Effects of elastic compression stockings on wall shear stress in deep and superficial veins of the calf

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Downie SP, Raynor SM, Firmin DN, Wood NB, Thom SA, Hughes AD, Parker KH, Wolfe JH, Xu XY. Effects of elastic compression stockings on wall shear stress in deep and superficial veins of the calf. Am J Physiol Heart Circ Physiol 294: H2112–H2120, 2008. First published March 7, 2008; doi:10.1152/ajpheart.01302.2007.—The purpose of this study was to estimate wall shear stress (WSS) in individual vessels of the venous circulation of the calf and quantify the effects of elastic compression based on change of vessel geometry and velocity waveform. The great saphenous vein and either a peroneal or posterior tibial vein have been imaged in four healthy subjects using magnetic resonance imaging, with and without the presence of a grade 1 medical stocking. Flow through image-based reconstructed geometries was numerically simulated for both a range of steady flow rates and ultrasound-derived transient velocity waveforms, scaled to give a standardized time averaged flow rate. For steady flow, the stocking produced an average percentage increase in mean WSS of ~100% in the great saphenous vein across a range of 0.125–1.25 ml/s. The percentage increase in the peroneal/posterior tibial veins varied from 490 to 650% across a range of 0.5–5 ml/s. In addition, application of the stocking eliminated periods of very low or zero flow from the transient waveforms. The average minimum value of WSS in all vessels without the stocking was <0.1 Pa. With the stocking, this was increased to 0.7 Pa in the great saphenous and 0.9 Pa in the peroneal/posterior tibial veins. The pathophysiological effects of these changes are discussed. In conclusion, the flight stocking was effective in raising venous WSS levels in prone subjects, and this effect was much more pronounced in the deep vessels. The stocking also tended to prevent cessation of flow during periods of increased downstream pressure produced by respiration.

calf veins; deep vein thrombosis; hemodynamics; numerical simulation

DEEP VEIN THROMBOSIS (DVT) is a common complication in hospitalized patients. It is often asymptomatic and resolves without intervention; however, it can lead to local injury to the vein wall and valves and is an important initiator of chronic venous insufficiency. Another more serious outcome is pulmonary thromboembolism, which is implicated in 10% of all hospital deaths (3).

Multiple forms of prophylaxis are available for DVT. Medicinal anticoagulants, such as low-molecular-weight heparin, are often used in conjunction with mechanical methods such as graduated compression stockings and intermittent pneumatic compression of the calf or foot. The mechanical methods are generally thought to act by the reduction of venous stasis, but their biomechanical effects and influence on the underlying vascular biology have not been fully elucidated. A more complete understanding would potentially help clinicians to use them more effectively and manufacturers to improve their design.

The etiology of DVT is generally explained within the framework of the three thrombogenic factors advanced by Virchow (31): stasis, hypercoagulability, and injury to the vessel wall. Injury to the vessel wall is an important factor in the arterial model of thrombosis, causing adhesion and activation of platelets and exposing them to subendothelial tissue factor. This chain of events is supported by the observation of a platelet-rich region at the attachment point of the thrombus, with red blood cell aggregates only visible at the boundaries (16).

In contrast, Sevitt (24) has shown venous thrombi to consist of a red blood cell-rich aggregate at the attachment point with platelet-rich zones only visible at the boundaries (24), suggesting a different mechanism of formation. In an autopsy study of 41 limbs, Sevitt (24) also failed to find obvious signs of vein wall injury in 49 out of 50 thrombi. It appears that stasis and hypercoagulability play the dominant role in venous thrombosis, but the source of tissue factor, in the absence of endothelial injury, remains a matter of some debate. Current evidence points to circulating microvesicles as the most likely source (16).

The lack of platelets at the heart of the thrombus also begs the question as to how the coagulation process is activated. Tracy (30) has shown that activated endothelial cells provide a surface for the assembly of the coagulation complex, which is equally efficient as activated platelets. However, there are further questions as to the stimulus for endothelial activation and the mechanism by which antithrombotic agents such as tissue factor pathway inhibitor and thrombomodulin are sufficiently suppressed to allow the coagulation cascade to proceed. A possible stimulus for endothelial activation is low hemodynamic wall shear stress (WSS) resulting from stasis. It is now well known that endothelial cells are highly responsive to WSS. Regions of low or oscillating WSS have been heavily linked with formation of atherosclerotic plaques, and it is generally theorized that high levels of unidirectional and pulsatile WSS promotes an anti-inflammatory phenotype (18). Much research has been devoted to the response of arterial endothelial cells to WSS, but similar mechanisms undoubtedly...
exist in venous endothelial cells. Eriksson et al. (10) have demonstrated an inflammatory response in large veins to tumor necrosis factor-α, which is stronger than in their corresponding arteries.

There is also a strong case for hypoxia as the stimulus for endothelial activation, but, since low WSS and hypoxia are both integral features of stasis, it is difficult to separate the two effects in vivo. Evidence for an important role for low WSS in the formation of venous thrombi comes from the study of Goel and Diamond (12), where adhesion of red blood cells to platelets, neutrophils, and polymerized fibrin was observed at WSS levels below 0.1 Pa but not above.

High WSS has also been shown to stimulate the production of various antithrombotic and fibrinolytic agents, including nitric oxide (5), prostacyclin (11), and tissue plasminogen activator (5, 7, 8). Optimization studies of intermittent compression devices have focused on WSS and flow rate enhancement as important parameters. Early development of these devices focused on the generation of high peak flows, with the assumption that this would aid the mechanical break-up of thrombi. As evidence mounted that the beneficial effects may lie instead in the endothelial response to induced flows, the objectives of optimization became less clear.

Much work has been done on this topic by Kamm and coworkers (4, 13, 14, 21, 23). Using the theoretical framework for flow in collapsible tubes developed by Shapiro and Kamm (15, 25), numerical and physical simulations were performed that shed light on the distributed hemodynamic effects of differing modes of compression. An important aspect of modeling flow in collapsible tubes is an accurate description of the pressure/volume relationship, known as the tube law. In a further study by the same group, a two-dimensional finite element model of a transverse section of calf was used to simulate vessel wall deformation under various circumferential pressure distributions (4). However, the model was highly idealized, and, while the overall approach has provided important general insights into the underlying hemodynamics, without validation of the simulated tube law against in vivo data it is not clear that the results are physiologically realistic.

The application of theoretical modeling to the design of graduated compression stockings has been less thoroughly pursued. The work of Sigel et al. (26) has provided an empirical basis for current designs, but their main criteria was the increase in velocities at the exit of the compressed region. This is a good general indicator of the stocking’s ability to reduce stasis but gives no information on the hemodynamic conditions in the upstream vessels. This may be important, since some beneficial effects of compression could be localized to only those regions directly exposed to antithrombotic hemodynamic conditions (4).

This study introduces the combined use of magnetic resonance imaging (MRI), pulsed Doppler ultrasound, and computational fluid dynamics (CFD) to estimate the effect of static compression on WSS in the major deep and superficial vessels of the calf. Image-based computational modeling has become an established tool in the study of arterial hemodynamics and offers the potential to provide data that cannot be measured by experiment alone, in particular, WSS distribution in realistic vessel geometries.

METHODS

Overview

Four healthy male subjects were studied, aged 24–32 yr without any history of venous disease. The study complied with the Declaration of Helsinki and was approved by the local Research Ethics Committee. All participating subjects gave written, informed consent. Vessel geometry was acquired from MRI to provide a realistic basis for numerical simulations of flow within the vessels using CFD.

It was not possible to simultaneously measure flow rates in the reconstructed vessels; therefore, the main focus of the simulations was to quantify the effect of the change in vessel geometry produced by the stocking, with time-averaged flow rate assumed to remain unchanged. Steady flow simulations were performed for a range of flow rates in each reconstructed vessel to calculate the resulting WSS distributions and percentage increase in spatial mean WSS resulting from compression.

The effect of the stocking on the velocity waveform was also examined. Pulsed Doppler ultrasound data were acquired from the same subjects on a separate occasion, with the conditions mirroring those under which the MRI data were acquired as closely as possible. Difficulties arising from the presence of the stocking and the depth of tissue surrounding the deep vessels made it impractical to make direct measurements of flow in the reconstructed vessels. Flow velocity was therefore measured downstream, above the level of the stocking, in the popliteal and great saphenous veins. Representative waveforms were then calculated for each vessel before and after compression and used to perform transient flow simulations.

Vessel Geometry

Image acquisition. The MRI were acquired from a Siemens Avanto 1.5T scanner, using a three-dimensional (3D) true fast imaging with steady procession sequence, as described previously (9). The images were acquired with and without the presence of a grade 1 medical stocking. Subjects were imaged in the prone position to avoid compressing the muscles of the calf against the table. After entering the bore, a period of 5 min was allowed to pass before the proximal third of the subject’s right calf was imaged. The subject was then partially removed from the bore to allow application of the stocking while remaining prone. A period of 10 min was then allowed to pass before imaging the same section of calf.

Image processing. The venous system of the calf is separated into the superficial system (external to the muscular fascia) and the deep system (internal to the muscular fascia). The major veins of each system are the great saphenous vein (superficial) and the peroneal and posterior tibial veins (deep), which are generally four in number and run alongside the peroneal and posterior tibial arteries before joining to form the popliteal vein.

In each subject, a segment of the great saphenous vein and one other deep vessel (a peroneal vessel in three subjects and a posterior tibial vessel in one) were selected for analysis based on the clarity of the MRI and the presence of a reasonable length of vessel free from bifurcations. All segments studied here were 4 cm long apart from the great saphenous vein in subject 4 where only a 3.2-cm segment met the necessary criteria. All segments were located in the proximal third of the calf, below the level of the popliteal venous confluence.

The vessel cross sections were segmented manually using in-house software written in MATLAB (version 7.0.1; The Mathwork), and these were then used to reconstruct the full 3D geometry. A smoothing function was applied in MATLAB during geometry reconstruction to reduce imaging artifacts and small manual errors from the segmentation process to facilitate mesh generation. The curve-fitting algorithm “scsps” was employed for this purpose; first to smooth the cross sections (smoothing parameter = 0.9) and then to smooth along the axial direction (smoothing parameter = 0.7).
Velocity Waveforms

Ultrasound data acquisition. The subjects were asked to lie in the prone position and perform diaphragm-dominated respiration, as described by Miller et al. (19), regulated by an analog metronome with a period of ~7 s (one full respiration cycle). Once regulated respiration had commenced, measurements were made after a 5-min interval.

Because of the depth of tissue surrounding the peroneal and posterior tibial vessels and the presence of the stocking in half the measurements, it was not possible to measure flow directly at the site of the vessels segmented from the MRI. Flow velocities were therefore recorded by pulsed Doppler ultrasound in the popliteal and great saphenous veins, just above the level of the stocking, using a Philips ATL 5000 Doppler ultrasound machine equipped with a 6-MHz linear array transducer. Digital data were transferred to a personal computer and analyzed using commercial software (HDI Lab version 1.19; ATL-Philips, Bothell, WA).

Doppler waveforms were recorded over a period of 50 s in both vessels, initially without the stocking. The insonation angle was 60°, and the entire vessel cross section was included in the sample volume, as has been shown previously to be optimal for venous flow measurements (20). Following this, an identical stocking to that used in the MRI scans was applied to the subject’s right leg, and measurements were repeated after a 10-min interval.

Signal processing. The peak velocity waveform was extracted using HDI Lab and used to calculate a representative waveform by segmenting the entire waveform into individual respiration cycles and taking an ensemble average of six cycles. Because the period was not accurately controlled, in each case the segment length was optimized to give the minimum root mean square value when the representative waveform was subtracted from the original waveform. Any remaining high-frequency noise was then removed using a low-pass filter with a cut off frequency of 0.5 Hz.

The presence of valves (if competent) in the venous system will cause flow to come abruptly to a halt rather than become reversed. Such discontinuities cannot be approximated well with low-frequency harmonics, and mathematical artifacts introduced to the waveform during filtering may falsely imply that reverse flow is taking place. Reverse flow was not observed in any of the measurements, so, for the duration of such artifacts, flow was set to zero. A sample comparison of computed representative waveforms against the raw data output from HDI Lab is shown in Fig. 1.

CFD analysis. Simulations were performed using the commercial CFD code CFX10 (ANSYS). Blood was modeled as a Newtonian fluid with density 1.060 kg/m and viscosity 3.5 mPa/s. The Reynolds number fell within the laminar regime in all simulations, so no turbulence model was used. Spatial discretization was performed via an hybrid first- and/or second-order scheme, whereas temporal discretization was performed via an implicit second-order backward Euler scheme.

Steady flow simulations were run for a range of flow rates between 0.5 and 5 ml/s in the case of the deep vessels and 0.125–1.25 ml/s in the case of the great saphenous vein. Because the inlet geometries were arbitrary, with irregular cross sections, velocity profiles could not be determined directly. To provide a consistent inlet boundary condition, the model inlet was therefore extended upstream by 10 hydraulic diameters, and the velocity profile was allowed to develop from an initial flat profile.

Grid dependency tests were run for one subject. Refining the mesh from 74,000 to 540,000 nodes produced a change of <5 mPa in WSS. A mesh size of 140,000 nodes was determined to provide a discretization error of <1.5 mPa relative to the WSS calculated from the 540,000 node mesh and was used throughout. Transient simulations were performed for three respiration cycles, and the results were taken from the final cycle. Uniform mean flow rates of 1 ml/s in the deep veins and 0.25 ml/s in the great saphenous vein were used for each subject. A study of the time step dependency revealed that increasing the time steps from 100 to 200 steps/cycle gave a root mean square difference of <0.1 mPa in WSS, and so 100 steps were used throughout.

RESULTS

Geometry Reconstruction

The volume of all reconstructed vessels was reduced by the stocking, but the effect was more pronounced in the deep veins than in the great saphenous vein. On average, the deep veins were reduced in volume by 59%, whereas the great saphenous vein was reduced by 40%. Elastic recoil in the vessel wall, implied by the reduction in vessel circumferences, was observed in all vessels. Bending of the vessel wall was more evident in the deep veins than in the great saphenous veins, with their cross sections taking on an approximately ellipsoid shape (further details are available from Ref. 9). Sample geometrical reconstructions from a peroneal vein and the great saphenous vein of subject 2 are shown in Fig. 2.

Velocity Waveforms

In the absence of the stocking during diaphragmatic breathing, velocity waveforms in all vessels showed a similar pattern to those observed by Miller et al. (19). During inspiration, flow was greatly reduced, often to below measurable levels, as the descending diaphragm increased intra-abdominal pressure (though an initial period of reversed flow was not observed during our measurements). As the expiration phase began and intra-abdominal pressure dropped, flow rapidly resumed and
continued until the next inspiration phase. With the presence of the stocking, the response was markedly different. The overall pattern of respiratory flow modulation remained, but the magnitude was much decreased. During inspiration, flow slowed somewhat but did not fully halt in any of the cases (see Fig. 3).

The effect was quantified based on the pulsatility index (PI = maximum velocity minus minimum velocity over mean velocity), which was calculated from the representative waveforms since the flow rate was not consistent from cycle to cycle. Without the stocking, the mean and SD of the PI were 1.56 ± 0.31 in the popliteal vein. With the stocking, this was reduced to 0.56 ± 0.35. A similar magnitude of effect was seen in the great saphenous vein, with a PI of 1.47 ± 0.60 reduced to 0.48 ± 0.38 upon application of the stocking.

Steady Flow Analysis

Flow simulations were performed for the great saphenous and deep veins using geometries reconstructed from MRI acquired before and after application of the stocking, for a range of physiologically relevant flow rates derived from the literature. No qualitative change in flow and WSS patterns was found with the increase in flow rate, although quantitative variations were observed. Spatial distribution of WSS in the great saphenous vein was relatively uniform, both with and without the stocking. More variation was seen in the deep veins, as illustrated in Fig. 4. Without the stocking, bulges in the vessels (possibly indicating the presence of valves) gave rise to very low values of WSS in some regions. With the stocking, WSS tended to be higher near the proximal ends of the reconstructed segments, approaching the junction of the peroneal and posterior tibial veins.

Table 1 gives a summary of spatial mean WSS values averaged among the four subjects, before and after compres-
sion, along with the corresponding Reynolds number at the segment inlets. The increase in WSS with respect to flow rate was approximately linear in the case of the great saphenous veins, giving a value of 100%. In the case of the deep veins, the percentage increase varied from 490 to 650% across the range of 0.5–5 ml/s. In both cases, a quadratic expression was required for an exact fit between WSS and flow rate.

**Transient Flow Analysis**

The transient simulations were performed using subject-specific velocity waveforms acquired before and after compression, assuming constant time-averaged flow rates (0.25 ml/s for the great saphenous vein and 1 ml/s for the deep veins). The results showed slightly higher values of time-averaged WSS but very close (within 1%) to that in the steady flow simulations at the same flow rate. Despite the reduced pulsatility of the velocity waveforms in the compressed vessels, the range of spatial mean WSS experienced by the vessel during a respiration cycle increased by ~100% in the deep veins. In the great saphenous vein, the WSS range was decreased by ~35% due to the lesser reduction in vessel volume.

Temporal variations in spatial mean WSS are shown in Fig. 5, with maximum and minimum values given in Table 2.

**DISCUSSION**

Segments of the great saphenous vein and either a peroneal or posterior tibial vein have been reconstructed from MRI in four subjects, before and after application of a grade 1 compression stocking. The increase in WSS levels produced by the change in geometry has been derived from CFD analysis for a range of steady flow rates. Two flow rates were selected and used to scale velocity waveforms measured downstream in the great saphenous and popliteal veins during diaphragmatic respiration. These data were then used in a transient CFD analysis.

The reconstructed vessel geometries demonstrated a marked difference between the deformation of the great saphenous and major deep veins. Not only was there a much greater reduction in volume in the deep veins (59% compared with 40%), but there was a greater degree of bending of the vessel wall, implied by the alteration of the cross-sectional shape under the influence of the stocking.

**Table 1. Subject-averaged values of spatial mean WSS and Reynolds number in great saphenous and deep veins**

<table>
<thead>
<tr>
<th>Flow rate, ml/s</th>
<th>0.125</th>
<th>0.25</th>
<th>0.625</th>
<th>1.25</th>
<th>0.5</th>
<th>1</th>
<th>2.5</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reu</td>
<td>15.55</td>
<td>31.09</td>
<td>77.73</td>
<td>155.45</td>
<td>34.43</td>
<td>68.87</td>
<td>172.17</td>
<td>344.33</td>
</tr>
<tr>
<td>U WSS, Pa</td>
<td>0.21</td>
<td>0.43</td>
<td>1.08</td>
<td>2.22</td>
<td>0.10</td>
<td>0.19</td>
<td>0.49</td>
<td>1.00</td>
</tr>
<tr>
<td>Rec</td>
<td>20.43</td>
<td>40.86</td>
<td>102.16</td>
<td>204.32</td>
<td>48.87</td>
<td>97.75</td>
<td>244.37</td>
<td>488.74</td>
</tr>
<tr>
<td>C WSS, Pa</td>
<td>0.44</td>
<td>0.88</td>
<td>2.22</td>
<td>4.56</td>
<td>0.57</td>
<td>1.20</td>
<td>3.33</td>
<td>7.54</td>
</tr>
</tbody>
</table>

U WSS, uncompressed spatial mean wall shear stress (WSS; without stocking); C WSS, compressed spatial mean WSS (with stocking); Reu/Rec, Reynolds number at inlet of uncompressed/compressed geometries, respectively, based on hydraulic diameter.
Because the flow rates in the reconstructed vessels at the time the MRI were acquired could not be measured directly, a range of steady flow rates was analyzed with the intention of providing data across a physiologically relevant range. The ranges of flow rates studied in the great saphenous and deep vessels were relatively wide. This was partly in recognition of the uncertainty resulting from the inability to measure this parameter during the course of this study and partly because of the high level of variability in lower limb venous flow.

No direct measurement of peroneal or posterior tibial vein flow could be found in the literature, but data exist for popliteal flow and for great saphenous flow close to the sapheno-femoral junction. Delis et al. (6) have demonstrated the strong dependence of lower limb venous flow rates on posture, making measurements from subjects in the horizontal position the most relevant to this study. Lurie et al. (17) examined 12 subjects and found an average flow rate of $3.8 \pm 0.6$ ml/s (mean $\pm$ SD) in the popliteal vein and $3.9 \pm 0.3$ ml/s in the great saphenous vein 5 cm upstream from the sapheno-femoral junction. An earlier study by the same investigators (20) did not measure popliteal flow but found an average great saphenous flow rate of 0.6 ml/s among 25 subjects, again acquired just upstream from the sapheno-femoral junction but this time in 30° reverse Trendelenburg’s position (legs down on tilted table). Delis et al. (6) found an average popliteal flow of 1.7 ml/s (estimated from figure in Ref. 6) in a study of 26 limbs from 13 healthy subjects in the horizontal position.

Given the range of popliteal flow values reported from the literature, it seems likely that, in the horizontal position, resting flow rates in the peroneal and posterior tibial veins are $1$ ml/s. From the steady flow results, this implies that normal WSS levels (without compression) in this position are $<0.2$ Pa.

Fig. 5. Transient simulation results showing time-dependent spatial mean wall shear stress in the peroneal/posterior tibial veins (left) and great saphenous veins (right) in all four subjects. The time scale has been normalized by the period of the respiration cycle.
In their study of the effect of WSS on secretion of tissue plasminogen activator, Diamond et al. (7) showed that WSS levels >0.4 Pa were required to stimulate increased secretion. Our results indicate that, under the action of the stocking, a flow rate of just 0.34 ml/s would be sufficient to generate this threshold level of WSS in the segments of deep vessel studied here. In the uncompressed vessel geometries, the same flow rate would give an average WSS level of 0.07 Pa. Without the stocking, a flow rate of <0.52 ml/s would generate WSS levels under 0.1 Pa, at which Goel and Diamond (12) observed adhesion of red blood cells. With the stocking, a flow rate of 0.52 ml/s gives a WSS value of 0.61 Pa.

It must be emphasized that, since these flow rates have not been acquired simultaneously with the imaging of the vessel geometries, the values presented should be viewed as illustrative. However, the results indicate that, for an equivalent flow rate before and after compression, the stocking was effective in raising WSS. It is particularly interesting to note the difference in response between the deep vessels and superficial vessels. WSS increased in the perforal and posterior tibial veins by an average of between 490 and 650% across the range of flow rates examined compared with just 100% in the great saphenous vein, illustrating the difference in compression of the deep and superficial veins. This assumes an unchanged mean flow rate, which may not be the case.

Studies have shown that static external compression can produce a reduction in femoral vein flow rates (22, 27). This effect will reduce the beneficial impact of the stocking on WSS and stasis in general, although from the steady flow simulations it would require a flow rate reduction of 51% in the great saphenous vein and 83% in the peroneal/posterior tibial vessels to negate the influence of the stocking on WSS entirely. The results of Sabri et al. (22) suggest that a reduction of ~10% in femoral vein flow rate could be expected for a grade 1 stocking.

The velocity waveforms obtained without the stocking showed similar behavior to that reported by Miller et al. (19). The oscillations in downstream (proximal) pressure caused by the movement of the diaphragm periodically slowed the flow velocity to very low values, often causing it to cease entirely (or at least reducing it below measurable levels). The effect of the stocking on the waveform was unexpectedly pronounced. The magnitude of the modulation was dramatically reduced, and a continuous flow toward the heart was always maintained. This effect has been previously observed by Macklon and Greer (17a), and an explanation will be suggested based on the theoretical model advanced by Takata et al. (29).

As the diaphragm descends, it tends to compress the abdominal veins. Assuming retrograde flow is prevented by the venous valves and a low resistance pathway to thoracic veins is maintained, this will tend to displace blood centrally without much change in local venous pressure in the abdomen. However, if the external pressure increases to the point where internal venous pressure is not high enough to prevent collapse of the inferior vena cava, then a high-resistance pathway to flow from the abdominal region is created. The implications of this are not straightforward, but, by consideration of mechanical equilibrium at the throat of the collapsed portion, we can assume that local venous pressure must have increased to a value close to that of the external abdominal compartment.

This increased back pressure will reduce the outflow from the upstream vessels and, if sufficiently high, will hold the upstream valves shut, preventing outflow from the leg. This causes venous pressure to rise exponentially toward an asymptotic value (32). The situation will be maintained until either the rising upstream pressure reverses the pressure gradient across the valve leaflets and reestablishes flow or the diaphragm ascends during expiration, removing the back pressure, and flow resumes with a transitory increase as the walls of the leg vessels recoil, expelling the blood volume that has accumulated during the period of increased back pressure.

The effect of the stocking may be twofold. The reduction in cross section of the veins under the stocking will increase the local vascular resistance. An accurate prediction of the effect of a change in resistance in one vessel in a flow network requires consideration of the resistance of all vessels in the network and is beyond the scope of this study. However, evidence exists in the literature to support an increase in local venous pressures.

Spiro et al. (27) have shown that the application of external pressure to the hindlimb of a dog produces a pressure increase in the femoral vein; at 15 mmHg of external pressure, an internal pressure rise of 8 mmHg was observed (27). An increase in venous pressure in the calf could explain the change in waveform since it would reduce the effect of the increase in downstream pressure produced by inspiration and could help to maintain a continuous flow.

In addition, the rate at which venous pressure rises when outflow is prevented is determined by the compliance of the system. The presence of the stocking should reduce the compliance of the vessels in the calf, since the compliance of the deep veins is dominated by the surrounding skeletal muscle and the blood will have to do more work to expand the vessel wall against compressed skeletal muscle. When the outflow from the leg decreases below the inflow from the microcirculation, pressure in the calf therefore rises faster than that in the thigh, potentially maintaining a continuous flow in the femoral network.

The main purpose of the transient analysis was to assess whether the changes in respiratory modulation of the velocity waveform induced by the stocking would alter the time-
average WSS. Time averaged transient WSS, with and without the stocking, was found to be the same as for an equivalent steady flow rate in the corresponding vessel geometry. The elimination of periods of very low or zero WSS in the presence of the stocking may be important though.

At the flow rates investigated, without the stocking WSS periodically dropped to an average value of \(<0.1\) Pa in all vessels; with the stocking, the average minimum values were 0.7 Pa in the great saphenous vein and 0.9 Pa in the peroneal/posterior tibial vessels. Not only did the stocking tend to prevent the cessation of flow, but, in the deep veins, the resulting reduction in cross-sectional area increased the range of WSS experienced during the respiratory cycle. A continuous flow would also hold the venous valves open, maintaining a constant vortical flow behind their leaflets, a frequent site of thrombus formation. The effect has only been shown here in prone subjects and may not apply with the limb in a dependent position such as seated in an airplane. However, the transient effects of static compression probably deserve greater attention.

The improvement in the methodology used here over previous studies, such as that of Sigel et al. (26), is the ability to examine hemodynamic conditions in the specific veins where thrombi are known to initiate. The main limitation is the difficulty in the measurement of flow rate in the deep veins. The depth of the surrounding skeletal muscle makes Doppler ultrasound unsuitable for this purpose, and MRI sequences for the measurement of venous flow will require some effort to develop. The degree of repeatability in venous waveforms is too low to allow a gated approach, meaning that real-time imaging would probably be required to capture transient effects.

Even with the potential to make simultaneous measurements of vessel geometry and flow, further effort will be required if the methodology presented here was to be extended to clinical studies or the optimization of stocking design. Endothelial phenotype varies throughout the cardiovascular system (1), and it is not yet clear what a healthy level of WSS in the large veins of the calf would be. It appears that very low values may promote (either actively or passively) the adhesion of red blood cells and that endothelial production of antithrombotic agents is stimulated above some threshold level, but the specific values obtained from the studies of Diamond et al. (7) and Goel and Diamond (12) may not be applicable to the vessels studied here.

Nevertheless, it is important that methodologies are developed to take advantage of developments in our understanding of the pathophysiology of venous thrombosis. In future studies, it would be desirable to improve the resolution and clarity of the MRI to allow the reconstruction of the smaller intramuscular veins of the soleus and gastrocnemius muscles, a frequent site of thrombosis (2). In the longer term, efforts should be made to include fluid structure interaction between the blood and vessel wall and eventually to include the venous valves.

The subjects used in this study were all young and healthy. A possible focus for future clinical study using this methodology would be hemodynamic differences between young and old populations. Stanton et al. (28) have reported that older subjects tend to exhibit “saccular dilatations” in the veins of the calf. This observation may be linked to the increased incidence of DVT in older populations and would make a valid target for investigation via this methodology.

In conclusion, these results indicate that, in prone subjects, grade I compression stockings are effective at increasing WSS in large deep and superficial veins in the calf, based solely on the change in vessel geometry, and the effect is more pronounced in the deep vessels. The presence of the stocking also seems to decrease the reduction in local flow velocities induced by periods of increased downstream (proximal) pressure, which acts to ensure that WSS is prevented from dropping to near zero. Both of these effects may play important roles in the overall mechanism by which compression stockings provide their clinical benefit.

REFERENCES