Eur J Vasc Endovasc Surg (2019) 58, 708–718

Aortic and Systemic Arterial Stiffness Responses to Acute Exercise in Patients With Small Abdominal Aortic Aneurysms

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WHAT THIS PAPER ADDS

Elevated arterial stiffness is associated with aneurysm progression and probably contributes to the high cardiovascular risk of patients with abdominal aortic aneurysms (AAA). It is demonstrated herein that the changes in aortic and systemic arterial stiffness are lower in patients with AAA after 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 patients with AAA. The findings support the use of interval based high intensity exercise as a safe intervention to improve cardiovascular function in patients with AAA and adds to the evidence that exercise prescription should be part of the routine care of patients with AAA.

Objective/background: 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 patients with AAA is unknown. The effect of moderate- and higher intensity exercise on arterial stiffness was assessed in patients with AAA and healthy adults.

Methods: Twenty-two men with small diameter AAAs (36 $\pm$ 5 mm; mean age 74 $\pm$ 6 years) and 22 healthy adults (mean age 72 $\pm$ 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: (i) moderate intensity continuous exercise; (ii) higher intensity interval exercise; or (iii) seated rest.

Results: At rest, PWV was higher in patients with AAA than in healthy adults ($p < .001$), while 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 than seated rest ($p < .001$). ΔPWV was lower immediately after higher intensity than after moderate intensity exercise ($p = .015$).

Conclusion: High resting aortic stiffness in patients with AAA 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 adjunctive therapy for patients with small AAAs.

Keywords: Pulse-wave velocity, Vascular disease, Wave reflection characteristics
Article history: Received 20 August 2018, Accepted 24 February 2019, Available online 17 October 2019

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1078-5884/
https://doi.org/10.1016/j.ejvs.2019.02.021

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 and human AAA.[3,4] 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 patients with AAA, short-term exercise therapy has been shown to improve cardiorespiratory fitness,[10,11] and is associated with reduced post-operative complications after 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 patients with AAA. 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 patients with AAA 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 patients with AAA. 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 patients with AAA. Such an increase in aortic stiffness after high intensity exercise might exacerbate cardiovascular risk,[19] and would be a concern in patients with AAA. 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 patients with AAA.

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 patients with AAA, and an insight into the potential value of higher intensity interval exercise for these patients.

METHODS

Participant recruitment

Twenty-two men with an AAA (diameters 30–45 mm) and 22 healthy men were included. Patients with AAAs were recruited through local clinics and had a confirmed diagnosis within the six months prior to study entry. Participants were included if they were aged 60–86 years and able to exercise; they were excluded if they were deemed unsuitable for exercise by a cardiologist, for example for reversible ischaemia 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 syndrome 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, crossover 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 24 h, and caffeine for 12 h, prior to each visit. Participants were fasted for $\geq$6 h and consumed a standardised breakfast 3 h before each session. Visit 1 consisted of anthropometric measurements, followed by a maximal incremental cycling test to determine cardiorespiratory fitness (VO_{2peak}) and peak power output (PPO). Experimental visits (visits 2–4) were counterbalanced, randomised, and consisted of either (i) moderate intensity continuous cycling exercise; (ii) higher intensity interval cycling exercise; or (iii) 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 $\pm$ 1°C).

Determination of cardiorespiratory fitness

A maximal incremental cycling test commenced at 20 W and then increased by 10 W/minute until volitional cessation. Pedal rate was maintained at 60–90 rpm. Expired gases were collected throughout and data were averaged every 15 s (Parvomedics, Sandy, UT, USA) for the determination of oxygen consumption (VO_2; $mL \cdot kg^{-1} \cdot min^{-1}$). VO_{2peak} was determined as the highest 15 s average of VO_2 over the last 60 s. Heart rate was continuously measured (Mortara, Milwaukee, WI, USA), along with the rate of perceived exertion (RPE).[21] PPO was used to establish the exercise intensity for the experimental visits.

Table 1. Characteristics of patients with abdominal aortic aneurysms and healthy adults

Characteristics	Abdominal aortic aneurysm (n = 22)	Healthy (n = 22)	p
Participant characteristics			
Age − y	74 ± 6	72 ± 5	.202
Height − m	1.73 ± 0.1	1.75 ± 6.6	.161
Weight − kg	84.1 ± 16	80 ± 12	.283
Body mass index − kg/m^2	28 ± 9.1	26 ± 3.6	.072
Body fat − %	28.6 ± 5.7	25 ± 5.2	.016
Resting heart rate − beats per min	59 ± 9	59 ± 7	.824
Brachial systolic blood pressure − mmHg	129 ± 13	124 ± 13	.258
Brachial diastolic blood pressure − mmHg	73 ± 7	74 ± 9	.785
Clinical information			
Maximum AAA diameter − mm	36 ± 0.5	–	–
Hypertension	15 (68)	5 (23)	.006
Dyslipidaemia	18 (82)	8 (36)	.005
Diabetes	2 (9)	0 (0)	.478
Smoking: current	2 (9)	1 (5)	.697
Smoking: previous	12 (55)	11 (50)	.701
Previous stroke	2 (9)	0 (0)	.488
Previous myocardial infarction	6 (27)	1 (5)	.021
Previous coronary artery bypass graft	11 (50)	1 (5)	.002
Medication use			
Angiotensin II receptor blockers/angiotensin converting enzyme inhibitors	9 (41)	4 (18)	.140
Antiplatelet	13 (59)	2 (9)	.003
Beta blockers	9 (41)	2 (9)	.034
Calcium channel blockers	4 (18)	1 (5)	.345
Statins	20 (91)	9 (41)	.001
Maximal incremental cycling test			
Absolute peak oxygen uptake (VO_{2peak}) − L/min	1.58 ± 0.36	1.94 ± 0.35	.002
Relative VO_{2peak} − mL/kg/min	19.03 ± 3.54	24.47 ± 2.78	.001
Peak power output − W	120 ± 20	150 ± 30	.001

Data are presented as mean ± standard deviation (SD) or n (%). All participants were male. AAA = abdominal aortic aneurysm; VO_{2peak} = maximal oxygen uptake during peak exercise; W = watts.

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 × 60 s bouts at 70% PPO, separated by 12 × 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 after 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). An aortic pressure waveform was generated by applying a proprietary digital signal processing and transfer function,[24] from which central systolic (cSBP), diastolic (cDBP), central pulse pressure (cPP), mean arterial pressure (MAP), augmentation pressure (AP), and AIx were derived. cPP was calculated as the difference between cSBP and cDBP. AP 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 beats per minute (bpm; AIx75). Wave separation analysis was applied (SphygmoCor CVMS software, version 9) to determine the aortic forward (Pf) and backward (Pb) pressure waveforms.[25] 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

Table 2. Heart rate and blood pressure during seated rest, moderate intensity continuous exercise, and higher intensity interval exercise in patients with abdominal aortic aneurysms (AAA) and healthy adults

Parameter	Group	Protocol	Baseline	Peak	*p* values				
					Time	Protocol	Group	P × T	P × G × T
Heart rate — beats per minute					.001	.001	.14	.001	.10
	AAA	REST	59 ± 9	67 ± 11					
		MOD	60 ± 9	97 ± 152[a,b]					
		HIGH	59 ± 9	102 ± 15[a,b]					
	Healthy	REST	60 ± 10	66 ± 11					
		MOD	58 ± 7	103 ± 12[a,b]					
		HIGH	58 ± 7	102 ± 10[a,b,c]					
Systolic blood pressure — mmHg					.001	.001	.53	.001	.53
	AAA	REST	128 ± 11	141 ± 20					
		MOD	130 ± 14	168 ± 25[a,b]					
		HIGH	130 ± 15	168 ± 21[a,b]					
	Healthy	REST	124 ± 15	141 ± 18					
		MOD	124 ± 12	166 ± 18[a,b]					
		HIGH	127 ± 14	171 ± 18[a,b]					
Diastolic blood pressure — mmHg					.001	.065	.57	.62	.91
	AAA	REST	72 ± 6	83 ± 10					
		MOD	74 ± 8	82 ± 11					
		HIGH	73 ± 8	83 ± 08					
	Healthy	REST	74 ± 12	86 ± 10					
		MOD	73 ± 9	83 ± 11					
		HIGH	74 ± 10	83 ± 10					
Mean arterial pressure — mmHg					.001	.001	.75	.75	.67
	AAA	REST	88 ± 7	104 ± 12					
		MOD	91 ± 9	109 ± 14[b]					
		HIGH	88 ± 9	109 ± 11[b]					
	Healthy	REST	88 ± 11	103 ± 12					
		MOD	88 ± 10	109 ± 12[b]					
		HIGH	89 ± 11	107 ± 11[b]					

Data are mean ± standard deviation (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; P × T = protocol × time interaction; P × G × T = protocol × group × time interaction.
[a] Significantly different to baseline based on P × T post-hoc comparisons.
[b] Significantly different to seated rest.
[c] Significantly different to moderate intensity.

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] the 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 $m \cdot s^{-1}$ between the AAA and healthy groups, assuming an alpha level of .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-square 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-exercise) 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 covariates.[15] Statistically significant interactions were further investigated with multiple comparisons using Fisher's least significant difference approach.[28] Analyses were conducted using SPSS (version 22; IBM, Armonk, NY, USA) and statistical significance was set at $p \leq .05$. Data are presented in the text as

Table 3. Arterial stiffness at baseline and after seated rest, moderate intensity continuous, and higher intensity interval exercise in patients with abdominal aortic aneurysm (AAA) and healthy adults

Parameter	Group	Protocol	Time point (min)						*p* values				
			Baseline	0 post	20 post	40 post	60 post	90 post	Time	Protocol	Group	P × T	P × G × T
Pulse wave velocity − m·s^{-1}									.001	.001	.001	.001	.61
	AAA	REST	14.0 ± 2	14.9 ± 2[a]	14.9 ± 2[a]	15.1 ± 2[a]	15.3 ± 2[a]	15.3 ± 2[a]					
		MOD	14.2 ± 2	14.0 ± 2	13.8 ± 2	14.3 ± 2	14.5 ± 2	15.0 ± 2[a]					
		HIGH	14.3 ± 2	13.2 ± 2[a]	13.8 ± 2	13.9 ± 2	14.3 ± 2	15.3 ± 2[a]					
	Healthy	REST	11.8 ± 2	12.5 ± 2[a]	12.9 ± 3[a]	12.6 ± 2[a]	12.9 ± 2[a]	13.1 ± 2[a]					
		MOD	12.3 ± 2	12.4 ± 2	12.4 ± 2	12.4 ± 2	12.4 ± 2	13.1 ± 2[a]					
		HIGH	12.5 ± 2	12.4 ± 2[a]	12.2 ± 2	12.7 ± 2	12.7 ± 2	13.3 ± 2[a]					
Augmentation index (AIx75) − %									.001	.001	.35	.39	.47
	AAA	REST	20.1 ± 10	17.2 ± 10	18.2 ± 11	15.8 ± 9	16.3 ± 12	15.9 ± 10					
		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					
	Healthy	REST	24.5 ± 10	20.3 ± 8	21.5 ± 8	18.2 ± 9	19.0 ± 11	22.0 ± 9					
		MOD	24.9 ± 10	22.4 ± 11	26.7 ± 11	21.0 ± 10	21.5 ± 11	23.2 ± 12					
		HIGH	24.5 ± 10	22.4 ± 9	25.1 ± 10	21.9 ± 11	20.5 ± 12	20.3 ± 10					
Reflection magnitude − %									.001	.001	.19	.001	.50
	AAA	REST	72 ± 11	74 ± 14	73 ± 10	72 ± 13	69 ± 8	73 ± 11					
		MOD	74 ± 12	63 ± 11[a]	71 ± 11[a]	70 ± 9[a]	70 ± 12[a]	72 ± 8[a]					
		HIGH	74 ± 11	60 ± 11[a]	67 ± 14[a]	68 ± 12[a]	72 ± 10[a]	72 ± 12[a]					
	Healthy	REST	73 ± 12	75 ± 13	78 ± 14	77 ± 13	79 ± 14	78 ± 10					
		MOD	80 ± 11	63 ± 11[a]	72 ± 8[a]	75 ± 12[a]	76 ± 13[a]	76 ± 14[a]					
		HIGH	81 ± 12	58 ± 13[a]	69 ± 14[a]	71 ± 10[a]	72 ± 13[a]	75 ± 12[a]					
Forward pressure waveform − mmHg									.001	.24	.090	.001	.53
	AAA	REST	26.5 ± 5	27.6 ± 5	26.9 ± 5	26.8 ± 5	27.5 ± 5	29.1 ± 5					
		MOD	27.1 ± 4	30.1 ± 5[a]	25.4 ± 4	27.2 ± 4	27.1 ± 5	28.0 ± 5					
		HIGH	26.4 ± 5	32.2 ± 6[a]	26.9 ± 6	26.3 ± 7	25.1 ± 5	28.4 ± 6[a]					
	Healthy	REST	24.8 ± 5	25.8 ± 6	24.1 ± 5	23.0 ± 6	24.2 ± 5	25.1 ± 5					
		MOD	23.8 ± 4	30.5 ± 7[a]	25.1 ± 6	24.0 ± 5	24.8 ± 6	25.4 ± 5					
		HIGH	23.3 ± 5	30.0 ± 6[a]	24.9 ± 5	23.7 ± 5	24.3 ± 5	24.6 ± 5[a]					
Backward pressure waveform − mmHg									.001	.001	.27	.036	.91
	AAA	REST	18.8 ± 3	20.3 ± 4	19.7 ± 4	19.2 ± 4	19.5 ± 5	21.2 ± 4					
		MOD	19.9 ± 3	19.0 ± 4	17.8 ± 2[a]	19.2 ± 4[a]	18.7 ± 3	20.1 ± 4					
		HIGH	19.5 ± 4	19.1 ± 4[a]	17.6 ± 3[a]	17.6 ± 4[a]	18.0 ± 3[a]	20.0 ± 3					
	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[a]	17.6 ± 3[a]	18.5 ± 4	18.7 ± 4					
		HIGH	18.3 ± 3	16.9 ± 3[a]	16.7 ± 3[a]	16.7 ± 3[a]	17.0 ± 3[a]	17.9 ± 4					

Data are mean ± standard deviation (SD). REST = seated rest; MOD = moderate intensity continuous exercise; HIGH = higher intensity interval exercise; AIx75 = augmentation index normalised to a heart rate of 75 beats per min; PWV = pulse wave velocity; P × T = protocol × time interaction; P × G × T = protocol × group × time interaction.
[a] Significantly different to baseline based on P × T post-hoc comparisons.

mean and 95% confidence interval (CI) unless otherwise stated.

RESULTS

Participant characteristics

The characteristics of the patients with AAA and healthy adults are provided in Table 1.

Heart rate, MAP, and perceived exertion during exercise

Mean power output (W) during exercise was significantly greater in healthy adults (moderate intensity: mean 58 W, 95% CI 53—61); higher intensity mean 100 W, 95% CI 93—107) compared with patients with AAA (moderate intensity: mean 48 W, 95% CI 43—51; higher intensity mean 83 W, 95% CI 76—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—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 patients with AAA and healthy adults for each protocol are shown in Figs. 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

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 abdominal aortic aneurysm (AAA) and healthy adults

Parameter	Groups	Protocol	Time point (min)						*p* values				
			Baseline	0 post	20 post	40 post	60 post	90 post	Time	Protocol	Group	P × T	P × G × T
Heart rate — beats per minute									.001	.001	.76	.001	.16
	AAA	REST	59 ± 9	56 ± 8[a]	56 ± 8[a]	56 ± 8[a]	56 ± 10[a]	57 ± 8[a]					
		MOD	60 ± 9	68 ± 12[a]	62 ± 9[a]	61 ± 8	58 ± 9	58 ± 9					
		HIGH	59 ± 9	69 ± 11[a]	65 ± 8[a]	62 ± 9[a]	60 ± 9	60 ± 8					
	Healthy	REST	60 ± 10	55 ± 9[a]	54 ± 7[a]	53 ± 7[a]	55 ± 7[a]	55 ± 7[a]					
		MOD	58 ± 7	68 ± 9[a]	62 ± 8[a]	59 ± 7	59 ± 6	59 ± 6					
		HIGH	58 ± 7	71 ± 14[a]	63 ± 11[a]	60 ± 9[a]	60 ± 8	58 ± 7					
Central systolic blood pressure — mmHg									.001	.001	.52	.001	.67
	AAA	REST	116 ± 10	124 ± 14[a]	124 ± 14[a]	123 ± 13[a]	125 ± 18[a]	129 ± 15[a]					
		MOD	119 ± 13	119 ± 14	113 ± 11[a]	118 ± 14	118 ± 14	124 ± 14[a]					
		HIGH	118 ± 14	118 ± 13	113 ± 10[a]	112 ± 11[a]	116 ± 12[a]	122 ± 13[a]					
	Healthy	REST	117 ± 14	121 ± 15[a]	118 ± 14[a]	119 ± 14[a]	119 ± 14[a]	124 ± 16[a]					
		MOD	117 ± 13	120 ± 12	114 ± 11[a]	114 ± 12	118 ± 15	122 ± 12[a]					
		HIGH	115 ± 11	117 ± 12	111 ± 12[a]	112 ± 12[a]	115 ± 12[a]	121 ± 12[a]					
Central diastolic blood pressure — mmHg									.001	.001	.74	.043	.61
	AAA	REST	73 ± 6	77 ± 7[a]	77 ± 8[a]	78 ± 8[a]	77 ± 9[a]	80 ± 9[a]					
		MOD	74 ± 8	75 ± 7	73 ± 7	74 ± 8	74 ± 8	77 ± 7[a]					
		HIGH	73 ± 7	74 ± 7	73 ± 7	72 ± 6	74 ± 8	76 ± 7[a]					
	Healthy	REST	74 ± 9	76 ± 9[a]	75 ± 10[a]	76 ± 10[a]	77 ± 9[a]	80 ± 11[a]					
		MOD	75 ± 10	77 ± 9	74 ± 10	74 ± 10	76 ± 12	80 ± 13[a]					
		HIGH	74 ± 10	77 ± 11	74 ± 10	74 ± 10	75 ± 11	78 ± 11[a]					
Central pulse pressure — mmHg									.001	.001	.13	.001	.42
	AAA	REST	43 ± 7	47 ± 8[a]	46 ± 9[a]	45 ± 9[a]	48 ± 11[a]	50 ± 7[a]					
		MOD	45 ± 8	44 ± 9	40 ± 6[a]	44 ± 9	44 ± 8	48 ± 9[a]					
		HIGH	45 ± 9	45 ± 8	41 ± 6[a]	40 ± 7[a]	42 ± 7[a]	46 ± 7					
	Healthy	REST	41 ± 9	45 ± 9[a]	43 ± 9[a]	43 ± 8[a]	44 ± 8[a]	44 ± 8[a]					
		MOD	42 ± 8	42 ± 8	40 ± 7[a]	40 ± 7	41 ± 8	43 ± 8[a]					
		HIGH	41 ± 7	40 ± 8	37 ± 6[a]	38 ± 5[a]	39 ± 6[a]	43 ± 9					

Data are mean ± standard deviation (SD). REST = seated rest; MOD = moderate intensity exercise; HIGH = higher intensity exercise; P × T, protocol × time interaction; P × G × T, protocol × group × time interaction.
[a] Significantly different to baseline based on protocol × time post-hoc comparisons.

(CV% = SD/mean × 100) for PWV, AIx75, and RM ranged between 5% and 10% in both groups. PWV measured at baseline was 2.2 $m \cdot s^{-1}$ (95% CI 0.9—3.5; $p < .001$) higher in patients with AAA vs. 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 patients with AAA 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) vs. 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 with seated rest (Fig. 1). In addition, ΔPWV was lower at 0 and 40 min after higher intensity exercise than after moderate intensity exercise (Fig. 1B and 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 it 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 patients with AAA 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 than with moderate intensity continuous exercise in both groups. While PWV was higher in the patients with AAA 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

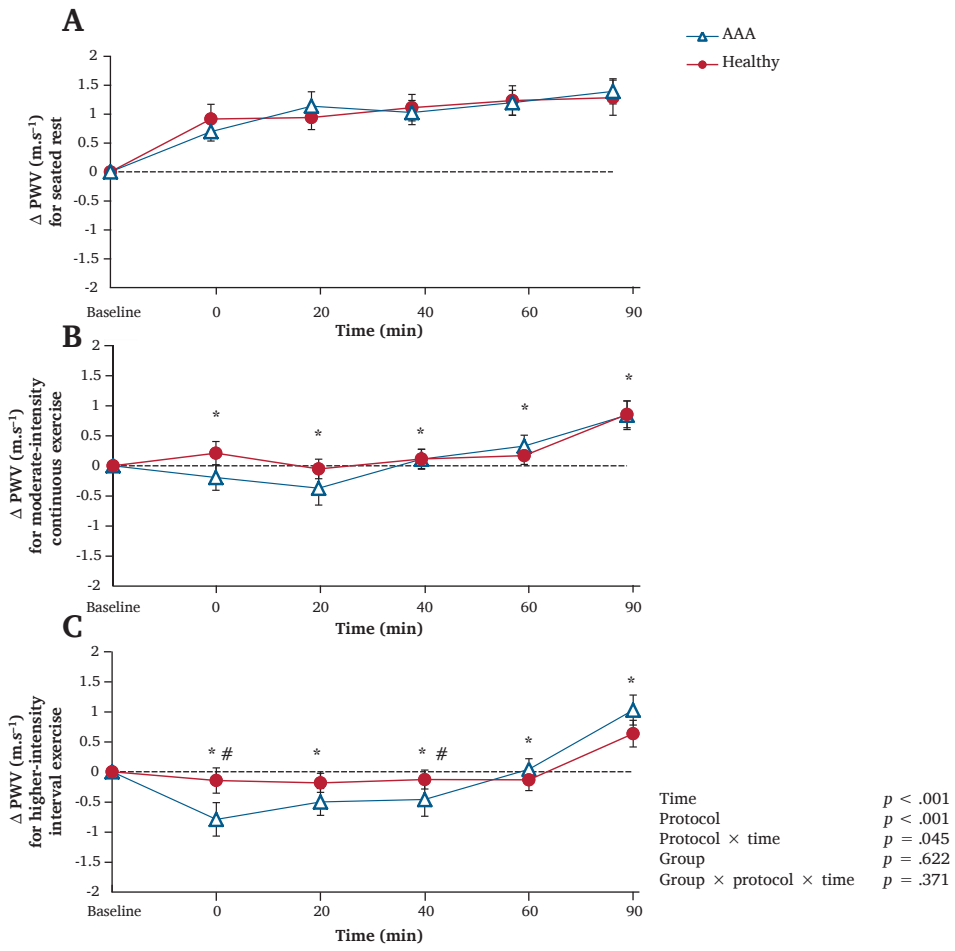

Figure 1. Delta (Δ) pulse wave velocity (PWV) response of abdominal aortic aneurysm (AAA) (white triangles) and healthy (red circles) groups to (A) seated rest, (B) moderate intensity continuous, and (C) higher intensity interval exercise. Data are mean ± standard error of the mean (SEM) open. PWV = pulse wave velocity. *Significantly different to seated rest; #significantly different to moderate intensity based on protocol × time post-hoc comparisons.

acute risks and potential benefits of exercise and the types of exercise that may be suitable for patients with AAA patients.

Aortic and systemic arterial stiffness at rest

Resting PWV was higher in patients with AAA 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 with the seated rest protocol, the responses of PWV and RM were attenuated following exercise in patients with AAA and healthy adults. This finding is in line with previous studies in younger and older adults.[15,32]

Despite a higher resting PWV in patients with AAA, 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 sub-maximal exercise, compared with seated rest, suggests there may be a reduction in aortic wall stress and an acute cardiovascular benefit from exercise for patients with AAA, similar to that reported for healthy adults.[19] This is probably 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

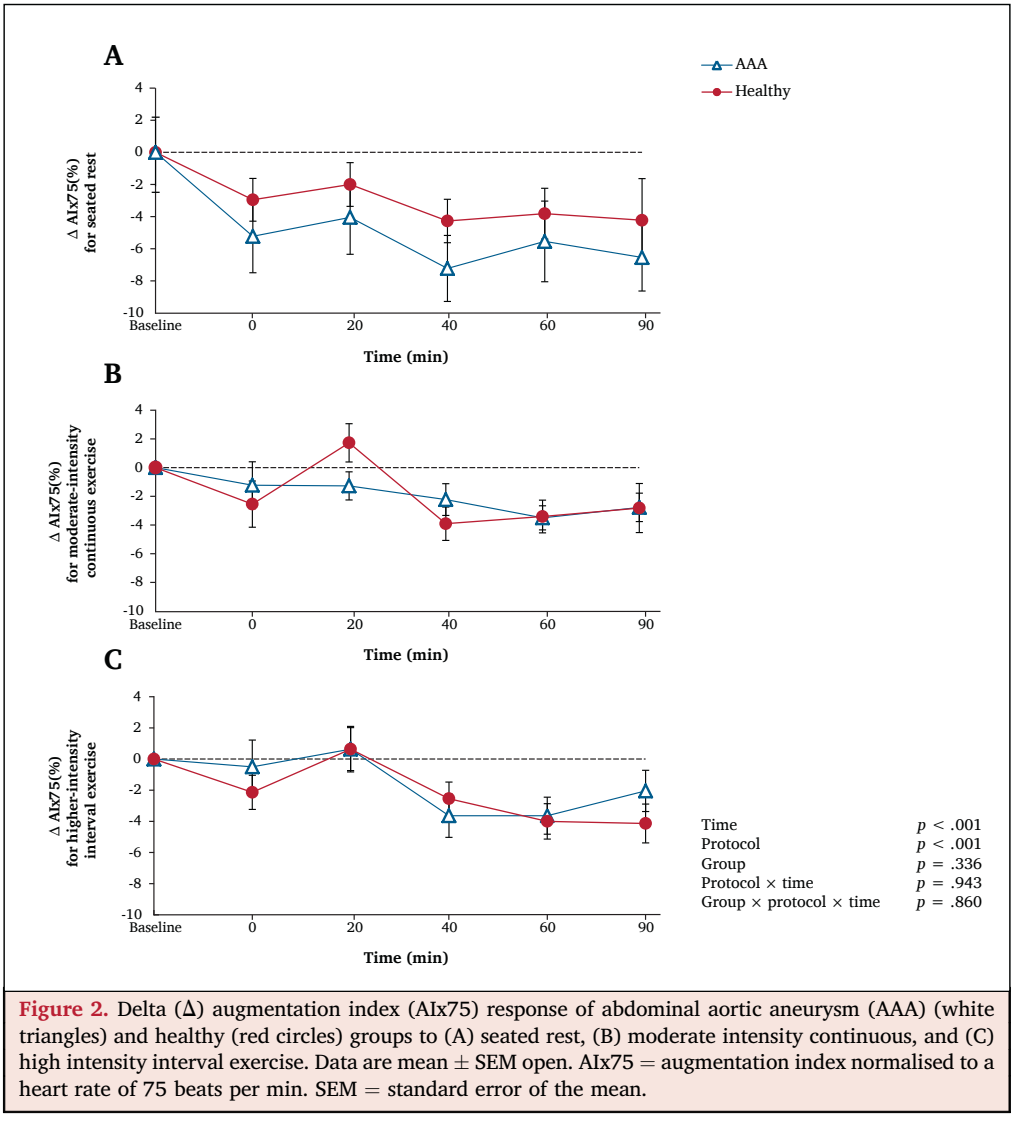

Figure 2. Delta (Δ) augmentation index (AIx75) response of abdominal aortic aneurysm (AAA) (white triangles) and healthy (red circles) groups to (A) seated rest, (B) moderate intensity continuous, and (C) high intensity interval exercise. Data are mean ± SEM open. AIx75 = augmentation index normalised to a heart rate of 75 beats per min. SEM = standard error of the mean.

remodelling with sustained exercise therapy, including longer term reductions in arterial stiffness.[36] In patients with AAA, the attenuation in aortic stiffness and wave reflection magnitude compared with 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 translational relevance of this finding has not yet been established, and further evidence is needed from human AAA exercise trials to confirm this benefit.[39]

Exercise as an adjunctive therapy for AAA

To date, several exercise therapy studies have demonstrated significant improvements in cardiorespiratory fitness in patients with small and large AAAs,[10,11,20] 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 patients with AAA may have contributed to exercise historically being contraindicated for these patients.[40] 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 patients with AAA.[10,11,39] In the current study, higher intensity interval exercise induced a lower post-exercise PWV than 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, than moderate intensity exercise.[37,38,41] The present 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 patients with AAA. Further longer term randomised controlled trials are

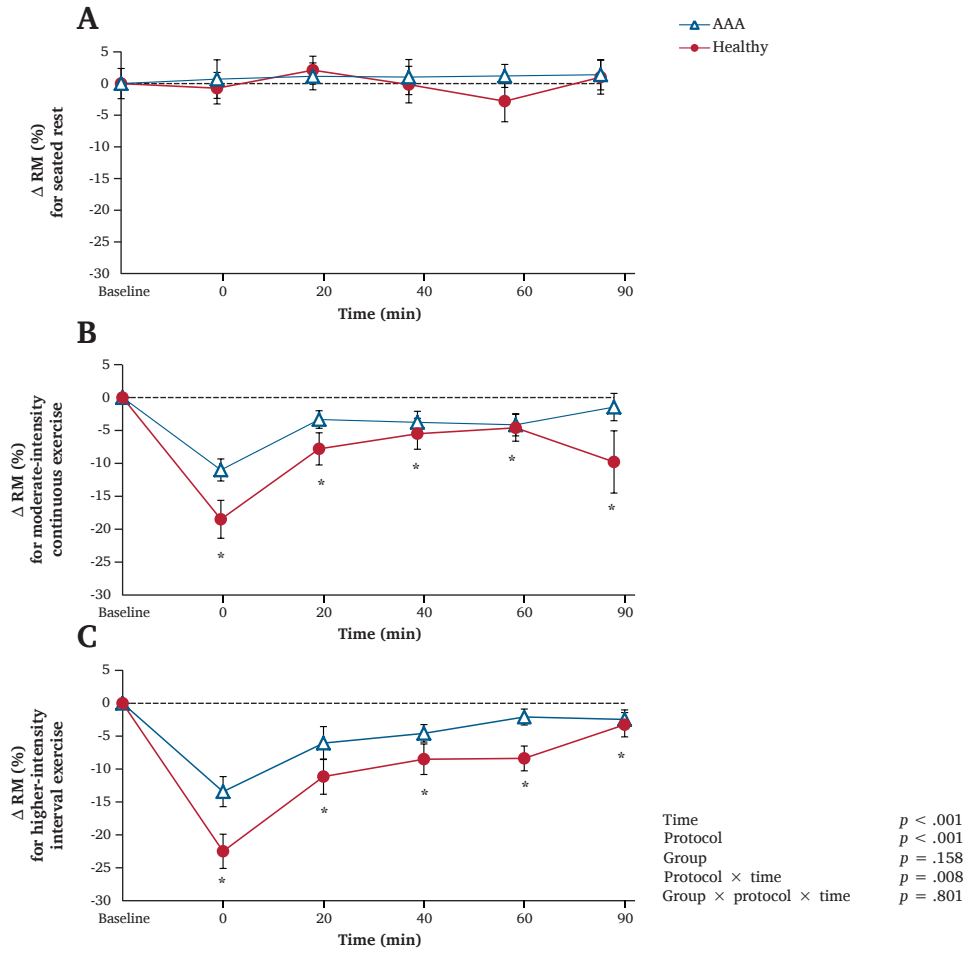

Figure 3. Delta (Δ) reflection magnitude (RM) response of abdominal aortic aneurysm (AAA) (white triangles) and healthy (red circles) groups to (A) seated rest, (B) moderate intensity continuous, and (C) high intensity interval exercise. Data are mean ± SEM open. RM = reflection magnitude; SEM = standard error of the mean. *Significantly different to seated rest.

needed to more thoroughly determine the effect of high intensity exercise therapy vs. standard care on clinical outcomes in patients with AAA.

Limitations

As would be expected, there were differences in medication prescription between patients with AAA and healthy adults. Beta blockers and other antihypertensive medications may affect the response of PWV to exercise;[17,42] 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 patients with AAA 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 the authors' laboratory (5.0 ± 4.1%).[23] With large AAAs there is an increase in PWV measurement error,[31] and thus the present 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 patients with AAA. In addition, this study only included men and thus the findings cannot be extrapolated to women.

CONCLUSION

This study suggests that a bout of exercise attenuates the arterial stiffness response, vs. seated rest, in patients with AAA 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 patients with AAA. Whether exercise training leads to a chronic lowering of aortic and systemic arterial stiffness in patients with AAA requires future investigation.

ACKNOWLEDGEMENTS

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

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 National Health and Medical Research Council (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.

CONFLICT OF INTEREST

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2019.02.021.

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