Original Research

Effects of Chronic Anaerobic Training on Markers of Sub-Clinical Atherosclerosis

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Introduction: Although several cardiovascular adaptations in response to different types of exercise are already known, data comparing the effects of the type of exercise training on early markers of atherosclerosis are limited.

Methods: Forty-nine tennis players, 28 weightlifters and 20 non-trained healthy volunteers were recruited for the study. Flow-mediated dilatation (FMD) and intima–media thickness (IMT) in the carotid and femoral arteries were measured in all volunteers for assessment of endothelial function and vascular remodelling, respectively.

Results: Systolic blood pressure (BP) differed significantly among the three study groups (p=0.002) independently of age, body mass index (BMI), frequency, duration and intensity of exercise (p=0.033). FMD was significantly lower in weightlifters than tennis players (p=0.002), while mean carotid IMT was significantly higher in weightlifters as compared to tennis players (p=0.009) and the control group (p=0.003). Although the differences found in FMD were not independent of blood pressure and shear stress, mean carotid IMT remained significantly higher in weightlifters after adjustment for age, BMI and systolic BP, as well as the frequency, duration and intensity of exercise.

Conclusions: The anaerobic exercise involved in weightlifting correlated with worse endothelial function and increased IMT as compared to exercise in the form of tennis. The type of anaerobic exercise may be an important determinant of subclinical atherosclerosis, possibly explaining the elevated cardiovascular risk seen in athletes performing anaerobic training.

Assessment of endothelial function and vascular remodelling has gained a lot of attention lately, as it is considered to be a premature indication of atherosclerosis and vessel damage.[1] Flow-mediated dilatation (FMD) is a non-invasive, easy to perform method for assessing endothelial function, which is closely related to coronary endothelial function,[2] and it has been associated with several established risk factors.[3] Intima–media thickness (IMT) is also a non-invasive method for the assessment of vascular remodelling, having both scientific and clinical value.[4] It is an important surrogate marker for cardiovascular disease,[5] which can be modified by several lifestyle changes, altering the prognosis for future cardiovascular events.[6,7]

Exercise is a cardinal lifestyle factor that is capable of altering several cardiovascular risk factors and improving the prognosis for cardiovascular disease.[8] It seems that exercise ameliorates endothelial function through increased nitric oxide (NO) production and bioavailability,[9]

while it also increases vessel diameter.[10] Regardless of type (aerobic, anaerobic), exercise increases heart rate and pulse volume, which consequently increases cardiac output. Increased blood flow and oxygen intake are also observed, together with a myocardial hypertrophy known as "athlete's heart".[11]

Both aerobic and anaerobic training cause important structural and functional adaptations in the heart and vessels.[12,13] It seems that aerobic training, such as long-distance running or playing a tennis match, improves vascular function through a favorable effect on lipid profile, insulin sensitivity, and body-fat storage,[12] while it decreases blood pressure (BP)[14] and arterial stiffness, and improves vessel distensibility.[15] Anaerobic training, such as weightlifting, increases heart rate and BP.[13] It also alters the collagen-to-elastin ratio in the arterial wall, an important structural alteration that decreases arterial distensibility.[16] However, the possible effect of anaerobic training on endothelial function is controversial.[17]

Although several cardiovascular adaptations in response to different types of exercise have already been investigated, no study has so far directly compared different types of exercise with each other, and with individuals who do not train regularly, as regards their effects on early markers of atherosclerosis. Tennis players demonstrate a relatively high aerobic capacity, as evidenced by their endurance and their mean maximal oxygen uptake values (55-65 ml/kg/min), very low body fat percentage (<10%), resting bradycardia (50 beats/min), increased heart volume (30% above normal), stroke volume, cardiac output, and peripheral vascularisation.[18,19] In contrast, weightlifters exhibit low aerobic energy requirements during training and competition, low aerobic capacity as evidenced by their limited endurance capacity and their mean maximal oxygen uptake values (38-48 ml/kg/min), higher resting heart rates (65-78 beats/min), and lower stroke volume, cardiac output and vascularisation.[20] Furthermore, weightlifting training has been shown to induce significant adaptations in left ventricular function and contractility, related to differences in the volume–afterload relationship, without affecting the myocardium.[20]

Therefore, the aim of the present study was to determine whether athletes competing in sports that induce considerable quantitative and qualitative adaptations in the cardiovascular system differ with respect to early markers of atherosclerosis, i.e. endothelial function and vascular remodeling.

Methods

Subjects

We studied 49 male tennis players with mean age 23.16 ± 2.01 years (mean ± SE) and 28 male weightlifters with mean age 23.93 ± 3.69 years (Table 1). All subjects from each group were following common training programmes conducted by professional trainers. On average, the training programme of tennis players consisted of 25% aerobic exercise and 75% anaerobic exercise (50% anaerobic glycolysis and 25% phosphagen system activation), while that of weightlifters consisted of 100% anaerobic exercise via phosphagen system activation. All subjects were healthy, had no history of hypertension, dyslipidaemia, diabetes mellitus, or coronary artery disease (CAD), while none had liver or endocrine diseases. As controls we used 20 healthy male volunteers, who were matched for age and had either no or very low physical activity, defined as not engaging in any aerobic or anaerobic exercise program for the last 2 years, or walking for no more than 30 minutes per day less than 4 times per week. Volunteers using antioxidant vitamins, nutritional supplements or any other medication, including anabolic steroids, or subjects dieting at the time of the study were excluded. The study was approved by the local scientific committee, was conducted according to the Declaration of Helsinki, and all subjects gave their written informed consent before participating.

Experimental protocol

Volunteers were instructed to attend the Vascular Laboratory of Alexandra Hospital, Athens, Greece, after a 10-12 hour fast and abstention from alcohol, coffee or caffeinated beverages, and smoking. Ultrasound scanning for assessing endothelial function and vascular remodelling was performed and the subjects completed analytical questionnaires about their family history, physical condition, and training. Training was assessed by questionnaires on the frequency of exercise (times/week), mean duration of exercise each time (in hours), and intensity of exercise (scale 1-10, describing the subjective perception of intensity by each athlete, irrespective of the type of exercise). All measurements were performed in a quiet room, at a temperature maintained within 20-25°C, with the subject in a supine position after a 10 min resting period.

Table 1. Characteristics of the study population (controls, tennis players and weightlifters).

Variable	Controls (n=20)	Tennis players (n=49)	Weightlifters (n=28)	Overall p-value	p1	p2	p3
Age (years)	23.65 ± 3.42	23.16 ± 2.06	23.93 ± 3.69	0.520	0.999	0.999	0.807
BMI (kg/m^2)	24.67 ± 2.52	23.89 ± 1.86	26.58 ± 3.09	<0.001	0.699	0.024	<0.001
Waist (cm)	89.33 ± 7.76	85.53 ± 6.94	87.82 ± 10.74	0.240	0.384	0.999	0.757
Waist/hip ratio	0.57 ± 0.15	0.58 ± 0.1	0.55 ± 0.1	0.357	0.999	0.539	0.846
SBP (mmHg)	126.3 ± 13.9	112.8 ± 11.3	120.5 ± 15.5	0.001	0.001	0.379	0.059
DBP (mmHg)	71.7 ± 11.2	69.4 ± 9.9	72 ± 10.3	0.501	0.999	0.999	0.892
Frequency of exercise (times/week)	1.6 ± 2.1	4.8 ± 1.7	4.9 ± 1.6	<0.001	<0.001	<0.001	0.999
Hours of exercise	0.8 ± 0.8	2.2 ± 0.9	2.4 ± 0.7	<0.001	<0.001	<0.001	0.815
Intensity of exercise (scale 1-10)	3.5 ± 3.4	6.8 ± 1.3	8.4 ± 0.9	<0.001	<0.001	<0.001	0.002

Variables are expressed as mean ± standard error; p1: p-value for comparison of control group with tennis players; p2: p-value for comparison of control group with weightlifters; p3: p-value for comparison of weightlifters with tennis players; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure.

Flow-mediated dilatation measurement

A 14.0 MHz multi-frequency linear array probe attached to a high-resolution ultrasound machine (Vivid 7 Pro, GE Healthcare) was used for the assessment of FMD. The method of assessing endothelial function has been described previously.[21,22] The measurement of the artery diameter was performed by two independent observers who were unaware of the study phase, at end-diastole, using electronic callipers, and the procedure was guided by electrocardiographic assessment. After the initial measurement under resting conditions, a cuff fitted 8 cm distal to the brachial artery and near the wrist was inflated at 250-300 mmHg, altering the arterial flow for 4.5 minutes. Then it was deflated, increasing the arterial flow (reactive hyperaemia). Cuff deflation was followed by a continuous scan for 90 s, and the vessel's maximal diameter was determined again at the same point as for the resting measurement (diameter during reactive hyperemia). Shear stress (in dyn/cm^2) was calculated using the formula $8 \times \mu \times$ mean flow velocity / resting diameter (where μ is the blood viscosity), as previously described.[23] FMD was defined as the percentage change in the artery diameter (endothelial-dependent vasodilation) and hyperaemia referred to the percentage increase in flow from flow at rest (at each time point of the study). FMD was also normalised for shear stress using the ratio FMD/shear stress. The inter- and intra-observer variability for brachial diameter measurements in our laboratory are 0.1 ± 0.12 and 0.08 ± 0.19 mm respectively, while FMD variability measured on 2 different days was 1.1 ± 1%.

After the last scan for FMD measurement, 0.4 mg glyceryl trinitrate was administered sublingually, and 4 min later a final scan was performed in order to measure endothelium-independent vasodilatation or nitrate-mediated dilatation and to exclude vascular smooth-muscle cell injury.

Carotid intima–media thickness

IMT was measured using similar equipment as that used for FMD. Scanning included the left and right carotid arteries, as previously described.[24] The carotid artery image was focused on the far wall and 3 segments were identified on each side: (i) common carotid artery (defined as the segment 1 cm proximal to carotid dilatation); (ii) carotid bulb (defined as the segment between the carotid dilatation and carotid flow divider); and (iii) internal carotid artery (defined as the 1 cm long arterial segment distal to the flow divider). In each segment three measurements of the maximal carotid IMT in the far wall were averaged. Subsequently, the average maximal carotid IMT of all 6 segments was calculated as the mean carotid IMT. The femoral IMT was measured in the far wall of a 1 cm long arterial segment proximal to the femoral bifurcation. The same operator performed IMT measurements for each patient in order to avoid inter-observer variability.

Statistical analysis

Continuous variables are presented as mean ± error (E). Their distribution was evaluated graphically by histograms and statistically by the non-parametric Shapiro–Wilk test. Differences in measured variables
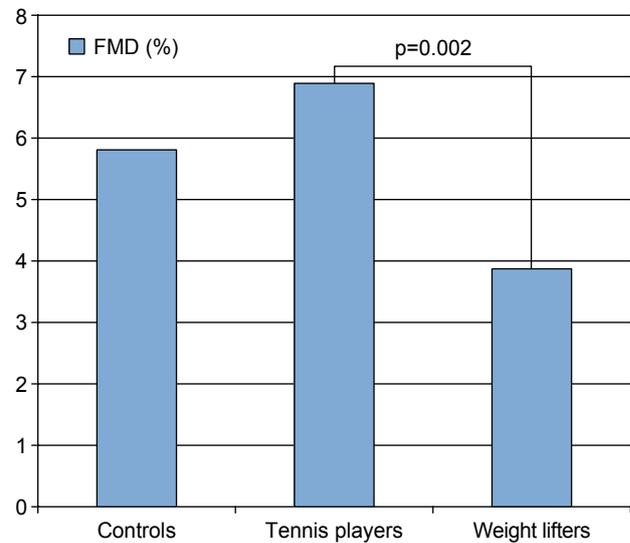
among the controls, weightlifters, and tennis players were evaluated using analysis of variance (ANOVA) and *post hoc* analysis (Bonferroni-corrected Student t-test for multiple comparisons). Multiple analysis of variance (MANOVA) was performed to evaluate differences among groups after adjustment for other confounders. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS 18 for Windows (SPSS Inc, Chicago IL, USA).

Results

Descriptive characteristics of the study population are presented in Table 1. Weightlifters had higher BMI levels compared with tennis players (p<0.001) and controls (p=0.024). Systolic BP in tennis players tended to be lower compared with weightlifters (p=0.059), but the difference reached statistical significance compared with the control group (p=0.001).

Although FMD in weightlifters (3.8 ± 2.06%) was significantly lower than in tennis players (p=0.002; Figure 1, Table 2), FMD normalised for shear stress did not differ among the groups (Table 2). Moreover, hyperaemic shear stress was significantly lower in both tennis players and weightlifters as compared to controls (Table 2).

Mean carotid IMT was significantly higher in weightlifters compared with tennis players (p=0.009) and controls (p=0.003; Figure 2). When the IMT at each site was analysed, IMT in the femoral artery, and in the common and internal carotid was found to be higher in weightlifters than in tennis players (Table 2). In regard to the assessed grading measures

Figure 1. Values of flow-mediated dilation (FMD) among the study groups (controls, tennis players, weightlifters).

of exercise, femoral IMT was positively correlated with the intensity of exercise (r=0.450, p=0.016) in the weightlifters, but no other significant correlations were observed with the vascular parameters of interest in any group.

Multivariate analysis showed that systolic BP differed significantly among the three study groups (p=0.002), independently of age and BMI, and the frequency, duration, and intensity of exercise (p=0.033). FMD differed significantly among the three study groups, independently of age, BMI, and the frequency, duration, and intensity of exercise (p=0.029), with weightlifters having significantly lower FMD than tennis players (p=0.044). However, the FMD difference lost its statistical significance among

Table 2. Markers of endothelial function and vascular remodelling.

	Controls (n=20)	Tennis players (n=49)	Weightlifters (n=28)	Overall p-value	p1	p2	p3
FMD (%)	5.81 ± 1.09	6.86 ± 0.51	3.88 ± 0.39	0.003	0.791	0.181	0.002
Resting shear stress (dyn/cm^2)	12.2 ± 10.6	11.3 ± 5.4	11.6 ± 10.7	0.935	0.999	0.999	0.999
Hyperaemic shear stress (dyn/cm^2)	29.4 ± 20.4	16.9 ± 8.0	18.2 ± 14.7	0.004	0.003	0.022	0.999
FMD/hyperaemic shear stress	0.36 ± 0.50	0.49 ± 0.34	0.38 ± 0.39	0.336	0.652	0.999	0.719
NMD (%)	15.74 ± 0.73	15.39 ± 1.89	14.75 ± 2.98	0.976	0.999	0.999	0.999
Mean carotid IMT (mm)	0.52 ± 0.021	0.54 ± 0.011	0.60 ± 0.014	0.002	0.999	0.003	0.009
Femoral IMT (mm)	0.50 ± 0.032	0.52 ± 0.015	0.60 ± 0.024	0.004	0.999	0.012	0.011
Common carotid IMT (mm)	0.54 ± 0.020	0.53 ± 0.014	0.59 ± 0.016	0.015	0.999	0.158	0.014
Carotid bulb IMT (mm)	0.55 ± 0.044	0.62 ± 0.018	0.65 ± 0.026	0.068	0.337	0.063	0.84
Internal carotid IMT (mm)	0.47 ± 0.025	0.48 ± 0.014	0.56 ± 0.018	0.003	0.999	0.012	0.006

Variables are expressed as mean ± standard error; p1: p-value for comparison of control group with tennis players; p2: p-value for comparison of control group with weightlifters; p3: p-value for comparison of weightlifters with tennis players; FMD – flow-mediated dilation; NMD – nitrate mediated dilatation; IMT – intima–media thickness.
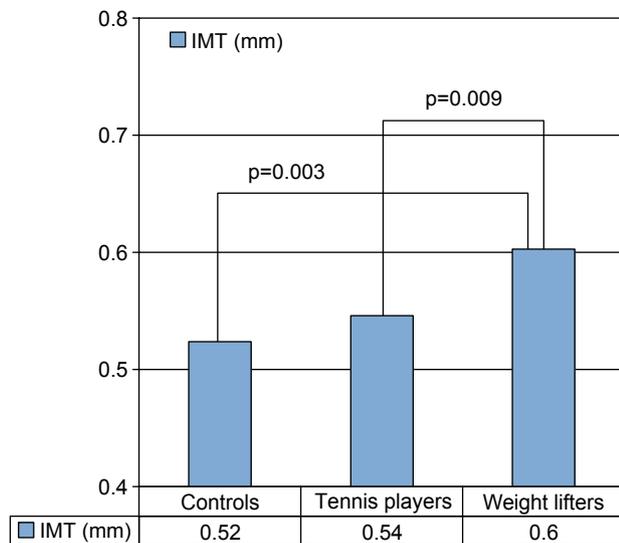
Figure 2. Values of carotid intima–media thickness (IMT) among the study groups (controls, tennis players, weightlifters).

groups when systolic BP (p=0.065) was entered into the multivariate model. Mean carotid, femoral artery, common carotid, and internal carotid IMT were significantly higher in weightlifters than in tennis players and the control group, independently of age, BMI, and systolic BP (p<0.05). Moreover, mean carotid (p=0.016) and femoral (p=0.009) IMT were significantly higher in weightlifters, independently of the frequency, duration and intensity of exercise.

Discussion

The present study demonstrates for the first time results from a direct comparison of early markers of atherosclerosis between athletes playing tennis, requiring high aerobic conditioning, and athletes in anaerobic training (weightlifters). Both endothelial function and IMT were found to be worse in weightlifters. More importantly, these differences in IMT were independent of possible confounders such as age, BMI, and systolic BP. On the other hand, tennis training was associated with a favourable effect on systolic BP, which was found to be lower in comparison with the control group. It seems that the type of exercise is an important determinant for a number of markers of subclinical atherosclerosis. In the present study, despite the significantly higher self-reported intensities of exercise in weightlifters than in tennis players, the observed differences in vascular function and structure were independent of this parameter. Given that tennis is a form of high-intensity interval

training that significantly improves the aerobic capacity of these athletes,[25] specific aerobic-related characteristics, not identified by the design of the current study, may mediate the possible beneficiary effects on endothelial function. In line with this, although we did not assess maximum oxygen uptake (VO_2max) in this population, available data from similar groups of individuals examined in our department of Physical Education and Sports Science confirm that VO_2max in tennis players is significantly higher (61.4 ± 2.9 mL/kg/min, p<0.05) than in weightlifters (42.1 ± 2.5 mL/kg/min) and untrained subjects (39.3 ± 2.1 mL/kg/min) of similar age and risk factor profile.

There are many studies investigating the effect of aerobic exercise on IMT, but anaerobic training has not yet been well evaluated.[26] Although data are in most cases inconsistent,[27,28] in general it has been shown that a sedentary lifestyle, obesity, and ageing increase thickening of the arteries, while aerobic training enables an improvement in IMT.[26,29] Both in animal models and in cross-sectional and interventional studies in endurance athletes (aerobic exercise), chronic changes in blood flow can produce directionally similar changes in the lumen diameter.[30,31] This flow-induced adaptation is thought to maintain basal levels of shear stress along the arterial wall. In addition to these effects on lumen diameter, chronically elevated blood flow leads to a reduction in the thickness of the intimal and medial layers of the artery, with the collective process being termed "expansive arterial remodelling".[32,33] Therefore, it was expected for tennis players to have almost the same levels of IMT as the control group. In a recent study by Rowley et al,[34] elite tennis players showed better IMT than that of controls. From our results, we failed to observe a beneficial effect of tennis on IMT; the different findings could be due to discrepancies in age and risk factors between the populations studied. Since our population consisted of young healthy adults without cardiovascular risk factors, and therefore IMT in the controls was not expected to be abnormal (high), the possibility of observing a better (lower) IMT in tennis athletes was rather low. Indeed, the carotid and femoral IMT of the control group in the above-mentioned study (0.618 ± 0.074 mm and 0.634 ± 0.015 mm, respectively) were substantially higher than those of our control group (0.54 ± 0.021 mm and 0.50 ± 0.020 mm, respectively), possibly indicating a higher risk factor burden in the former population. On the other hand, the level and type of training (elite versus habitual athletes) might also affect differences between athletes

and controls. However, the observed results concerning IMT in weightlifters could be explained through the already known direct relation between arterial stiffness and carotid atherosclerosis.[35] It seems that resistance training (anaerobic) increases arterial stiffness,[36] while aerobic exercise may increase arterial distensibility.[37] It is hypothesised that increased arterial stiffness may lead to vessel wall damage and atherosclerosis. It is possible that without the shock-absorbing capacity, the stiff arterial wall may be subjected to increased intraluminal stress, which in consequence gradually increases arterial thickness.

The FMD was found to be lower in weightlifters than in tennis players, and a direct comparison with tennis players demonstrated a statistically significantly lower value, which was independent of age and BMI. It has already been reported that, regardless of type, exercise increases NO production and bioavailability,[9] which in turn improves endothelial function. However, it was found that as the intensity of exercise increases, there is a remarkable increase in oxidation.[38] Heavy physical exercise has been determined to be associated with a dramatic increase in oxygen uptake, both by the whole body and particularly by the skeletal muscle. Most of the oxygen consumed is utilised in the mitochondria for substrate metabolism and ATP production, which has been linked in several studies with increased free radical production.[39] It could be hypothesised that weightlifters may have developed increased oxidative stress, which reduces NO bioavailability, leading to decreased FMD levels. However, it would be necessary to assess several markers of oxidation in our volunteers in order to support this hypothesis. Additionally, the observed difference in FMD between tennis players and weightlifters lost its significance when systolic BP was entered into the multivariate analysis, which could be explained by the established inverse relation between FMD and systolic BP. Recently, Plavnik et al showed that in a healthy normotensive (systolic BP <140 mmHg) population aged 35-50 years, without any risk factors for atherosclerotic disease, subjects with systolic BP ≥115 mmHg, when compared with subjects with systolic BP <115 mmHg, had a significant reduction in FMD for every 10 mmHg increase in systolic BP.[40] Finally, after normalising for shear stress these differences were lost because of the difference in shear stress responses between controls and athletes. This may be attributed to a higher level of adaptation to short-term challenges of increased shear stress in athletes as compared to sedentary individuals.

It might be argued that it is unexpected that tennis players did not show a better FMD than sedentary controls, since following endurance training, particularly in middle-aged or older adults, an improved vascular profile is expected as compared to their age-matched counterparts.[41] However, the tennis players in our population engaged in both aerobic and anaerobic exercise, and therefore a pure effect of aerobic exercise could not be expected. Furthermore, although in these age groups endothelial dysfunction is very commonly encountered, in our non-smoking young healthy population without risk factors it is difficult to observe significant improvements in endothelial function in an already normal vascular environmement. In contrast, a deteriorating effect, such as that observed in weightlifters, would become more prevalent in a vascular system that is relatively naïve to challenges. Indeed in a recent study by Phillips et al,[42] FMD significantly improved after a hypertension challenge in athletes, including weightlifters, but not in sedentary persons. Interestingly, in that study weightlifters showed FMD values better than runners and similar to sedentary controls; however, this was acknowledged by the authors of that manuscript to be unexpected and contradictory to most results from previous trials with much larger samples, as discussed above.

The observed results regarding BMI were expected and are in accordance with previous studies. Although body composition analysis was not performed in this study, weightlifters demonstrate more developed skeletal muscles, and therefore a higher body weight and BMI than tennis players, which is quite normal and typical.[43]

On the other hand, systolic BP was found to be lower in tennis players than in the control group, and tended to be lower compared with weightlifters. Additionally, the observed findings for systolic BP were independent of age and BMI. There is increasing evidence that continuous aerobic training may lead to significant reductions in BP,[44] while high intensity anaerobic training is frequently responsible for BP elevations.[13] Observations concerning systolic BP could also be partly justified by the different effects of aerobic and anaerobic training on arterial stiffness. It seems that continuous aerobic training may have beneficial effects leading to an increase in arterial distensibility.[37] On the other hand, recent studies conducted in healthy individuals have concluded that resistance training increases arterial stiffness.[36] Therefore, it is possible that the tennis players and weightlifters

in our study may have had significant differences in arterial stiffness, which in turn could directly affect BP measurements. However, in the present study we did not measure any relevant markers and can only speculate based on previous findings.

It is also important to acknowledge a number of limitations in our study. Specifically, the blood lipid profile was not assessed, but at the age of our volunteers, dyslipidaemias are almost exclusively familial. A detailed family history was taken for all volunteers and no family history of dyslipidaemia was detected. There was also no subjective measure of assessing anaerobic components within aerobic training, which is mostly present in tennis playing. However, tennis players must have increased aerobic conditioning in order to avoid fatigue during long matches, which is why this sport was selected in our study. Finally, the diet and dietary patterns of our volunteers were not assessed.

Conclusions

The present study suggested that anaerobic training may significantly worsen markers of subclinical atherosclerosis such as IMT and FMD. It seems that the type of exercise could be an important determinant of significant markers of early atherosclerosis and consequently the risk of future cardiovascular events.

References

1. Quyyumi AA. Prognostic value of endothelial function. Am J Cardiol. 2003; 91: 19H-24H.
2. Celermajer DS, Sorensen KE, Bull C, Robinson J, Deanfield JE. Endothelium-dependent dilation in the systemic arteries of asymptomatic subjects relates to coronary risk factors and their interaction. J Am Coll Cardiol. 1994; 24: 1468-1474.
3. Anderson TJ, Uehata A, Gerhard MD, et al. Close relation of endothelial function in the human coronary and peripheral circulations. J Am Coll Cardiol. 1995; 26: 1235-1241.
4. Graham I, Atar D, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice: full text. Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts). Eur J Cardiovasc Prev Rehabil. 2007; 14 Suppl 2: S1-113.
5. Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. Circulation. 1986; 74: 1399-1406.
6. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. Circulation. 2007; 115: 459-467.
7. Ahmed HM, Blaha MJ, Nasir K, Rivera JJ, Blumenthal RS. Effects of physical activity on cardiovascular disease. Am J Cardiol. 2012; 109: 288-295.
8. Pitsavos C, Chrysohoou C, Koutroumbi M, et al. The impact of moderate aerobic physical training on left ventricular mass, exercise capacity and blood pressure response during treadmill testing in borderline and mildly hypertensive males. Hellenic J Cardiol. 2011; 52: 6-14.
9. Fukai T, Siegfried MR, Ushio-Fukai M, Cheng Y, Kojda G, Harrison DG. Regulation of the vascular extracellular superoxide dismutase by nitric oxide and exercise training. J Clin Invest. 2000; 105: 1631-1639.
10. Laurent S, Tropeano AI, Lillo-Lelouet A, Jondeau G, Laloux B, Boutouyrie P. Local pulse pressure is a major determinant of large artery remodelling. Clin Exp Pharmacol Physiol. 2001; 28: 1011-1014.
11. Pavlik G, Major Z, Varga-Pintιr B, Jeserich M, Kneffel Z. The athlete's heart Part I (Review). Acta Physiol Hung. 2010; 97: 337-353.
12. Sasaki JE, dos Santos MG. The role of aerobic exercise on endothelial function and on cardiovascular risk factors. Arq Bras Cardiol. 2006; 87: e226-231.
13. Tanasescu M, Leitzmann MF, Rimm EB, Willett WC, Stampfer MJ, Hu FB. Exercise type and intensity in relation to coronary heart disease in men. JAMA. 2002; 288: 1994-2000.
14. Duncan GE, Perri MG, Anton SD, et al. Effects of exercise on emerging and traditional cardiovascular risk factors. Prev Med. 2004; 39: 894-902.
15. Vaitkevicius PV, Fleg JL, Engel JH, et al. Effects of age and aerobic capacity on arterial stiffness in healthy adults. Circulation. 1993; 88: 1456-1462.
16. Umpierre D, Stein R. Hemodynamic and vascular effects of resistance training: implications for cardiovascular disease. Arq Bras Cardiol. 2007; 89: 256-262.
17. Green DJ, Spence A, Rowley N, Thijssen DH, Naylor LH. Vascular adaptation in athletes: is there an 'athlete's artery'? Exp Physiol. 2012; 97: 295-304.
18. König D, Huonker M, Schmid A, Halle M, Berg A, Keul J. Cardiovascular, metabolic, and hormonal parameters in professional tennis players. Med Sci Sports Exerc. 2001; 33: 654-658.
19. Kovacs MS. Tennis physiology: training the competitive athlete. Sports Med. 2007; 37: 189-198.
20. Sagiv M, Sagiv M, Ben-Sira D. Weight lifting training and left ventricular function in adolescent subjects. J Sports Med Phys Fitness. 2007; 47: 329-334.
21. Celermajer DS, Sorensen KE, Gooch VM, et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet. 1992; 340: 1111-1115.
22. Corretti MC, Anderson TJ, Benjamin EJ, et al. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the International Brachial Artery Reactivity Task Force. J Am Coll Cardiol. 2002; 39: 257-265.
23. Aznaouridis KA, Stamatelopoulos KS, Karatzis EN, Protogerou AD, Papamichael CM, Lekakis JP. Acute effects of renin-angiotensin system blockade on arterial function in hypertensive patients. J Hum Hypertens. 2007; 21: 654-663.
24. de Groot E, Jukema JW, Montauban van Swijndregt AD, et al. B-mode ultrasound assessment of pravastatin treatment effect on carotid and femoral artery walls and its correlations with coronary arteriographic findings: a report of the Regression Growth Evaluation Statin Study (REGRESS). J Am Coll Cardiol. 1998; 31: 1561-1567.

25. Kubukeli ZN, Noakes TD, Dennis SC. Training techniques to improve endurance exercise performances. Sports Med. 2002; 32: 489-509.

26. Kadoglou NP, Iliadis F, Liapis CD. Exercise and carotid atherosclerosis. Eur J Vasc Endovasc Surg. 2008; 35: 264-272.

27. Moreau KL, Silver AE, Dinenno FA, Seals DR. Habitual aerobic exercise is associated with smaller femoral artery intima-media thickness with age in healthy men and women. Eur J Cardiovasc Prev Rehabil. 2006; 13: 805-811.

28. Myers J, Wagner D, Schertler T, et al. Effects of exercise training on left ventricular volumes and function in patients with nonischemic cardiomyopathy: application of magnetic resonance myocardial tagging. Am Heart J. 2002; 144: 719-725.

29. Stabouli S, Kotsis V, Karagianni C, Zakopoulos N, Konstantopoulos A. Blood pressure and carotid artery intima-media thickness in children and adolescents: the role of obesity. Hellenic J Cardiol. 2012; 53: 41-47.

30. Ben Driss A, Benessiano J, Poitevin P, Levy BI, Michel JB. Arterial expansive remodeling induced by high flow rates. Am J Physiol. 1997; 272: H851-858.

31. Langille BL. Arterial remodeling: relation to hemodynamics. Can J Physiol Pharmacol. 1996; 74: 834-841.

32. Dinenno FA, Tanaka H, Monahan KD, et al. Regular endurance exercise induces expansive arterial remodelling in the trained limbs of healthy men. J Physiol. 2001; 534: 287-295.

33. Mattsson EJ, Kohler TR, Vergel SM, Clowes AW. Increased blood flow induces regression of intimal hyperplasia. Arterioscler Thromb Vasc Biol. 1997; 17: 2245-2249.

34. Rowley NJ, Dawson EA, Birk GK, et al. Exercise and arterial adaptation in humans: uncoupling localized and systemic effects. J Appl Physiol. 2011; 110: 1190-1195.

35. van Popele NM, Grobbee DE, Bots ML, et al. Association between arterial stiffness and atherosclerosis: the Rotterdam Study. Stroke. 2001; 32: 454-460.

36. Miyachi M, Kawano H, Sugawara J, et al. Unfavorable effects of resistance training on central arterial compliance: a randomized intervention study. Circulation. 2004; 110: 2858-2863.

37. Otsuki T, Maeda S, Iemitsu M, et al. Effects of athletic strength and endurance exercise training in young humans on plasma endothelin-1 concentration and arterial distensibility. Exp Biol Med (Maywood). 2006; 231: 789-793.

38. Coyle EF. Physical activity as a metabolic stressor. Am J Clin Nutr. 2000; 72: 512S-20S.

39. Banerjee AK, Mandal A, Chanda D, Chakraborti S. Oxidant, antioxidant and physical exercise. Mol Cell Biochem. 2003; 253: 307-312.

40. Plavnik FL, Ajzen SA, Christofalo DM, Barbosa CS, Kohlmann O Jr. Endothelial function in normotensive and high-normal hypertensive subjects. J Hum Hypertens. 2007; 21: 467-472.

41. DeVan AE, Seals DR. Vascular health in the ageing athlete. Exp Physiol. 2012; 97: 305-310.

42. Phillips SA, Das E, Wang J, Pritchard K, Gutterman DD. Resistance and aerobic exercise protects against acute endothelial impairment induced by a single exposure to hypertension during exertion. J Appl Physiol. 2011; 110: 1013-1020.

43. Longhurst JC, Stebbins CL. The power athlete. Cardiol Clin. 1997; 15: 413-429.

44. Fagard RH. Effects of exercise, diet and their combination on blood pressure. J Hum Hypertens. 2005; 19 Suppl 3: S20-24.