Original article

Randomized feasibility trial of high-intensity interval training before elective abdominal aortic aneurysm repair

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Background: **This study assessed the feasibility of a preoperative high-intensity interval training (HIT) programme in patients awaiting elective abdominal aortic aneurysm repair.**

Methods: **In this feasibility trial, participants were allocated by minimization to preoperative HIT or usual care. Patients in the HIT group were offered three exercise sessions per week for 4 weeks, and weekly maintenance sessions if surgery was delayed. Feasibility and acceptability outcomes were: rates of screening, eligibility, recruitment, retention, outcome completion, adverse events and adherence to exercise. Data on exercise enjoyment (Physical Activity Enjoyment Scale, PACES), cardiorespiratory fitness (anaerobic threshold and peak oxygen uptake), quality of life, postoperative morbidity and mortality, duration of hospital stay and healthcare utilization were also collected.**

Results: **Twenty-seven patients were allocated to HIT and 26 to usual care (controls). Screening, eligibility, recruitment, retention and outcome completion rates were 100 per cent (556 of 556), 43·2 per cent (240 of 556), 22·1 per cent (53 of 240), 91 per cent (48 of 53) and 79–92 per cent respectively. The overall exercise session attendance rate was 75·8 per cent (276 of 364), and the mean(s.d.) PACES score after the programme was 98(19) ('enjoyable'); however, the intensity of exercise was generally lower than intended. The mean anaerobic threshold after exercise training (adjusted for baseline score and minimization variables) was 11·7 ml per kg per min in the exercise group and 11·4 ml per kg per min in controls (difference 0·3 (95 per cent c.i. −0·4 to 1·1) ml per kg per min). There were trivial-to-small differences in postoperative clinical and patient-reported outcomes between the exercise and control groups.**

Conclusion: **Despite the intensity of exercise being generally lower than intended, the findings support the feasibility and acceptability of both preoperative HIT and the trial procedures. A definitive trial is warranted. Registration number: ISRCTN09433624 (https://www.isrctn.com/).**

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Introduction

Abdominal aortic aneurysms (AAAs) are found in 5–7·5 per cent of men and 1·5–3 per cent of women aged 65 years or more[1]. They usually remain asymptomatic until they rupture, which causes huge internal bleeding and carries an overall mortality rate in excess of 80 per cent[2]. Elective open surgical or endovascular repair is the most effective treatment for preventing aneurysm-related rupture and death. It is usually reserved for AAAs of at least 5·5 cm in diameter[3], with more than 4000 elective AAA repairs performed in the UK each year[4]. However, elective aortic surgery also carries significant risk. For example, data from the UK in 2014 indicated in-hospital mortality rates of 3·2 and 0·8 per cent for open and endovascular aneurysm repair respectively[4], with non-fatal postoperative complications several times more common[5–7].

Aneurysm repair, especially open surgery, results in neuroendocrine, metabolic and inflammatory changes that lead to an increase in global tissue oxygen uptake of up to 50 per cent[8]. Patients with low cardiorespiratory fitness are less able to meet these extra perioperative demands, which may lead to tissue hypoxia and debilitative or life-threatening complications. This notion is supported by observational studies[9–12] showing an association between preoperative cardiorespiratory fitness and mortality and major morbidity following elective AAA repair. Up to half of patients presenting for intra-abdominal surgery do not have the prerequisite fitness, quantified using cardiopulmonary exercise testing, to be deemed at low risk of perioperative complications[13]. It is therefore intuitive that improving cardiorespiratory fitness before surgery should translate into reduced complication rates after major surgery.

The clinical effectiveness and cost-effectiveness of preoperative exercise training before AAA repair has yet to be established in a large multicentre trial. Pilot and feasibility studies are often appropriate as part of a phased approach to the development, testing and evaluation of healthcare interventions[14,15]. During protocol development, the project team was not aware of any published or ongoing studies in this respect. Two small studies[16,17] demonstrated that moderate-intensity exercise training was feasible and could improve cardiorespiratory fitness in people under surveillance for a small AAA. However, it was unclear whether meaningful cardiorespiratory fitness improvements could be achieved safely in patients with a large AAA in the limited window available before surgery (typically 4–6 weeks)[18–20].

High-intensity interval training (HIT) is characterized by brief (for example 1–4 min) bouts of vigorous exercise (such as running or cycling) interspersed by periods of passive or active recovery. A recent meta-analysis of six trials (229 participants)[21] demonstrated a greater improvement in peak oxygen uptake following HIT compared with moderate-intensity continuous training in patients with coronary artery disease. However, the absence of HIT studies involving patients with AAA or in the present setting (UK National Health Service, NHS) make it difficult to draw inferences about the potential success of a definitive trial. Therefore, it was concluded that a randomized feasibility trial of preoperative HIT *versus* usual care (no exercise) for people awaiting elective AAA repair was required.

The overall aims of the HIT-AAA (High-intensity Interval Training before Abdominal Aortic Aneurysm repair) study were to assess whether HIT is a feasible and acceptable intervention for the preoperative optimization of patients with a large AAA (examine intervention implementation potential) and to test the feasibility of the protocol design (examine methodological standard). Thus, the main purpose of the study was to assess whether it was appropriate to progress to a larger-scale trial and, if so, to optimize its design. Accordingly, this article reports on rates of screening, eligibility, recruitment, retention, outcome completion, adherence to exercise and adverse events, as well as reasons for exclusion and non-consent, sample characteristics and the distribution of potential primary outcomes. For completeness, preliminary data on effectiveness and healthcare resource use are also presented.

Methods

A full description of the methods has been published[22]. The study was a two-arm, parallel-group, randomized controlled feasibility trial conducted in three teaching hospitals in England (James Cook University Hospital, Middlesbrough; Northern General Hospital, Sheffield; and York Hospital, York). Ethics approval was granted by the North East-Tyne and Wear South Research Ethics Committee (reference 13/NE/0116), and all participants provided written informed consent before enrolment. The trial was registered prospectively (ISRCTN09433624).

Participants

Participants were recruited from vascular surgical or preoperative assessment clinics at each of the trial sites. Patients aged at least 18 years who had been listed, following routine clinical assessment and vascular multidisciplinary team consideration, for an open or endovascular repair of an infrarenal AAA with a diameter of 5·5–7·0 cm were invited to participate. Exclusion criteria were: refusal or inability to provide informed consent, AAA managed non-operatively, not an infrarenal aneurysm (juxtarenal, suprarenal or thoracic), infrarenal AAA diameter exceeding 7·0 cm, emergency AAA repair, contraindication to exercise testing or training[23], specialist referral required (for example to cardiology) and BMI below 20 or above 40 kg/m^2.

Randomization and concealment

Following baseline assessment, participants were allocated using minimization to receive either usual care alone (control) or usual care plus a preoperative exercise programme. There were three minimization factors: sex, type of procedure (open or endovascular repair) and study centre. Allocation was concealed from those assessing eligibility and recruiting patients, with eligible patients allocated remotely via e-mail by the trial statistician. The research nurses in charge of recruitment were unaware of the specific minimization factors and so could not deduce future group assignments by keeping track of the previous allocations. Minimization was performed using Minim software[24], with a 1 : 1 allocation ratio and equal weighting for the three minimization factors.

Interventions

All participants received usual care, which comprised evidence-based medical optimization. Participants allocated to the exercise group were also invited to complete three hospital-based exercise sessions per week, for the 4 consecutive weeks (weeks 1–4; main phase) immediately preceding their intended operation date (in week 5). Participants whose operation was delayed beyond week 5 (for example owing to lack of availability of a hospital bed) also received a maintenance phase of training (1 exercise session per week). All exercise was undertaken on a cycle ergometer (Optibike Med; Ergoline, Bitz, Germany). Each of the first three sessions comprised a 10-min warm-up of unloaded cycling, eight 2-min intervals of high-intensity cycling interspersed with 2-min rest periods of unloaded cycling, and then a 5-min cool-down of unloaded cycling. In all subsequent sessions, participants had the choice of performing eight 2-min or four 4-min 'work' intervals for the main body of the workout. In the first exercise session, the 2-min work intervals were performed at the power output corresponding to anaerobic threshold on a baseline cardiopulmonary exercise test (CPET). The power output in all subsequent sessions was guided by participants' ratings of perceived exertion (RPE), which were assessed separately for legs (RPE-L) and breathlessness/chest (RPE-C) at the end of each interval using Borg's CR-10 scale[25]. The aim was for all work intervals to be undertaken at a hard to very hard level of exertion (RPE-L or RPE-C of 5 and 7 respectively). For safety reasons, the power output of the work intervals was reduced if systolic BP (measured manually via sphygmomanometer at the end of each interval) exceeded 180 mmHg or if heart rate (recorded continuously via telemetry; Polar RS400™, Polar, Kempele, Finland) exceeded 95 per cent of the maximum observed on the baseline CPET. All occurrences of power output reduction were recorded for safety, and all exercise-related adverse events were noted. Each session was supervised directly by a research nurse and a physiotherapist who were trained in immediate life support, with full resuscitation equipment available immediately. Sessions were also attended intermittently by one of two experienced exercise scientists, who had overall responsibility for ensuring treatment fidelity of the exercise programme.

Study schedule and assessments

An overview of the assessment schedule has been published[22]. A baseline assessment visit was conducted in week 0, during which the following were recorded: medical history, current medications, baseline characteristics, maximum AAA diameter (transabdominal ultrasound imaging), cardiorespiratory fitness (anaerobic threshold and peak oxygen uptake recorded during an incremental cycle ergometer test to maximum volitional exertion), health-related quality of life (Short Form (SF) 36 physical function (PF) and mental health (MH) subscales (SF-36v2®, Optum, Eden Prairie, Minnesota, USA)[26]; EuroQol (EQ) 5D utility index (version EQ-5D-5 L) and EQ visual analogue scale (EQ-VAS) (EuroQol, Rotterdam, The Netherlands)[27], and preference for allocation to exercise or control.

In week 5, 24–48 h before the planned operation date, participants attended for reassessment of cardiorespiratory fitness and quality of life. Anaerobic threshold was determined by two experienced investigators blinded to group allocation, as described previously[28]. The exercise group also provided an overall rating of enjoyment of the exercise programme, using the Physical Activity Enjoyment Scale (PACES)[29], as well as having their maximum AAA diameter reassessed.

Surgical repairs were performed by the open or endovascular route, according to the routine clinical practice in each institution. Surgery was planned in week 5 (breeches recorded) with members of the clinical teams blinded to the group allocation. During the in-hospital postoperative period, an investigator blinded to the group allocation recorded data on the following: organ-specific morbidity (Post-Operative Morbidity Survey (POMS)[7], recorded daily), mortality, and duration of critical care and hospital stay.

Following discharge from hospital, participants were asked to record their healthcare use for a 12-week interval using a structured diary (*Appendix S1*, supporting information). At 6 weeks, participants received a telephone call from a study investigator encouraging accurate diary completion. Research nurses retrieved this information from participants during a face-to-face visit after 12 weeks. Health-related quality of life (SF-36® and EQ-5D™) was also reassessed at this visit.

Feasibility and acceptability outcomes

Outcomes used to assess the feasibility and acceptability of key trial parameters were rates of: screening,

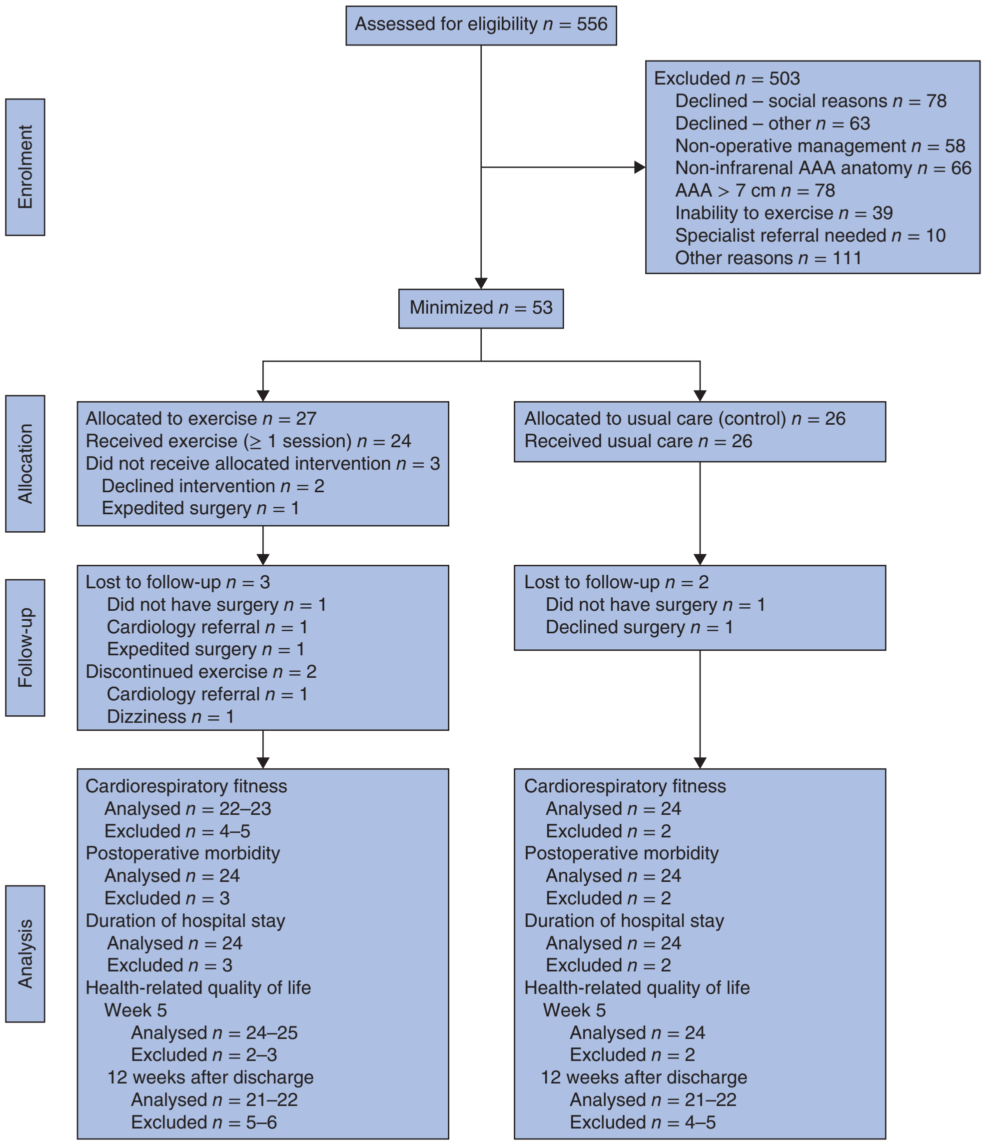

Fig. 1 Flow of participants through the trial

eligibility, recruitment, retention, outcome completion and adherence to exercise. Participants defined as adherent completed at least 75 per cent of the main-phase sessions (at least 9 of 12 sessions), plus all weekly maintenance sessions if surgery was delayed. Adverse events were recorded in a local adverse event log. Events were classified according to severity and whether they were related to the study intervention.

Group preference and reasons for exclusion and non-consent were recorded, and data on sample characteristics and the distribution of potential primary outcomes were also collected.

Sample size

The aim of the study was not to provide a definitive estimate of treatment effect, so the sample size calculation (*Appendix S1*, supporting information) was based on adherence to exercise rather than a clinical or patient-reported outcome. The aim was to recruit at least 50 participants within 21 months.

Analysis of clinical and patient-reported outcomes

For all clinical and patient-reported outcomes, point estimates and their uncertainty are presented as an indication of the range of effect sizes consistent with the data. No robust inference was attempted, as this was a feasibility study that was not powered to detect small yet clinically meaningful effects. For cardiorespiratory fitness at week 5, a conventional analysis of co-variance model was used to estimate the mean difference between groups in anaerobic threshold and peak oxygen uptake, adjusted for baseline score, operative procedure and trial site. Although sex was a minimization factor, it was not included as a factor in the analysis, as the study group comprised almost exclusively men. Interindividual differences in the fitness response to the exercise programme (treatment heterogeneity) were also quantified, as described in *Appendix S1* (supporting information).

For morbidity, a linear mixed model was used to explore differences between groups in total POMS score (maximum score 9). The model included operative procedure and trial site, fixed effects for group and number of days after operation, and a day × group interaction term. For duration of hospital stay, median (i.q.r.) number of days was calculated for each group, together with the hazard ratio (exercise *versus* control) for discharge alive using Cox regression, adjusting for operative procedure and trial site. For the EQ-5D™ utility index, EQ-VAS, and SF-36® PF and MH subscales at week 5 and 12 weeks after discharge from hospital, a linear mixed model was used with restricted maximum likelihood, adjusted for baseline score, operative procedure and trial site. This model included all three time points in the same analysis, a principled method for handling any data missing at random on the dependent variable[30]. All effects are presented with 95 per cent confidence intervals.

Economic evaluation

A prospective economic evaluation was rehearsed to develop and refine the methods for a subsequent definitive trial. The methods for this evaluation are described in *Appendix S1* (supporting information).

Results

Recruitment took place between September 2013 and July 2015, with all follow-up data collection completed by January 2016. The trial was stopped at the end of the grant funding interval, with the target sample size having been achieved.

Screening, eligibility and recruitment

All potentially eligible patients with an AAA were screened during the recruitment interval, giving a screening rate of 100 per cent. Of 556 patients screened for participation, 240 met the eligibility criteria and 53 were recruited, giving eligibility and recruitment rates of 43·2 and 22·1 per cent respectively. The three sites recruited 24, 21 and eight participants. Reasons for non-consent and exclusion are shown in *Fig. 1*, the most common of which were social (such as work commitments or difficulty travelling; 78 patients). Others included AAA diameter exceeding 7 cm (78) and non-infrarenal AAA anatomy (66).

Group allocation, group preference and participant characteristics

Twenty-seven participants were allocated to exercise and 26 to usual care. Of the 47 participants who expressed a preference for a specific group before allocation, 30 preferred exercise. Fifty men (94 per cent) and three women (6 per cent) were recruited to the study. Participant characteristics at baseline are shown in *Table 1*; the groups were well balanced for the majority of variables. Eleven participants in each group underwent open AAA repair, whereas 16 in the exercise group and 15 in the usual-care group received endovascular AAA repair.

Retention

The retention rate was 91 per cent. Five of 53 participants formally left the study (3 exercise, 2 control). One person from each group withdrew as they were no longer undergoing surgery, one control participant withdrew after declining surgery, one exercise participant withdrew before having completed any sessions because surgery was expedited, and one exercise participant withdrew after completing just one exercise session. The latter participant reported feeling unwell approximately 8 h after the exercise session; subsequent cardiology assessment showed no abnormality, but the subject decided to withdraw from the study at that stage.

Exercise adherence, exercise enjoyment and safety data

A detailed description of the training data has been presented elsewhere[31]. Of the 27 exercise participants, 15 had a delayed operation and therefore required at least one maintenance exercise session (range attended 0–9). No surgical delays occurred because of the exercise programme; the main reason for delayed operations was lack of a hospital bed for postoperative care on the day of surgery. In total, 324 main-phase and 40 maintenance exercise sessions were scheduled, of which 240 (74·1 per cent) and 36 (90 per cent)

Table 1 Baseline characteristics of participants

	Exercise ($n = 27$)	Control ($n = 26$)
Age (years)*	74·6(5·5)	74·9(6·4)
Sex ratio (M : F)	25 : 2	25 : 1
Body mass index (kg/m^2)*	26·5(4·1)	26·8(3·4)
AAA diameter (cm)*	6·0(0·4)	5·8(0·4)
Repair procedure		
Open repair	11	11
EVAR	16	15
Current or recent (within 6 months) smoker	8	2
Co-morbidities		
Coronary artery disease	11	14
Cerebrovascular disease	7	7
Peripheral arterial disease	0	2
Diabetes mellitus	4	2
Chronic obstructive pulmonary disease	6	7
Medications		
Antiplatelet	12	11
Statin	20	23
ACE inhibitor	9	14
Beta-blocker	9	9
Calcium channel blocker	7	10
Diuretic	1	5
Anaerobic threshold (ml per kg per min)*	11·0(2·1)†	10·9(2·7)‡
Peak oxygen uptake (ml per kg per min)*	16·5(3·7)†	15·7(3·1)
SF-36® physical function subscale*	50(7)†	48(8)‡
SF-36® mental health subscale*	57(6)	53(10)
EQ-5D™ utility index*	0·812(0·155)	0·822(0·157)
EQ visual analogue scale*	73(17)	73(16)‡

*Values are mean(s.d.). Based on †26 patients. ‡Based on 25 patients. AAA, abdominal aortic aneurysm; EVAR, endovascular aneurysm repair; ACE, angiotensin-converting enzyme; SF, Short Form; EQ, EuroQol.

were completed respectively (overall attendance rate 75·8 per cent). Seventeen of the 27 exercise participants (63 (95 per cent c.i. 45 to 81) per cent) achieved the prespecified adherence criterion. Three participants did not complete any sessions: two declined the exercise programme and one had expedited surgery. In addition, two participants did not complete the exercise programme: one was a full withdrawal after completing one session and referral to cardiology (described above); the other was a withdrawal from exercise after completing five sessions and referral to cardiology. This latter participant experienced prodromal symptoms (dizziness) on four separate occasions when the power output was increased beyond approximately 80 W. These symptoms resolved quickly on reducing the power output, with the participant completing the exercise sessions. Subsequent investigator review of the participant's baseline CPET resulted in a cardiology review to exclude significant underlying cardiac pathology. This review was normal; however, the participant was withdrawn from the exercise programme for logistical reasons.

The intensity of all work intervals completed by the 17 adherent participants is summarized as follows: mean(s.d.) RPE-L 4·1(2·0), RPE-C 3·5(1·9) and heart rate 81·7(8·5) per cent maximum. Some 30 per cent of work intervals were reported in the hard to very hard range (RPE-L 5–7). The mean improvement in cycling power output from baseline to week 4 sessions for all participants was 8 W. The mean(s.d.) PACES score was 98(19) of 119, equating to participants reporting the exercise sessions as enjoyable.

Twenty of the 27 exercise participants had at least one episode of cycling power output reduction owing to safety criteria being triggered (such as systolic BP over 180 mmHg). Of all work intervals, there were 36 instances of power output reduction among the 17 adherent participants, and 40 instances among the ten non-adherent participants (rates of 3 and 10 per cent respectively). One adverse event occurred that resulted in the termination of an exercise session: a single episode of short-lived angina that was relieved by self-administration of glyceryl trinitrate. Twenty-two exercise participants had maximal AAA diameter measurements at both baseline and week 5; mean(s.d.) values were 6·0(0·4) and 5·9(0·4) cm respectively.

A summary of the feasibility and acceptability data is presented in *Table S1* (supporting information).

Cardiorespiratory fitness

A week 5 anaerobic threshold value was available for 46 participants (22 exercise, 24 control), of whom one control participant had a missing baseline value, which was imputed using mean imputation[32]. The anaerobic threshold at week 5 was 11·7 ml per kg per min in the exercise group and 11·4 ml per kg per min in the control group (difference 0·3 (95 per cent c.i. −0·4 to 1·1) ml per kg per min). The s.d. for individual differences in response to the exercise programme was 1·0 (−0·7 to 1·5) ml per kg per min, a moderate effect size indicating potentially substantial interindividual differences in treatment response. For exercise *versus* control, assuming a minimum clinically important difference of 1·5 ml per kg per min, one individual was very likely to be a positive responder, three were likely to be positive responders, four were possibly positive responders, nine were trivial (non-) responders, and five were possibly negative responders.

A week 5 peak oxygen uptake value was available for 47 participants (23 exercise, 24 control). Peak oxygen uptake at week 5 was 16·8 ml per kg per min in the exercise group and 16·3 ml per kg per min in the control group (difference 0·5 (95 per cent c.i. −0·6 to 1·7) ml per kg per min). There was no evidence of substantial interindividual response to exercise.

Table 2 Summary of cost data in both groups from National Health Service and personal social services perspective

	Cost per participant (£)		
	Exercise	Control	Bootstrapped mean difference*
Cost of exercise programme	1176(0)	0	1176
Costs of AAA repair	10 481(2247)	10 880(2209)	−399 (−1719, 1000)
Postdischarge costs	862(2653)	1129(2290)	−267 (−1622, 1312)
Total costs	12 519(3107)	12 009(3107)	510 (−1393, 2498)

Values are bootstrapped mean(s.d.) unless indicated otherwise; *values in parentheses are 95 per cent confidence intervals. AAA, abdominal aortic aneurysm.

Postoperative morbidity and mortality

POMS data were collected for all 48 participants who completed the study. Mean total POMS count up to the point of discharge from hospital was 2·3 in the exercise group and 2·1 in the control group (difference 0·2, 95 per cent c.i. −0·3 to 0·7). There was no substantial group × postoperative day interaction. For example, on postoperative day 1, the mean total POMS count was 3·7 in the exercise group *versus* 3·4 in the control group. On days 3 and 5, the POMS counts were 2·4 *versus* 2·3 and 1·3 *versus* 1·2 respectively. There were no in-hospital or 30-day deaths in either group. One participant in the exercise group died from a myocardial infarction 12 weeks after discharge from hospital.

Duration of hospital stay

The unadjusted median duration of hospital stay was 7 (i.q.r. 4·5–8·5) days in the exercise group and 6 (4–8) days in the control group (48 participants). The hazard ratio for discharge alive in exercise *versus* control groups was 0·96 (95 per cent c.i. 0·53 to 1·74).

Health-related quality of life

EQ-5D™ utility scores were available for 49 participants at week 5 (25 exercise, 24 control) and 43 at 12 weeks after discharge (21 exercise, 22 control). The mean EQ-5D™ utility index score at week 5 was 0·864 in the exercise group and 0·796 in controls (difference 0·068, 95 per cent c.i. 0·002 to 0·135). Respective values at 12 weeks were 0·837 and 0·760 (difference 0·077, 0·005 to 0·148). The mean EQ-VAS score at week 5 was 81·9 in the exercise group and 75·8 in the control group (difference 6·1, −0·3 to 12·6). At 12 weeks, the scores were 79·6 and 74·4 respectively (difference 5·2, −1·7 to 12·0).

A SF-36® PF score was available for 48 participants at week 5 (24 exercise, 24 control) and 43 at 12 weeks after discharge (22 exercise, 21 control). The mean SF-36® PF score at week 5 was 49·6 in the exercise group and 49·9 in controls (difference −0·3, −2·7 to 2·1). At 12 weeks, respective scores were 49·4 and 46·5 (difference 2·9, 0·4 to 5·4). A SF-36® MH score was available for 49 participants at week 5 (25 exercise, 24 control) and 42 at 12 weeks after discharge (21 exercise, 21 control). The mean SF-36® MH score at week 5 was 54·6 in the exercise group and 55·1 in the control group (difference −0·5, −3·3 to 2·3). At 12 weeks, the scores were 55·6 and 55·0 respectively (difference 0·6, −2·4 to 3·6).

Health economic data

There were no missing data for the costs of the exercise programme and AAA repair procedures. The costs of the exercise programme are presented in *Table S2* (supporting information); the mean cost per participant was £1176. Unit costs for open and endovascular AAA repair procedures (including resource inputs during hospital stay) were based on NHS National Tariff Schedules: £8285·56 and £12 675·50 respectively[33].

Data on health and social care costs after discharge from hospital were available for 43 participants (21 exercise, 22 control). The mean costs per participant for each cost category at follow-up are shown *Table S3* (supporting information). Data regarding personal costs to each trial participant, including informal care-givers time, was not included owing to the unreliability of the data. Hospital readmission (for any reason) was the highest resource-use category across all categories in the study. There were no hospital readmissions in the exercise group, and three in the control group (owing to shortness of breath, rectal bleeding and oesophageal varices). The costs of outpatient visits were also high across both study groups; however, it must be noted that the costs of any diagnostic tests undertaken at these visits were included. The cost of district nursing was also notably high in the exercise group; this was because one participant recorded 17 visits in the first 3 weeks of follow-up.

The mean total cost per participant for each group is presented in *Table 2*. It was £12 519 in the exercise group and £12 009 for controls (bootstrapped mean difference £510, 95 per cent c.i. −1393 to 2498) (€13 707 and 13 149 respectively; bootstrapped mean difference €558, −1525 to 2735; exchange rate 21 August 2017).

Discussion

This study successfully tested recruitment and group allocation procedures, the logistics of study measurements and follow-up, and the feasibility and preliminary effectiveness of a preoperative HIT programme in people awaiting elective AAA repair. A key finding was that the trial procedures were mostly feasible. The preoperative HIT programme was also generally feasible and acceptable; however, exercise progression was often limited by the safety criteria, which resulted in an inconsistent and lower-than-prescribed intensity of exercise. This issue may have contributed to the observation that cardiorespiratory fitness did not change substantially at the group level, although there was evidence of interindividual heterogeneity, with around one-third of the exercise participants possibly-to-very likely to be positive responders (improvement in anaerobic threshold more than 1·5 ml per kg per min). The findings also indicate a potential small beneficial effect of the exercise programme on health status and physical function up to 12 weeks after discharge from hospital.

The feasibility and acceptability of preoperative HIT in people with a large AAA was a key area of uncertainty before conducting this work. The participant characteristics are consistent with those of a high-risk, elderly and unfit population, and there was insufficient relevant literature to inform whether such patients would engage with this intervention or if they could complete it safely. Overall, the findings generally support the feasibility and acceptability of the intervention. For example, recruitment was to time and target, there were few postrandomization withdrawals, and ratings of enjoyment were high. The preliminary safety data were also favourable in that there were few adverse events and no evidence of aneurysm expansion owing to exercise. Although data were not collected from non-consenting patients to allow a comparison of their characteristics with those of trial participants, the participants' fitness data were comparable to those observed in routine preoperative assessment[34]. Therefore, any potential concern about recruitment bias in favour of physically active patients was not supported by the data. Finally, the overall session attendance rate was good at 75·8 per cent. The trial protocol specified a success criterion of a lower limit of the 90 per cent confidence interval of 67 per cent for the proportion of the exercise group meeting the prespecified adherence rate[22]. Strictly, as only 17 of the 27 exercise participants (63 per cent) were adherent, this criterion was not met. The present study did not employ any specific adherence-enhancing components; however, cognitive behavioural strategies could easily be employed as part of any future trial.

In the context of the UK healthcare system, it was essential that the intervention did not interfere with the national target of patients being operated on within 8 weeks of referral[35]. All participants completing the exercise programme did so within this treatment window, with no surgical delays consequent to this. The exercise programme was also generally considered easy to deliver, owing to its relatively simple design. However, two issues were identified. First, the research nurses found it burdensome to take manual BP readings at the end of every work interval. This practice was necessary given the lack of published evidence on exercise for people with a large AAA. In future, it seems reasonable to suggest that the frequency of BP recordings could be reduced.

Regarding costs, although additional resources (such as staff and equipment) would be required to offer a preoperative exercise service, the overall additional costs are likely to be modest, lower than those reported in *Table 2*, and not markedly different from the cost of running a physiotherapy-led cardiac rehabilitation service. Another issue regarding intervention delivery was that the intensity of exercise, as predominantly indicated by RPE, was generally inconsistent and lower than prescribed. Although the possibility of participant under-reporting of RPE cannot be excluded, this finding is more likely explained by exercise progression being limited by the exercise safety criteria. Indeed, most participants (20 of 27) had at least one episode of cycling power output reduction owing to a safety criterion being triggered. This observation is important because suboptimal exercise progression may limit adaptations in cardiorespiratory fitness, which in turn may limit the potential for improvements in postoperative outcomes.

The HIT-AAA feasibility trial was essentially a small version of a full-scale trial, what is sometimes referred to as an external pilot trial[36]. A benefit of this design was that it allowed a test of whether the components of the main trial could all work together. One potential area of concern for a future trial is the low completion rates of the postdischarge questionnaires/diaries. Here, missing data approached 20 per cent, the level above which there may be threats to trial validity[37]. Feedback from participant interviews suggests that the diaries were lengthy and repetitive. A systematic review[38] of 38 randomized retention trials evaluating broad types of strategy to increase questionnaire response rates found that monetary incentives, recorded delivery of questionnaires, and a package of postal communication strategies with reminder letters all increased postal questionnaire response.

Other factors, besides feasibility and acceptability, need to be considered when deciding whether or not to pursue a full-scale trial. A key factor is whether the evidence base has developed in such a way that an evidence gap no longer exists. The recent study of Barakat and colleagues[19] included 124 patients, and used a circuit-style, moderate-intensity aerobic and resistance training programme delivered three times weekly for 6 weeks. The authors reported significant improvements in anaerobic threshold and peak oxygen uptake in exercise *versus* control groups in a subset of 48 participants who completed repeat CPET assessments, and a significant reduction in postoperative complications. No adverse events were recorded. It is possible that a 6-week programme of mixed aerobic/resistance training could be superior to a 4-week programme of HIT. Recent studies have shown that short-term preoperative interval training programmes can improve cardiorespiratory fitness in patients having surgery for lung[39] and rectal[40] cancer. Many participants with an AAA may be limited in their ability to perform high-intensity exercise, typically because of safety criteria limiting exercise progression. Therefore, it might be that longer-duration moderate-intensity training is preferential for such patients. Alternatively, a mixture of interval- and continuous-type exercise may also be worth considering. Indeed, a recent crossover study[41] showed that the incidence of non-response to exercise training may be reduced by changing from interval- to continuous-type training, or vice versa. Alternatively, there could be scope to intervene earlier in the surveillance population, for example, starting prehabilitation when the AAA diameter exceeds 4·5 cm rather than waiting until aneurysm repair is indicated (AAA larger than 5·5 cm).

Regardless of the optimal timing and content of a preoperative exercise programme for this population, it seems that a large, multicentre trial that is pragmatic in design and explores both clinical effectiveness and cost-effectiveness is needed before recommendations can safely be made about whether or not the healthcare systems should adopt this type of intervention.

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Supporting information

Additional supporting information may be found online in the supporting information tab for this article.

Editor's comments

Prehabilitation has the potential to improve outcomes across a range of major elective procedures. Abdominal aortic aneurysm (AAA) repair is an ideal model as so many men are monitored in surveillance programmes. There are many options for prehabilitation and the first priority is to find an exercise regimen that is practical, but that demonstrably improves fitness. High-intensity interval training may be too extreme for unfit patients (who might expect to benefit most). Prolonged, lower-intensity training may work better in men with an AAA. This is another example of a feasibility study contributing to the information required before a major RCT. Conducting the right definitive trial has the best chance of defining the optimal prehabilitation programme. Many men with an AAA in surveillance are overweight and continue to smoke; more focus on these simple issues should also be considered a component of the prehabilitation process.

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