Fluid wall shear stress measurements in a model of the human abdominal aorta: oscillatory behavior and relationship to atherosclerosis

James E. Moore Jr.\textsuperscript{a},\textsuperscript{†}, Chengpei Xu\textsuperscript{b}, Seymour Glagov\textsuperscript{b}, Christopher K. Zarins\textsuperscript{c}, David N. Ku\textsuperscript{a}\textsuperscript{*}

\textsuperscript{a}School of Mechanical Engineering, Georgia Institute of Technology, Atlanta, GA 30332-0405, USA
\textsuperscript{b}Department of Pathology, \textsuperscript{c}Department of Surgery, The University of Chicago, Chicago, IL, USA

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Abstract

Clinically significant atherosclerosis in the human aorta is most common in the infrarenal segment. This study was initiated to test the hypothesis that flowfield properties are closely related to the localization of plaques in this segment of the arterial system. Wall shear stress was calculated from magnetic resonance velocity measurements of pulsatile flow in an anatomically accurate model of the human abdominal aorta. The wall shear stress values were compared with intimal thickening from 15 post-mortem aortas measured by quantitative morphometry of histological cross sections obtained at standard locations. Wall shear stress oscillated in direction throughout most of the infrarenal aorta, most prominently in the distal region. The time-averaged mean wall shear stress ($-1.7$ to $1.4$ dyn/cm$^2$) was lowest near the posterior wall in this region. These hemodynamic parameters coincided with the locations of maximal intimal thickening. Statistical correlation between oscillatory shear and intimal thickness yielded $r = 0.79$, $P < 0.00001$. Low mean shear stresses correlated nearly as well ($r = -0.75$, $P < 0.00005$). Comparison of our data with surface maps of Sudan Red staining and early lesions as reported by others revealed similar conclusions. In contrast, pulse and maximum shear stresses did not correlate with plaque localization as has been shown for other sites of selective involvement by atherosclerosis ($r < 0.345$). Simulated exercise conditions markedly changed the magnitude and pattern of wall shear stress in the distal abdominal aorta. These results demonstrate that in the infrarenal aorta, regions of low mean and oscillating wall shear stresses are predisposed to the development of plaque while regions of relatively high wall shear stress tend to be spared.

Keywords: Atherosclerosis; Shear stress; Aorta; Oscillatory shear; Intimal thickening; Exercise; Hemodynamics

\textsuperscript{†}Present address: Biomedical Engineering Laboratory, Swiss Federal Institute of Technology at Lausanne, Champs Courbes 1, 1024 Ecublens, Switzerland.

\textsuperscript{*}Corresponding author.
1. Introduction

Atherosclerosis is a frequent cause of morbidity and mortality. The disease tends to be focal, involving mainly the carotid bifurcation, the coronary arteries, the abdominal aorta and the arteries of the legs. The localized nature of the disease has led to the hypothesis that mechanical factors related to differences in geometry and flow patterns are involved in the selective localization of the disease.

Low wall shear stress, high wall shear stress, oscillating wall shear stress, flow separation, non-laminar blood flow patterns, and turbulence have been suggested as possible atherogenic factors. Turbulence is rare in the normal cardiovascular system and has not been found to promote atherosclerosis in animal models [1]. Fox and Hugh [2] proposed that local variations in blood flow patterns, specifically boundary layer separation, could play a role in atherogenesis. Caro et al. [3] modified this theory to state that low wall shear stress could produce an area of low mass transfer. In contrast, Fry [4] showed that wall shear stresses in excess of 400 dyn/cm² could damage the endothelial cell layer, and suggested that high wall shear stresses could cause an injury mediated process leading to the formation of a plaque. However, the maximum wall shear stress on any artery in the normal cardiovascular system would be expected to be less than 100 dyn/cm². Zarins et al. [5,6] showed that at the carotid bifurcation, regions of low flow velocity and wall shear stress in arteries are susceptible to atherosclerosis, whereas areas of high flow velocity and elevated wall shear stress appear to be relatively spared.

In subsequent studies of the carotid bifurcation, Ku et al. [7] showed that intimal thickening correlated most strongly with the inverse of the maximum wall shear stress in regions of low mean wall shear stress. Correlations with the inverse of the mean wall shear stress and the oscillatory shear index were nearly as good. Similar relationships between the reciprocal of wall shear stress and plaque localization have been demonstrated in a primate model of aortic stenosis [8]. Friedman et al. have compared intimal thickness and wall shear stress measurements in casts of the aortic bifurcation [9,10] and of the coronary arteries [11]. A negative correlation slope was noted with the mean, maximum and pulse wall shear stress. Low, pulse, and oscillating shear appear to coincide for these correlative studies [12]. The general trend of selective atherosclerosis development in areas of low and oscillating wall shear stress has been suggested for all arteries [1,13].

In the human aorta, atherosclerosis is most prominent in the infrarenal segment [14]. Studies of atherosclerosis in young subjects reveal that the lateral and posterior walls of the aorta distal to the inferior mesenteric artery (IMA) are involved with the highest frequency [15]. The present study was undertaken to quantify the hemodynamic wall shear stresses in an accurate model of the human abdominal aorta, to determine statistically which flowfield characteristics are most closely related to atherosclerotic plaque location and thickness, and to demonstrate changes in wall shear stress during exercise conditions.

2. Methods

An anatomic model of the abdominal aorta was designed, and axial velocities were measured using magnetic resonance velocimetry. The velocity data were used to estimate the wall shear stress distribution in the human abdominal aorta. The wall shear stress was then statistically compared with several morphologic measures of early atherosclerosis.

2.1. Aorta flow model

The three-dimensional geometric configuration of the abdominal aorta model was obtained from the measurements of 55 bi-planar angiograms and 10 cadaver aortas. The model included the curvature of the aorta in the lumbar region, the aortic bifurcation, and the celiac, superior mesenteric (SMA), inferior mesenteric (IMA) and the right and left renal arteries (Fig. 1a). The flow rates through each vessel were controlled with precision needle valves and based on physiologic values [16]. Flow conditions corresponding to normal resting conditions as well as to vigorous lower limb exercise were simulated. Under resting conditions,
Fig. 1. (a) Diagram of abdominal aortic model with measurement sites indicated at: A, supra renal; B, infrarenal; and C, bifurcation. (b) Flow waveforms in the model suprarenal aorta simulating resting and exercise flow conditions. (c) Definition of the shear stress indices obtained from each shear stress vs. time plot. An index of oscillations in shear direction was calculated for the axially directed wall shear stress according to the formula

\[ OSI = \frac{|A_{\text{neg}}|}{A_{\text{pos}} + |A_{\text{neg}}|} \]

where \( A_{\text{neg}} \) and \( A_{\text{pos}} \) are the areas under the shear stress versus time curve when the shear is negative and positive, respectively.
two-thirds of the blood flowing through the thoracic aorta exits through the celiac, SMA and renal arteries. For exercise conditions, the overall flow rate was increased by 300%, with only 20% of the thoracic aortic flow exiting the celiac, SMA and renal arteries. The pulsatile characteristics of flow in the abdominal aorta were modeled by reproducing the bi-phasic flow waveform present in the suprarenal aorta and the tri-phasic flow waveform found in the infrarenal aorta under resting conditions [17] (Fig. 1b). For the suprarenal thoracic aorta, the corresponding 'stroke volume' was 38 ml, and 45% of the volume flow occurred in systole. For exercise conditions, the flow waveforms were bi-phasic in the entire aorta, with forward flow throughout the cardiac cycle. The working fluid for the flow system was water with 1 uM CuSO4 as a magnetic doping agent, which required that the flow and pulse rates be scaled according to the Reynolds number and Womersley parameter [18,19]. This fluid had a kinematic viscosity of 0.01 cm²/s and a density of 1.0 g/cm³.

2.2. MRI velocimetry

MRI phase-velocity encoding was used to quantify the axial velocity profiles in the aorta model. General explanations of this method may be found in Moran [20], Firmin et al. [21], and Oshinski [22]. Additional details on the particular MRI sequence used in this study may be found in Ku et al. [23] and Moore and Ku [24]. The matrix size for each measurement, or slice, was 256 x 256 with a pixel resolution of 1 x 1 mm. The timing between measurements was set such that sixteen velocity profiles were obtained during the cardiac cycle. The images were obtained with a Philips 1.5-tesla whole body MRI scanner (Philips Medical Systems, NA, Shelton, CT), then exported to a Sun 3/260 workstation for post-processing. Measurements were taken at three anatomical locations which were noted to have strong flowfield differences seen in previous flow visualization studies [16,25]. The first measurement was located in the suprarenal aorta, 37 mm proximal to the celiac artery [24]. The second measurement was located in the infrarenal aorta, 12 mm distal to the left renal artery. The third slice location was in the aortic bifurcation, 10 mm proximal to the apex (Fig. 1a).

2.3. Wall shear stress calculation

Estimations of wall shear stresses in the abdominal aorta model were extrapolated from the pulsatile velocity field data. The wall shear rate was calculated as the spatial derivative of the velocity at the wall from the velocity profiles as a function of position around the circumference of the vessel for sixteen time points throughout the cardiac cycle. The basic procedure involved first locating the tube wall, and then calculating the radial derivative of the velocity profile as a function of time and position around the circumference. This procedure is presented in detail in Appendix 1.

Six shear stress indices were recorded around the circumference at each slice location. The mean wall shear stress was calculated by averaging the shear stress values over the cardiac cycle (Fig. 1b). Maximum and minimum wall shear stresses were identified and subtracted to give the pulse wall shear stress for each position. One method for quantifying the degree of oscillation in shear direction which was proposed by Ku et al. [7] is the Oscillatory Shear Index (OSI). An index of oscillations in shear direction was calculated for the axially directed wall shear stress according to the formula

\[ \text{OSI} = \frac{|A_{neg}|}{A_{pos} + |A_{neg}|} \]

where \(A_{neg}\) and \(A_{pos}\) are the areas under the shear stress versus time curve when the shear is negative and positive, respectively, as defined in Fig. 1c. Alternatively, another index of oscillation was studied. The fraction of time that the wall shear stress was negative in direction was calculated and is referred to as the NEG index (NEG = \(t_{neg}/T\)).

The flow in the suprarenal aorta was modelled as fully developed pulsatile flow through a straight rigid tube, allowing the experimental values of the six shear stress indices to be compared with theoretically determined wall shear stress values [26,27]. The experimental maximum and mean wall shear stresses measured by MR velocimetry were very close to the theoretically expected values with an error of 3% or less (see Fig. 2 and Table 1). Slightly more discrepancy between theory and
Fig. 2. Shear stress indices evaluated in the suprarenal aorta under resting conditions. MEAN refers to the time average wall shear stress, MAX and MIN to the maximum and minimum values, respectively, and PULSE refers to the pulse shear stress (MAX-MIN). The NEG index refers to the fraction of the cardiac cycle that the shear stress is negative and OSI in the non-dimensional oscillatory shear index, defined in the text and in Fig. 1. The horizontal axes represent the position around the 360° circumference of the vessel, with data values every 15°. The straight lines in the graphs represent the theoretical values. The average measured shear stress indices were close to the theoretical values.

2.4. Morphometry

To assess the spatial distribution of intimal thickening in human aortas, 15 aortas were obtained at autopsy from subjects who had had no clinical symptoms referable to the aorta. The subjects were men, ranging in age from 41 to 92 (mean, 55 years). Transverse sections were removed at standard locations along the axial length of each aorta and each section was indexed with regard to posterior location. The pathology samples taken approximately 2 cm proximal to the aortic bifurcation flow divider were used for correlation with the hemodynamic shear indices at the bifurcation. Histologic preparations were stained with hemotoxylin and eosin. Images of the histologic sections were projected onto a digitizing tablet. An on-line computer program was used to provide intimal area and mean intimal thickness in each of 24 equal circumferential sectors with the posterior location indexed at 0°. Results were recorded as the mean ± S.E.M. of each sector for each aorta. The data were stored in a spreadsheet for later statistical comparison with the hemodynamic data.

Since this study was intended to analyse flow-related alterations in healthy aortas, we determined the precise localization of relatively small but definite intimal thickenings. Small thickenings are usually discrete and well circumscribed, permitting accurate determination of preferential circumferential localization. With advanced atherosclerosis, intimal plaques tend to become confluent and are associated with modifications of aortic

Table 1
Comparisons of measured shear stress with theoretical shear stress indices (dyn/cm²) in the suprarenal aorta

<table>
<thead>
<tr>
<th></th>
<th>Mean shear stress</th>
<th>Maximum shear stress</th>
<th>Minimum shear stress</th>
<th>Pulse shear stress</th>
<th>NEG</th>
<th>OSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theory</td>
<td>1.30</td>
<td>8.68</td>
<td>-4.54</td>
<td>13.2</td>
<td>0.42</td>
<td>0.26</td>
</tr>
<tr>
<td>Measured</td>
<td>1.32</td>
<td>8.38</td>
<td>-4.08</td>
<td>12.5</td>
<td>0.38</td>
<td>0.26</td>
</tr>
<tr>
<td>Spatial S.D.</td>
<td>0.64</td>
<td>1.26</td>
<td>1.52</td>
<td>1.8</td>
<td>0.10</td>
<td>0.10</td>
</tr>
<tr>
<td>Percent error</td>
<td>2%</td>
<td>3%</td>
<td>10%</td>
<td>5%</td>
<td>10%</td>
<td>0%</td>
</tr>
</tbody>
</table>

NEG and OSI are non-dimensional indices.
curvature and dimensions. Therefore, selected aortas with minimal atherosclerotic disease were chosen for analysis. In these vessels, non-confluent intimal changes amenable to precise determination of circumferential localization occurred mainly in the distal abdominal aorta at and near the bifurcation, while such changes were sparse in the thoracic and proximal abdominal aortic segments. In this report, significant correlations of hemodynamic factors with the localization of intimal thickening in the distal abdominal aorta are presented. The term 'intimal thickening' rather than 'atherosclerosis' is used in the presentation of the results. Intimal thickening includes atherosclerosis as well as intimal fibrocellular hypertrophy, so-called diffuse intimal thickening or neointima formation. These changes are usually localized to the same regions and are likely to be related to the same physical forces.

The probability-of-occurrence maps for Sudan IV staining and gross appearance of raised lesions on the lumen surface of the human abdominal aorta have been demonstrated by Cornhill et al. [15] as part of the P-DAY study. Using the landmarks of the aortic bifurcation, and renal and superior mesenteric arteries on the probability-of-occurrence maps, we identified an axial location corresponding approximately to our distal abdominal aortic measurement site for wall shear stress. The probability-of-occurrence maps were digitized and the color scale converted into quintiles of probability-of-occurrence as defined by Cornhill et al. [15]. For statistical comparison, the distribution of lesions were assumed to be symmetric about the midline. Thus, probability-of-occurrence of the right half of the aorta was taken to duplicate that given for the left half. A histogram of probability-of-occurrence around the circumference of the aorta was then used as an indicator of lesion localization in the distal abdominal aorta.

Linear regression analyses were performed between the hemodynamic shear indices and the morphology data of intimal thickening. Statistical correlation coefficients were used to evaluate the statistical significance at the $P < 0.05$ level.

3. Results

3.1. Resting conditions

Shear stress was predominantly unidirectional around the circumference of the vessel in the modelled suprarenal descending aorta under simulated normal resting conditions. The spatially averaged mean wall shear stress around the circumference was 1.3 dyn/cm², with a spatial standard deviation of 0.6 dyn/cm² (Fig. 2). The average maximum, minimum and pulse wall shear stresses were $8.4 \pm 1.3$, $-4.0 \pm 1.5$, and $13.5 \pm 1.8$ dyn/cm², respectively. Wall shear stresses were negative for $38 \pm 10\%$ of the pulse cycle, and the average OSI was $0.26 \pm 0.10$. 

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**Fig. 3.** Shear stress indices evaluated in the infrarenal aorta under resting conditions. Note that the mean, maximum, minimum and pulse shear stresses are lowest at the posterior wall, and highest at the anterior wall. The NEG and OSI are highest at the posterior wall.
In the infrarenal aorta under resting conditions, the time-averaged mean wall shear stress was negative along the posterior wall in an area that extended 45° laterally to the side walls (Fig. 3). The mean shear stress reached −5.0 dyn/cm² at the posterior wall. Elsewhere around the circumference, the mean wall shear stresses were positive, being 4.3 dyn/cm² at the lateral walls. The spatial distribution of maximum and minimum wall shear stresses were similar, with the least values located at the posterior wall. The fraction of cycle during which shear stress was negative (NEG) and the OSI were greatest at the posterior wall (0.86 and 0.94, respectively). The least values for NEG and OSI were 0.18 and 0.13, respectively, located at the right lateral wall.

Shear stress measurements at the distal abdominal aorta revealed that the greatest shear stress reversal moved toward the lateral walls. The most negative mean wall shear stresses were −0.9 and −1.7 dyn/cm², located near the left and right lateral walls (Fig. 4). Mean wall shear stresses at the anterior and posterior walls were 1.4 and 0.8 dyn/cm². Maximum wall shear stress was greatest at the left and right lateral walls (10.2 and 10.4 dyn/cm²). Minimum wall shear stress reached its lowest value at the lateral walls (−11.0 and −12.2 dyn/cm²). Pulse shear stress was greatest near the

Fig. 4. Shear stress indices evaluated in the aortic bifurcation under resting conditions. In this location, the mean and minimum shear stresses are lowest at the lateral posterior walls. The maximum and pulse shear stresses, and the NEG and OSI are highest at the lateral posterior walls.
left and right lateral posterior walls (21.1 and 22.5 dyn/cm²). The NEG and OSI were greatest at the lateral walls, but lowest at the anterior and posterior walls in the distal abdominal aorta.

3.2. Exercise conditions
Under simulated exercise conditions, shear stress indices in the modelled suprarenal aorta were relatively constant around the circumference of the vessel. The mean wall shear stress remained positive about the circumference, with an average value of 2.6 ± 0.6 dyn/cm² (Fig. 5). The average values of the maximum, minimum and pulse wall shear stresses were 6.8 ± 0.8, −1.5 ± 0.9, and 8.4 ± 0.9 dyn/cm², respectively. The average NEG and OSI were 0.26 ± 0.09 and 0.08 ± 0.06, respectively.

Wall shear stress measurements in the infrarenal aorta under simulated exercise conditions revealed a marked reduction of shear stress reversal at the posterior wall compared with resting conditions. Mean wall shear stresses were all positive at this location, ranging from 5.4 dyn/cm² at the posterior wall to 10.6 dyn/cm² at the left lateral wall. Minimum wall shear stresses were positive except for a region extending from the posterior wall to 30° toward the right lateral wall (Fig. 6). The least minimum wall shear stress occurred at the posterior wall and was −1.8 dyn/cm². Shear stress was negative for a maximum of 18% of the region near the posterior wall.

Fig. 5. Shear stress indices evaluated in the suprarenal aorta under exercise conditions. The shear stresses are higher than under resting conditions, and feature less reversal in direction.

Fig. 6. Shear stress indices evaluated in the infrarenal aorta under exercise conditions. The shear stress reversal found under resting conditions was eliminated, except for a small region near the posterior wall.
cardiac cycle in this region. The OSI was 0.03 at the same location. Elsewhere around the circumference, NEG and OSI were zero.

At the aortic bifurcation, there was a slight, transient wall shear stress reversal along the posterior and lateral posterior walls under exercise conditions. Mean wall shear stresses ranged from 3.1 dyne/cm² at the posterior wall to 11.6 dyne/cm² at the anterior wall (Fig. 7). Maximum wall shear stress was least (9.6 dyne/cm²) at the right wall approximately 45° lateral from directly posterior, and greatest (20.5 dyne/cm²) at the anterior wall. Minimum wall shear stress was negative along the posterior half of the circumference. The most negative value for minimum wall shear stress was −4.8 dyne/cm² which occurred at the posterior wall. The NEG and OSI reached their greatest values of 0.35 and 0.16 at the posterior wall, but fell to zero toward the anterior wall.

3.3. Statistical comparison to atherosclerosis

Shear stress measurements reported above were compared with two data sets representing the localization of atherosclerosis in the distal abdominal aorta: intimal thickening and probability of occurrence maps of sudanophilic staining and raised lesions. Comparisons were limited to the distal abdominal aorta due to the low incidence and size of early plaques in the thoracic and proximal abdominal aorta.

The first set of data was generated by measuring intimal thickness in standard sections of abdominal aortas harvested at autopsy. Intimal thickness was greatest at the postero-lateral walls of the distal aorta, proximal to the bifurcation. The spatial variation in mean intimal thickness around the circumference is given in Fig. 8, where the maximum thickness at 180° was greater than at 0° with \( P < 0.01 \).

The distribution of intimal thickening around the circumference of the aorta (Fig. 8) was similar to the distribution of shear stress plots in Fig. 4. Linear regression of hemodynamic and morphologic data is given in Table 2. The strongest positive correlation between the intimal thickness data and the shear stress indices was with the OSI (\( r = 0.75, P < 0.00005 \)). The correlations of lesions with NEG were only slightly less significant (\( r = 0.68, P < 0.00005 \)). A negative correlation was noted with the mean wall shear stress (\( r = -0.72, P < 0.0001 \)). A slight correlation was found for the minimum wall shear stress (\( r = -0.47 \)). The direct correlations of plaque localization with the other wall shear stress indices were not statistically significant. Comparisons using the inverses of the mean, pulse and maximum wall shear stresses were also not significant.

A second set of data came from the probability of occurrence maps of sudanophilic staining and raised lesions in left axial halves of aortas from young accident victims [15]. Linear regression analysis of probability of occurrence and shear stress also demonstrated the best correlations.
using mean and oscillatory shear indices (Table 2). The regression analysis indicated that probability of occurrence of plaque location correlated strongly and positively with oscillations in shear stress direction with coefficients between 0.75 and 0.80 and $P < 0.00005$. The probability of occurrence maps and mean shear stress had a negative correlation ($r = -0.72$ to $-0.80$, $P < 0.0001$) indicating that low mean shear stresses were most associated with atherosclerosis localization.

Since the evaluation of wall shear stress involved taking the derivative of already noisy velocity data, a statistical test was performed to ensure that the correlations noted above would not be affected by the presence of measurement error. The most extreme relative error was noted in the mean shear stress, where the measured standard deviation in the suprarenal aorta was 0.6 dyn/cm$^2$. This uncertainty was applied to the mean shear stress measurements in the aortic bifurcation using the

![Graph](image)

**Fig. 8.** Atherosclerosis localization in the aortic bifurcation as a function of position around the circumference of the vessel. The distribution of the disease was found to be similar to the distributions of low mean and oscillating wall shear stress, shown in Fig. 4.

<table>
<thead>
<tr>
<th>Shear stress index</th>
<th>Intimal thickness</th>
<th>Raised lesions</th>
<th>Sudan staining</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$P$</td>
<td>$r$</td>
</tr>
<tr>
<td>OSI</td>
<td>0.788</td>
<td>$&lt; 0.00001$</td>
<td>0.748</td>
</tr>
<tr>
<td>MEAN</td>
<td>$-0.748$</td>
<td>$&lt; 0.00005$</td>
<td>$-0.724$</td>
</tr>
<tr>
<td>NEG</td>
<td>0.729</td>
<td>$&lt; 0.00001$</td>
<td>0.680</td>
</tr>
<tr>
<td>MIN</td>
<td>$-0.465$</td>
<td>$&lt; 0.05$</td>
<td>$-0.437$</td>
</tr>
<tr>
<td>MAX</td>
<td>0.084</td>
<td>NS</td>
<td>0.000</td>
</tr>
<tr>
<td>PULSE</td>
<td>0.300</td>
<td>NS</td>
<td>0.245</td>
</tr>
<tr>
<td>1/MEAN</td>
<td>$-0.202$</td>
<td>NS</td>
<td>$-0.095$</td>
</tr>
<tr>
<td>1/PULSE</td>
<td>$-0.341$</td>
<td>NS</td>
<td>$-0.243$</td>
</tr>
<tr>
<td>1/MAX</td>
<td>$-0.055$</td>
<td>NS</td>
<td>0.000</td>
</tr>
<tr>
<td>OSI $\leq 0.5$</td>
<td>0.141</td>
<td>NS</td>
<td>$-0.184$</td>
</tr>
</tbody>
</table>

NS, not significant ($P > 0.05$)

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Table 2

Correlation coefficients and level of significance for comparisons between wall shear stress indices and indicators of early atherosclerotic disease.
Additional shear stress versus position curves were generated by randomly choosing points around the measured values at each position. These randomly chosen values were constrained so that their mean would equal the measured value, and their standard deviation would be 0.6 dyn/cm². This method was used to generate 500 new shear stress versus position plots which were all correlated with the intimal thickness plot. The slope of the best fit regression line was always negative, confirming that the experimental uncertainty did not affect the correlations noted above ($P = 0$).

4. Discussion

This study reveals a strong, significant correlation between oscillations in the direction of, and low mean values of wall shear stress to two different markers of early atheroma distribution in the distal abdominal aorta. These hemodynamic conditions correlate with intimal thickness data from 15 aortas in adults and probability-of-occurrence (POC) maps of atherosclerosis in 1378 young subjects as identified by Sudan Red staining or by gross appearance as raised lesions. It is also important to note that the distribution of intimal thickening and probability-of-occurrence surface maps of Sudan staining and raised lesions were not identical at the distal abdominal aorta. The different markers provide slightly different locations of disease. However, all three measures of early atheroma indicate the disease begins at the postero-lateral walls of the distal aorta.

The results can be compared with previous studies linking hemodynamics with atherosclerosis. The results of the present study of the distal abdominal aorta are consistent with previous studies of the iliac, left coronary, and carotid arteries in that intimal thickness correlated in general with low and oscillating shear stress. Friedman et al. [9] performed a model study of flow through casts of the aortic bifurcation under the assumption of developed flow conditions proximal to the aortic bifurcation. Comparisons of intimal thickness with mean and maximum near-wall velocity measurements along the inner and outer walls of the aortic bifurcation resulted in a negative correlation, implying that low mean and maximum wall shear stresses were associated with intimal thickening. Negative correlations of the distribution of plaque with mean and maximum, as well as pulse shear stresses were also reported for the coronary artery [12]. Ku et al. [7] found a negative correlation between mean shear stress and intimal thickness at the carotid bifurcation. They also noted a strong correlation with oscillations in shear stress and inverse relationships to the maximum and mean shear stresses.

There are, however, important differences between our results and previous correlations of hemodynamics and atherosclerosis localization. There was no statistically significant relationship found between intimal thickness and maximum shear stress or its inverse for the distal abdominal aorta. At other atherosclerotic sites, maximum shear stress was low in the same anatomical locations where the mean shear stress was low. The hemodynamics of the distal abdominal aorta are different from other sites of atherosclerosis in that the maximum shear stress reached its greatest values where the mean shear stress was lowest. The development of atherosclerosis was most prominent at these lateral sites and a negative correlation between intimal thickening and the maximum shear stress was not found. Thus, the correlations here suggest that maximum shear stress does not determine plaque localization in the distal abdominal aorta.

A notable difference exists between these results and those previously published in relation to the OSI. OSI is meant to express the amount of shear stress oscillation the arterial wall experiences. In Ku et al. [7], the OSI was 'corrected' to range from 0 to 0.5 by subtracting the difference between the actual value of the OSI and 0.5 from 0.5 (i.e., an OSI value of 0.62 would become 0.38). The reasoning for this was that if the wall shear stress is mostly negative, then a positive shear stress would essentially constitute a reversal. In the present study, the correlation between intimal thickness and the 'uncorrected' OSI was found to be very strong, while the correlation with the 'corrected' OSI was not as significant. An 'uncorrected' OSI of greater than 0.5 indicates that most of the shear stress is directed in the opposite direction of the
mainstream flow. The persistence of reverse flow itself may be atherogenic.

The hemodynamic modeling in this study differs slightly from previously reported studies of hemodynamics in the aorta. The studies by Mark et al. [29] and Friedman et al. [9] measured shear rates from 1.5 cm proximal to about 2 cm distal from the flow divider. This is generally further downstream than our most distal measurement. Their proximal entrance conditions did not include the curvature of the aorta, nor the proximal visceral arteries which take away two-thirds of the thoracic aorta blood flow and contribute to secondary flow development. Furthermore, their statistical comparison included only velocity data from the inner and outer (medial and lateral) walls of the iliac arteries instead of the entire circumference. The studies of Adamson et al. [30] and Liepsch et al. [31] concentrated on the effects of the renal artery branches without inclusion of the celiac and superior mesenteric arteries or the curvature of the aorta. In the present study, the curvature and branches were included, and shear stresses were measured just proximal to the aortic bifurcation around the entire circumference of the vessel. Additionally, the effects of exercise conditions on the flow field were quantified.

The wall shear stress measurements for resting conditions presented here are lower than previously reported values. Friedman et al. [9] found mean wall shear stress values between 2 and 18 dyn/cm² at the aortic bifurcation of a cast of a human aorta. Adamson et al. [30] presented values between 2.8 and 8.8 dyn/cm² just distal to the renal arteries in an in vitro model flow study. We determined mean shear stress values between -1.7 and 1.4 dyn/cm². In this regard, it should be noted that the mean and peak flow rates used by Friedman et al. [9] were 10% and 180% higher than the values used in our study, and there was less reversal in the cam-driven flow waveform. The flow rates used in our study were within the expected normal physiologic range, albeit at the lower end of that range [24]. Flow visualization studies in this model showed similar areas of shear reversals at higher mean and peak flow rates when the same flow waveform shape was used. Although the spatial distribution of relative shear stress levels would remain roughly the same, the actual magnitudes of shear stress may vary from individual to individual. The similarity of the velocity profiles used in this study to profiles measured in vivo has been verified, although the in vivo flow rates were higher [32].

The wall shear stress reversal that was present in the infrarenal aorta and aortic bifurcation during resting conditions was nearly eliminated for simulated exercise conditions in all locations. There was much less reversal in direction, and exercise mean wall shear stresses were positive and higher than the resting values. At the posterior wall of the infrarenal aorta and aortic bifurcation, there was still a small amount of shear stress reversal. The changes in wall shear stress during simulated exercise conditions are primarily due to the change in flow division to the branches of the aorta and the elimination of the tri-phasic flow waveform [33]. It is likely that the marked changes in wall shear stress with exercise may account for some of the reduction in atherosclerosis progression seen clinically in association with exercise [34].

Although the results were not shown here, measurements of wall shear stress under simulated postprandial conditions were also performed, i.e. with increased superior mesenteric artery flow [35]. The changes in flow field patterns from the resting to the postprandial state were minor and resulted in a slight reduction in wall shear stress along the left anterior wall of the infrarenal aorta.

The hemodynamic model of the abdominal aorta was based on measurements made on 55 biplanar angiograms and, therefore, represents an average flow geometry [24]. Our previous studies have demonstrated that the angle of the renal and mesenteric arteries are not critical [36]. In addition, the walls of the model were rigid and a Newtonian fluid was used. The effects of these simplifications have been shown to be relatively minor for this relatively high flow part of the arterial tree [10]. The wall shear stress measurements presented here represent only the axial component of the wall shear stress. The contributions of the secondary flows to the wall shear stress were extremely small in the locations where measurements were taken as seen by flow visualization [16].
Intimal thickening and atheroma formation in the aortas in our study had an average of thickness of approximately 1 mm. Thus, no statements can be made regarding the more advanced stages of atherosclerosis, including occlusive or aneurysmal disease. The use of aortas with relatively small intimal thickening provides an opportunity to avoid changes in wall configuration which could affect flow. Furthermore, the lesions in our material are similar in size to those studied by Cornhill et al. [15].

Shear stress results are presented for a site of clinically important atherosclerosis. Low mean and oscillatory shear stress were found to coincide with three different sets of data atherosclerosis localization. These results, in combination with other evidence, directly identify low and oscillating shear stresses as important primary factors in atherogenesis. Contrary to previous studies, no statistically significant relationship was found with maximum shear stress. Under simulated exercise conditions, shear stress reversal was virtually eliminated. These data suggest that exercise may help inhibit the development of atherosclerosis by increasing the flow phenomena which favor sparing, and decreasing those which favor intimal thickening and atherogenesis.

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Appendix 1

Details of shear stress calculation

The procedure that was used to calculate the wall shear stresses from the velocity data is outlined as follows. First, the wall of the vessel was outlined from the MR magnitude image, where the vessel lumen was easily distinguished from the surroundings, and the wall could be defined as the border between the two regions. In a typical MR image, where pixel values were coded from 0 to 4095, the pixels inside the lumen had a value of around 2700, while the pixels outside the lumen had values of approximately 1000. A mask file was generated for each slice location in which a value of ‘1’ was given to pixels inside the lumen, and a value of ‘0’ was given to pixels outside the lumen. These mask files were multiplied with the velocity data to give the final velocity profiles.

The masked file for each slice was then used to determine the center of the tube and the radii along the circumference. Then, the center of the tube was calculated by averaging the edge point coordinates. Based on this center coordinate, the edge point locations were converted to polar coordinates, with the anterior side of the slice being the 0° reference. Since some of the row edge points were also column edge points, duplications were eliminated, and the resulting list was sorted in order of increasing angular location.

The next step was to calculate the radius at 24 locations equally spaced around the circumference of the tube (every 15°). The program picked the four closest values from the edge points and used a linear least squares approximation to calculate the radius, R, at the desired location. Therefore, each R represents the radius on an arc through the neighboring edge points. For round tubes with a 20-25 mm radius, the calculated radii were an average of 3.2% larger than the actual radius of the tube. Therefore, the radii were all multiplied by 0.97 to give better estimates of the actual radii. The

Table A1
Correlations between shear stress calculated using linear and quadratic approximations of the experimental velocity data (FIT) and theoretical shear stress (TH) using two different values of Δr

<table>
<thead>
<tr>
<th></th>
<th>Linear</th>
<th>Quadratic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δr = 0.5 mm</td>
<td>FIT = 0.858 + 0.494 TH</td>
<td>FIT = 0.297 + 0.822 TH</td>
</tr>
<tr>
<td></td>
<td>r = 0.891</td>
<td>r = 0.966</td>
</tr>
<tr>
<td>Δr = 0.7 mm</td>
<td>FIT = 1.06 + 0.373 TH</td>
<td>FIT = 0.524 + 0.709 TH</td>
</tr>
<tr>
<td></td>
<td>r = 0.828</td>
<td>r = 0.926</td>
</tr>
</tbody>
</table>
final results were found to be within a standard deviation of 0.2 mm of the actual tube radius.

Using the radii calculated above, along with the measured velocity profiles, the wall shear stress as a function of time and position around the circumference of the tube was determined. At each of the locations around the edge of the circle, the Cartesian coordinates of the four points closest to $R_i - \Delta r$, $R_i - 2\Delta r$, and $R_i - 3\Delta r$ were found ($\Delta r$ being a small radial increment). Then, for each of
the 16 heart phases measured with MRI, an interpolated velocity was computed using a weighted bi-linear interpolation scheme for each new point \( R_i - \Delta r, R_i - 2\Delta r, \) and \( R_i - 3\Delta r. \)

Two different least squares approximations of the shear rate at the wall were compared: (A) a quadratic least squares approximation through the wall (velocity = 0) and the three inner radius velocity values, and (B) a linear least squares approximation using the wall and two inner radius velocity values. For method A, the derivative of the parabola was evaluated at the wall. If the parabola did not extrapolate to the wall, the derivative was calculated at \( R_i \), and an error message was printed. For method B, the derivative was taken from the slope of the fitted line.

The linear and quadratic approximations of the wall shear rate were compared with the theoretical wall shear rate using Womersley's solution and the volume flow waveform measured by the ultrasonic flow meter inserted upstream of the aorta model and Womersley's solution [26,27]. Several shear stress waveforms were generated using the theoretical near-wall velocities at different \( \Delta r \) values (Table A1). Not surprisingly, the smallest \( \Delta r \) values gave the most accurate shear stress waveforms.

Unfortunately, the spatial resolution of the actual measured velocity profiles places a stochastic minimum on the value that can be used for \( \Delta r \). This minimum value can be estimated by examining the case when the velocities along a 45° line are desired, and the wall of the tube is located exactly in the middle of a pixel. The bi-linear interpolation scheme must not 'create' data by obtaining 5 or more new velocity values from four neighboring measured values. Therefore, with this constraint, the minimum value for \( \Delta r \) in these experimental data is 0.3 mm.

There is an additional practical limit on the minimum value of \( \Delta r \). Due to large changes in magnetic properties over a small distance near the tube walls (Gibbs artifacts), the velocity data near the walls fluctuated more than those in the center of the tube. With larger values of \( \Delta r \), the problem of near-wall fluctuations in measured velocity is minimized. For the final results, a quadratic approximation with \( \Delta r = 0.5 \) mm was used, and

the wall shear stress values measured under resting conditions were corrected using this comparison of experimental versus theoretical wall shear for resting pulsatile flow given in Table A1. The measured shear stress indices compared well with the theoretical values. The error in the maximum shear stress (underestimated by 3%) is in exact accordance with the predictions given by Lou et al. [37] for this type of calculation. No correction was applied for the exercise results, since the flow was mostly forward, and the corrections obtained for resting conditions would not apply to the higher Womersley parameter in exercise.

A comparison of the theoretical velocity profile and the quadratic, \( \Delta r = 0.5 \) mm approximation is shown in Fig. A1, for several points in the cardiac cycle. The quadratic approximation worked well in systole, but not as well later in the cardiac cycle. The quadratic approximation underestimated the shear stress at peak reversal (Fig. A1c), and had trouble with the complex profile shape that occurred at the diastolic forward peak (Fig. A1d). This complex profile arose because of the relatively high value of the Womersley parameter \( (\alpha = 16) \), which caused many of the unsteady changes in velocity to be confined to the near wall region. This analysis demonstrates that one must be aware of the limitations of experimental methods used to estimate wall shear stress from near wall velocity measurements. Further details, along with the computer program listings, may be found in Moore [35].

References

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