Original Article

Postural Changes May Influence Popliteal Atherosclerosis by Modifying Local Circumferential Wall Tension

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Atherosclerosis of peripheral arteries typically affects vessels of the lower limbs, suggesting that local hemodynamic stimuli play a role in this process. Our study evaluated the effects of body postural changes on carotid and popliteal blood pressure, circumferential wall tension (CWT) and arterial strain, and investigated the relationship between such hemodynamic parameters and intima-media thickness (IMT) of these arteries. One hundred seventeen nondiabetic, nonhypertensive, nonsmoker subjects (48 men and 69 women) were enrolled and had their blood pressure measured in the arm and calf in supine and orthostatic positions. Echo-doppler analysis evaluated the common carotid and popliteal arteries after blood pressure measurements, while CWT was calculated according to Laplace's law. The results showed that changing from supine to orthostatic posture increased blood pressure and CWT in popliteal but not in carotid arteries. Partial correlation analysis adjusted for age and body mass index revealed no major relationship between IMT of the studied vessels and local blood pressure or arterial strain. Conversely, supine and orthostatic CWT exhibited comparable correlation coefficients with carotid IMT, while orthostatic CWT displayed a stronger relationship with popliteal IMT than with supine CWT. These results were confirmed by multiple linear regression analysis that included age, sex, body mass index, lipid fractions and glucose as independent variables. Overall, our results indicate that orthostatic CWT is a stronger hemodynamic predictor of popliteal IMT than supine CWT, suggesting that erectile posture may be a potential risk factor for popliteal atherosclerosis because it increases the local hemodynamic burden. (*Hypertens Res* 2008; 31: 2059–2064)

***Key Words*: atherosclerosis, blood pressure, body posture, circumferential wall tension, intima-media thickness**

Introduction

Atherosclerosis is a systemic disease that is caused or accelerated by systemic risk factors. It often localizes in particular regions of the arterial tree, as a consequence of local predisposing factors (*1*). Among the predisposing factors, hemodynamic forces generated by blood pressure are of the utmost importance (*1*, *2*). Circumferential wall tension (CWT) is a hemodynamic force that leads to an extensional (dilating) effect on the vessel and has been shown to influence vascular structure (*3*, *4*). In addition, several lines of evidence have demonstrated a direct relationship between CWT and carotid intima-media thickness (IMT) in human beings (*5*, *6*), supporting the notion that evaluation of this hemodynamic parameter might be a useful approach in predicting local development of atherosclerosis.

Peripheral artery disease is a manifestation of atheroscle-

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rotic burden that shares similar systemic risk factors with stroke and coronary heart disease (*7*). Nevertheless, it typically occurs in arteries of the lower limbs (*8*), indicating that local stimuli play a major role in this process. In accordance with this assumption, previous reports have shown that leg arteries are exposed to greater hemodynamic burden in human beings, including higher pulse pressure (*9*) and increased hydrostatic pressure in the orthostatic position (*10*), which might explain why atherosclerosis preferentially develops in such vessels. However, although some reports have hypothesized that erectile posture might be a risk factor for arterial remodeling in the legs (*11*, *12*), it remains unknown the role of hemodynamic forces on the atherogenesis of these limbs. To date, researchers have also not yet uncovered the impact of body postural changes in this regard. Accordingly, our study reported herein aimed to evaluate the influence of supine and orthostatic position on blood pressure, CWT and arterial strain measurements of carotid and popliteal arteries to determine whether these hemodynamic parameters correlate with IMT of these vessels.

Methods

One hundred seventeen healthy subjects, recruited from June 2006 to January 2008, were enrolled in the study. The participants were nonsmokers, nondiabetics (fasting blood glucose <126 mg/dL), nonhypertensive (blood pressure <140/90 mmHg), and with normal low-density–lipoprotein cholesterol and triglyceride levels according to the National Cholesterol Education Program ATP III (*13*). None of the patients was taking any medication. The study was approved by the Ethics Committee of the State University of Campinas, and written consent was obtained from all participants.

Blood pressure was measured by the same investigator (T.G.) using validated digital oscillometric devices (Omron HEM-705CP, Omron Healthcare, Kyoto, Japan) with appropriate cuff sizes. 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 and right calf with the subject lying in the supine position for 10 min. Then, blood pressure was concomitantly measured in the same arm and calf after the patient remained in an upright position for 10 min. In order to eliminate the influence of muscle contraction on calf blood pressure measured in the orthostatic position, the subject was asked to support his or her body weight on the contralateral leg during blood pressure measurement. Mean blood pressure was obtained using the formula (systolic blood pressure + 2 × diastolic blood pressure)/3, and pulse pressure was calculated as the difference between systolic and diastolic blood pressure.

Height and weight were measured by routine methods. Body mass index was calculated as body weight (kg) divided by height (m) 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.

Table 1. Clinical Features of Studied Subjects

Variable	
Male sex, *n* (%)	48 (41)
Age, years	32.7±1.1
Height, m	1.67±0.01
Weight, kg	69.4±1.3
Body mass index, kg/m^2	24.6±0.4
Total cholesterol, mg/dL	183.5±1.9
Low-density–lipoprotein cholesterol, mg/dL	107.3±1.6
High-density–lipoprotein cholesterol, mg/dL	53.2±0.8
Triglycerides, mg/dL	138.0±3.1
Glucose, mg/dL	85.3±0.4

n=117.

Carotid and popliteal arteries were evaluated by the same investigator (T.G.) with a Vivid 3 Pro (General Electric, Milwaukee, USA) apparatus equipped with a 10-MHz linear-array transducer as previously described (*14*). The exams were performed with the subjects in supine and orthostatic positions after blood pressure measurement. The right common carotid artery IMT was measured in the far wall 1 cm proximal to the bulb and the right popliteal artery IMT was measured in the far wall 1 cm distal to the emergence of the genyculate artery. The IMT was obtained during the diastolic phase from five contiguous sites at 1-mm intervals for each vessel, and the average value of the five measurements was used for analyses. All measurements were made using an automatic border recognizer (Vivid 3 Pro IMT software analyzer) on still images obtained during sonographic scanning and were never acquired at the location of a discrete plaque. End-diastolic and peak-systolic internal diameters were obtained using continuous tracing of the intimal-luminal interface of the near and far walls of the common carotid and popliteal artery in three cycles and averaged.

Peak and mean CWT as well as peak and mean tensile stress were calculated according to Laplace's law (*5*, *6*):

$$\text{Peak CWT (dyn/cm)} = \text{systolic blood pressure} \times \text{peak-systolic internal diameter}/2.$$

$$\text{Mean CWT (dyn/cm)} = \text{mean blood pressure} \times ((\text{systolic internal diameter} + 2 \times \text{diastolic internal diameter})/3)/2.$$

$$\text{Peak tensile stress (dyn/cm}^2\text{)} = \text{peak CWT/IMT}.$$

$$\text{Mean tensile stress (dyn/cm}^2\text{)} = \text{mean CWT/IMT}.$$

Arterial strain in the circumferential direction of the carotid and popliteal arteries was calculated using the formula ([peak-systolic internal diameter] − [end-diastolic internal diameter])/end-diastolic internal diameter (%) (*6*).

To test the reproducibility of measurements, they were

Table 2. Vascular and Hemodynamic Features of Studied Subjects

Variable	Carotid supine	Carotid orthostatic	Popliteal supine	Popliteal orthostatic
Intima-media thickness, mm	0.55±0.01	—	0.76±0.01*	—
Systolic internal diameter, mm	6.4±0.1	6.6±0.1	5.8±0.1*,†	5.6±0.1*,†
Diastolic internal diameter, mm	5.8±0.1	6.0±0.1	5.2±0.1*,†	5.0±0.1*,†
Systolic blood pressure, mmHg	124.5±1.0	127.1±1.0	131.7±1.2*	186.8±2.0*,†,‡
Diastolic blood pressure, mmHg	77.9±0.7	80.2±0.6	75.9±0.7†	106.9±1.3*,†,‡
Mean arterial pressure, mmHg	93.4±0.7	95.8±0.7	94.5±0.7	133.5±1.4*,†,‡
Pulse pressure, mmHg	46.6±0.8	46.9±0.8	55.8±1.2*,†	80.0±1.6*,†,‡
Peak CWT, 10^4 dyn/cm	5.4±0.1	5.6±0.1	5.1±0.1†	7.0±0.1*,†,‡
Mean CWT, 10^4 dyn/cm	3.8±0.1	3.9±0.1	3.4±0.1†	4.7±0.1*,†,‡
Peak tensile stress, 10^4 dyn/cm^2	100.0±1.8	104.4±1.8	67.4±1.1*,†	92.1±1.5*,†,‡
Mean tensile stress, 10^4 dyn/cm^2	70.2±1.2	73.2±1.2	45.3±0.7*,†	61.7±1.1*,†,‡
Strain (%)	10.7±0.3	10.4±0.3	10.6±0.4	11.0±0.4

CWT, circumferential wall tension. *$p<0.05$ in comparison with carotid supine; †$p<0.05$ in comparison with carotid orthostatic; ‡$p<0.05$ in comparison with popliteal supine.

repeated weekly for 4 weeks in 10 subjects. The variation coefficients averaged 1% and 2% for peak-systolic internal diameter and end-diastolic internal diameter; 6% for systolic blood pressure and 5% for diastolic blood pressure; 2% for peak CWT and 1% for mean CWT; 3% for carotid IMT and 2% for popliteal IMT.

Descriptive statistical results are given as mean±SEM. Differences between carotid and popliteal IMT were assessed using an unpaired *t*-test, and differences in hemodynamic and other vascular parameters were evaluated by one-way ANOVA followed by the Tukey test for pairwise comparisons. Pearson's or Spearman's methods were used to assess univariate correlations between clinical features and carotid or popliteal IMT. Partial correlation analysis controlled for potential confounders was performed between hemodynamic forces and IMT. Standard and stepwise multiple linear regression analyses were used to evaluate the independent predictors of carotid and popliteal IMT, respectively. A *p*-value of less than 0.05 was considered significant.

Results

Table 1 summarizes the clinical features of the subjects in our study, and vascular and hemodynamic characteristics are shown in Table 2. Popliteal arteries displayed increased average IMT but exhibited a lower luminal diameter in comparison with carotid arteries. Carotid CWT values acquired in either supine or orthostatic positions were statistically similar, whereas popliteal peak and mean orthostatic CWT were markedly higher in comparison with popliteal supine CWT measurements. Conversely, peak and mean tensile stress of popliteal arteries were significantly lower than those of carotid arteries measured in the same postures.

Univariate correlation analysis between popliteal or carotid IMT and clinical features of the studied subjects were evaluated with the aim of identifying potential confounding variables. Carotid IMT was found to be correlated with age ($r=0.27$; $p<0.01$), whereas popliteal IMT was correlated with both age ($r=0.35$; $p<0.001$) and body mass index ($r=0.19$; $p<0.05$). We then performed a partial correlation analysis between local hemodynamic forces and IMT that controlled for these potential confounders. Mean CWT measured in both orthostatic and supine positions exhibited the highest correlation coefficients with carotid IMT, whereas peak orthostatic CWT was the hemodynamic parameter that displayed the strongest correlation with popliteal IMT, followed by peak supine CWT (Table 3). On the other hand, further partial correlation analyses showed no significant relationship between carotid/popliteal IMT and local blood pressure or arterial strain measurements (data not shown).

Table 3. Partial Correlation Analyses between Local Circumferential Wall Tension and Intima-Media Thickness

Circumferential wall tension	Carotid IMT (adjusted for age)	Popliteal IMT (adjusted for age and BMI)
Peak supine	0.17	0.25†
Peak orthostatic	0.22*	0.29‡
Mean supine	0.26†	0.22*
Mean orthostatic	0.27†	0.20*

IMT, intima-media thickness; BMI, body mass index. *$p<0.05$; †$p<0.01$; ‡$p<0.001$.

In order to determine whether hemodynamic parameters were independent predictors of carotid IMT, we conducted standard multiple regression analyses including age, body mass index, low-density–lipoprotein cholesterol, high-density–lipoprotein cholesterol, triglycerides and glucose as independent variables (Table 4). Given the significant collinearity between mean orthostatic and mean supine CWT ($r=0.93$), these hemodynamic parameters did not have addi-

Table 4. Multiple Regression Analysis for Carotid Intima-Media Thickness

	Carotid IMT (Model 1) r^2=0.18	Carotid IMT (Model 2) r^2=0.18
Male sex	0.124±0.095	0.134±0.095
Age	0.294±0.107*	0.304±0.106*
Body mass index	−0.084±0.103	−0.100±0.105
LDL-cholesterol	0.085±0.117	0.092±0.117
HDL-cholesterol	0.021±0.094	0.013±0.094
Triglycerides	−0.096±0.112	−0.117±0.112
Glucose	−0.186±0.108	−0.187±0.108
Mean orthostatic CWT	0.255±0.096*	—
Mean supine CWT	—	0.250±0.095*

LDL, low-density–lipoprotein; HDL, high-density–lipoprotein; CWT, circumferential wall tension; IMT, intima-media thickness. *$p<0.01$.

Table 5. Stepwise Regression Analysis for Popliteal Intima-Media Thickness

Step	Variable	r^2 change	F ratio	p
1	Peak orthostatic CWT	0.14	17.8	<0.0001
2	Age	0.08	10.8	0.001

Peak supine CWT, orthostatic systolic blood pressure, gender, body mass index, low-density–lipoprotein cholesterol, high-density–lipoprotein cholesterol and glycemia did not significantly improve the regression. CWT, circumferential wall tension.

tive effects. Mean orthostatic CWT and mean supine CWT were shown to be strongly associated with carotid IMT under two different statistical analyses that yielded similar variability prediction parameters (r^2=0.18). Conversely, stepwise regression analysis revealed that peak orthostatic CWT and age were the only significant predictors of popliteal IMT in a model that also included as independent variables peak supine CWT, orthostatic systolic blood pressure, gender, body mass index, low-density–lipoprotein cholesterol, high-density–lipoprotein cholesterol and glycemia (Table 5).

Discussion

Hemodynamic forces acting on the arterial wall have been shown to contribute to the development of atherosclerosis as local factors (*1–3*). Our study evaluated a healthy population with low cardiovascular risk and found that: 1) changing from supine to orthostatic posture increased CWT in popliteal but not in carotid arteries; 2) mean CWT measured in either supine or orthostatic positions exhibited a similar relationship with carotid IMT; 3) peak orthostatic CWT, rather than peak supine CWT, was the major hemodynamic predictor of popliteal IMT. Overall, these data extend to lower limb arteries the notion that CWT is a predictor of local vascular IMT (*5*, *6*) and further suggest that this relationship may be modulated by changes in body posture.

Atherosclerosis of peripheral arteries typically affects vessels of the lower limbs (*8*). Although the reason for this predilection is poorly understood, it is possible that the greater hemodynamic burden imposed on leg arteries plays a role. For instance, pulse pressure is consistently higher in leg arteries than in vessels closer to the heart (*9*), whereas blood pressure values increase in leg arteries in the erectile position as a consequence of higher local hydrostatic pressure (*10*) and activation of the venous-arteriolar reflex (*15*). Our study aimed to determine which hemodynamic components were related to popliteal atherosclerosis. In this regard, pulse pressure was found to be higher in popliteal than in carotid arteries but displayed no significant relationship with popliteal IMT. On the other hand, we confirmed that systolic, diastolic and mean blood pressure as well as peak and mean CWT markedly increased in popliteal arteries when subjects switched from supine to orthostatic posture. Interestingly, local orthostatic CWT, but not supine CWT, emerged as the best hemodynamic predictor of popliteal IMT. In general, our findings indicate that IMT growth in leg arteries is sensitive to CWT changes induced by postural alterations, thus providing a potential pathophysiological mechanism by which to explain how atherosclerosis develops in these vessels.

The results of our study also suggested that carotid and popliteal arteries display distinct hemodynamic and structural responses to variation in body posture. In contrast to popliteal arteries, carotid CWT measured in either supine or orthostatic postures was statistically similar and displayed comparable relationships with carotid IMT. These findings support the notion that changes in body posture exert no major effect on carotid hemodynamic burden and therefore do not impact local IMT growth. Moreover, carotid and popliteal arteries also seemed to present distinct responses to hemodynamic forces *per se*. For example, mean CWT was the best predictor of carotid IMT, and peak CWT was the major hemodynamic determinant of popliteal IMT. On the other hand, tensile stress of popliteal arteries was significantly lower than that of carotid arteries measured in the same postures. The reasons for such discrepancies are not apparent. Nevertheless, the explanation may be partly related to the structural properties of these vessels. Common carotid arteries are central elastic vessels, while popliteal arteries are considered more muscular (*16*, *17*). Thus, it is possible that differences in elastic fiber content as well as on the extent of smooth muscle layers may influence the vascular response to hemodynamic stimuli. However, this hypothesis seems to be challenged by recent evidence demonstrating that popliteal arteries are actually unusual muscular arteries that share similar mechanical properties with central elastic vessels, such as the aorta and common carotid arteries (*18*).

Our study found that values of peak and mean tensile stresses in the carotid arteries were ~100 and ~70×10^4

dyn/cm^2, respectively. We note that these values were higher than those reported by Carallo *et al*. (*5*), who found peak and mean tensile stress of 73 and 51×10^4 dyn/cm^2 in carotid arteries of healthy subjects. Even though the explanations for such divergences are not apparent, it is possible that ethnic differences between the studied samples as well as examiner variation played a role in this regard. Furthermore, our enrolled subjects were younger (32.7 *vs*. 46.0 years) and therefore displayed lower carotid IMT (0.55 *vs*. 0.67 mm), which could also help explain the higher values of tensile stress.

Mechanical stretch is a recognized stimulus for the development of a pro-atherogenic phenotype in vascular cells. Most of this knowledge relies on data from *in vitro* studies that investigated the effect of expansion of endothelial and vascular smooth muscle cells cultured on an elastic membrane mounted in a stretch device (*2*, *19*). Clinically, CWT obtained by Laplace's law has been used as the stretch stimulus *in vivo* (*5*, *6*). Nevertheless, it is important to acknowledge that CWT and circumferential deformation might be distinct mechanical forces *in vivo*. In this regard, Dobrin showed that medial thickening occurred in response to circumferential deformation but not to CWT in a vein-graft model, in which he discriminated tension and deformation by using a band to narrow the carotid artery proximal to the vein graft (*20*). This finding suggests that the effect of CWT and strain may be different *in vivo*. In our study, we found an association between CWT and IMT but not between arterial strain and IMT, a result that is in accordance with other sources (*6*) and further agrees with previous data from *ex vivo* studies demonstrating that the arterial intimal layer increases in order to normalize local CWT (*4*).

Some methodological aspects of our study deserve further comment. Blood pressure values used to calculate CWT in popliteal arteries were measured in the calf, which differed from earlier reports where popliteal CWT was calculated using blood pressure measurements from the arms (*21*, *22*). Given that blood pressure values vary along the arterial tree and particularly in the legs (*9*), we believe that our approach ensured a more accurate popliteal hemodynamic assessment. Conversely, blood pressure values used to calculate CWT in carotid arteries were recorded at the brachial artery. Although this procedure has been extensively used in studies evaluating carotid hemodynamics (*5*, *6*, *23*), there may be limitations associated with this approach. For instance, we cannot overlook the fact that we may have overestimated the carotid systolic wall tension in the supine posture, especially in younger, tall subjects (*24*). In addition, it can be argued that brachial blood pressure does not reflect changes in carotid blood pressure following postural adjustment. Indeed, we found no significant variation in brachial blood pressure values when we switched the subjects in our study from a supine to orthostatic position. Noticeably, these findings are in agreement with data from other sources that demonstrated that carotid pulse pressure did not change in response to postural variation (*25*). Although slight differences in the absolute values cannot be excluded, these results suggest that there might be a strong correlation between brachial and carotid blood pressure in response to postural stress.

It is known that IMT measurement does not allow for differentiation of the two components of the arterial wall (*i.e.*, intima and media) (*26*). Thus, in our study, it was impossible to discriminate between wall thickening caused by tunica media hypertrophy and that caused by a properly defined atherosclerotic process. Nevertheless, despite this limitation, several trials have provided strong evidence that IMT is a good indicator of atherosclerotic burden. In this regard, both carotid and popliteal IMT have been directly associated with a higher rate of clinically manifested cardiovascular disease and with an increased incidence of atherosclerotic risk factors (*27–29*).

In conclusion, our study demonstrated that changing from supine to orthostatic posture increased CWT in popliteal arteries and revealed that orthostatic CWT was a better hemodynamic predictor of popliteal IMT than was supine CWT. These findings point toward erectile posture as a risk factor for IMT growth in leg arteries. Nevertheless, further studies are necessary to evaluate the role of body posture as a predictor of peripheral artery disease.

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