Calculations of Pulsatile Flow through a Branch

IMPLICATIONS FOR THE HEMODYNAMICS OF ATHEROGENESIS

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ABSTRACT

Numerical simulations of pulsatile blood flow through a symmetrical branch modeling the aortic bifurcation were carried out to assess several hemodynamic theories of atherogenesis by comparing the distribution of hemodynamic variables with that of early lesions in arterial branches. Considerable spatial and temporal variations in wall shear were found when the flow was pulsatile; the highest values occurred at the convex corner on the outer wall of the branch and in the neighborhood of the flow divider tip, and the lowest shears were experienced by the outer wall of the daughter vessel a short distance distal to the corner. Transient flow reversal occurred almost everywhere in the branch, and a transient separated region was found corresponding to the low-shear region in the daughter vessel. The shear profiles and the calculated separated region were influenced to some degree by the extent of flow development at the branch inlet and markedly by the branch area ratio. All of the proposed hemodynamic promoters of atherosclerosis that were examined—high shear, low shear, and separation—were found at sites in the branch where lesions commonly develop. Comparisons with a steady-flow calculation at the same mean flow rate showed that the severity of all of these proposed hemodynamic determinants was increased by pulsatility.

KEY WORDS geometric effects in arteries wall shear profiles flow reversal flow separation flow development vascular model

Certain regions in the arterial tree such as the inside walls of bends and the neighborhoods of branches and ostia are particularly prone to develop atheromatous lesions (1-6). These predisposed segments probably differ from straighter segments in a variety of ways, but, since the blood flow patterns in bends and branches are patently different from those in straight segments, this focal aspect of atherosclerosis has led to a number of hemodynamic theories of atherogenesis.

Only a fraction of these theories are supported by either fluid mechanical calculations or an experimental demonstration of the proposed determining hemodynamic factor. Fry (7) has suggested that in areas where the wall shear rate is high increased amounts of mechanical energy are stored in the wall with damaging effects on the intimal endothelium. The harmful effects of acutely elevated shear have also been demonstrated previously (8). Along similar lines, Gutstein et al. (9), employing hot-wire anemometry, have found flow disturbances at the aortic bifurcation in vivo; they have proposed that these irregularities expose the adjacent intima to high shearing stresses. Hugh and Fox (3) have observed that in the internal carotid artery the sites of intra-arterial stasis as demonstrated radiographically are those at which lesions are characteristically found; they have suggested that thrombogenesis is facilitated in such stagnant regions. Similarly, Jorgensen et al. (10) have presented histological evidence suggesting that a harmful platelet-leukocyte interaction with the vessel wall is most pronounced in regions of flow separation. The role of low ambient shear as a hemodynamic factor in atherogenesis has been stressed by Caro et al. (4), who combined steady-flow estimates of shear distribution in the arterial tree with their own and other studies of lesion distribution to develop their thesis that natural atherosclerosis originates at sites where wall shear is unusually low rather than unusually high.

Besides the foregoing theories based on high shear, stasis-separation phenomena, and low shear, a fourth hemodynamic hypothesis derives from the calculations of pulse-wave reflection at a branch reported by Gosling et al. (11). This theory proposes that impedance mismatching at the aortic bifurcation causes a damaging increase in hydrostatic stress proximally. Newman et al. (12) and Lallemand et al. (5) have shown that this hypothesis is consistent with measurements of the area ratio at the bifurcation.

Only some of the proposed hemodynamic theo-
ries of atherogenesis are summarized in this introduction. These theories and others are the subject of a more comprehensive critical review which has recently appeared in Circulation Research (13).

A proper experimental fluid mechanical study of arterial hemodynamics is difficult, since the required measurements must be made in vivo and so as not to perturb the flow. At the same time, numerical simulations are hindered by the threedimensionality of arterial geometry, the unsteadiness of the flow, and the possible need to describe and incorporate into the analysis wall mechanics and blood rheology. Nonetheless, it is reasonable to hope that, by converging on the real problem through increasingly sophisticated experimental procedures and increasingly realistic numerical simulations, a sufficient appreciation of the role of hemodynamics in atherogenesis can be obtained without encountering insuperable experimental or computational obstacles.

The present study presents a numerical simulation of blood flow through a symmetrical branch. The branch area ratio and the mean flow parameters were selected to correspond to those at the aortic bifurcation. The intent of this work was to establish the distributions of hemodynamic variables in vessel segments, such as the bifurcation, which are known to be prone to develop atherosclerotic disease, and, by comparing these distributions with the distribution of lesions, to gain an appreciation of the hemodynamic variables and associated phenomena most likely to be implicated in atherogenesis. As implied earlier, the modeling was far from perfect—the branch was two-dimensional because of computational limitations, its walls were rigid, and the contained fluid was Newtonian. Steady flows through such branches have been the subject of numerical studies by Lynn et al. (14), and Hung and Naff (15) have presented a limited selection of their results for a flow impulse from rest. In the present paper, the flow was more realistically pulsatile, and the effect of this unsteadiness on the hemodynamics in the branch was assessed by comparing the results with the corresponding steady-flow solution. However, the qualitative aspects of this unsteady flow through a bifurcating geometry and the qualitative effect of changes in geometry and flow conditions should persist in three-dimensional blood flow through an elastic artery.

**Mathematical Methods**

The model geometry is shown in Figure 1. The geometry and the flow are two-dimensional in the plane of the figure. The branch and the flow are symmetrical

![Figure 1: Model geometry. Because of symmetry, calculations only have to be carried out for the half-branch region outlined heavily. See text for definition of abbreviations.](http://circres.ahajournals.org/)

The equations which govern the viscous flow in this region are derived from the normalized two-dimensional Navier-Stokes equation for a Newtonian incompressible fluid.

\[
\frac{\eta}{2} \frac{\partial^2 \Omega}{\partial \tau^2} - \text{Re}_m (\psi_x \Omega_y - \psi_y \Omega_x) = \nabla^2 \Omega, \quad (1a)
\]

\[
\nabla^2 \psi = -\Omega, \quad (1b)
\]

where \( \eta = (2U^2 \omega \nu)^{1/3} \), \( \Omega(x,y,\tau) \) is nondimensional vorticity, differentiation is indicated by subscripting, \( \tau = \omega t \), \( \text{Re}_m = UL/\nu \) (note that this value is half the Reynolds number as it is usually defined), \( \psi(x,y,\tau) \) is the nondimensional stream function, \( \hat{x} = uL, \hat{y} = yL, \omega \) is angular frequency, \( \nu \) is the kinematic viscosity of the fluid, \( t \) is time, and \( U \) is the mean inlet flow velocity averaged over \( y \) and \( t \). In two dimensions, the vorticity and the stream function are related to the nondimensional velocity components \( \hat{u}(x,y,\tau) \) and \( \hat{v}(x,y,\tau) \) by \( \Omega = \partial \hat{v}/\partial \hat{x} - \partial \hat{u}/\partial \hat{y} \), \( \psi = \hat{u} \), and \( \hat{u} = \nabla \psi \), where \( u \) = \( U \), \( \hat{u} = uL \), and \( u \) and \( v \) are the components of fluid velocity in the \( x \) and \( y \) directions, respectively. The method of solution of these equations is described elsewhere (16).
All unsteady-flow calculations given in the present paper are for an idealized pulsatile flux wave form consisting of a constant Re component of 100 on which is superimposed a sinusoidal flow whose Re amplitude is 100 and whose frequency is such that \( T/J = 10 \) in the parent vessel. Thus, the maximum instantaneous flow is twice the mean, the minimum flow is zero, and the values of \( Rm \) and \( \eta \) in Eq. 1a are 100 and 10, respectively. Two inlet profiles given by \( \psi(0,y,T) \) are employed: a fully developed parallel-flow profile and an entrance-flow, flat velocity profile. A few steady-flow calculations with \( R = Rm = 100 \) and a fully developed inlet boundary condition were also carried out for comparison purposes. These and the other boundary conditions employed in the calculations are straightforward and are discussed in detail by Ehrlich (16).

The vessel walls are impermeable, so \( \psi \) is instantaneously uniform along them. At the wall, from Eq. 1b, \( \Omega_w = - (\partial \psi / \partial n)_w \), where the subscript \( w \) denotes evaluation at the wall and \( n \) is the nondimensional normal coordinate at the wall. The stream function defines the nondimensional velocity field, so \( \Omega_w \) can be related to the nondimensional velocity gradient at the wall. The shear stress, in turn, is given by \( \tau_w = \mu (\partial u'/ \partial n)_w \), where \( \mu \) is the viscosity of the fluid, \( u' \) is the velocity parallel to the wall, and \( n \) is the dimensional normal coordinate. Substituting the nondimensionalizing factors given previously and replacing \( v \) by \( y/p \) (\( p \) is fluid density),

\[
\tau_w = \frac{\mu Rm}{D^2} \Omega_w. \tag{2}
\]

Thus, the wall vorticity can be regarded as a nondimensional wall shear. It is easy to show that the sign of \( \Omega_w \) depends on the direction (forward or reverse) of the flow past the wall.

A number of measures of wall shear were obtained from the computed values of \( \Omega_w(x,T) \) at each mesh point along the walls of the region. The only two whose meanings are not immediately evident are:

**Average nondimensional shear** \( \langle \Omega_w \rangle(\xi) = \frac{1}{2\pi \int_0^\infty \Omega_w(\xi,\tau)d\tau} \)

**Average nondimensional shear magnitude** \( \langle |\Omega_w| \rangle(\xi) = \frac{1}{2\pi \int_0^\infty |\Omega_w(\xi,\tau)|d\tau} \)

In many of the calculations to be presented in this paper, the direction of flow past a vessel wall at a given instant of time is directed distally along part of the wall and proximally along the remainder. Since the sign of \( \Omega_w \) indicates the flow direction at the wall, \( \Omega_w \) will change sign, that is, pass through zero, at that point along the wall at which the flow direction changes from forward to reverse. The closed separation regions of interest in this analysis are manifested as eddies in which the flow past a wall segment is oppositely directed to the flow proximal and distal to the segment. Hence, such a region is bounded by *two* zeros of \( \Omega_w \) along a wall; the zeros are at the instantaneous separation and reattachment points. It should be noted that, in general, the positive identification of separation requires an examination of the stream function values in this neighborhood.

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**Results and Discussion**

**BASE CASE CALCULATION**

The base case calculation was carried out for the idealized pulsatile flux wave form described in Methods, a fully developed parallel-flow inlet boundary condition, a mesh size of \( \Delta x = \Delta y = 1/16 \), and an area ratio of \( \alpha = 0.796 \).

Figures 2 and 3 present a number of wall shear measures for the base case and steady-flow runs. In general terms, the instantaneous and time-averaged spatial wall shear profiles adhere to a fairly common pattern. The shear on the outer wall of the parent maintains the parallel-flow
Shear measures on the inner wall of a bifurcation plotted against $\dot{x}$. The curves of $\langle \Omega_w \rangle$ and $-\langle |\Omega_w| \rangle$ for the base case are labeled; inner wall vorticities are negative when flow is in the direction of increasing $\dot{x}$. - - - = steady flow calculation, $Re = 100$; - - - = algebraic minimum wall vorticity in the pulsatile case. Curves start one mesh point beyond the flow divider tip. The position of the tip and the length $L$ are given to define the horizontal scale.

Shear rises rapidly to reach its highest value at the corner mesh point. The shear drops drastically to a much lower value at the next outer wall mesh point and then continues to fall for a short distance into the daughter. A minimum shear is reached, and then the shear rises smoothly to the parallel-flow solution corresponding to the $Re$ and $\eta$ which characterize the daughter. As regards the inner wall, the vorticity at the flow divider tip is fixed at zero by symmetry.

As would be expected from parallel-flow considerations, the value of $\eta$ is such that wall shear cannot be regarded as quasi-steady. There are considerable differences between the spatial wall shear profiles at the two times during the cycle when the sinusoidal flow component is zero (accelerating vs. decelerating). These profiles, in turn, differ from the steady-flow result at the same $Re$. The inclusion of the inertial term leads in the present geometry to nonsinusoidal wall shear histories at points within the branch, and the extrema and zeros of these (temporal) profiles are not in phase.

As might be expected, the maximum shears in the pulsatile-flow case can be several multiples of the average shear or the steady shear at the same $Re_m$. The largest instantaneous shear is at the corner; it occurs during flow acceleration just before the maximum instantaneous $Re$ is reached. When this value of $\Omega_w$ (79.6) is inserted into Eq. 2, identifying $L$ with an arterial radius of 0.67 cm (17) and using accepted values of $\mu$ and $\rho$ for blood, the maximum calculated shear stress at the corner, and hence in the entire segment save possibly the immediate neighborhood of the flow divider tip, is only about 30 dynes/cm$^2$.
During a cycle, the algebraic range of wall vorticity, $\omega_{w,max}(\xi) - \omega_{w,min}(\xi)$, at each wall mesh point is close to the extremum of $\omega_{w}(\xi)$, so the extrema in Figures 2 and 3 are representative of the rates at which shear stress is applied to the intimal endothelium. The possibility of a deleterious viscoelastic response to continued periodic changes in stress or to stress rate per se cannot be ruled out at this time.

The variation of $\omega_w$ with $x$ and $\tau$ can be represented by $\omega_w$ contours in $x$-$\tau$ space. The $\omega_w = 0$ contours for the inner and outer walls are presented in Figures 4 and 5. These contours divide the space into areas of positive and negative wall vorticity. Flow at the wall is directed distally when the vorticity is positive on the outer wall or negative on the inner wall; flow reversal occurs at the outer wall when $\omega_w < 0$ and at the inner wall when $\omega_w > 0$. Every point on the outer wall experiences flow reversal during some fraction of the cycle; this situation explains why, in Figure 2, $\langle \omega_w \rangle$ is everywhere less than $\langle |\omega_w| \rangle$. Along the inner wall, there is no flow reversal for some distance distal to the flow divider, and the curves of $\langle \omega_w \rangle$ and $\langle |\omega_w| \rangle$ in Figure 3 do not separate until a point further downstream is reached.

As observed earlier, stasis and low shear have been thought to be hemodynamic causes of atherosclerosis. A fluid mechanical event which is strongly geometry dependent and which can promote low mural shears is separation; indeed, a transient closed separation "bubble" is observed in Figure 4. The bubble is found only when the instantaneous flow is nearly maximum; it extends a short distance along the outer wall of the daughter from a separation point just distal to the corner. Both the temporal and the spatial extent of the calculated separated region are reduced when the computational mesh is made finer; hence, it cannot be stated with certainty that the governing equations and boundary conditions do in fact give separation in this geometry. In real arteries, the anatomic equivalent of the corner is gently rounded, a deviation from the present geometry which might be expected to oppose the formation of a separated region. In sum, the calculations presented in this paper suggest that separation in the arterial tree is a relatively rare phenomenon compared with the number of sites at which early lesions are found. It would follow that separation is not a necessary condition for the initiation of atherosclerotic involvement.

This inference is not unrealistic; separation per se, and particularly transient separation, is not a phenomenon which would be expected to have a direct effect on the arterial wall. The wall responds to mural shear and to its chemical environment rather than directly to the presence of a dividing streamline. The important aspect of separated regions as they influence the wall is that they are usually associated with low wall shears and reduced replenishment of fluid in their vicinity. The first of these associated phenomena is manifest in Figure 2, where a minimum $\langle \omega_w \rangle$ is found just distal to the corner; the second is evident from a simple consideration of particle paths in a time-varying shear layer. Thus, in regions where shear is low, transport of nutrients or oxygen to and wastes away from the intima would be expected to proceed with relative difficulty, a condition which can be harmful to the tissue. The possibility that formed elements of the blood accumulate in regions of stasis has been suggested (10), but the present work, which regards blood as a homogeneous incompressible fluid, does not address this eventuality.

**COMPARISON WITH THE STEADY-FLOW CALCULATION**

The wall shear profiles for a steady flow at the
same mean Re as that employed in the pulsatile-flow calculations (Re = 100) are also presented in Figures 2 and 3. At any point in the branch, the maximum shear in the steady-flow case is, understandably, considerably less than the maximum in pulsatile flow. The vorticity on the outer wall is always positive in steady flow; hence, there is no flow separation. This result is not inconsistent with the pulsatile-flow calculation, inasmuch as the transient bubble observed in the unsteady case (Fig. 4, mesh size = 1/16) does not appear until the instantaneous Re is 182 during flow acceleration and collapses when the instantaneous Re has fallen from its peak value to 180.

Interestingly, the steady-flow minimum wall vorticity distal to the corner is more than three times the corresponding value of (D^2) found for pulsatile flow at the same Re m. Thus, if low wall shear is a part of the etiology of atherosclerosis, pulsatility evidently exacerbates the situation at a branch.

EFFECT OF INLET VELOCITY PROFILE

The calculations just described were all carried out using an inlet boundary condition y(0,y,r) corresponding to fully developed parallel flow. Owing to the treelike topology of the arterial system, it is unlikely that such inlet flows actually exist in vivo. To examine the effect of incomplete flow development, calculations were carried out for the case in which the inlet velocity profile was flat. The r dependence of instantaneous Re and ψ(0,1,r) were as before. To maintain a flat profile, ψ(0,y,r) was set equal to 0ψ(0,1,r); by Eq. 1b, the inlet vorticity was always zero.

The shear measures on the outer wall for an undeveloped inlet are compared with those for a fully developed inlet in Figure 6. Naturally, the wall shear at the inlet is infinite for the entrance flow used in this analysis. The shear measures develop at different rates; (|ωw|) is essentially equal to the fully developed value only a few mesh points into the branch, while (ωw) never reaches the fully developed value in the short space between the inlet and the corner. The minimum average vorticity distal to the corner is 0.8 when the inlet flow is undeveloped compared with 1.8 for the base case calculation. Although the absolute difference of mean shears is trivial, the percent difference is large. Hence, entrance effects may be important to processes, such as diffusion, which depend on shear directly.

The calculated separated region when the inlet flow is undeveloped is greater in temporal and spatial extent than that when the inlet is fully developed. For a mesh size of Δx = Δy = 1/16, the maximum extent of separation along the outer wall of the daughter is doubled when the inlet velocity profile is made flat and the duration of separation is increased by nearly 50%.

EFFECT OF BRANCH AREA RATIO

An important geometric parameter of any arterial branch, which varies with age (11, 12) and among individuals, is the area ratio a. Essentially all aspects of branch hemodynamics depend on a, and if one or more of these aspects play a role in atherogenesis it follows that the branch area ratio may be importantly related to the epidemiology of atherosclerosis. Branch angle, a parameter that was not varied in this analysis, may play a similar role as the basis of an architectural risk factor.

The branch area ratio was raised from 0.796 to 1.061 by translating the inner wall in the positive x direction. No other change from the base case calculation was made. The average vorticities (ωw) on the outer wall for the two values of a are compared in Figure 7. The increased distal cross section results in a general reduction in shear levels in the branch. Except near the inlet, all shear measures along the outer wall of the parent channel are lowered when a is raised. The maximum wall vorticity at the corner is only 41.2,
PULSATILE FLOW THROUGH A BRANCH

Average vorticity on the outer wall of a bifurcation plotted against $\dot{x}$. Solid line = base case calculation, area ratio $\alpha = 0.796$; dotted line $\alpha = 1.061$. The curves are broken between the corner mesh point and the first mesh point in the daughter. The position of the corner and the length $L$ are given to define the horizontal scale.

About half of the base case value. The minimum average vorticity along the daughter vessel outer wall is reduced from the base case value to $\langle \Omega_w \rangle = 0.1$. The spatial extent of this low-shear region is considerably greater when $\alpha = 1.061$ than it is when $\alpha = 0.796$.

The reduction in flow velocity in the daughter channel when $\alpha$ is raised has a striking effect on the outer wall zero vorticity contours (Fig. 8). The separated region originates similarly to the base case (Fig. 4), but as the flux through the branch diminishes, the eddy on the daughter channel wall does not die out. Rather, it continues to grow as the reattachment point moves distally, and it persists until reverse flow is established throughout the branch. As a consequence, the duration of reverse flow distal to the corner is much greater when the area ratio is raised. This phenomenon is reflected in the low mean vorticities in Figure 7. The influence of area ratio on shear profiles within the branch suggests that individual variations in arterial geometry may to some extent be responsible for corresponding variations in their predisposition to arterial disease. Such a causal relationship, if proven, could be exploited to identify persons at risk at an early enough age to permit effective intervention. Furthermore, the striking influence of geometry on the hemodynamic variables at the wall might be employed with appropriate epidemiological data to infer the principal fluid mechanical parameters involved in atherogenesis.

IMPLICATIONS WITH RESPECT TO ATHEROGENESIS

Both high and low wall shears have been proposed as hemodynamic states predisposing arteries to atherosclerosis. It is interesting to note that for a give $Re_m$, the introduction of pulsatility acts to the disadvantage of the arterial wall, irrespective of the proposed damage mechanism. The peak shears experienced by the wall are raised when the flow is made pulsatile, largely because the maximum instantaneous flow through the branch is greater than the mean flow, the latter being identical to the reference steady flow. In the high-shear areas of the branch, $\langle \Omega_w \rangle$ is somewhat greater in magnitude than the corresponding steady-flow vorticity (Figs. 2, 3). The region of lowest shear and the most likely site for separation to occur (if in fact it does) is just distal to the corner on the outer wall vorticity contours in $x-\tau$ space for the outer wall of a bifurcation having an area ratio of 1.061. Mesh size $\Delta \tilde{x} = \Delta \tilde{y} = 1/16$. The flux maximum occurs at $\tau = 0$; the flux through the branch is zero at $\tau = \pm \pi$ (see wave form at bottom of Fig. 4). The position of the corner (C) and the length $L$ are given to define the vertical scale; $\tilde{x}$ increases distally.
The wall of the daughter channel. The results in Figure 2 show that the extent to which the mean shear in this region is reduced from the parallel-flow value in the distal daughter (where the average shear is the same for pulsatile and steady flow at the same Re number) is greater in the pulsatile case.

As noted earlier in this paper, the largest wall vorticity in the base case calculation corresponds to a mural shear stress of only about 30 dynes/cm², much less than the acute stress of 380 dynes/cm² found (8) to cause endothelial damage. This inequality, however, is not a firm basis on which to discount high-shear hypotheses of atherogenesis, although it is clearly not supportive of such hypotheses. It can be argued that the computed stress is an underestimate of the true stress or that it is an overestimate. Higher stresses would be computed if the Reynolds number were higher, as it may be at the bifurcation and surely is proximally. In contrast, in real arterial geometries, the outer wall is rounded at the branch and the lumen grows in diameter proximal to the flow divider, so the peak shear along the outer wall is probably a smaller multiple of the mean shear in the parent artery than that computed in this analysis. Perhaps more important, it should be noted that Fry’s (8) critical stress is an acute value, but atherosclerosis is generally accepted to be a progressive disease. The chronic effects of small elevations in shear are unknown; Fry (7) has found that the uptake of protein by the vessel wall is increased by shear at levels below the acute critical stress. In short, the merits of high-shear hypotheses are best evaluated by examining the coincidence of high-shear regions with sites predisposed to vascular disease rather than by comparing the magnitude of the calculated or experimental shear in these regions with an uncertain critical value.

The spatial and temporal variations in wall shear stress are considerable when the flow is pulsatile and branching and cannot be predicted entirely from steady-flow considerations. In spite of these variations, one cannot infer a principal hemodynamic factor in atherogenesis from the observed distribution of lesions. Caro et al. (4), using Sudan III staining, found that in the initial segment of aortic side branches (celiac, superior mesenteric, renal), the quadrant corresponding to the site of the carotid siphon and the localization of atheromatous plaques. Pol Med J 7:238-243, 1968


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