[Primary Care]

Impaired Femoral Vascular Compliance and Endothelial Dysfunction in 30 Healthy Male Soccer Players: Competitive Sports and Local Detrimental Effects

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Background: Despite beneficial effects of physical activity on cardiovascular risk, discordant data on elite athletes (high atherosclerotic damage in activity comprising strenuous exertion) and retired sportsmen are reported in the literature.

Hypothesis: We hypothesize that long-lasting daily physical activity could affect the morphology and function of the carotid and femoral vessel walls differently, as assessed in elite male athletes aged 20 to 30 years compared with age- and sex-matched healthy controls.

Study Design: Retrospective case-control study.

Level of Evidence: Level 3.

Methods: Sixty male subjects (30 athletes and 30 controls) underwent medical examination for ankle brachial index, augmentation index (AIX) and AIX corrected for heart rate (AIXr), peripheral arterial tonometry (PAT), and intima media thickness and pulse wave velocity assay at common carotid (carotid–intima media thickness [c-IMT], carotid–pulse wave velocity [c-PWv]) and femoral arteries (femoral–intima media thickness [f-IMT], femoral–pulse wave velocity [f-PWv]) assessed by ultrasonography using Doppler ultrasound.

Results: Athletes showed a significantly lower heart rate (HR) at rest and a better lipid profile than controls. In athletes, c-PWv (5.87 ± 0.80 vs 6.62 ± 1.02 m/s, $P = 0.001$) and f-PWv (8.96 ± 1.29 vs 7.89 ± 1.39, $P = 0.002$) were, respectively, significantly lower and higher than values found in controls; accordingly, carotid AIX (4.03 ± 6.21 vs 7.81 ± 5.21, $P = 0.003$) and femoral AIX (8.56 ± 10.21 vs 6.09 ± 7.95, $P = 0.042$) were lower and higher than control values, even after correction for heart rate ($P = 0.03$). On the other hand, IMT values were significantly higher in controls than in athletes (c-IMT, $P < 0.0001$; f-IMT, $P < 0.0001$). A positive significant correlation between HR and c-IMT and f-IMT ($r = 0.527$, $P < 0.001$ and $r = 0.539$, $P < 0.0001$, respectively) and between HR and c-PWv ($r = 0.410$, $P = 0.01$) was found when controls and athletes were considered as a whole group. Soccer players showed lower PAT values in comparison with controls ($P = 0.002$).

Conclusion: Elite sports positively affect c-IMT, f-IMT, and carotid PWv and AIX but not femoral PWv, AIX, AIXr, or PAT.

Clinical Relevance: Physical activity affects vascular beds in elite athletes differentially, depending on the rate of superior or inferior limb involvement in different sports. In soccer players, physical activity has a protective effect on carotid and femoral vessel walls but worsens femoral arterial and endothelial function. These findings highlight how different results can be shown on carotid and femoral districts, when these vascular districts are differently stressed during sport activity.

Keywords: intima media thickness; arterial stiffness; peripheral arterial tonometry

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Possible effects of physical activity on the vascular arterial wall have been well summarized by Green et al.[10] Several studies have investigated carotid and femoral intima media thickness (c-IMT and f-IMT, respectively)[13] and vascular compliance,[17] showing decreased atherosclerotic involvement for athletes in comparison with the general population; however, retired or older elite sportsmen[1] had similar or higher atherosclerotic burden than the general population, suggesting a relationship between the type and intensity of sport and subclinical vascular damage.[5,6] Moreover, vigorous exertion[15] was significantly associated with sudden death[2] and coronary atherosclerosis.[19]

Ultrasound-measured IMT and vascular compliance, assessed by pulse wave velocity (PWv),[4] at common carotid and femoral arteries[7,8] are early morphologic and functional markers of atherosclerotic vessel wall damage and are proven to optimize stratification of cardiovascular (CV) risk in primary prevention.[11,24]

Intima media thickness reflects structural morphologic changes of the arterial wall strictly related to the development of atherosclerotic plaque.[5] PWv and augmentation index (AIX)[4] are markers of functional vascular wall properties[12] and reflect local intrinsic damage of biophysical properties of the vascular wall[17] due to increased vascular wall stiffness rather than hemorheologic or blood characteristics.[14]

Several physiologic and pathologic determinants modulate arterial stiffness, and age, physical activity, hypertension, dyslipidemia, and diabetes are reported as the most important ones.[12] PWv is considered an intermediate end point in CV events, showing an independent predictive power for death for all causes and for CV mortalities, fatal and nonfatal coronary events, and fatal strokes.[12,34] Similarly, AIX is an independent predictor of CV events in hypertensive patients[6]; nevertheless, data regarding AIX in sports are scarce. Evidence suggests that arterial stiffness and IMT may express differently without overlapping assessments, and both are concurrent in optimizing the cardiovascular profile.[26]

Peripheral arterial tonometry (PAT) is a novel technique to noninvasively assess endothelial function.[6,16] Low PAT values are associated with endothelial dysfunction and high CV risk in both primary and secondary prevention populations.[6,16]

This study evaluated the effects of professional daily and intensive sports activity on vascular morphology (IMT) and function (PWv and AIX) at the carotid and femoral vessel walls of 30 elite soccer athletes aged 20 to 30 years in comparison with 30 age- and sex-matched healthy controls not participating in sports at competitive levels. To this aim, a comprehensive assessment of local and systemic vascular characteristics was provided, as recommended by current guidelines, to identify subclinical organ damage.

MATERIALS AND METHODS

Study Population

Sixty healthy white men (30 athletes playing aerobic activity [soccer] and 30 healthy male controls) were enrolled at the Office for Vascular Function Assessment, Careggi Hospital, Florence, Italy, for routine vascular function assessment. All subjects gave written informed consent to the collection and analysis of data. The investigation was performed in accordance with the Declaration of Helsinki.[35]

Study Design

A retrospective analysis of data collected during activities was performed. Athletes were soccer players participating at a competitive level with different Italian teams and actively taking part in weekly soccer-specific training and competitions.

All athletes had engaged a competitive sport career for at least 4 ± 0.2 years. At the time of the visit, all soccer players had obtained clinical eligibility for competitive sports by first-line investigators, as required under Italian law. Players with a long history of injuries as well as goalkeepers were eliminated from the study.

Control subjects included 30 healthy, sedentary men, not performing aerobic physical activity. No control subjects had previously played sports at a competitive level or participated in aerobic exercise programs.

Clinical Assessment

Exclusion criteria comprised acute illness or pathologic conditions; history of disease; other systemic disorders such as dyslipidemia, diabetes, hypertension, autoimmune, pulmonary, or hematologic disorders; and anxiety or depression. All subjects were nonsmokers, of normal weight, and were not alcoholics.

Clinical assessment of athletes was performed during the sport season, exclusively on Mondays, and included a medical questionnaire, physical examination (heart rate [HR], blood pressure, height, weight, body mass index [BMI], waist circumference), 12-lead electrocardiogram at rest, blood venous sampling (complete blood count, fasting glucose, lipid profile, kidney and liver function markers), ultrasound assessment (IMT, PWv, and AIX), and ankle-brachial index (ABI).

The presence of CV risk factors was assessed in each subject according to current guidelines (Table 1).[3,28-32]

Ultrasound Assessment

All patients underwent echographic assessment by a MyLab 70 XVisionEsaote machine (Esaote Medical Systems). The system used dedicated software (RF data technology involving RF quality intima media thickness [^{RF}QIMT] and RF quality arterial stiffness [^{RF}QAS]).[8,21]

Intima media thickness of the right and the left common carotid arteries (c-IMT) was measured 1 cm proximal to the carotid dilation with B-mode ultrasonography using a computerized probe with a 7.5-MHz transducer attached to a MyLab 70 XVision Esaote machine. f-IMT was measured in the far wall of a 1-cm-long arterial segment proximal to the femoral bifurcation.

For each subject, the maximum c-IMT and f-IMT values were used for statistical analysis. According to the guidelines of the

Table 1. Clinical risk factors accounted in risk assessment

Risk Factor	Description
Hypertension	Systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg,[32] or receiving antihypertensive treatment
Hyperlipidemia	Total serum cholesterol level >160 mg/dL[33] or taking lipid-lowering medication
Diabetes mellitus	Treated with an oral hypoglycemic agent, insulin, or both or having fasting glucose levels >126 mg/dL[34]
Family history for coronary artery disease	Having first- or second-degree relatives with premature cardiovascular disease
Overweight	Body mass index ≥25 kg/m^2
Smoking habit	Current smokers or ex-smokers ≤1 year

European Society of Hypertension,[28,31] c-IMT values >0.9 mm and f-IMT values >1.2 mm were considered pathologic.

The Esaote machine software automatically assessed the vascular diameter of the carotid and femoral arteries. Arterial stiffness was expressed as local PWv according to the distensibility of the right and left common carotid arteries and it was measured 1 cm proximal to the carotid dilation. f-PWv was measured in the far wall of a 1-cm-long arterial segment proximal to the femoral bifurcation. The cutoff value for c-PWv and f-PWv was considered 12 m/s, according to current literature.[28,31] For each subject, the maximum c-PWv and f-PWv values were used for statistical analysis.

The assay of AIX was performed at the common carotid and femoral arteries, simultaneous to the ultrasound investigation. The AIX analysis was automatically performed by MyLab 70 XVisionEsaote software according to a previously described method.[18] For each subject, the maximum carotid and femoral AIX values were used for statistical analysis.

We followed recommendations for standardization of subject conditions.[19,33]

Ankle-brachial index was obtained by the ratio tibial/brachial systolic blood pressure measured by Doppler ultrasound and a value of <0.9 was the cut-off for the diagnosis of peripheral arterial disease according to current guidelines.[30]

Peripheral Arterial Tonometry

Endothelial function was noninvasively assessed via PAT values (expressed as a natural logarithm of reactive hyperemia index values [ln RHI]).[19] PAT signals were obtained using the EndoPAT 2000 device (Itamar Medical Ltd), a noninvasive validated technology used to assess peripheral arterial tone.[6,20,21]

Statistical Analysis

Database construction and statistical analysis were performed using SPSS for Windows (version 19; IBM Corp). Categorical variables were expressed as frequencies and percentages; analysis of data distribution was evaluated using the chi-square test (statistical significance, $P < 0.05$). Continuous variables were expressed as mean ± SD.

Analysis of variance was used. The nonparametric Mann-Whitney test was used for analysis of unpaired data. Correlation analysis was measured using the Spearman correlation test. A P value <0.05 was considered to indicate statistical significance.

RESULTS

Characteristics of the study population are listed in Table 2. Data regarding instrumental markers of atherosclerosis are listed in Table 3.

DISCUSSION

The effect of elite sport activity improved endothelial function and was associated with lower IMT values at the carotid and femoral walls; however, elite sports improved markers of arterial stiffness (PWv and AIX) only in carotid districts but not in femoral arteries.

The lower HR values found in athletes could be because of an increase in basal vagal tone and/or cardiopulmonary performance in athletes that is associated with vascular protection. Recent reports identify high HR as an independent CV risk factor, and low, as observed in our athletes, could mark for a lower cardiovascular risk profile.[9,25]

All biochemical parameters were within normal values. Differences in lipid parameters showed a better profile for sportsmen than for controls. In particular, lower plasma levels of triglycerides and higher levels of high-density lipoprotein cholesterol found in sportsmen in comparison with controls could reflect the positive effects exerted by physical activity on metabolic pathways and CV risk. The direct associations between markers of arterial stiffness (PWv, AIX, and AIXr) and glucose levels are consistent with other data.[12]

The slight decrease in c-IMT and f-IMT found in athletes in comparison with sedentary controls highlights the positive effects of physical activity on early markers of morphologic

Table 2. Characteristics of the study population

Variable	Athletes (n = 30)	Controls (n = 30)	*P* Value[a]
Anthropometric parameters			
Age, y, mean ± SD	28.1 ± 2.5	27.1 ± 3.1	0.7
Heart rate, bpm	61.1 ± 3.6	70.2 ± 3.9	**<0.0001**
Waist circumference, cm	82.90 ± 5.23	81.80 ± 4.89	0.07
BMI, kg/m^2[b]	22.7 ± 1.5	22.4 ± 1.4	0.6
SBP, mm Hg	121.1 ± 3.6	121.9 ± 3.4	0.7
DBP, mm Hg	72.4 ± 5.1	71.6 ± 5.1	0.7
Mean blood pressure, mm Hg	96.75 ± 24.9	96.75 ± 25.6	0.7
Biochemical parameters			
Hematocrit, %	42.65 ± 2.02	45.98 ± 3.76	**0.035**
Hemoglobin, g/dL	15.23 ± 0.77	14.86 ± 0.82	0.08
Fibrinogen, mg/dL	323 ± 37.9	338 ± 42.8	0.09
Glucose, mg/dL	83 ± 12	85 ± 15	0.7
Total cholesterol, mg/dL	181.8 ± 13.5	184.9 ± 13.3	0.2
HDL-c, mg/dL	69.2 ± 15.7	54.5 ± 13.4	**0.030**
LDL-c, mg/dL	98 ± 23	119 ± 31	0.06
Triglycerides, mg/dL	96.3 ± 20.9	111.1 ± 26.2	**0.026**
Serum creatinine, mg/dL	0.62 ± 0.04	0.64 ± 0.07	0.8
AST, U/L[c]	16 ± 3	17 ± 3.5	0.8
ALT, U/L[c]	15 ± 4	14 ± 5	0.8
GGT, U/L[c]	13 ± 6	16 ± 5	0.7

ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; DBP, diastolic blood pressure; GGT, gamma-glutamyl transpeptidase; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; SBP, systolic blood pressure.
[a]Boldfaced values indicate significant *P* values.
[b]Significant correlation between BMI and waist circumference ($r = 0.44$, $P = 0.001$).
[c]BMI significantly correlated with indices of hepatic function: AST ($r = 0.382$, $P = 0.043$), ALT ($r = 0.399$, $P = 0.037$), and GGT ($r = 0.363$, $P = 0.044$).

arterial wall damage.[13] Moreover, the positive relationship found between the decrease in HR and in c-IMT and f-IMT may suggest that the decrease in IMT could be the expression of a better cardiopulmonary performance.

We calculated the f-IMT/c-IMT ratio and the f-PWv/c-PWv ratio to appreciate whether changes of IMT and PWv in carotid and femoral districts, evaluated in 2 study groups, are harmonious. The similar f-IMT/c-IMT ratios found in soccer players and sedentary individuals shows positive effects of physical activity on morphologic markers of arterial wall damage and were equally obtained at carotid and femoral districts ($P = 0.5$).

On the contrary, in our athletes, the effect of physical activity on early markers of functional arterial wall damage were opposite at the carotid and femoral districts. The different pattern of the f-PWv/c-PWv ratio and of AIX values found in soccer players and sedentary subjects supports the selective regional-based effects of physical activity and shows that selective local functional damage at the femoral wall occurs in athletes in contrast with the contemporaneous systemic improvement found in IMT at both carotid and femoral vessels.

These findings could be related to the fact that soccer players mainly use muscles of inferior limbs during physical activity. Indeed, femoral arteries are resistance arteries, and an increase

Table 3. Instrumental markers of atherosclerosis and vascular compliance[a]

Variable	Athletes (n = 30)	Controls (n = 30)	*P* Value[b]
c-IMT, μm[c,d]	408.5 ± 63.2	463.6 ± 53.8	**<0.0001**
f-IMT, μm[c,d]	446.5 ± 105.2.9	527.0 ± 85.0	**<0.0001**
c-PWv, m/s[e,f]	5.87 ± 0.80	6.62 ± 1.02	**0.001**
f-PWv, m/s	8.96 ± 1.29	7.89 ± 1.39	**0.004**
Carotid diameter, mm[g]	7.74 ± 0.94	7.18 ± 0.87	**0.03**
Femoral diameter, mm[g]	8.24 ± 0.74	7.71 ± 0.90	**0.014**
Carotid thickness/diameter ratio	0.053 ± 0.03	0.069 ± 0.04	**0.01**
Femoral thickness/diameter ratio	0.055 ± 0.04	0.068 ± 0.04	**0.02**
ABI	1.1 ± 0.03	1.1 ± 0.02	0.9
Carotid AIX, %	4.03 ± 6.21	7.81 ± 5.21	**0.003**[h]
Femoral AIX, %	8.56 ± 10.21	6.09 ± 7.95	**0.042**[i]
ln RHI[j]	0.65 ± 0.08	0.94 ± 0.10	**0.002**

ABI, ankle brachial index; AIX, augmentation index; c-, carotid; f-, femoral; IMT, intima media thickness; PWv, pulse wave velocity; RHI, reactive hyperemia index.

[a]All continuous variables are expressed as mean ± SD.

[b]Boldfaced values indicate significant *P* values.

[c]Positive correlation between heart rate and c-IMT ($r = 0.527$, $P < 0.0001$) and f-IMT ($r = 0.539$, $P < 0.0001$).

[d]Positive correlation between fasting glucose and c-IMT ($r = 0.402$, $P = 0.034$) and f-IMT ($r = 0.398$, $P = 0.042$).

[e]Positive correlation between c-PWv and heart rate ($r = 0.410$, $P = 0.01$).

[f]Positive correlation between c-PWv and fasting glucose ($r = 0.389$, $P = 0.032$).

[g]Inverse correlation between c-IMT and f-IMT and carotid and femoral diameters ($r = –0.41$, $P = 0.033$ and $r = –0.40$, $P = 0.02$, respectively).

[h]After correction for heart rate, AIXr, $P = 0.003$.

[i]After correction for heart rate, AIXr, $P = 0.03$.

[j]Positive correlations between ln RHI values and carotid and femoral wall thickness/diameter ratio ($r = 0.38$, $P = 0.02$ and $r = 0.40$, $P = 0.03$, respectively).

in vascular resistance at the muscular level occurs during walking and running activities. Moreover, the increased leg muscle mass due to training can further relate to the decrease in vascular compliance at the femoral district of athletes.

Repeated efforts of the lower limb muscles associated with hemodynamic strain on the femoral vessel wall can result in excessive stress on the femoral wall, alter the elastic elements, and lead to their mechanical and structural fatigue.[22] Strenuous activity, in particular marathon running,[36] is associated with an increased inflammatory burden that can worsen arterial stiffness.[11,20,23,27]

Aortic stiffness is an independent marker of coronary and peripheral atherosclerosis and a strong predictor of CV events and all-cause mortality in different populations.[18] Femoral compliance is strictly related to aortic stiffness,[20,33] and the decrease in femoral compliance found in our soccer players might contribute to explain the increased CV mortality reported in some athlete populations.[20]

Lower PAT values discovered in our athletes could reflect a systemic negative effect of sport activity on endothelial function, be related to the impairment of femoral vessel function, and contribute to structural arterial remodeling.[9] We cannot rule out that the reduction in PAT values found in our athletes was almost in part because of the fact that the measurements were obtained during the sporting season. Dedicated studies are needed to evaluate whether PAT values increase in the resting period.

Our findings seem to confirm different patterns of early morphologic (IMT) and functional (PWv and AIX) markers of vascular damage in the detection and quantification of early atherosclerotic damage of the arterial wall in different vascular districts in athletes.

CONCLUSION

Elite soccer participation resulted in beneficial effects on c-IMT thickness, femoral intima media thickness, and carotid pulse wave velocity, but also was associated with worsened femoral stiffness values and systemic endothelial function.

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