Effects of posture on shear rates in human brachial and superficial femoral arteries

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Newcomer SC, Sauder CL, Kuipers NT, Laughlin MH, Ray CA. Effects of posture on shear rates in human brachial and superficial femoral arteries. Am J Physiol Heart Circ Physiol 294: H1833–H1839, 2008. First published February 1, 2008; doi:10.1152/ajpheart.01108.2007.—Shear rate is significantly lower in the superficial femoral compared with the brachial artery in the supine posture. The relative shear rates in these arteries of subjects in the upright posture (seated and/or standing) are unknown. The purpose of this investigation was to test the hypothesis that upright posture (seated and/or standing) would produce greater shear rates in the superficial femoral compared with the brachial artery. To test this hypothesis, Doppler ultrasound was used to measure mean blood velocity (MBV) and diameter in the brachial and superficial femoral arteries of 21 healthy subjects after being in the supine, seated, and standing postures for 10 min. MBV was significantly higher in the brachial compared with the superficial femoral artery during upright postures. Superficial femoral artery diameter was significantly larger than brachial artery diameter. However, posture had no significant effect on either brachial or superficial femoral artery diameter. The calculated shear rate was significantly greater in the brachial (73 ± 5, 91 ± 11, and 97 ± 13 s−1) compared with the superficial femoral (53 ± 4, 39 ± 77, and 44 ± 5 s−1) artery in the supine, seated, and standing postures, respectively. Contrary to our hypothesis, our current findings indicate that mean shear rate is lower in the superficial femoral compared with the brachial artery in the supine, seated, and standing postures. These findings of lower shear rates in the superficial femoral artery may be one mechanism for the higher propensity for atherosclerosis in the arteries of the leg than of the arm.

atherosclerosis; conduit artery diameter; leg and arm vasculature; lesion formation

The vasculature of the lower extremities is highly susceptible to atherosclerotic lesion formation in contrast with that of the upper extremities, which seem protected against the deleterious effects of atherosclerosis (16, 21, 27, 30). Stress, a frictional force exerted by blood moving across endothelial cells, is a potential mechanism that may contribute to limb differences in atherosclerosis through the modification of proteins associated with atherosclerosis (19, 39). Consistent with this hypothesis, Wu et al. (37) reported that shear rates (SRs) in the superficial femoral artery were significantly lower than those of the brachial artery of supine subjects. Based on these observations, these authors noted that wall SRs in the vasculatures of the upper and lower extremities reflected the differences in propensity for atherosclerosis (17, 37). Since this proposal of Wu et al. (37) is based on brachial and superficial femoral artery SRs measured only in the supine position, this conclusion should be considered cautiously, because the average American spends only one-third of the day in the supine position (10, 17). The remaining two-thirds of the day are spent in either the seated or standing postures. Resting conditions contribute to the majority of this time spent in the upright posture since the average American spends only 1 h a day walking or running (38). Therefore, measurements of limb vasculature SRs in these postures during rest are critical for a complete understanding of the potential role of shear stress on the heterogeneous distribution of atherosclerosis in the limb vasculatures (10, 17).

There are at least three mechanisms whereby posture may differentially impact limb vascular shear stress in the brachial and femoral arteries. First, upright posture unloads the baroreceptors, causing a similar increase in arm and leg muscle sympathetic nerve activity (MSNA) (4, 13) but a greater increase in total peripheral resistance in the leg compared with the arm vasculature (13). Higher total peripheral resistances in the legs compared with the arms, during upright posture, may suggest a greater reduction in the arterial diameter in the leg vasculature. It is unknown whether changes in the diameter of the resistance arteries, which occur with upright posture, are associated with changes in conduit artery diameter. If leg conduit artery diameter changes with posture, this would directly impact SR in the leg vasculature. A second possible mechanism is the effect that upright posture has on arterial blood pressure in the dependent limb, which may contribute to increases in SR in the leg vasculature during upright posture. It is well established that the gravitational force of the Earth produces an elevation in leg blood pressure during upright posture that does not occur in arm vasculature due to its proximity to the heart (20, 28). This elevation in leg blood pressure during upright posture could impact SR by altering conduit artery diameter through myogenic mechanisms as proposed by Imadojemu et al. (13). Third, upright posture even when standing at rest engages the skeletal muscle in the lower extremities, which may also impact leg conduit artery SR through an increase in blood flow to the active muscle.

The purpose of this investigation was to determine the effect of posture on conduit artery diameter and SR in the brachial and superficial femoral arteries in an attempt to elucidate potential mechanisms underlying limb differences in atherosclerosis. Contrary to what has been previously reported in the supine posture (37), we hypothesized that an upright posture
subjects (seated and/or standing) would produce greater SRs in the superficial femoral compared with the brachial artery. To test this hypothesis, we calculated SR from measurements of brachial and superficial femoral artery mean blood velocity (MBV) and diameter during supine, seated, and standing postures.

METHODS

Subjects

Studies were performed on 21 normally active healthy young men (n = 10) and women (n = 11). The average age of the subjects was 26 ± 1 yr. Health status was evaluated through a questionnaire and a physical examination. All subjects were normotensive (<140/90 mmHg), nonsmokers, not currently taking any medication, and nonobese (body mass index, <30). Subject characteristics are reported in Table 1. Before participation, each subject was verbally informed of the potential risks and discomforts associated with the study and signed a written informed consent form, and the study was approved by the Institutional Review Board of the Milton S. Hershey Medical Center.

Experimental Protocol

On the day of the study, each subject reported in a postabsorptive state and abstained from caffeine and exercise. Upon arrival, subjects were instrumented for blood pressure using a finometer (Finapres Medical Systems, Amsterdam, The Netherlands) and heart rate (ECG) measurements. At the completion of instrumentation, subjects were asked to rest quietly for 10 min in the supine, seated, or standing postures. After 10 min, blood velocities were recorded simultaneously by two separate investigators for 60 s in the brachial and superficial femoral arteries of the nondominant limbs. This was followed by a 15-s recording of brachial and superficial femoral artery diameter. The brachial and superficial femoral arteries were chosen based on their relatively similar anatomical location within each limb, tortuosity (2, 35), lack of branching points (2), and a greater propensity for atherosclerotic lesion formation in the superficial femoral compared with the brachial arteries (2, 21, 27, 35). These procedures were replicated in all three postures for each subject. The order of the three postures was randomized in an attempt to alleviate any ordering effects. During the upright trials, subjects were tilted to a fully weight-bearing 80°. This tilt angle was utilized in an attempt to decrease measurement errors associated with postural sway during free standing. Consistent arterial measurements between postures were ensured through anatomical landmarks and marking the transducer location on the skin with a permanent marker. The artery measured by each investigator was the same within the subject but randomized between subjects in an attempt to alleviate an investigator effect.

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Average</th>
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</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>21</td>
</tr>
<tr>
<td>Age, yr</td>
<td>26±1</td>
</tr>
<tr>
<td>Height, cm</td>
<td>171±2</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>69±3</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>61±3</td>
</tr>
<tr>
<td>Supine systolic blood pressure, mmHg</td>
<td>115±3</td>
</tr>
<tr>
<td>Supine diastolic blood pressure, mmHg</td>
<td>64±3</td>
</tr>
<tr>
<td>Supine mean blood pressure, mmHg</td>
<td>80±2</td>
</tr>
</tbody>
</table>

Values are means ± SE.

Measurements

Maximum (peak antegrade), minimum (peak retrograde), and mean blood velocities (BVs) and diameters were measured in the brachial and superficial femoral arteries of the nondominant limb with Doppler ultrasound (HD1 5000; ATL Ultrasound, Bothell, WA). A 12.5-MHz transducer was positioned between the antecubital fossa and anterior axillary fold for brachial measurements and ~8 to 10 cm distal to the bifurcation of the common femoral artery for superficial femoral artery measurements. BV was measured at an insonation angle of ≈60°. The sample volume was maximized in an attempt to minimize overestimations of BV (26). Arterial diameter was measured using a longitudinal view of the artery. The measurements of arterial diameter were performed during diastole and systole (determined by ECG) by measuring the distance between the near and far wall intima. The diameter over the cardiac cycle was calculated as diameter = 0.33 (systolic diameter) + 0.66 (diastolic diameter) (26).

Blood viscosity was not measured because blood samples from the brachial and the superficial femoral artery were not collected in the current investigation. Therefore, SR (in s⁻¹) was used as a surrogate measure for shear stress (25). SR was calculated as SR = 4 × BV/Dia, where BV is in centimeters per second, and arterial diameter over the cardiac cycle (Dia) is in centimeters. Oscillatory shear index (OSI) is defined as the cyclic departure of the wall shear stress vector from its predominant axial alignment and was calculated as previously described (37): OSI = [min shear rate]/[max shear rate] + [min shear rate]/.

Blood flow and conductance were also calculated in addition to SR. Blood flow in the brachial and superficial femoral arteries was calculated as Q = πr² × MBV × 60, where Q (in ml/min) is blood flow, r (in cm) is radius, MBV is in centimeters per second, and 60 is the conversion factor for minutes. Conductance in the brachial and superficial femoral arteries was calculated as Conductance = Q/MAP, where mean arterial pressure (MAP) is in millimeters of mercury. MAP at the level of the heart/brachial artery was measured using a finometer (Finapres Medical Systems).

Data Analysis

Continuous measurements of heart rate and blood pressure were collected online with MacLab 16sp (ADI Instruments, New Castle, Australia) and analyzed offline using Chart 5.4.2 software (ADI Instruments). The analysis of heart rate and blood pressure was analyzed over the same time duration as MBV and diameter measurements. Repeated-measures ANOVAs (SuperANOVA version 1.11) were applied to compare the brachial and superficial femoral artery hemodynamic responses with supine, seated, and standing postures. Comparisons between postures were performed using a Bonferroni test. Statistical significance was set at P < 0.05. All data are presented as means ± SE.

RESULTS

Effects of Posture on Heart Rate and Blood Pressure

Heart rate was significantly elevated in the upright (88 ± 4) compared with supine (61 ± 3) and seated (65 ± 3 beats/min) postures (Fig. 1A). However, arm MAP was not significantly different between the supine (80 ± 2), seated (87 ± 4), and upright (85 ± 3 mmHg) postures (Fig. 1B).

Effects of Posture on Peripheral Hemodynamic Variables Within Vasculatures

Brachial artery. Posture had no significant effect on brachial artery blood flow (Fig. 2A) or conductance (Fig. 2B). In addition, there were no significant effects of posture on minimum BV (Fig. 3A), MBV (Fig. 3C), and diameter (Fig. 3D) in
the brachial artery. However, maximum BV in the brachial artery was significantly reduced in the standing compared with the seated and supine postures (Fig. 3B). Posture had no significant effect on either minimum (Fig. 4A) or mean SRs (Fig. 4C) in the brachial artery. In contrast, standing significantly reduced brachial artery maximum SR compared with seated and supine postures (Fig. 4B) and increased OSI compared with sitting postures (Fig. 4D).

Superficial femoral artery. Posture had no significant effect on superficial femoral artery blood flow (Fig. 2A) or conductance (Fig. 2B). There was also no significant effect of posture on superficial femoral artery MBV (Fig. 3C) and diameter (Fig. 3D), whereas upright posture (sitting and standing) significantly increased minimum and decreased maximum BVs (Fig. 3, A and B) and SRs (Fig. 4, A and B). These significant alterations in superficial femoral artery minimum and maximum SRs during upright posture did not significantly alter either mean SR (Fig. 4C) or OSI (Fig. 4D).

Effects of Posture on Peripheral Hemodynamic Variables Between Vasculatures

Blood flow, conductance (Fig. 2A and B), and diameters (Fig. 3D) were significantly greater in the superficial femoral compared with the brachial artery across all postures. In contrast, minimum BV in the superficial femoral artery was significantly lower compared with that in the brachial artery in all three postures (Fig. 3A). Maximum BV was significantly greater in the superficial femoral artery in the supine posture and lower in the standing posture compared with that in the brachial artery (Fig. 3B), whereas MBV in the superficial femoral artery was significantly lower than that in the brachial artery in both upright postures (Fig. 3C).

Mean and maximum SRs were significantly lower in the superficial femoral compared with the brachial arteries across all three postures (Fig. 4, B and C). Lower minimum SRs were also calculated in the superficial femoral compared with the brachial arteries in the supine and seated postures (Fig. 4A). These differences in minimum and maximum SRs between brachial and superficial femoral arteries produced a significantly higher OSI in the superficial femoral compared with the brachial arteries independent of posture (Fig. 4D).

DISCUSSION

The objective of this investigation was to test the hypothesis that upright posture (seated and/or standing) would produce greater SRs in the superficial femoral compared with the brachial artery. Contrary to our hypothesis, our current findings indicate that minimum, maximum, and mean SRs are lower in the superficial femoral compared with the brachial artery in the supine, seated, and standing postures. These findings of reduced SRs in the superficial femoral artery are the product of
interactions between the differences in diameter and BVs of the respective vascular beds.

It has been previously reported that mean SRs in the brachial arteries are \( \sim 50\% \) higher than those measured in the superficial femoral arteries of supine subjects using MRI (37). Our current data using Doppler ultrasound demonstrated \( \sim 40\% \) greater SRs in the brachial compared with superficial femoral arteries in the supine posture, confirming these previous results. Interestingly, results from hemodynamic modeling of the brachial and common femoral arteries suggest greater SRs in the common femoral compared with the brachial arteries (31). These discrepancies in the results of Stroev et al. (31) may be indicative of differences between common and superficial femoral artery hemodynamics, limitations associated with hemodynamic modeling versus direct measurements and/or that the data generated for modeling calculations were derived from a single subject. Limb differences in SR do not appear to be isolated to just brachial and superficial artery comparisons since lower mean SRs have also been reported in the popliteal compared with the brachial artery under resting supine conditions (23, 24).

The current study has extended these measurements of brachial and superficial femoral artery SRs in the supine position across the seated and standing postures. It is important to describe brachial and superficial femoral artery SRs in the seated and upright postures because the average American spends two-thirds of his or her day in these postures (10, 17). We hypothesized that increases in MSNA associated with upright posture would decrease superficial femoral artery diameter to a greater extent than brachial diameter. This hypothesis was based on previous findings of greater vascular resistance in the leg compared with the arm during 40° head-up tilt (13). It is well established that changes in vascular resistance during 40° head-up tilt are mediated through arterioles, but little is known about the effects of upright posture on femoral artery diameter. The ability of adrenoreceptor stimulation to alter femoral artery diameter has been revealed in a recent report demonstrating that intra-arterial infusions of phenylephrine (\( \alpha_1 \)-adrenoreceptor agonist) produced a 25% reduction in femoral artery diameter (29). Present results demonstrate that no significant changes occur to either brachial or superficial femoral artery diameter after 10 min of sitting or standing. This finding suggests that any increases in MSNA that may be associated with 10 min of upright posture (4, 13) have a limited to no effect on the diameter of the brachial and superficial femoral arteries. These findings are consistent with pharmacological data suggesting that increased norepinephrine release through intra-arterial infusions of tyramine had no significant effect on femoral artery diameter but decreased leg vascular conductance (29).

We also hypothesized that the MBV, the second component of the SR calculation, would increase in the superficial femoral artery due to the greater metabolic demands of the postural muscles in the legs. However, upright posture was not associated with an increase in MBV to the superficial femoral artery. These findings are consistent with previous data that reported no significant change in MBV in the femoral artery during a
modest weight-bearing posture, a 40° head-up tilt (13). The relative lack of an increase in MBV and blood flow to the leg during upright posture is also consistent with data suggesting only a minimal increase (13 ± 8%) in energy expenditure when going from the supine to standing posture (18) and could be accounted for by an increase in oxygen extraction rather than delivery. Interestingly, data derived from nonweight-bearing head-up tilt suggest that blood flow is reduced in the femoral arteries during upright posture (14, 15). Future studies will be needed to determine the mechanisms underlying the differences in leg blood flow during weight-bearing versus nonweight-bearing upright posture.

Interestingly, OSI has previously been reported to be lower in the brachial compared with the superficial femoral arteries of supine humans (37). Our current results both confirm and extend these previous findings by demonstrating that OSI is lower in the brachial compared with the superficial femoral arteries in the supine, seated, and standing postures during rest. These differences in the OSI are indicative of significantly lower minimum and maximum SRs in the superficial femoral artery under resting conditions.

Clinical Relevance

The current findings of lower SRs and higher OSIs in the superficial femoral compared with the brachial artery in all postures examined may add insight to why limb-specific differences in atherosclerotic lesion formation exist in humans. It is well known that the vasculatures of the leg, including the superficial femoral artery, have a higher incidence of atherosclerosis than the arm vasculatures (16, 21, 27, 30). It has been hypothesized that the hydrostatic pressure column created by gravity during upright posture may contribute to this heterogeneous distribution of atherosclerosis between the limbs (7, 20, 22, 34). However, lower SRs and vascular tortuosity have also been proposed to contribute to limb differences in atherosclerosis (35, 37). The current findings of chronically higher SRs in the brachial compared with the superficial femoral artery across all postures during resting conditions are consistent with the hypothesis that chronically lower SRs contribute to increased atherosclerosis in the leg vasculature. Similar increases in the magnitude of shear stress have been reported to increase endothelial nitric oxide synthase (eNOS) protein expression in cultured endothelial cells (33). In vivo data, obtained from mouse aortas at rest, also demonstrate that regions with low mean wall shear stress (i.e., inner curvature of the aortic arch) exhibit a significantly elevated expression of vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) compared with that of regions exposed to a mean wall shear stress (i.e., lateral walls of the ascending aorta), which is double of that in the inner curvature of the aortic arch (32). Based on these data, we speculate that lower resting SRs in the superficial femoral artery produce a proatherogenic environment through the heterogeneous expression of eNOS, VCAM-1, and ICAM-1. Our findings of higher OSIs in the superficial femoral compared with the brachial arteries are also of interest relative to in vitro data demonstrating that oscillatory shear initiates a proatherogenic environment through the downregulation of...
the average American spends only 1 h a day being physically active (39). We recognize that the oscillatory shear patterns applied to cultured endothelial cells are unlike those currently reported in the brachial and superficial femoral arteries and that this limits the ability to draw direct inferences from these in vitro studies to our current in vivo results. Nonetheless, these in vitro studies represent the extent of our current knowledge concerning the effect of oscillatory shear on markers of atherosclerosis. The combination of relatively lower SRs and high OSIs in the superficial femoral artery, coupled with elevated blood pressure in the leg vasculature during seated and standing postures, may contribute to a proatherogenic environment in the lower extremities compared with the upper extremities (1, 39).

Limitations

A limitation of the current study is the fact that by design, SR was measured under resting conditions. It is well documented that increases in physical activity are protective against lower extremity peripheral arterial disease (9). Increased SRs in the brachial and superficial femoral arteries during exercise may contribute to these protective effects. Although the overall effects of exercise are important, recent data demonstrate that the average American spends only 1 h a day being physically active (38). Therefore, resting SRs represent the hemodynamic environment in which the brachial and the superficial femoral arteries are chronically exposed. Our results make it tempting to speculate that resting SRs also significantly influence the vascular health of the brachial and superficial femoral arteries perhaps through similar mechanisms. Evidence for the significance of resting SR on vascular health can be derived from research investigating the effects of chronic inactivity on lower extremity vascular function, which demonstrates that 52 days of either bed rest or spinal cord injury is associated with preserved endothelial function in the superficial femoral artery (3, 6). This preservation of lower extremity endothelial function, in the face of chronic lower extremity inactivity, can potentially be explained by the dramatic increases in superficial femoral artery SRs that are associated with the inward remodeling and subsequent diameter changes that occur to the superficial femoral artery in these conditions (3, 6). Therefore, indirect evidence exists to support the notion that both resting and exercise-induced SRs contribute to the peripheral vasculatures susceptibility to atherosclerosis.

Another potential limitation of this study is the fact that the brachial artery is smaller than the superficial femoral artery in most people. This could be of significance because the greater shear stress in the brachial artery could simply be the result of the difference in the size of the arteries. However, SR is determined by the interaction of artery diameter and BV in the artery. Comparisons have been made of brachial artery SRs and SRs in other sized arteries of the lower extremities. Thus a comparison in the relationship between artery diameter and SR in the brachial versus common femoral artery (36) and brachial versus popliteal artery (23) indicates that the difference in resting SR between the brachial artery and arteries of the lower extremities is not simply due to the difference in artery size.

An additional potential limitation of this investigation is that hemodynamic measurements were performed in sitting (straight leg) and standing (80°) postures, which are less likely to be utilized throughout the course of a day compared with bent leg sitting and 90° standing. To address this potential limitation, additional experiments were performed in five subjects to evaluate the effects of straight versus bent leg sitting and 80° versus 90° standing on superficial femoral artery SRs. The results of these experiments suggest that superficial femoral artery mean SR is significantly reduced in bent leg sitting compared with straight leg sitting (straight, 52.9 ± 15.0; and bent, 36.0 ± 12.3 s⁻¹), whereas there is no significant effect of 80° versus 90° standing on superficial femoral artery mean SR (80°, 35.3 ± 3.3; and 90°, 37.2 ± 3.5 s⁻¹). The results of this pilot study confirm the results presented in Figs. 1 and 2, demonstrating that lower SRs are observed in the superficial femoral versus the brachial artery in the upright postures.

In conclusion, the results of this investigation indicate that mean SRs in the brachial and superficial femoral artery are unaffected by posture. Furthermore, the results of this investigation indicate that SRs of the superficial femoral artery are chronically lower than those of the brachial artery under resting conditions across all postures.

GRANTS

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