THE AORTIC AND SYSTEMIC ARTERIAL STIFFNESS RESPONSES TO ACUTE EXERCISE IN PATIENTS WITH SMALL ABDOMINAL AORTIC ANEURYSMS

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ARTICLE TYPE: ORIGINAL ARTICLE

DECLARATIONS OF INTEREST: NONE

WORD COUNT: 4174

SHORT TITLE: Exercise and aortic stiffness in AAA

FIGURES: 3 TABLES: 4

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WHAT THIS PAPER ADDS

Elevated arterial stiffness is associated with aneurysm progression and likely contributes to the high cardiovascular risk of AAA patients. We demonstrate that the change in aortic and systemic arterial

stiffness are lower in AAA patients following exercise compared with seated rest. This effect was most marked following higher-intensity interval exercise. This attenuation in arterial stiffness suggests there may be an acute cardiovascular benefit of exercise in AAA patients. Our findings support the use of interval-based high-intensity exercise as a safe intervention to improve cardiovascular function in AAA patients and adds to the evidence that exercise prescription should be part of routine care of AAA patients.

ABSTRACT

Objective: Elevated arterial stiffness is a characteristic of abdominal aortic aneurysm (AAA), and is associated with AAA growth and cardiovascular mortality. A bout of exercise transiently reduces aortic and systemic arterial stiffness in healthy adults. Whether the same response occurs in AAA patients is unknown. The effect of moderate- and higher-intensity exercise on arterial stiffness was assessed in AAA patients and healthy adults.

Methods: Male patients with small AAAs (AAA diameter 36±5 mm; n=22; mean age 74±6 years) and healthy adults (n=22; mean age 72±5 years) were included. Aortic stiffness was measured using carotid to femoral pulse wave velocity (PWV), and systemic arterial stiffness was estimated from the wave reflection magnitude (RM) and augmentation index (AIx75). Measurements were performed at rest and during 90 min of recovery following three separate test sessions in a randomised order: 1) moderate-intensity continuous exercise; 2) higher-intensity interval exercise; or 3) seated-rest.

Results: At rest, PWV was higher in AAA patients compared with healthy adults (P<0.001), whilst AIx75 and RM were similar between groups. No differences were observed between AAA patients and healthy adults in post-exercise aortic and systemic arterial stiffness after either exercise protocol. When assessed as the change from baseline (delta, Δ), post-exercise ΔAIx75 was not different to the seated rest protocol. Conversely, post-exercise ΔPWV and ΔRM were both lower at all time-points compared to seated rest (P<.001). ΔPWV was lower immediately after higher-intensity compared with moderate-intensity exercise (P=.015).

Conclusions: High resting aortic stiffness in AAA patients is not exacerbated after exercise. There was a similar post-exercise attenuation in arterial stiffness between patients with AAA and healthy

adults compared with seated rest. This effect was most pronounced following higher-intensity interval exercise, suggesting that this form of exercise may be a safe and effective adjunct therapy for patients with small AAAs.

Key Words: pulse wave velocity, wave reflection characteristics; vascular disease

INTRODUCTION

An established deficiency in the current management of abdominal aortic aneurysm (AAA) is the absence of effective therapies to limit progression of early stage disease.[1] Patients with AAA also have an increased incidence of cardiovascular events.[2] Increased aortic stiffness is implicated in the progression of experimental [3] and human AAA.[4] Carotid-femoral pulse wave velocity (PWV), the gold-standard non-invasive measure of aortic stiffness,[5] is elevated in adults with AAAs.[6] Increased PWV is also associated with greater AAA progression and rupture risk.[7] Additionally, measures of systemic arterial stiffness, such as augmentation index (AIx) and reflection magnitude (RM), are strongly associated with cardiovascular mortality risk.[8] Therefore, interventions that attenuate the rise in arterial stiffness may help limit AAA growth and cardiovascular risk.

Exercise therapy is widely recommended as part of the routine management of patients with cardiovascular disease.[9] In AAA patients, short-term exercise therapy has been shown to improve cardiorespiratory fitness [10, 11] and is associated with reduced postoperative complications following aneurysm repair.[12] A recent retrospective study also reported that exercise rehabilitation was associated with reduced AAA growth and a lower requirement for AAA repair.[13] Despite these reports, there is a lack of understanding regarding the risks of exercise and mechanisms by which exercise may provide benefit to AAA patients. There is also a lack of knowledge regarding which forms of exercise are most likely to be beneficial. As such, exercise therapy remains underutilised in AAA patients and specific guidelines for its safe and effective use are absent from the current management guidelines.[14]

Exercise may be an effective approach for reducing arterial stiffness in AAA patients. A single bout of moderate-intensity exercise transiently lowers PWV and central blood pressure (cBP) in healthy

adults,[15] and higher-intensity exercise has been reported to induce larger reductions in PWV and cBP.[16] In contrast, increases in PWV were reported after high-intensity exercise in adults with hypertension and obesity,[17, 18] comorbidities commonly observed in AAA patients. Such an increase in aortic stiffness following high-intensity exercise might exacerbate cardiovascular risk,[19] and would be a concern in AAA patients. Interval-based exercise consisting of intermittent bouts of higher-intensity exercise interspersed with periods of low-intensity recovery has recently been proposed as a feasible intervention to improve fitness prior to AAA repair.[20] To date, there have been no investigations of how this form of exercise affects haemodynamics and arterial stiffness in AAA patients.

This study aimed to compare the effect of moderate-intensity continuous and higher-intensity interval exercise on the aortic and systemic arterial stiffness responses between AAA patients and healthy adults. Determining the acute arterial stiffness response to exercise will provide better understanding of the potential risks and benefits of exercise in AAA patients, and an insight into the potential value of higher-intensity interval exercise for these patients.

METHODS

Participant recruitment

Twenty-two male AAA patients (diameter: 30-45 mm) and 22 healthy males were included. AAA patients were recruited through local clinics and had a confirmed diagnosis within the 6 months prior to study entry. Participants were included if they were aged 60-86 years and able to exercise; and were excluded if they were deemed unsuitable for exercise by a cardiologist, e.g. for reversible ischemia during exercise or uncontrolled cardiac arrhythmia. Healthy participants were excluded if they had a family history of aneurysm. Exclusion criteria for both groups included uncontrolled hypertension (>140/>90 mmHg), heart failure, critical aortic stenosis, ankylosing spondylitis, peripheral neuropathy, limiting venous insufficiency, or any other diagnosed vascular disease (e.g. Raynaud's or vasculitis). All participants provided written informed consent to participate in the study, which conformed to the Declaration of Helsinki. The study was approved by the human research ethics committees of the University of the Sunshine Coast and the Prince Charles Hospital, Brisbane.

Experimental Overview

This was a randomised, cross-over experimental study. Participants in both groups underwent four separate visits and continued to take all prescribed medication throughout the study. Participants refrained from alcohol and exercise for 24h, and caffeine for 12h, prior to each visit. Participants were ≥6h fasted and consumed a standardised breakfast 3h before each session. Visit 1 consisted of anthropometric measurements, followed by a maximal incremental cycling test to determine cardiorespiratory fitness ($\dot{V}O_{2peak}$) and peak power output (PPO). Experimental visits (2-4) were counter-balanced, randomised, and consisted of either: 1) moderate-intensity continuous cycling exercise; 2) higher-intensity interval cycling exercise; or 3) seated-rest. Measures of aortic and systemic arterial stiffness were recorded in the supine position at rest and during the recovery period after each protocol (0, 20, 40, 60 and 90 min). Laboratory conditions were standardised for each visit (room temperature: 23 ± 1°C).

Determination of cardiorespiratory fitness

A maximal incremental cycling test commenced at 20 W and then increased by 10 W/min until volitional cessation. Pedal rate was maintained at 60-90 rpm. Expired gases were collected throughout and data were averaged every 15 s (Parvo Medics, UT, USA) for the determination of oxygen consumption ($\dot{V}O_2$; $mL \cdot kg^{-1} \cdot min^{-1}$). $\dot{V}O_{2peak}$ was determined as the highest 15 s average of $\dot{V}O_2$ over the last 60 s. Heart rate was continuously measured (Mortara Inc., WI, USA), along with the rate of perceived exertion (RPE).[21] PPO was used to establish the exercise intensity for the experimental visits.

Experimental exercise and seated-rest protocols

Following pre-test measurements of aortic and systemic arterial stiffness, and blood pressure, participants performed a 3-min warm up at 0 W followed by moderate-intensity continuous (24 min moderate-intensity at 40% PPO) or high-intensity interval (12 x 60 s bouts at 70% PPO, separated by 12 x 60 s bouts at 10% PPO) cycling. The seated-rest protocol was a duration-matched period of seated rest. Heart rate was recorded every 2 min and brachial blood pressure was measured manually every 6 min. Immediately following each protocol, participants were moved back to the supine position for recovery measurements of arterial stiffness.

Aortic and systemic arterial stiffness measurements

Measures of aortic (carotid-femoral PWV) and systemic arterial stiffness (wave reflection indices: AIx and RM) were measured while supine using the SphygmoCor XCEL device (AtCor Medical, West Ryde, NSW, Australia). Wave reflection measurements always preceded PWV measurements and followed recently published guidelines.[22] The reliability of the post-exercise arterial stiffness indices was recently established in older adults.[23]

Wave reflection characteristics: Blood pressure was measured in triplicate before the collection of brachial artery waveforms for wave reflection characteristics (SphygmoCor Xcel, AtCor Medical, Sydney, Australia). An aortic pressure waveform was generated by applying a proprietary digital

signal processing and transfer function,[24] from which central systolic (cSBP), diastolic (cSDP), central pulse pressure (cPP), mean arterial pressure (MAP), augmentation pressure (AP) and AIx, were derived. Central pulse pressure was calculated as the difference between cSBP and cDBP. Augmentation pressure was the difference between cSBP and the pressure at the inflection point (the merging of the forward and reflected pressure waves). AIx is augmentation pressure expressed as a percentage of pulse pressure. As AIx is affected by heart rate, it was corrected for a heart rate of 75 bpm (AIx75). Wave separation analysis was applied (SphygmoCor CVMS software, version 9) to determine the aortic forward (Pf) and backward (Pb) pressure waveforms.[25] Reflection magnitude (RM) was calculated as the ratio of Pb to Pf magnitude and expressed as a percentage [RM = (Pb/Pf)*100].

Pulse wave velocity: Simultaneous measures of the pulse wave were taken from the right carotid artery using a hand-held high-fidelity applanation tonometer, and the right femoral artery using a cuff placed at mid-thigh level. Once a stable carotid pulse was detected, the thigh cuff was inflated to 80 mmHg to obtain a concurrent femoral pulse waveform. Measurements were based on 10 s pulse wave traces that were free of artefact and met the quality control threshold of the SphygmoCor Xcel device for pulse-to-pulse variability. PWV was determined as the ratio of the distance between the carotid and femoral arteries to the transit time of the pulse wave between sites.[26]

Statistical analysis

Based on previous reports in patients with cardiovascular disease and hypertension [17] and the established variance of the outcome measures,[23] our sample size estimates revealed that 18 participants per group would be required to detect differences in the post-exercise PWV response of 1.2±2.0 m s^{-1} between the AAA and healthy groups, assuming an alpha level of 0.05 and >80% power. Normality of the outcome data was confirmed based on kurtosis and skewness analyses.[27] A single-factor linear mixed model (LMM) was used to compare anthropometric characteristics and cardiorespiratory fitness between AAA and healthy adults. Pearson's chi squared test was used to compare categorical data between groups. A two-factor (group*protocol) LMM was used to compare

baseline PWV, AIx75 and RM between groups across the study visits. The factor "time" was added to the LMM to detect differences in heart rate, blood pressure and perceived exertion during each protocol. The same analysis was used to compare PWV, AIx75 and RM between AAA and healthy adults, across "time" (baseline, 0-, 20-, 40-, 60-, and 90-min post) and between each protocol (seated-rest, moderate- and higher-intensity exercise). Post-exercise data were also analysed as changes from baseline (delta,Δ) to account for individual day-to-day baseline variance. Cardiorespiratory fitness and AAA size were added as co-variates.[15] Statistically significant interactions were further investigated with multiple comparisons using Fisher's least significant difference approach.[28] Analyses were conducted using the Statistical Package for Social Sciences (Version 22; IBM SPSS Inc., Chicago, IL) and statistical significance was set at $P \leq .05$. Data are presented in the text as mean and 95% confidence interval (95%CI) unless otherwise stated.

RESULTS

Participant characteristics

Characteristics of AAA patients and healthy adults are provided in Table 1.

Heart rate, mean arterial pressure and perceived exertion during exercise

Mean power output (W) during exercise was significantly greater in healthy adults [moderate-intensity: mean = 58W, (95% CI, 53 to 61); higher-intensity: mean = 100W (95% CI, 93 to 107)] compared to AAA patients [moderate-intensity: mean = 48W, (95% CI, 43 to 51); higher-intensity: mean = 83W (95% CI, 76 to 90), P<.001]. Increases in heart rate, blood pressure and RPE throughout each protocol were similar between groups (Table 2).

Central blood pressure, aortic stiffness and systemic stiffness at baseline and in response to exercise

Mean central blood pressure, PWV, AIx75 and RM at baseline and during recovery (0 to 90 min) after exercise and seated-rest protocols for AAA and healthy groups are shown in Tables 3 and 4. The change (Δ) from baseline in PWV, AIx75 and RM in AAA patients and healthy adults for each protocol are shown in Figures 1-3. Findings are summarised below.

Baseline central blood pressure and arterial stiffness indices

Arterial stiffness indices measured at baseline were similar across the three protocols (P>.05). Coefficient of variation (CV% = SD / mean x 100) for PWV, AIx75 and RM ranged between 5-10% in both groups. PWV measured at baseline was 2.2 $m.s^{-1}$ (95% CI 0.9 to 3.5, P<.001) higher in AAA patients compared with the healthy group (Table 3).

Effect of exercise on central blood pressure and arterial stiffness indices

There was no significant three-way (protocol*group*time) interaction for any of the arterial stiffness and central blood pressure indices hence, the responses to exercise did not differ between AAA patients and healthy adults for any of these measures (Tables 3 and 4). In both groups, following the seated-rest protocol, PWV increased from baseline at all time-points, whereas after moderate-intensity exercise, PWV was only elevated from baseline at 90 min. Conversely, PWV decreased immediately after higher-intensity exercise (0-min after) compared with baseline, before increasing above baseline at 90 min (Table 3). After both exercise protocols the response of ΔPWV was

attenuated and significantly lower at all time-points compared to seated-rest (Fig 1). In addition, ΔPWV was lower at 0 and 40 min after higher-intensity exercise compared with after moderate-intensity exercise (Fig 1B/C).

In both groups, AIx75 decreased and remained below baseline for 90 min after all three protocols; however, there was no protocol*time interaction (Table 3, Fig 2). After seated-rest, RM remained unchanged, whereas RM decreased after both exercise protocols compared with baseline (Table 3). After both exercise protocols ΔRM was lower at all time-points compared with seated-rest, however there was no difference between exercise protocols (Fig 3).

In both participant groups, heart rate decreased below baseline for 90 min after seated-rest and was increased above baseline for 20-40 min after exercise (Table 4). Central blood pressure indices (cSBP, cDBP, cPP) increased above baseline for 90 min after seated-rest (Table 4).

DISCUSSION

This study investigated the effect of a bout of exercise on post-exercise measures of aortic (PWV) and systemic artery stiffness (RM, AIx75) in AAA patients compared with healthy adults. Post-exercise PWV and RM responses were attenuated following exercise compared with seated-rest. With higher-intensity interval exercise, post-exercise PWV was lower compared with moderate-intensity continuous exercise in both groups. While PWV was higher in the AAA patients at rest, the change in aortic and systemic arterial stiffness after exercise was similar compared with healthy adults. These findings provide important information about the acute risks and potential benefits of exercise and the types of exercise that may be suitable for AAA patients.

Aortic and systemic arterial stiffness at rest

Resting PWV was higher in AAA patients compared with healthy adults, which is consistent with most,[7, 29] but not all previous reports.[30] Conversely, there was no significant difference in systemic arterial stiffness between groups. PWV represents aortic stiffness,[5] while wave reflection characteristics represent the net reflected pressure wave that travels from the peripheral vascular tree back to the proximal aorta, which may not be directly affected by AAA.[31] These findings suggest that the presence of small AAA is associated with localised stiffening of the aorta, but not peripheral arterial stiffness relative to healthy adults.

Aortic and systemic arterial stiffness after exercise

In both groups, there were transient significant decreases from baseline in RM after both exercise protocols, and in PWV only after higher-intensity interval exercise. Following the seated-rest period, there was a progressive rise in PWV, but no change in RM. Compared to the seated-rest protocol, the responses of PWV and RM were attenuated following exercise in both AAA patients and healthy adults. This finding is in line with previous studies in younger [32] and older adults.[15]

Despite a higher resting PWV in AAA patients, exercise did not exacerbate aortic stiffness, with the changes in PWV during exercise recovery being similar between groups. The attenuation in aortic and systemic arterial stiffness after submaximal exercise, compared with seated-rest, suggests there may be a reduction in aortic wall stress and an acute cardiovascular benefit from exercise for AAA patients, similar to that reported for healthy adults.[19] This is likely due to exercise-induced improvements in arterial tone,[33] sympathetic nervous activity [34] and increases in shear stress mediated endothelial function.[35] Importantly, these acute physiological changes have been suggested to contribute to positive vascular remodelling with sustained exercise therapy, including longer-term reductions in arterial stiffness.[36] In AAA patients, the attenuation in aortic stiffness and wave reflection magnitude compared to seated rest may contribute to a reduced central blood pressure and may alleviate stress on the AAA wall, perhaps limiting growth and rupture risk. While there is evidence that exercise reduces the likelihood of AAA formation in a mouse model of Marfan

syndrome, [37, 38] the translation relevance of this finding have not yet been established, and further evidence is needed from human AAA exercise trials to confirm this benefit.[39]

Exercise as an adjunct therapy for AAA

To date, several exercise therapy studies have demonstrated significant improvements in cardiorespiratory fitness in patients with small [10, 11] and large AAAs, [40] and reductions in complication rates following AAA repair. [12] However, a lack of evidence regarding the safety and effectiveness of exercise in providing cardiovascular benefit in AAA patients may have contributed to exercise historically being contraindicated for these patients.[41] The most recent European Society for Vascular Surgery guidelines encourage exercise as part of strategies towards a healthy lifestyle, although specific recommendations on what an exercise program should consist of are not currently available.[14] Most prior exercise studies have adopted a conservative prescription of low- or moderate-intensity continuous exercise in AAA patients [10, 11, 39]. In the current study, higher-intensity interval exercise induced a lower post-exercise PWV compared with moderate-intensity continuous exercise. Interval exercise is increasingly being recommended in adults with cardiovascular disease as it allows for a greater volume and intensity of exercise, and has potential for additional cardiovascular and systemic benefit, compared with moderate-intensity exercise.[37, 38, 42] Our findings, and a recent feasibility study reporting no adverse events with exercise in patients with large AAA,[20] provide support for the use of interval-based high-intensity exercise as a safe intervention to improve cardiovascular function in AAA patients. Further longer-term randomised controlled trials are needed to more thoroughly determine the effect of high-intensity exercise therapy compared with standard care on clinical outcomes in AAA patients.

Limitations

As would be expected, there were differences in medication prescription between AAA patients and healthy adults. Beta-blockers and other anti-hypertensive medications may affect the response of PWV to exercise;[17, 43] but this study found no differences in PWV responses between those who were receiving prescribed medications and those who were not. The reliability of PWV has not been yet

established in patients with small AAA. However, in the current study the between-day CV% for AAA patients was excellent (5.9±3.1%), similar to that in the healthy adults (6.2±4.2%), and in line with previous published work from our lab (5.0±4.1%).[23] With large AAAs there is an increase in PWV measurement error [31] and thus our findings may not be generalisable to those with large AAA. This study only included patients with small (<45 mm) asymptomatic AAA who had been cleared to exercise by a cardiologist. Thus, care should be taken in generalising the findings of this study to all AAA patients. In addition, this study only included male participants and thus the findings cannot be extrapolated to females.

CONCLUSION

In conclusion, this study suggests that a bout of exercise attenuates the arterial stiffness response, compared with seated-rest, in both AAA patients and healthy adults. This effect is most marked following higher-intensity interval exercise and supports the safety and potential efficacy of exercise training as part of the management of AAA patients. Whether exercise training leads to a chronic lowering of aortic and systemic arterial stiffness in AAA patients requires future investigation.

FUNDING

This research was funded by grants from the National Health and Medical Research Council (1000967, 1022752, 1079369) and The Townsville Hospital. Professor Jonathan Golledge's work is supported by fellowships from the NHMRC (1117061) and the Queensland Government (Senior Clinical Research Fellowship). Support for this work was also provided through the Inflammation and Healing Research Cluster at the University of the Sunshine Coast.

ACKNOWLEDGEMENTS

The authors thank the patients and volunteers for taking part in the study. We thank Lauren Northey at the Sunshine Coast University Hospital and Health Service, and the administrative team at Sunshine Vascular Clinic, for their support with patient recruitment.

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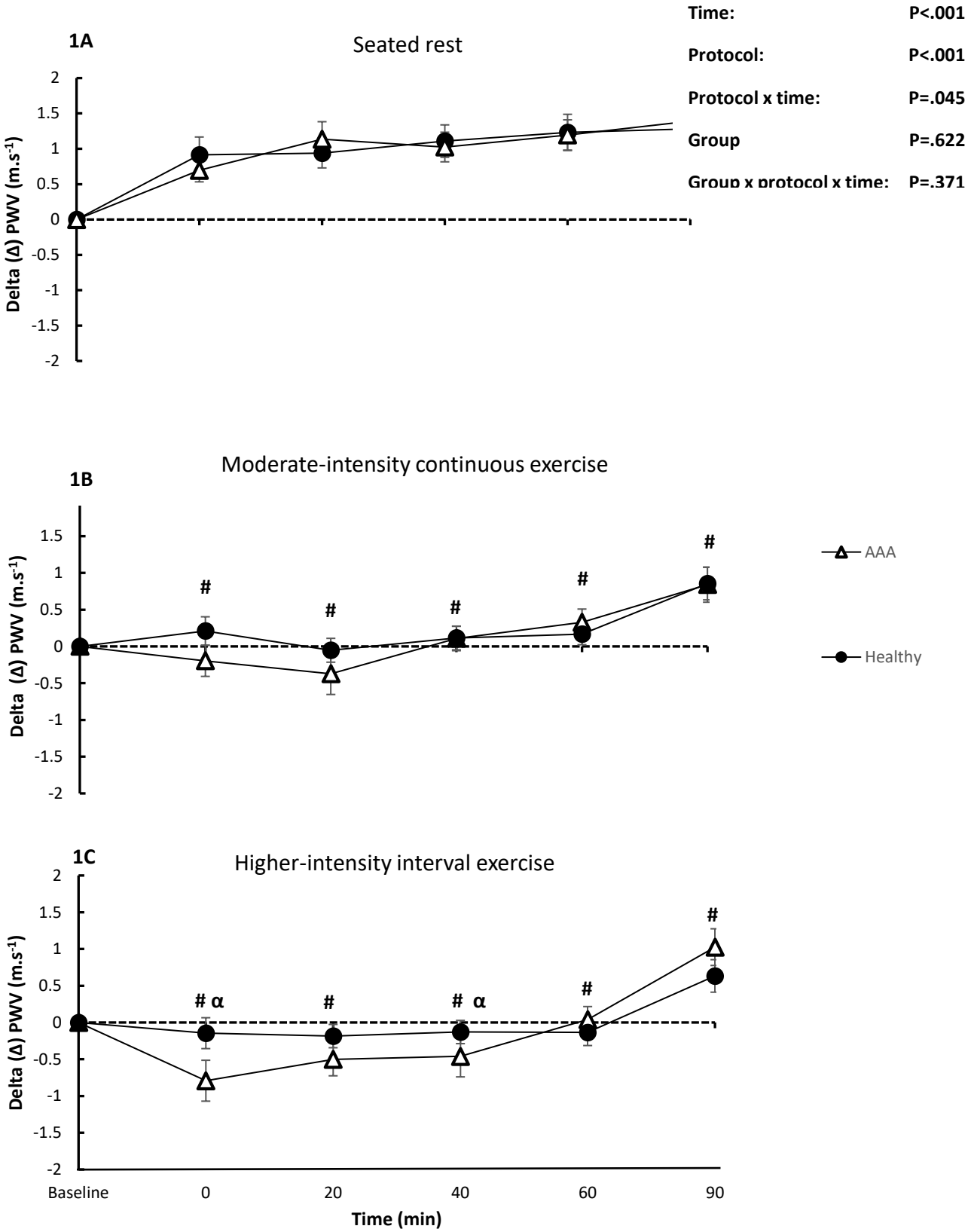

Figure 1: Delta PWV response of AAA (white triangles) and healthy (black circles) groups to seated rest (A), moderate-intensity continuous (B) and higher-intensity interval (C) exercise. Data are mean and SEM; PWV, pulse wave velocity. [#]Significantly different to seated rest; [α] significantly different to moderate-intensity based on protocol*time post-hoc comparisons.

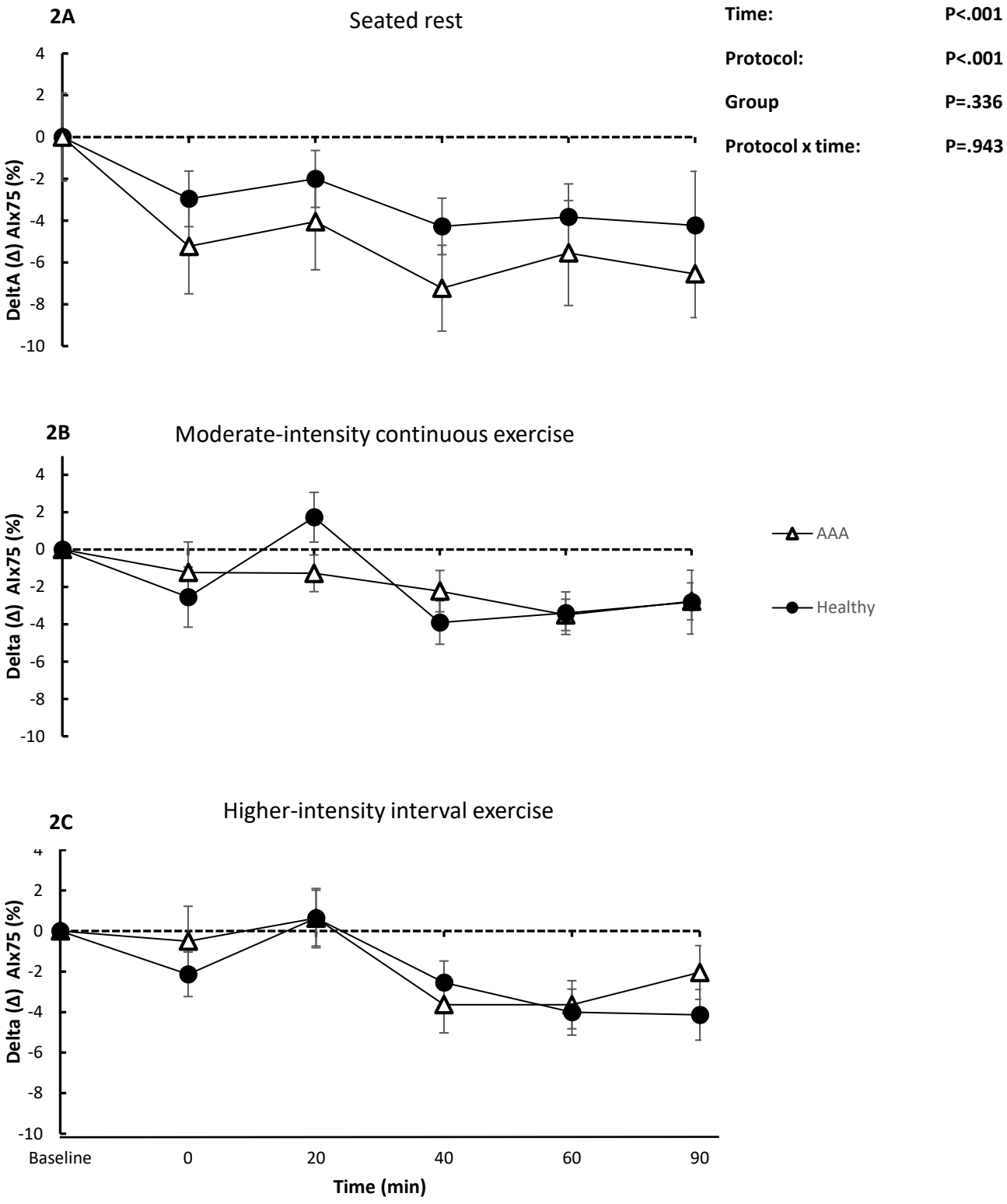

Figure 2: Delta AIx75 response of AAA (white triangles) and healthy (black circles) groups to seated rest (A), moderate-intensity continuous (B) and high-intensity interval (C) exercise. Data are mean and SEM; AIx75, augmentation index normalised to a heart rate of 75 bpm. [#]Significantly different to seated rest; [α] significantly different to moderate-intensity based on protocol*time post-hoc comparisons.

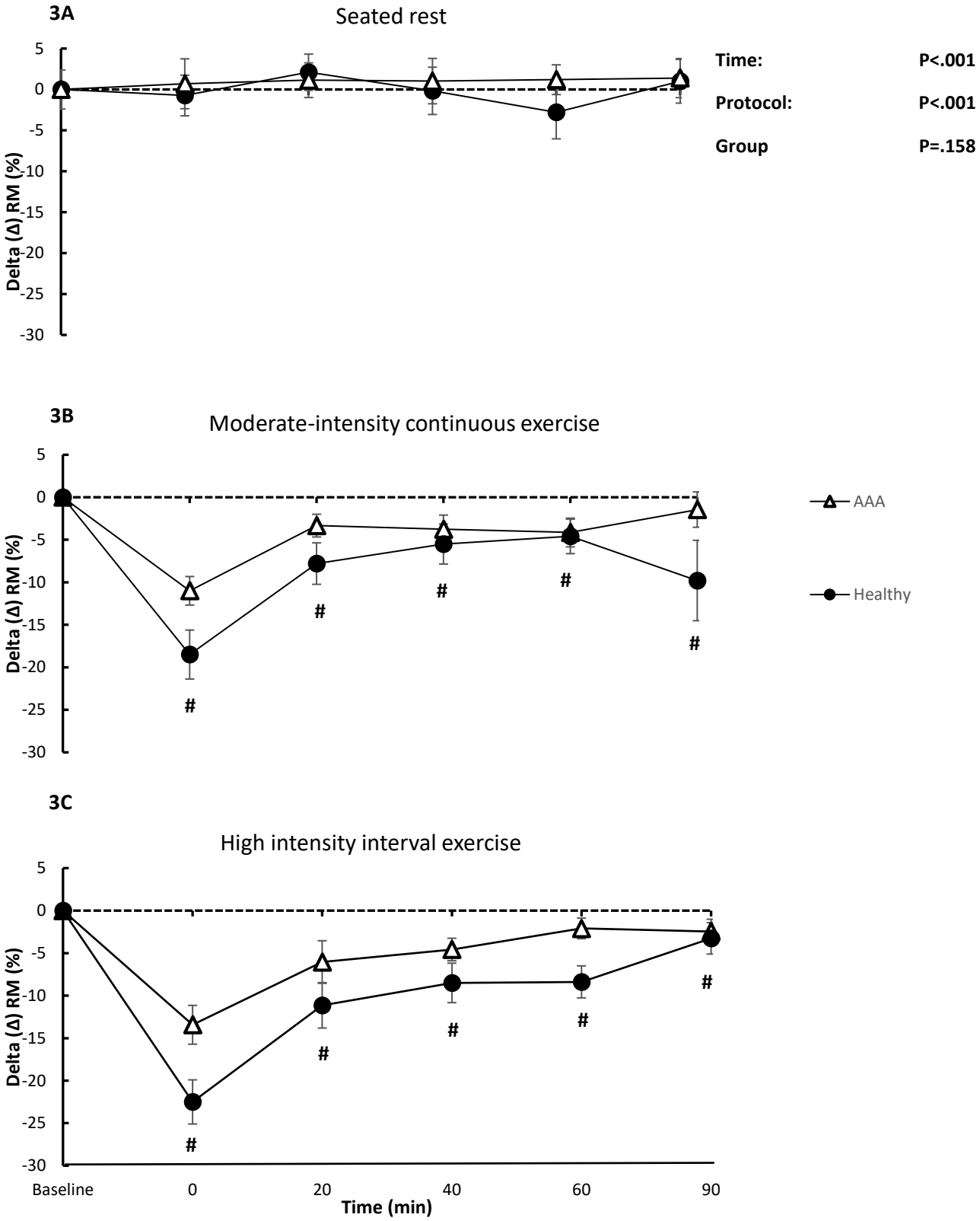

Figure 3: Delta RM response of AAA (white triangles) and healthy (black circles) groups to seated rest (A), moderate-intensity continuous (B) and high-intensity interval (C) exercise. Data are mean and SEM; RM, reflection magnitude. [#]Significantly different to seated rest; [α] significantly different to moderate-intensity based on protocol*time post-hoc comparisons.

Table 1. Characteristics of AAA patients and healthy adults. Data are presented as mean ±SD or percentage (%). All participants are male. BMI, body mass index; AAA, abdominal aortic aneurysm; MI, myocardial infarction; CABG, coronary artery bypass graft; ARB, Angiotensin II receptor blockers; ACE, angiotensin converting enzyme; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; $\dot{V}O_{2peak}$, peak oxygen uptake; RER, respiratory exchange ratio.

	AAA (n=22)	**Healthy (n=22)**	***P* value**
Participant characteristics			
Age (years)	74 ± 6	72 ± 5	.202
Height (m)	1.73 ± 0.1	1.75 ± 6.6	.161
Weight (kg)	84.1 ± 16	80 ± 12	.283
BMI ($kg.m^{-2}$)	28 ± 9.1	26 ± 3.6	.072
Body fat (%)	28.6 ± 5.7	25 ± 5.2	.016
Resting heart rate (bpm)	59 ± 9	59 ± 7	.824
Brachial SBP (mmHg)	129 ± 13	124 ± 13	.258
Brachial DBP (mmHg)	73 ± 7	74 ± 9	.785
Clinical information			
Maximum AAA diameter (mm)	36 ± 0.5	-	-
Hypertension, N (%)	15 (68)	5 (22)	.006
Dyslipidaemia, N (%)	18 (82)	8 (36)	.005
Diabetes, N (%)	2 (9)	0 (0)	.478
Smoking - current, N (%)	2 (9)	1 (5)	.697
Smoking -previous, N (%)	12 (55)	11 (50)	.701
Previous stroke, N (%)	2 (9)	0 (0)	.488
Previous MI, N (%)	6 (27)	1 (5)	.021
Previous CABG, N (%)	11 (50)	1 (5)	.002
Medication use			
ARB/ACE inhibitors, N (%)	9 (40)	4 (18)	.140
Anti-platelet, N (%)	13 (60)	2 (9)	.003
Beta-blockers, N (%)	9 (40)	2 (9)	.034
Calcium channel blockers, N (%)	4 (18)	1 (5)	.345
Statins, N (%)	20 (90)	9 (40)	.001
Maximal incremental cycling test			
Absolute $\dot{V}O_{2peak}$, $L.min^{-1}$	1.58 ± 0.36	1.94 ± 0.35	.002
Relative $\dot{V}O_{2peak}$, $mL.kg^{-1}.min^{-1}$	19.03 ± 3.54	24.47 ± 2.78	.001
Peak power output, W	120 ± 20	150 ± 30	.001

Table 2. Heart rate and blood pressure during seated rest, moderate-intensity continuous and higher-intensity interval exercise in patients with AAA and healthy adults. Data are presented as mean ±SD and baseline data are an average of resting measures collected at the three experimental visits. REST, seated rest; MOD, moderate intensity continuous exercise; HIGH, higher- intensity interval exercise; HR, heart rate; SBP systolic blood pressure; SDP, diastolic blood pressure; MAP, mean arterial pressure. P*T, protocol*time interaction; P*G*T, protocol*group*time interaction; *significantly different to baseline based on protocol*time post-hoc comparisons; #significantly different to seated rest; αsignificantly different to moderate-intensity.

Heart rate and blood pressure during the experimental protocols

	Groups	Protocol	Baseline	Peak	P values		Interactions	
HR (bpm)	**AAA**	REST	59 ± 9	67 ± 11	**Time**	.001	**P*T**	**.001**
		MOD	60 ± 9	97 ± 152*#				
		HIGH	59 ± 9	102 ± 15*#	**Protocol**	.001		
	Healthy	REST	60 ± 10	66 ± 11				
		MOD	58 ± 7	103 ± 12*#	**Group**	.135	**P*G*T**	**.997**
		HIGH	58 ± 7	102 ±10*#α				
SBP (mmHg)	**AAA**	REST	128 ± 11	141 ± 20	**Time**	.001	**P*T**	**.001**
		MOD	130 ± 14	168 ± 25*#				
		HIGH	130 ± 15	168 ± 21*#	**Protocol**	.001		
	Healthy	REST	124 ± 15	141 ± 18				
		MOD	124 ± 12	166 ± 18*#	**Group**	.532	**P*G*T**	**.523**
		HIGH	127 ± 14	171 ± 18*#				
DBP (mmHg)	**AAA**	REST	72 ± 6	83 ± 10	**Time**	.001	**P*T**	**.621**
		MOD	74 ± 8	82 ± 11				
		HIGH	73 ± 8	83 ± 08	**Protocol**	.065		
	Healthy	REST	74 ± 12	86 ± 10				
		MOD	73 ± 9	83 ± 11	**Group**	.567	**P*G*T**	**.912**
		HIGH	74 ± 10	83 ± 10				
MAP (mmHg)	**AAA**	REST	88 ± 7	104 ± 12	**Time**	.001	**P*T**	**.747**
		MOD	91 ± 9	109 ± 14#				
		HIGH	88 ± 9	109 ± 11#	**Protocol**	.001		
	Healthy	REST	88 ± 11	103 ± 12				
		MOD	88 ± 10	109 ± 12#	**Group**	.747	**P*G*T**	**.671**
		HIGH	89 ± 11	107 ± 11#				

Table 3. Arterial stiffness at baseline and after seated rest, moderate-intensity continuous and higher-intensity interval exercise in patients with AAA and healthy adults. Data are presented as mean ±SD; REST, seated rest; MOD, moderate intensity continuous exercise; HIGH, higher- intensity interval exercise; AIx75, augmentation index normalised to a heart rate of 75 bpm; RM, reflection magnitude; PWV, pulse wave velocity. P*T, protocol*time interaction; P*G*T, protocol*group*time interaction; *significantly different to baseline based on protocol*time post-hoc comparisons.

Arterial stiffness indices												
			Time point (min)									
	Groups	Protocol	Baseline	0 post	20 post	40 post	60 post	90 post	P value		Interactions	
PWV ($m.s^{-1}$)	AAA	REST	14.0 ± 2	14.9 ± 2*	14.9 ± 2*	15.1 ± 2*	15.3 ± 2*	15.3 ± 2*	Time	.001	P*T	.001
		MOD	14.2 ± 2	14.0 ± 2	13.8 ± 2	14.3 ± 2	14.5 ± 2	15.0 ± 2*				
		HIGH	14.3 ± 2	13.2 ± 2*	13.8 ± 2	13.9 ± 2	14.3 ± 2	15.3 ± 2*	Protocol	.001		
	Healthy	REST	11.8 ± 2	12.5 ± 2*	12.9 ± 3*	12.6 ± 2*	12.9 ± 2*	13.1 ± 2*			P*G*T	.614
		MOD	12.3 ± 2	12.4 ± 2	12.4 ± 2	12.4 ± 2	12.4 ± 2	13.1 ± 2*	Group	.001		
		HIGH	12.5 ± 2	12.4 ± 2*	12.2 ± 2	12.7 ± 2	12.7 ± 2	13.3 ± 2*				
AIx75 (%)	AAA	REST	20.1 ± 10	17.2 ± 10	18.2 ± 11	15.8 ± 9	16.3 ± 12	15.9 ± 10	Time	.001	P*T	.388
		MOD	22.0 ± 10	20.8 ± 12	20.7 ± 10	19.8 ± 9	18.5 ± 9	19.3 ± 9				
		HIGH	22.0 ± 10	21.5 ± 11	22.7 ± 9	18.4 ± 11	18.4 ± 10	20.0 ± 9	Protocol	.001		
	Healthy	REST	24.5 ± 10	20.3 ± 8	21.5 ± 8	18.2 ± 9	19.0 ± 11	22.0 ± 9			P*G*T	.466
		MOD	24.9 ± 10	22.4 ± 11	26.7 ± 11	21.0 ± 10	21.5 ± 11	23.2 ± 12	Group	.346		
		HIGH	24.5 ± 10	22.4 ± 9	25.1 ± 10	21.9 ± 11	20.5 ± 12	20.3 ± 10				
RM (%)	AAA	REST	72 ± 11	74 ± 14	73 ± 10	72 ± 13	69 ± 8	73 ± 11	Time	.001	P*T	.001
		MOD	74 ± 12	63 ± 11*	71 ± 11*	70 ± 9*	70 ± 12*	72 ± 8*				
		HIGH	74 ± 11	60 ± 11*	67 ± 14*	68 ± 12*	72 ± 10*	72 ± 12*	Protocol	.001		
	Healthy	REST	73 ± 12	75 ± 13	78 ± 14	77 ± 13	79 ± 14	78 ± 10			P*G*T	.499
		MOD	80 ± 11	63 ± 11*	72 ± 8*	75 ± 12*	76 ± 13*	76 ± 14*	Group	.190		
		HIGH	81 ± 12	58 ± 13*	69 ± 14*	71 ± 10*	72 ± 13*	75 ± 12*				
Pf (mmHg)	AAA	REST	26.5 ± 5	27.6 ± 5	26.9 ± 5	26.8 ± 5	27.5 ± 5	29.1 ± 5	Time	.001	P*T	.001
		MOD	27.1 ± 4	30.1 ± 5*	25.4 ± 4	27.2 ± 4	27.1 ± 5	28.0 ± 5				
		HIGH	26.4 ± 5	32.2 ± 6*	26.9 ± 6	26.3 ± 7	25.1 ± 5	28.4 ± 6*	Protocol	.241		
	Healthy	REST	24.8 ± 5	25.8 ± 6	24.1 ± 5	23.0 ± 6	24.2 ± 5	25.1 ± 5			P*G*T	.533
		MOD	23.8 ± 4	30.5 ± 7*	25.1 ± 6	24.0 ± 5	24.8 ± 6	25.4 ± 5	Group	.090		
		HIGH	23.3 ± 5	30.0 ± 6*	24.9 ± 5	23.7 ± 5	24.3 ± 5	24.6 ± 5*				

Pb (mmHg)	**AAA**	REST	18.8 ± 3	20.3 ± 4	19.7 ± 4	19.2 ± 4	19.5 ± 5	21.2 ± 4	**Time**	.001	**P*T**	.036
		MOD	19.9 ± 3	19.0 ± 4	17.8 ± 2*	19.2 ± 4*	18.7 ± 3	20.1 ± 4				
		HIGH	19.5 ± 4	19.1 ± 4*	17.6 ± 3*	17.6 ± 4*	18.0 ± 3*	20.0 ± 3	**Protocol**	.001		
	Healthy	REST	17.4 ± 4	18.9 ± 4	18.4 ± 4	17.7 ± 3	18.8 ± 4	19.2 ± 5				
		MOD	18.8 ± 4	18.6 ± 3	17.9 ± 3*	17.6 ± 3*	18.5 ± 4	18.7 ± 4	**Group**	.266	**P*G*T**	.909
		HIGH	18.3 ± 3	16.9 ± 3*	16.7 ± 3*	16.7 ± 3*	17.0 ± 3*	17.9 ± 4				

Table 4. Heart rate and blood pressure indices at baseline and after seated rest, moderate-intensity continuous and higher-intensity interval exercise in patients with AAA and healthy adults. Data are presented as mean ±SD; REST, seated rest; MOD, moderate-intensity exercise; HIGH, higher-intensity exercise; SBP systolic blood pressure; SDP, diastolic blood pressure; cPP, central pulse pressure. P*T, protocol*time interaction; P*G*T, protocol*group*time interaction; *significantly different to baseline based on protocol*time post-hoc comparisons.

Heart rate and central blood pressure indices											
	Groups	Protocol	Time point (min)						P Values		Interactions	
			Baseline	0 post	20 post	40 post	60 post	90 post				
HR (bpm)	AAA	REST	59 ± 9	56 ± 8*	56 ± 8*	56 ± 8*	56 ± 10*	57 ± 8*	Time	.001	P*T	.001
		MOD	60 ± 9	68 ± 12*	62 ± 9*	61 ± 8	58 ± 9	58 ± 9				
		HIGH	59 ± 9	69 ± 11*	65 ± 8*	62 ± 9*	60 ± 9	60 ± 8	Protocol	.001		
	Healthy	REST	60 ± 10	55 ± 9*	54 ± 7*	53 ± 7*	55 ± 7*	55 ± 7*				
		MOD	58 ± 7	68 ± 9*	62 ± 8*	59 ± 7	59 ± 6	59 ± 6	Group	.755	P*G*T	.158
		HIGH	58 ± 7	71 ± 14*	63 ± 11*	60 ± 9*	60 ± 8	58 ± 7				
cSBP (mmHg)	AAA	REST	116 ± 10	124 ± 14*	124 ± 14*	123 ± 13*	125 ± 18*	129 ± 15*	Time	.001	P*T	.001
		MOD	119 ± 13	119 ± 14	113 ± 11*	118 ± 14	118 ± 14	124 ± 14*				
		HIGH	118 ± 14	118 ± 13	113 ± 10*	112 ± 11*	116 ± 12*	122 ± 13*	Protocol	.001		
	Healthy	REST	117 ± 14	121 ± 15*	118 ± 14*	119 ± 14*	119 ± 14*	124 ± 16*				
		MOD	117 ± 13	120 ± 12	114 ± 11*	114 ± 12	118 ± 15	122 ± 12*	Group	.515	P*G*T	.674
		HIGH	115 ± 11	117 ± 12	111 ± 12*	112 ± 12*	115 ± 12*	121 ± 12*				
cDBP (mmHg)	AAA	REST	73 ± 6	77 ± 7*	77 ± 8*	78 ± 8*	77 ± 9*	80 ± 9*	Time	.001	P*T	.043
		MOD	74 ± 8	75 ± 7	73 ± 7	74 ± 8	74 ± 8	77 ± 7*				
		HIGH	73 ± 7	74 ± 7	73 ± 7	72 ± 6	74 ± 8	76 ± 7*	Protocol	.001		
	Healthy	REST	74 ± 9	76 ± 9*	75 ± 10*	76 ± 10*	77 ± 9*	80 ± 11*				
		MOD	75 ± 10	77 ± 9	74 ± 10	74 ± 10	76 ± 12	80 ± 13*	Group	.741	P*G*T	.611
		HIGH	74 ± 10	77 ± 11	74 ± 10	74 ± 10	75 ± 11	78 ± 11*				

cPP (mmHg)	**AAA**	REST	43 ± 7	47 ± 8*	46 ± 9*	45 ± 9*	48 ± 11*	50 ± 7*	**Time**	.001	**P*T**	.001
		MOD	45 ± 8	44 ± 9	40 ± 6*	44 ± 9	44 ± 8	48 ± 9*				
		HIGH	45 ± 9	45 ± 8	41 ± 6*	40 ± 7*	42 ± 7*	46 ± 7	**Protocol**	.001		
	Healthy	REST	41 ± 9	45 ± 9*	43 ± 9*	43 ± 8*	44 ± 8*	44 ± 8*				
		MOD	42 ± 8	42 ± 8	40 ± 7*	40 ± 7	41 ± 8	43 ± 8*	**Group**	.128	**P*G*T**	.416
		HIGH	41 ± 7	40 ± 8	37 ± 6*	38 ± 5*	39 ± 6*	43 ± 9				