Atherosclerosis 229 (2013) 282–286

Contents lists available at SciVerse ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Local and systemic effects of leg cycling training on arterial wall thickness in healthy humans

Dick H.J. Thijssen [a,b,*], Ellen A. Dawson [a], Inge C.L. van den Munckhof [b], Gurpreet K. Birk [a], N. Timothy Cable [a], Daniel J. Green [a,c]

[a] Research Institute for Sport and Exercise Science, Liverpool John Moores University, Tom Reilly Building, Byrom Street, Liverpool L3 3AF, United Kingdom
[b] Department of Physiology, Radboud University Nijmegen Medical Centre, The Netherlands
[c] School of Sport Science, Exercise and Health, The University of Western Australia, Crawley, Western Australia 6009, Australia

ARTICLE INFO

Article history:
Received 9 March 2013
Received in revised form
17 April 2013
Accepted 1 May 2013
Available online 21 May 2013

Keywords:
Intima-media thickness
Cardiovascular risk
Exercise training
Ultrasound

ABSTRACT

Exercise training is associated with direct effects on conduit artery function and structure. Cross-sectional studies suggest the presence of systemic changes in wall thickness as a result of exercise in healthy subjects, but no previous study has examined this question in humans undertaking exercise training.

Objective: To examine the change in superficial femoral (SFA, i.e. local effect) and carotid (CA, i.e. systemic effect) artery wall thickness across 8 weeks of lower limb cycle training in healthy young men.

Methods: Fourteen healthy young male subjects were assigned to an 8-week training study of cycling exercise ($n = 9$) or a control period ($n = 5$). Before, during (2, 4 and 6 weeks) and after training, SFA and CA wall thickness was examined using automated edge-detection of high resolution ultrasound images. We also measured resting diameter and calculated the wall:lumen(W:L)-ratio.

Results: Exercise training did not alter CA or SFA baseline diameter ($P = 0.14$), but was associated with gradual, consistent and significant decreases in wall thickness and W:L-ratio in both the CA and SFA ($P < 0.001$ and 0.002, respectively). Two-way ANOVA revealed a comparable magnitude of decrease in wall thickness and W:L-ratio in both arteries across the 8-week period (interaction-effect; $P = 0.29$ and 0.12, respectively). No changes in artery diameter, wall thickness or W:L-ratio were apparent in controls (0.82, 0.38 and 0.52, respectively).

Conclusion: We found that cycle exercise training in healthy young individuals is associated with modest, but significant, decreases in wall thickness in the superficial femoral and carotid arteries. These findings suggest that exercise training causes systemic adaptation of the arterial wall in healthy young subjects.

1. Introduction

Regular exercise training has strong and independent cardioprotective effects [1] which may partly be mediated through the direct effect of exercise on the vasculature [2]. Indeed, exercise training improves vascular function in active and non-active regions [3]. Previous studies have also demonstrated that exercise training can be associated with decreases in arterial wall thickness [4–7]. However, it is not clear whether exercise training leads to local or systemic adaptations of wall thickness.

Rowley et al. recently examined carotid (i.e. an artery representing systemic adaptations) and peripheral (i.e. brachial and superficial femoral artery, supplying active muscle beds) wall thickness of elite athletes [8], including racquet sportsmen [9]. They found a generally lower wall thickness in athletes compared to healthy, age-and sex-matched controls [9]. In the racquet sportsmen, wall thickness was lower than controls, but similar in both arms, despite larger artery lumen diameter in the preferred limb [9]. Although these findings suggest that changes in arterial wall thickness in response to exercise training may be generalised throughout the vasculature, other studies have presented conflicting results [4]. Indeed, one cross-sectional study reported smaller wall thickness of the femoral, but not carotid artery, in endurance trained post-menopausal women compared to sedentary controls [10]. Some of the conflict between previous data may relate to study design, including the assumption that differences

* Corresponding author. Department of Physiology, Radboud University Nijmegen Medical Centre, The Netherlands. Tel.: +31 243614222; fax: +31 245342512.
E-mail addresses: D.Thijssen@ljmu.ac.uk, d.thijssen@fysiol.umcn.nl (D.H.J. Thijssen).

0021-9150/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.atherosclerosis.2013.05.013

between subjects relate to impact of exercise *per se*. [11]. To date, no study has adopted a longitudinal design to examine whether exercise training leads to systemic or local adaptations in conduit artery wall thickness in humans. We therefore examined the impact of 8 weeks of supervised lower limb cycle ergometer training on superficial femoral (i.e. local) and carotid artery (i.e. systemic) wall thickness in healthy young men. We hypothesised that exercise training in healthy men would lead to comparable changes in wall thickness in the superficial femoral and carotid arteries across the 8-week training period.

2. Methods

2.1. Subjects

Fourteen healthy men were recruited and allocated to 8-weeks of exercise training ($n = 9$, 22 ± 2 years, 23.6 ± 3.9 kg/m^2) or control period (n = 5, 23 ± 2 years, 25.8 ± 2.1 kg/m^2). Subjects were healthy, none reported having been diagnosed with cardiovascular diseases, diabetes, insulin resistance or cardiovascular risk factors such as hypercholestolaemia or hypertension. Subjects who smoked or were on medication of any type were excluded. All subjects were recreationally active (1–5 h of physical activity per week) and were instructed to maintain their level of physical activity throughout the study. Informed consent was gained from all subjects prior to the experimental procedures. The study procedures were approved by the Liverpool John Moores Ethics Committee and adhered to the Declaration of Helsinki.

2.2. Experimental measures

Subjects were allocated to 8-weeks cycling exercise training (continuation of their regular activity pattern + 3 supervised exercise training per week) or a control period (continuation of their regular activity pattern). Each laboratory exercise session was supervised and consisted of 30-mins of cycle exercise (80% HR_{max}) performed at the same time of day. Assessments were performed before and after 8-week leg cycling exercise training (exercise training and control group), but also during the intervention (every 2 weeks) to track the nature and time-course of any adaptation in conduit artery wall thickness across the training period. All studies were conducted in a quiet, temperature controlled environment and each visit for a given subject was performed at the same time of day. Subjects were asked to fast for >4 h, abstain from alcohol and caffeine for 16 h, and not to perform any exercise for 24 h to exclude variation in resting tone [12].

After reporting to the laboratory, body characteristics were measured. Subsequently, subjects were positioned in the supine position on a comfortable bed. After a rest period of at least 15 min, blood pressure was measured twice using a manual sphygmomanometer. This was followed by assessment of baseline resting diameter and wall thickness of the carotid and superficial femoral artery by a trained sonographer. A 10 MHz multifrequency linear array probe attached to a high-resolution ultrasound machine (T3000, Terason, Burlington, MA) was used to image the artery lumen and wall thickness (WT). Clearly demarcated intimal-medial boundaries were obtained via perpendicular incidence imaging in relation to the orientation of the vessel. Images were optimized by using contrast controls on the ultrasound machine, which was consistently maintained between arteries for each individual [13]. Ultrasound parameters were set to optimize longitudinal B-mode images of the lumen/arterial wall interface. Diameter and WT was collected from 3 distinct angles and data was recorded for at least 10 s at a sampling frequency of 30 Hz.

Assessment of the common carotid artery was performed with the subject supine and the neck slightly extended to allow scanning of the artery. Images for the carotid artery were made on the proximal 1.5 cm straight portion of this artery. This was followed by assessment of the superficial femoral artery diameter and wall thickness which was performed in the proximal third of the thigh, at least 3 cm distal from the bifurcation. The repeated measurements were made on the same segment of the artery.

2.3. Analysis of conduit artery diameter and wall thickness

Post-test analysis of the carotid and superficial femoral arteries was performed by a researcher who was blinded to the subject identity and timing of the assessments. Furthermore, we used custom-designed edge-detection and wall-tracking software which is largely independent of investigator bias [13,14]. Briefly, the echo signal was encoded in real-time and stored as a DICOM file using an IMAQ-PCI-1407 card. Subsequent software analysis of this data was performed at 30 Hz using an icon-based graphical programming language and toolkit (LabVIEW™ 6.02, National Instruments, Austin, TX). The initial phase of image analysis involved the identification of regions of interest (ROI) on the first frame of every individual study. The ROI enables automated calibration for diameters on the B-mode image. A ROI was then drawn around the optimal area of the B-mode image and within this ROI a pixel-density algorithm automatically identified the angle-corrected near and far-wall e-lines for every pixel column within the ROI. The same algorithm also identifies the far wall media–adventitia interface. Detection of the near and far wall lumen edges and the far wall media–adventitia interface is performed on every frame. We have shown that the diameter measurements using this semi-automated software possess an intra-observer CV of 5.1% [14]. Furthermore, our method of WT assessment is closely correlated with a "phantom" artery system [13]. To correct for differences in diameter, we also calculated the wall-to-lumen ratio (W:L).

2.4. Statistics

Statistical analyses were performed using SPSS 20.0 (SPSS, Chicago, Illinois). A two-way repeated measures ANOVA was used to examine whether the effect of the 8-week intervention ('time'; 0, 2, 4, 6 and 8 weeks) on arterial diameter, wall thickness and wall-to-lumen ratio differed between the arteries ('artery'; carotid *versus* superficial femoral artery). Post-hoc comparisons were performed when a main effect was found. According to recent guidelines we adopted the least significant difference approach to multiple comparisons [15,16]. All data are reported as mean (SE) and statistical significance was assumed at $P < 0.05$.

3. Results

We found no differences between both groups before the intervention (Table 1). Across the 8-week exercise training period,

Table 1
Baseline characteristics of healthy subjects allocated to 8-weeks of exercise training (Intervention group, $n = 9$) or the control group ($n = 5$) who continued their usual levels of physical activity.

Parameter	Intervention group	Control group	*P*-value
Age (years)	23 ± 2	22 ± 2	0.34
Height (m)	1.81 ± 0.09	1.80 ± 0.05	0.81
Weight (kg)	84.8 ± 8.9	77.0 ± 15.4	0.33
Body mass index (kg/m^2)	25.9 ± 2.1	23.6 ± 3.9	0.26
Systolic blood pressure (mmHg)	118 ± 6	128 ± 12	0.12
Diastolic blood pressure (mmHg)	64 ± 6	66 ± 5	0.45