ORIGINAL ARTICLE

Endurance Exercise Training in Patients With Small Abdominal Aortic Aneurysm: A Randomized Controlled Pilot Study

Garry A. Tew, PhD, James Moss, BSc, Helen Crank, PhD, Pauline A. Mitchell, MA, Shah Nawaz, MD

ABSTRACT. Tew GA, Moss J, Crank H, Mitchell PA, Nawaz S. Endurance exercise training in patients with small abdominal aortic aneurysm: a randomized controlled pilot study. Arch Phys Med Rehabil 2012;93:2148-53.

Objective: To investigate the feasibility of endurance exercise training in patients with small abdominal aortic aneurysm (AAA), and to obtain preliminary data of its impact on important health outcomes.

Design: Randomized controlled pilot study.

Setting: University rehabilitation facility.

Participants: Patients with small AAA (N=28; mean age ± SD, 72±7y).

Intervention: Participants were randomized to a 12-week program of moderate-intensity endurance exercise or standard care control (encouragement to exercise only).

Main Outcome Measures: Safety was assessed in terms of the frequency of adverse events and changes in maximum AAA diameter. Outcomes were assessed at baseline and 12 weeks including cardiopulmonary fitness (ventilatory threshold), health-related quality of life (Medical Outcomes Study 36-Item Short-Form Health Survey [version 2]), and markers of vascular risk (eg, blood pressure and high-sensitivity C-reactive protein).

Results: Of 545 patients contacted, 28 (5%) entered the trial. There were 3 (11%) dropouts. Adherence to the exercise program was 94%. There were no paradoxical increases in AAA size or adverse clinical events. Ventilatory threshold increased in the exercise group, but not the control group (adjusted mean difference, 2.5mL·kg^{-1}·min^{-1}; 95% confidence interval, 0.5–4.5; d=.82). Systolic blood pressure and high-sensitivity C-reactive protein decreased in the exercise group compared with the control group (d=.34 and d=.58, respectively). There were no substantial changes in anthropometric variables or quality of life.

Conclusions: Despite a low recruitment rate, the findings suggest that moderate-intensity endurance exercise training is feasible in patients with small AAA, and can evoke improvements in important health outcomes.

Key Words: Exercise therapy; Feasibility studies; Physical fitness; Rehabilitation; Vascular diseases.

ABDOMINAL AORTIC aneurysm (AAA) is a frequently lethal age-related disease affecting 5% to 7.5% of men and 1.5% to 3% of women aged >65 years.[1] Rupture of an AAA and its associated catastrophic physiologic insult carries overall mortality in excess of 80%,[2] and 2% of all deaths are AAA-related in men aged 65 to 74 years.[3] Mechanical intervention (open surgical or endovascular repair) is currently the only treatment shown to be effective in preventing AAA rupture and aneurysm-related death; it is reserved for AAAs ≥55mm in diameter for men and ≥50mm in women.[4] Fortunately, 90% of AAAs detected during screening fall below these thresholds[5] and expansion rates are gradual, with mean growth rates for small AAAs (30–49mm) of 2 to 3mm per year.[6] There are currently few treatment options available for people with small AAAs[4,6]; most patients simply enter a surveillance program to monitor the progression of their aneurysm.

Endurance exercise training might be a useful intervention for patients with early AAA disease for several reasons. First, exercise might reduce the excessive risk of all-cause mortality and cardiovascular disease events that characterizes this population.[7] For example, epidemiologic data indicate that a 3.5mL·kg^{-1}·min^{-1} increase in maximum oxygen consumption is associated with 13% and 15% decrements in risk of all-cause mortality and cardiovascular disease events, respectively.[8] Second, indirect evidence suggests that exercise might inhibit AAA enlargement through mechanisms including improved aortic hemodynamics and reduced inflammation. For example, a study in a rat experimental model demonstrated that increased aortic flow inhibited AAA expansion.[9] Finally, exercise might reduce the risk of perioperative morbidity and mortality in patients progressing to elective aneurysm repair via enhanced cardiopulmonary fitness.[10] Indeed, preoperative fitness levels have been associated with higher survival rates in individuals undergoing open surgical AAA repair[11] and other major intra-abdominal surgery.[12]

At present, little is known about the effects of exercise training in patients with AAA disease, most likely because this condition was not as widely recognized in the past as it is today, and perhaps because of concerns about excessive rises in double product (systolic blood pressure × heart rate) causing aneurysm rupture. However, such concerns about the risks of exercise, particularly that of moderate intensity, appear unfounded. For example, Myers et al[13] recently assessed the safety of maximal treadmill exercise testing in 306 patients with small AAAs ranging from 30 to 50mm in diameter.

List of Abbreviations

AAA	abdominal aortic aneurysm
hs-CRP	high-sensitivity C-reactive protein
MMP-9	matrix metalloproteinase-9
Vo_2peak	peak oxygen consumption

From the Centre for Sport and Exercise Science (Tew, Moss, Crank) and the Faculty of Health and Wellbeing (Mitchell), Sheffield Hallam University, Sheffield; and the Sheffield Vascular Institute, Northern General Hospital, Sheffield (Nawaz), UK.

Presented to the European College of Sport Science, July 8, 2011, Liverpool, UK and British Association of Sport and Exercise Sciences, September 7, 2011, Colchester, UK.

Supported by Sheffield Hallam University and the Sheffield Vascular Institute.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit on the authors or on any organization with which the authors are associated.

Correspondence to Garry A. Tew, PhD, Centre for Sport and Exercise Science, Collegiate Crescent Campus, Sheffield Hallam University, Sheffield, S10 2BP, UK, e-mail: *g.tew@shu.ac.uk*. Reprints are not available from the author.

In-press corrected proof published online on Sep 26, 2012, at www.archives-pmr.org.

0003-9993/12/9312-00303$36.00/0
http://dx.doi.org/10.1016/j.apmr.2012.07.012

Despite the incidence of exercise-induced hypotension and hypertension being higher in AAA patients than in age-matched adults referred for clinical reasons (2.9% and 3.6% vs <1.0%, respectively; $P<.001$), there were no serious adverse events (eg, ventricular tachycardia, aneurysm rupture). Of note, the American College of Cardiology/American Heart Association Practice Guidelines for the Management of Patients with Peripheral Vascular Disease suggest that AAA patients should not be fearful of vigorous activity and that efforts should be made to improve fitness in the event that surgery is required.[14]

To date there have only been 2 published reports of exercise training in patients with AAA.[15,16] In the first of these, Kothmann et al[16] randomized 30 patients with small AAAs (30–51mm) to either a 6-week endurance exercise program (30min continuous moderate-intensity cycle ergometry, twice weekly) or usual care control. Twenty-five of the participants completed this pilot study, and ventilatory threshold increased by 10% in the intervention group compared with the controls ($P=.007$). This modest change is probably largely because of the low overall training volume. No other health outcomes were reported. In the other report, which described preliminary data from the AAA Simple Treatment or Prevention trial,[15] 57 patients with small AAA (30–50mm) were randomized to either exercise or usual care control. The exercise regimen involved a combination of moderate-intensity endurance and resistance exercises performed in-house and/or at home over the period of 1 year. Thus, the exact training stimulus likely varied somewhat between patients. Nevertheless, no participants in training experienced AAA-related symptoms, exercise-related clinical events, or excessive aneurysm growth rates. Although the increases in peak oxygen consumption (V_{O_2}peak) did not reach statistical significance ($P=.29$), the increase in treadmill test duration was considerable (42% vs 2%, respectively; $P=.01$), and the mean recreational energy expenditure equated to over 1 hour of moderate-intensity exercise per day.

Although these previous reports have provided some insight into the safety, acceptability, and efficacy of exercise training in patients with small AAAs, further research is needed to assess its feasibility and impact on a broad range of important health outcomes. Furthermore, we believe it is important to assess the effects of different training regimes. Therefore, the aim of this study was to investigate the feasibility of a 12-week program of supervised endurance exercise training in patients with small AAAs, as well as its impact on cardiopulmonary fitness, health-related quality of life, and several disease-specific and cardiovascular risk markers by comparison with patients receiving standard care only.

METHODS

Participants

Based on the pilot study guidelines of Lancaster et al,[17] we aimed to recruit 60 patients with early AAA disease between January 2010 and September 2011. Only 28 patients were recruited during this period (fig 1). Potential participants were identified from vascular clinics and aneurysm surveillance lists at the Northern General Hospital, Sheffield and Rotherham Hospital, Rotherham, UK. Inclusion criteria were men and women patients aged 50 to 85 years with an asymptomatic, infrarenal AAA 30 to 50mm in diameter. Exclusion criteria were any contraindications to exercise testing and training (eg, severe hypertension, unstable angina, and uncontrolled cardiac arrhythmias), an inability or unwillingness to undertake the commitments of the study, and current participation in regular purposeful exercise (≥30min, ≥3 times per wk). This research was carried out in accordance with the Declaration of Helsinki of the World Medical Association, and was approved by the South Yorkshire Research Ethics Committee. Participants provided written informed consent before being included in the study. The study was registered in ClinicalTrials.gov under reference no. NCT01234610.

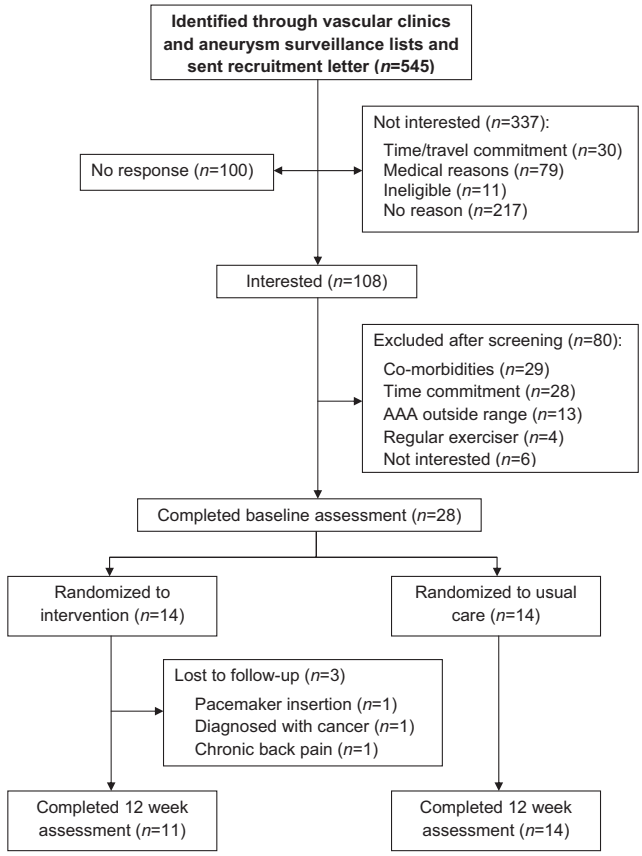

Fig 1. Consolidated Standards of Reporting Trials flow diagram.

Design

This was a randomized controlled pilot trial. After completion of baseline assessments, participants were randomly assigned 1:1 either to exercise training or standard care control. Both groups had access to standard care, which consisted of a basic recommendation to be physically active, but to avoid strenuous lifting. Allocation to exercise or control was done using a randomization sequence created by an independent researcher before study commencement.[a] The study researchers were made aware of this sequence on a case-by-case basis after baseline assessments were completed.

Study methods for all participants included extraction of medical history and drug information from medical records and patient questioning, and assessment of the following outcomes at baseline and after 12 weeks of follow-up: health-related quality of life using the Medical Outcomes Study 36-Item Short-Form Health Survey (version 2) questionnaire,[18] maximum AAA diameter via transabdominal ultrasound,[b] and ventilatory threshold via cardiopulmonary exercise testing. Fasting venous blood samples were collected for analysis of lipid profiles, high-sensitivity C-reactive protein (hs-CRP), matrix metalloproteinase-9 (MMP-9),[c] and glucose (all serum).