Atherosclerosis 224 (2012) 118–122

Contents lists available at SciVerse ScienceDirect

Atherosclerosis

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

Increased popliteal circumferential wall tension induced by orthostatic body posture is associated with local atherosclerotic plaques

Tiago Gemignani [a], Renata C. Azevedo [b], Celina M. Higa [b], Otávio R. Coelho [a], José R. Matos-Souza [a], Wilson Nadruz Jr. [a,*]

[a] Department of Internal Medicine, School of Medical Sciences, State University of Campinas, Cidade Universitária "Zeferino Vaz", 13081-970 Campinas, São Paulo, Brazil
[b] Department of Medical Psychology and Psychiatry, School of Medical Sciences, State University of Campinas, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 13 April 2012
Received in revised form
2 June 2012
Accepted 29 June 2012
Available online 13 July 2012

Keywords:
Peripheral artery disease
Body posture
Circumferential wall tension
Popliteal artery
Gender

ABSTRACT

Objective: Lower limb arteries are exposed to higher hemodynamic burden in erectile posture. This study evaluated the effects of body posture on popliteal, carotid and brachial circumferential wall tension (CWT) and investigated the relationship between local CWT and atherosclerotic plaques in subjects with cardiovascular risk factors.
Methods: Two hundred and three subjects (118 women and 85 men) with cardiovascular risk factors (smoking, hypertension or diabetes mellitus) underwent clinical and laboratory analysis and had their blood pressure measured in the arm and calf in supine and orthostatic positions. Arteries were evaluated by ultrasound analysis, while CWT was calculated according to Laplace's law.
Results: Among the enrolled participants, 47%, 29% and none presented popliteal, carotid and brachial plaques, respectively. Carotid CWT measurements were not associated with local plaques after adjustment for potential confounders. Conversely, general linear model and logistic regression analyses adjusted for potential confounders demonstrated that peak orthostatic CWT was the only local hemodynamic parameter showing significant relationship with popliteal plaques in the whole sample. In gender-specific analyses, although positively correlated with popliteal plaques in both genders, local peak orthostatic CWT exhibited an independent association with popliteal plaques after adjustment for potential confounders only in women.
Conclusion: Popliteal CWT measured in orthostatic posture, rather than in supine position, is associated with popliteal atherosclerotic plaques, particularly in women. These findings suggest that erectile posture might play a role in the atherogenesis of leg arteries by modifying local hemodynamic forces and that there may be gender differences in this regard.

1. Introduction

Atherosclerosis is a systemic and inflammatory disease, caused or favored by systemic risk factors, that localizes in particular regions of the arterial tree, through interaction with local predisposing factors [1,2]. Among the local factors, hemodynamic forces generated by blood pressure are of greatest importance, given their ability to stimulate inflammatory response and remodeling of vascular cells [1,3,4]. Circumferential wall tension (CWT) is a hemodynamic force that leads to an extensional (dilating) effect on the vessel and has been directly related to atherosclerotic burden in human beings [5–7], supporting the notion that evaluation of this hemodynamic parameter might be useful to predict local development of atherosclerosis.

Peripheral artery disease is a manifestation of atherosclerosis and shares similar systemic risk factors with stroke and coronary heart disease [8]. Nevertheless, it typically occurs in arteries of the lower limbs [9], indicating that local stimuli play a major role in this process. Leg arteries are known to be exposed to greater hemodynamic stress than arm arteries, particularly in orthostatic posture [10,11], which might provide a potential explanation whereby atherosclerosis preferentially develops in these vessels. In agreement with this assumption, recent data from our group demonstrated that orthostatic CWT was a stronger hemodynamic predictor of popliteal intima-media thickness (IMT) than supine CWT in normotensive subjects without cardiovascular risk factors [11]. Nevertheless evaluation of IMT is an approach unable to discriminate between artery wall thickening caused by tunica

* Corresponding author. Tel./fax: +55 19 3521 7836.
E-mail address: wilnj@fcm.unicamp.br (W. Nadruz).

0021-9150/© 2012 Elsevier Ireland Ltd. Open access under the Elsevier OA license.
http://dx.doi.org/10.1016/j.atherosclerosis.2012.06.069

media hypertrophy and that caused by a properly defined atherosclerotic process [12]. Atherosclerotic plaques are instead recognized to be a manifestation of atherosclerotic disease [13]. Therefore, the present study evaluated the influence of supine and orthostatic position on CWT measurements of popliteal, carotid and brachial arteries and determined whether these hemodynamic parameters were related to respective atherosclerotic plaques in a sample of subjects with cardiovascular risk factors for atherosclerosis.

2. Methods

2.1. Study participants

Two hundred and three subjects (118 women and 85 men) followed in outpatient clinics of a university hospital were included in the study from September 2008 to January 2011. Inclusion criteria were the presence of at least one of the following risk factors for peripheral artery disease: 1) current smoking; 2) hypertension (blood pressure $\geq$ 140/90 mmHg or use of antihypertensive medications) or 3) diabetes mellitus (fasting blood glucose $\geq$ 126 mg/dL or use of hypoglycemic medications). Exclusion criteria were age under 18 years, previous stroke and supine calf/brachial systolic blood pressure ratio $<$0.90 or $>$1.20 [14]. The study was approved by the Ethics Committee of the State University of Campinas and written consent was obtained from all participants.

2.2. Clinical data

Height and weight were measured by routine methods. Body mass index was calculated as body weight divided by height squared (kg/m^2). Fasting blood total cholesterol, low-density-lipoprotein-cholesterol, high-density-lipoprotein-cholesterol, triglycerides and glucose were measured using standard laboratory techniques [15]. Women with reported amenorrhea for more than 12 months, except for pregnancy, were identified as postmenopausal.

2.3. Blood pressure measurements

Blood pressure was measured by the same physician using validated digital oscillometric devices (HEM-705CP; Omron Healthcare, Kyoto, Japan) with appropriate cuff sizes [11]. Two readings were averaged and if they differed by more than 5 mmHg, one additional measurement was performed and then averaged. Initially, blood pressure was concomitantly measured in the right arm with one device and in the right calf with another device with the subject lying in supine position for 10 min. Then blood pressure was concomitantly measured in the same limbs after the patient remained in upright position for 10 min. In order to abolish the influence of muscle contraction on calf blood pressure measured in orthostatic position, the subject was asked to support the body weight on the contralateral leg during blood pressure measurement. Mean blood pressure was obtained as (systolic blood pressure + 2 $\times$ diastolic blood pressure)/3.

2.4. Vascular analysis

Carotid and popliteal arteries were evaluated by the same physician with a Vivid 3 Pro apparatus (General Electric, Milwaukee, WI) equipped with a 10-MHz linear-array transducer as previously described [11,16]. The exams were performed with the subjects in supine and orthostatic position after blood pressure measurement. Measurements of IMT were done at the following levels: 1) right common carotid artery: 2 cm proximal to the carotid bifurcation, 2) right brachial artery: 2 cm above the elbow, and 3) right popliteal artery: 1 cm distal to the emergence of the geniculate artery. All IMT measurements were made using an automatic border recognizer (Vivid 3 Pro IMT software analyzer) on still images obtained during the sonographic scanning and were never taken at the level of a discrete plaque. End-diastolic and peak-systolic internal diameters were obtained by continuous tracing of the intimal–luminal interface of the near and far walls of the studied arteries in 3 cycles and averaged. Atherosclerotic plaques were defined as the presence of wall thickening $\geq$1.5 mm [17,18].

Peak and mean CWT were calculated according to Laplace's law (3, 4): peak CWT (dyne/cm) = systolic blood pressure $\times$ peak-systolic internal diameter/2; mean CWT (dyne/cm) = mean blood pressure $\times$ end-diastolic internal diameter/2. Brachial blood pressure was used to calculate brachial and carotid CWT while popliteal blood pressure was used to calculate popliteal CWT.

To test the reproducibility of measurements, they were repeated weekly for 2 weeks in 20 subjects. The variation coefficients averaged 2% and 3% for peak-systolic internal diameter and end-diastolic internal diameter; 5% for systolic blood pressure and 5% for diastolic blood pressure; 4% for peak CWT and 3% for mean CWT; 4% for carotid IMT, 3% for popliteal IMT and 3% for brachial IMT; 1% for carotid atherosclerotic plaques and 2% for popliteal atherosclerotic plaques.

2.5. Statistical analysis

Continuous parametric and non-parametric variables are presented as mean $\pm$ standard error and median (25–75th percentile), respectively. The Kolmogorov–Smirnov test was used to test for normal distribution of the variables. Differences in continuous parametric variables were evaluated by unpaired *t*-test and one-way ANOVA followed by the Tukey test for pairwise comparisons. Differences between continuous non-parametric variables were evaluated by Mann–Whitney test. χ^2 was used to compare categorical variables. Bivariate correlation analysis between atherosclerotic plaques and local CWT measurements were carried out using the Spearman's method. General linear models were used to evaluate the relationship between carotid/popliteal plaques and local CWT and blood pressure measurements adjusted for potential confounding factors. Logistic regression analysis was used to evaluate the independent predictors of popliteal plaques. The median was used as the cut-off point of continuous independent variables included in logistic regression models. A *p*-value of less than 0.05 was considered significant.

3. Results

Table 1 summarizes the clinical features of studied subjects in the whole sample and according to gender. No differences in the clinical features were detected between the genders. Vascular and hemodynamic characteristics in the whole sample and according to gender are shown in Table 2 and Supplementary Table 1, respectively. Popliteal arteries displayed higher IMT and prevalence of atherosclerotic plaques, but lower luminal diameter compared to carotid arteries. Brachial arteries presented no plaques and exhibited lower IMT and luminal diameter than the other studied arteries. Changing from supine to standing was associated with increased peak CWT in carotid and popliteal arteries and with higher mean CWT only in popliteal vessels (Table 2). In addition, similar vascular and hemodynamic features were observed in both genders, except for higher carotid, popliteal and brachial diameters and CWT measurements in men (Supplementary Table 1).