician with termination criteria taken from the ATS statement on CPET [30].

AT defined as the oxygen consumption above which aerobic energy production is supplemented by anaerobic mechanisms, causing a sustained increase in lactate and metabolic acidosis [32], was determined by three independent assessors blinded to the participants, using both the V slope [33] and respiratory equivalents methods [34], with the mean of these values used [35].

Imaging

Whole-body DXA scanning (Lunar Prodigy II, GE Medical Systems, Buckinghamshire, UK) was used to assess body composition before and after HIT. Whole-body lean and fat tissue values were assessed along with specific regions of interest (ROI) for abdominal and leg tissue composition. Sagittal plane US images of the left *M. vastus lateralis* were taken before and after HIT to quantify muscle thickness.

HIT sessions

All HIT sessions comprised 16.5 min of cycling per session. After 2 min of unloaded warm-up participants cycled for 60 s against a resistance set at the wattage of the highest interval completed during an assessment session (100–110 % Watt max achieved during pre HIT CPET), followed by 90 s of unloaded cycling. These intervals were repeated five times followed by a 3.5-min cool down period.

Statistical analysis

Assuming a coefficient of variation of 25 % in VO_2 peak (from our previous work [36]), to detect a mean clinically significant increase in VO_2 peak of 2 ml/kg/min [37], with 80 % confidence and 5 % significance, we recruited 24 individuals in order to achieve> 20 complete data sets (assuming a drop out rate of 20 %, in keeping with our previous studies) for our primary endpoint for this study.

Normality of data was tested using D'Agostino and Pearson omnibus test. Normal data are expressed as mean ± standard deviation (SD), and nonparametric data as median ± interquartile range (IQR). Paired Student's *t* tests were used to test the parametric data, the Wilcoxon matched-pairs signed-rank test was used for nonparametric data. Pearson's correlation was used to explore relationships between changes in *M. vastus lateralis* thickness, lean leg mass, and VO_2 peak. GraphPad Prism 6 (San Diego, CA, USA) was used for data analysis with level of significance set at $p < 0.05$.

Results

Twenty-four volunteers began the study and 21 completed (Table 1; 8 male and 13 female; 67 (62–73) years; BMI: 26.1 ± 2.9 kg/m^2). Three volunteers were excluded: one failed to reach AT during the CPET, one suffered claustrophobia in the facemask, and one was withdrawn due to pre-existent paroxysmal atrial fibrillation. Participants who completed the study reported 1.5 ± 1.4 episodes of weekly exercise prior to the start of the study. Mean workload during the HIT intervals was 148 ± 44 W. There was full compliance with the training programme with all participants completing 12 HIT sessions in a mean of 28 days (±3.5 days).

Cardiovascular measurement data

There was a significant reduction in both diastolic blood pressure (84 ± 8 vs. 75 ± 14 mmHg, $p < 0.01$) and mean arterial pressure (101 ± 8 vs. 93 ± 11 mmHg, $p < 0.01$) after HIT (Fig. 1). Systolic blood pressure was not significantly lower after HIT (134 IQR 14.5 vs. 132 IQR 22.5 mmHg, $p = 0.107$), and resting heart rate was unchanged (67.8 ± 9.6 vs. 68.9 ± 6.7 bpm, $p = 0.292$). There was a significant reduction in submaximal heart rate taken at specific intensities in the post-HIT CPET compared to the baseline CPET. This was true at 50, 75, and 100 W (97 ± 20.3 vs. 88 ± 12.3 bpm; 113 ± 23.0 vs. 102 ± 16.5 bpm and 122 ± 24.7 vs. 115 ± 21.3, all $p < 0.001$, respectively). Haemoglobin was unchanged following HIT (143 ± 10.3 vs. 144.8 ± 11.2 g/l, $p = 0.563$).

Cardiorespiratory exercise test data

There was a significant increase in CPET time to failure (737 IQR 95 vs. 772 IQR 155 s, $p < 0.001$) and CPET wattage at failure (118 IQR 83.5 vs. 142 IQR 85 W, $p < 0.001$) after HIT. There was a significant increase in both VO_2 peak (23.9 ± 4.7 vs. 26.2 ± 5.4 ml/kg/min, $p < 0.001$) and AT (17.86 ± 4.45 vs. 20.21 ± 4.11 ml/kg/min, $p < 0.01$; Fig. 2) after HIT. Neither VO_2 peak nor AT improvements were correlated with baseline values. There was a significant increase in peak O_2 pulse (17.1 ± 3.7 vs. 18.5 ± 3.7 100 ml/beat/kg, $p < 0.001$) after HIT.

Body composition data

Due to unavoidable delays in ethics approval for DXA scanning, only 15 out of 21 participants had DXA scans before and after HIT. All participants had US scans before and after HIT. Weight and BMI were unaltered by HIT (BMI 26.1 ± 3 vs. 26.1 ± 3 kg/m^2, $p = 0.329$). DXA-derived data showed that there was no significant change in total body tissue mass (68490 ± 10503 vs. 68186 ± 10395 g, $p = 0.185$), total body fat mass (23336 ± 7026 vs. 22904 ± 6693 g, $p = 0.073$), or total body lean mass (45154 ± 11142 vs. 45282 ± 11068 g, $p = 0.668$) following HIT. Lean leg mass significantly increased with HIT (4133 ± 1271 vs. 4220 ± 1236 g, $p < 0.05$), coupled with a significant increase in the thickness of the *M. vastus lateralis* (2.04 ± 0.27 vs. 2.17 ± 0.28 cm, $p < 0.05$) (Fig. 3). Abdominal fat mass (2783 ± 938 vs. 2690 ± 913 g, $p < 0.05$) was significantly reduced following HIT.

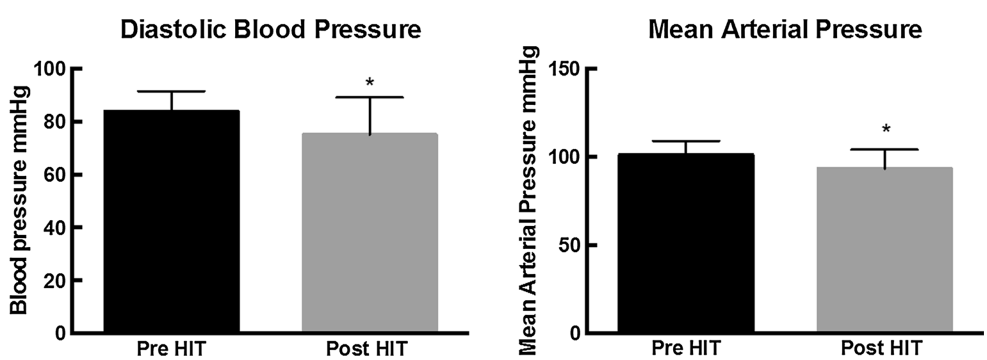
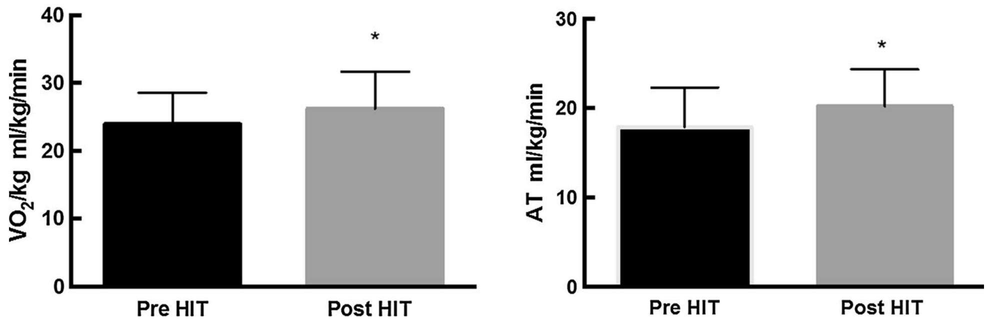


Fig. 1 Diastolic blood pressure and mean arterial pressure before and after HIT. Values are mean ± SD; *$p < 0.05$. Analysis via paired Student's *t* test

Fig. 2 VO_2 peak and AT before and after HIT. Values are mean ± SD; $*p < 0.05$. Analysis via paired students *t* test



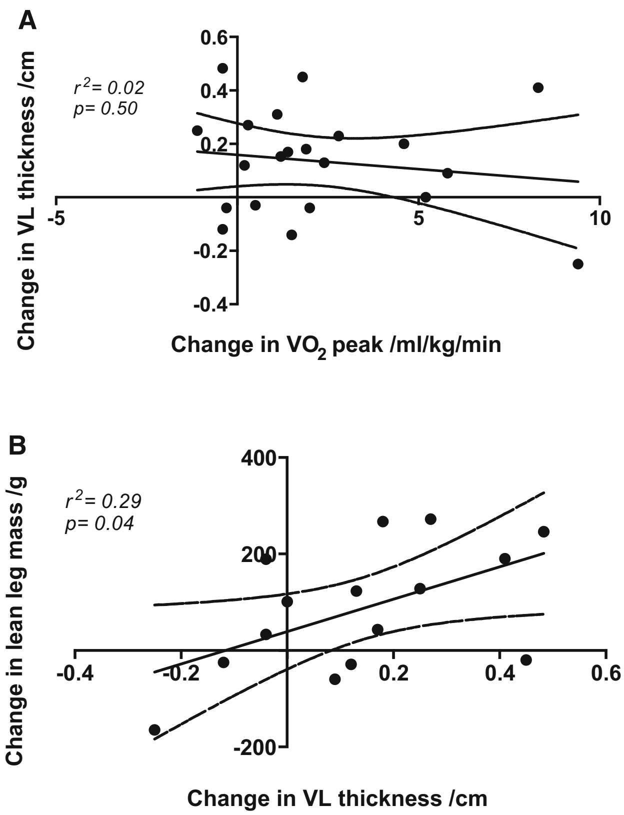


Fig. 3 **a** Change in lean leg mass *versus* change in *M. vastus lateralis* (VL) thickness following HIT. Analysis via Pearson's correlation. **b** Change in *M. vastus lateralis* (VL) thickness *versus* change in VO_2 peak following HIT. Analysis via Pearson's correlation

Acceptability of HIT

On a five-point Likert scale, the HIT programme was deemed highly acceptable by the majority of participants (Table 2).

Discussion

This observational, cohort study shows that it is possible to improve cardiorespiratory fitness in healthy, older people within 31 days using a HIT exercise programme. The regime was safe, acceptable, and not associated with any serious medical complications. Improvement in fitness was evidenced by significant improvements in VO_2 peak, AT, time to failure, and wattage at failure. Even though the baseline value for these participants was above the threshold for increased post-operative complications in CRC patients, the ability to improve fitness in a short time frame is encouraging. It is conceivable that those who are less fit at baseline (which maybe the case for many CRC patients) may demonstrate an even greater improvement in fitness.

To our knowledge, this is the first study to assess the efficacy of HIT on cardiorespiratory fitness in healthy, older individuals within the 31-day UK cancer target window. Other groups have reported an improvement in VO_2 peak in healthy older individuals and those with cardiovascular pathology, but training programmes have lasted 9–14 weeks [25, 26]. In 60-year-olds following coronary artery bypass grafting, an increase in VO_2 peak from 27 to 30 ml/kg/min in 4 weeks was reported, but with a higher training frequency [11].

In addition to fitness improvements, we also report reductions in diastolic and mean arterial blood pressure following HIT. Perioperatively elevated blood pressure increases risk of myocardial ischaemia, dysrhythmias, and renal impairment [38]. This observation is of particular note as several studies report reductions in blood pressure after prolonged duration HIT mirroring the reductions seen following endurance training, suggesting a non-specific effect of exercise training [39]. However, shorter duration HIT regimens in fit individuals have failed to replicate these improvements [12]. In contrast we have been able to show significant reductions in blood pressure after just 4 weeks of HIT in the elderly.

BMI and weight remained unchanged after HIT, despite a significant increase in lean leg mass as evidenced by DXA and US. These two measures of muscle mass/thickness showed close correlation ($r^2 = 0.29$, $p = 0.04$), suggesting that simple ultrasound measurements of the *M. vastus lateralis* could be used clinically to measure muscle-based changes (Fig. 3), with new ultrasound methods recently developed to give a measure of leg muscle mass

Table 2 Acceptability of HIT

Comment	Median score (range) 5—Strongly agree 1—Strongly disagree
HIT was well explained	5 (4–5)
I enjoyed HIT	5 (4–5)
HIT was a time burden	1 (1–5)
I would recommend HIT to others	5 (4–5)
HIT was more demanding than expected	2 (1–5)
I would do HIT again	5 (4–5)
The travelling involved with HIT interfered with my life	1 (1–5)
The physical strain interfered with my life	1 (1–5)
I believe my fitness has improved	5 (3–5)
I would like to have exercised in a group	1 (1–4)
I would like to have exercised at home	1 (1)

HIT high-intensity interval training

[40]. Similar HIT protocols in younger age groups have failed to show comparable changes in body composition in the recreationally active [41], but have shown an improvement in body composition in inactive and overweight groups [42]. Although observed increases in lean leg mass may confer an ability to attain higher VO_2 peak values and explain the increases in time to failure and wattage at failure, we failed to demonstrate a relationship between changes in muscle mass and VO_2 peak (Fig. 3), suggesting that HIT-induced increases in cardiorespiratory performance observed in this group are not solely attributable to increases in muscle mass.

Our participants found HIT both enjoyable and effective reporting benefit in exercising away from the home, with little time burden. Psychological support gained from attending an exercise programme has been reported in an older population [36], while increases in perceived fitness have been shown after exercise training [43], with self-efficacy central in adoption and maintenance of exercise programmes [44].

There are limitations to this study: despite demonstrating proof of principle that HIT is well liked, well tolerated, and effective in improving fitness in the elderly, those who had significant cardiorespiratory comorbidities were excluded from this study (to minimize risk of exercise related complications during this initial feasibility study), and our voluntary recruitment may have created selection bias, only appealing to those individuals already interested in improving their fitness.

It is also difficult to predict precisely how the findings of this study would translate to a group of CRC patients. It is possible that a patient group would have more co-morbidities and be less likely to exercise regularly; however, this may mean that greater improvements in fitness are seen with HIT.

Recruitment was limited to those between 60 and 75 years to provide a similarly aged cohort to those with the highest incidence of bowel cancer (95 % bowel cancer diagnosed in those over 50 years [2]). Most major colorectal resections occur in those between 65 and 74 years so a cohort with a mean age of 67 years is representative. As this was a feasibility study, there was no control group or randomization of participants with the primary objective of this study to assess whether improvements in fitness were possible in the limited time frame in a manner acceptable to the participants.

To summarize the importance of this work, CRC patients with an AT of less than 10 ml/kg/min or a VO_2 peak of less than 17 ml/kg/min are significantly more likely to suffer post-operative complications [37]. In this study subjects rapidly achieved a significant and clinically meaningful improvement in VO_2 peak within the time limits imposed by the UK National Cancer Action Team. This study provides the foundation for future work in a pre-operative CRC population to assess the efficacy and acceptability of HIT in patients. Translation of our findings to a patient population could allow pre-operative fitness to become a modifiable risk factor in operative cancer management.

Conclusions

This work provides evidence that it is possible to safely and significantly improve the cardiorespiratory fitness of individuals of an age comparable to those presenting for major CRC surgery, in a time frame compliant with UK national cancer management guidelines and by a method acceptable to subjects. Future work will assess the efficacy of the same exercise programme in a pre-operative CRC population.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

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