Analysis of Coronary Flow Fields in Thoracotomized Dogs

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ABSTRACT

A nonlinear theory of pulsatile flow was used to investigate the detailed flow field in the left circumflex coronary artery of anesthetized open-chest dogs. Studies were carried out under a wide range of blood pressures and flow rates induced by intravenous infusions of dipyridamole. The results indicated that (1) the flow profiles, although less blunt than those in the descending aorta, are still nonparabolic, (2) the wall shear in the coronary arteries maintains a high value through diastole, and (3) during intravenous infusions of dipyridamole both coronary flow and wall shear increase. The peak value of the shear stress during these infusions, which reached 360 dynes/cm², can approach the yield stress value of 400 dynes/cm² reported by Fry for endothelial cells.

Studies by Fry (1) and others (2-4) have shown that adjacent hydrodynamic events alter the permeability of the intimal surface of the aorta and the coronary arteries. Such events might play a significant role in the development of discrete atherosclerotic lesions. Thus, for a better understanding of the atherosclerotic process, it becomes important to study flow fields in critical areas of the circulatory system such as the coronary arteries. Previously, attempts have been made to measure the velocity distribution in the coronary arteries of horses using a hot-film anemometer (5) and a pulsed ultrasound Doppler velocity meter (6). However, because of technical limitations, it is not possible to compute the shear stress at the wall from such data. In the present study, we undertook to compute the detailed flow field at a given site in the left circumflex coronary arteries of dogs using a nonlinear theory developed by Ling and Atabek (7) and Ling et al. (8). The theory takes into account the nonlinear terms of the Navier-Stokes equations as well as the nonlinear behavior of the arterial wall. Using the locally measured values of the pressure and the pressure-gradient waves, the pressure-radius function, and the taper angle of the arterial wall, the theory predicts velocity distribution, wall shear, and flow waves. The theory is valid for a relatively straight artery that is at least ten diameters distal from a major branch site. This requirement is reasonably satisfied at the middle length of the left circumflex coronary artery approximately 2 cm distal to its origin. Since the nonlinear theory of blood flow has been described in detail previously, only a short summary of the theory will be presented in this paper.

Theory

To determine the flow field, a system of equations governing the motions of the blood and the arterial wall must be solved simultaneously. The analysis of this system is difficult, but with certain justifiable assumptions the problem can be simplified. First, the inertial force due to the effective mass of the arterial wall has been shown to be negligible in comparison with both the pressure and the elastic forces (9). Moreover, the wall viscosity in the circumferential direction is also negligible (10). Therefore, the radial motion of the arterial wall can be determined directly from the pressure wave and the pressure-radius function of the artery. Let \( p \) be the pressure and \( R \) the inner radius of the artery. Hereafter, we will assume that the relationship between the two, \( R = R(p) \), is determined experimentally and available for calculations. Second, the longitudinal motion and the velocity of the arterial wall are very small (9). Therefore, their effect on the flow field can be neglected. Thus, since the pressure wave is measured and the pressure-radius function is known, the problem of determining the flow field is reduced to obtaining periodic solutions to the fluid equations that satisfy the prescribed radial wall motion.

In studying the flow field, we will also assume that blood is a Newtonian fluid and that at the location of interest the flow is axially symmetric. Then, the equations expressed in cylindrical coordinates \( r, \theta, \) and \( z \), with \( z \) along the axis of the vessel, are:

\[
\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial r} + \frac{1}{r} \frac{\partial}{\partial \theta} (ru) + \frac{\partial u}{\partial z} = -\frac{1}{\rho} \frac{\partial p}{\partial r} + \nu \left( \frac{\partial^2 u}{\partial r^2} + \frac{1}{r} \frac{\partial u}{\partial r} + \frac{\partial^2 u}{\partial \theta^2} - \frac{u}{r^2} \right),
\]

\( (1) \)
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\[
\frac{\partial w}{\partial t} + u \frac{\partial w}{\partial r} + w \frac{\partial w}{\partial z} = -\frac{1}{\rho} \frac{\partial p}{\partial z} + \nu \left( \frac{\partial^2 w}{\partial r^2} + \frac{1}{r} \frac{\partial w}{\partial r} + \frac{\partial^2 w}{\partial z^2} \right),
\]

(2)

\[
\frac{\partial u}{\partial r} + \frac{u}{r} + \frac{\partial w}{\partial z} = 0,
\]

(3)

where \( t \) denotes time, \( u \) and \( w \) denote the components of the fluid velocity along the \( r \) and \( z \) directions, respectively, \( p \) is the pressure, \( \rho \) is the mass density, and \( \nu \) is the kinematic viscosity of blood.

Since both the radial velocity and the acceleration are small, we can infer from Eq. 1 that the radial variation of pressure, \( \partial p/\partial r \), is negligible; thus, within the artery the pressure field is essentially a function of \( z \) and \( t \). Therefore, if we measure \( \partial p/\partial z \) along the arterial wall, the pressure will cease to be an unknown variable in the equation system, and the remaining unknown variables, \( u \) and \( w \), can be determined using Eqs. 2 and 3. By a series of mathematical manipulations these equations can be transformed into the following forms, which are suitable for numerical integrations:

\[
\frac{\partial w}{\partial t} = F(z, t) + \left( \frac{\partial R}{\partial \eta} \right) \left( \frac{\partial u}{\partial \eta} \right) + \frac{\nu}{R^2} \left( \frac{\partial^2 w}{\partial \eta^2} + \frac{1}{\eta} \frac{\partial w}{\partial \eta} \right),
\]

(4)

\[
u u = -\left( \tan \psi + \rho F_0 \frac{\partial R}{\partial \eta} \right) \left[ \frac{\partial R}{\partial \eta} \int_\eta^1 \eta \left| \frac{w}{\partial \eta} \right| \mathrm{d\eta} - \int_0^\eta \frac{w}{\partial \eta} \mathrm{d\eta} \right] \bigg/ \int_0^1 \eta \left| \frac{w}{\partial \eta} \right| \mathrm{d\eta},
\]

(5)

where \( F(z, t) = -\rho^{-1} \partial p / \partial z \), \( R = R(\eta, t) \) denotes the inner radius of the artery, \( \eta = r/R \) denotes the normalized radius of the artery. In Eq. 5, \( \tan \psi \) represents the natural taper of the artery, and \( \rho F_0 \partial R / \partial \eta \) expresses the arterial taper generated by the pressure wave. The factor \( \partial R / \partial \eta \) is the derivative of the radius with respect to \( \rho \). The remaining terms are related to the axial velocity distribution and the radial velocity of the arterial wall, \( \partial R / \partial t \), which can be obtained from the pressure wave and the pressure-radius function.

Since all explicit dependence on \( z \) has been eliminated from Eqs. 4 and 5, it is not necessary to specify the boundary conditions in the \( z \) direction. However, these equations still have to satisfy the boundary conditions

\[
w|_{z=1} = 0 \quad \text{and} \quad \frac{\partial w}{\partial \eta} \bigg|_{\eta=0} = 0.
\]

(6)

Furthermore, Eq. 5 reduces to \( u = \partial R / \partial t \) at \( \eta = 1 \), thus satisfying the condition that on the wall the radial velocity of the fluid must be equal to the velocity of the wall.

After this set of equations has been written in the finite-difference form, the equations can be integrated numerically at a fixed \( z \) to obtain \( w \) and \( u \) as functions of radius and time. (For further details, see refs. 7 and 8.)

Methods

EXPERIMENTAL PROTOCOL

Eight dogs weighing 23.2-31.6 kg (average 27.7 kg) were studied under sodium pentobarbital anesthesia (approximately 30 mg/kg, iv). The dogs were thoracotomized, and ventilation was maintained with a positive-pressure respiratory pump. Heparin was administered intravenously (approximately 100 U.S.P. units/kg) to prevent blood clotting. Throughout the experiment, dextran was given (approximately 60 drops/min) intravenously to replace the fluid lost from the circulatory system. In addition, intravenous infusions of dipyridamole were administered in various doses (160-200 \( \mu \)g/min) to increase coronary blood flow.

For measurement of both the pressure and the pressure gradient, two taps were made in small branches of the left circumflex coronary artery. These taps were connected to two Statham P23Gb pressure transducers through two stiff nylon catheters (1.2 mm, i.d.) and a special duplex three-way valve as shown in Figure 1. The duplex three-way valve provided the means for obtaining both the "forward" and the "backward" pressure-difference signals either by connecting the first transducer, \( p_1 \), to the proximal tap, \( p_p \), and the second transducer, \( p_2 \), to the distal tap, \( p_d \), or by reversing these connections. The average distance between the cannulated branches was 2 cm. Any branch between the two pressure taps was ligated. Each of the catheters was tipped with a 1 cm long 22-gauge hypodermic needle. After insertion into the arterial branches, the needles were tied to the heart at two points. Wet sponges were placed along the catheters to dampen their motions. Flushing of the system was accomplished by connecting the first transducer, \( p_1 \), to a drip bottle containing deaerated saline solution. This setup enabled us to flush the system periodically during the experiment.

An electromagnetic flowmeter (Micron Instruments Inc.) was used to monitor left circumflex flow in six dogs. Whenever there was enough space between the proximal
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nary artery, an electromagnetic flowmeter probe was pressure tap and the origin of the left circumflex coro-

end of an experiment, a hot-film velocity probe (11) was placed at this location, as indicated in Figure 1, to monitor the flow rate continuously. However, when this space was less than 1 cm, the electromagnetic flowmeter probe was placed proximal to the proximal pressure tap, \( p_p - p_d \) = distal pressure tap.

Six basic signals were recorded on FM magnetic tape: (1) the event-code signal, (2) the electrocardiograph signal, (3) the forward or backward pressure-difference signal, (4) the proximal pressure signal, (5) the distal pressure signal, and (6) the electromagnetic flowmeter signal. The event-code signal was created by an event-code generator that provided the identification number for the beginning and the ending of a file of recorded data. The electrocardiograph signal provided the means for separating the serially recorded signals into individual heart beats. The forward pressure-difference signal was the difference of the first pressure transducer with respect to the second transducer, \( p_s - p_d \). After the pressure connections through the duplex three-way valve were reversed, the backward pressure-difference signal was obtained. These difference signals were obtained through a precision differential operational amplifier. Because the pressure-difference signal was a small fraction of the pressure signal, it was magnified by a factor of two or five through the operational amplifier to utilize the maximum range of the tape recorder. Two separate data files were required to record the forward and the backward pressure-difference signals, with each file containing a minimum of 30 heart beats. To minimize any change in heart rate during the recording period, the two files were normally recorded immediately one after the other. Also to avoid possible loss of data due to irregularity of heart beats during any one recording, one or two extra sets of recordings were usually made. Since the hot-film velocity measurement could not be performed simultaneously with the recording of pressure signals, it was generally recorded immediately after the last pressure-difference measurement as a separate file with the electrocardiograph signal.

Three or four times during each experiment, the viscosity of blood, \( \mu \), was measured by a cone-and-plate viscometer. The values of viscosity varied between 0.04 and 0.05 poise.

**CALIBRATION OF INSTRUMENTS**

The pressure transducers were calibrated both statically and dynamically. The static calibration was performed by setting the duplex three-way valve to an intermediate position where the pressure transducers were disconnected from the pressure taps and connected to the drip bottle. Then, by raising and lowering the drip bottle to known heights, the transducers could be calibrated. One gauge was first adjusted to an output level for maximum utilization of the range of the FM magnetic tape, and the second gauge was then adjusted to track the first one. Fine adjustment of both zero bias and gain was performed by observing the magnified difference of the output of the gauges through a precision differential amplifier. In one of its positions, the duplex three-way valve connected both transducers to the distal pressure tap. This position was used for the dynamic calibrations of the transducers during the experiment. Since both pressure transducers were connected to the same pressure source, ideally the outputs of the two transducers should have been identical and their difference should have been zero. Thus, the operating condition of the system was determined two or three times during each experiment by observing the magnified difference of the two signals through the precision differential amplifier. The individual dynamic response of each measuring system was also tested. The damped natural frequency was around 100 Hz, and the damping coefficient was 0.2, which was considered adequate for our purposes.

The electromagnetic flowmeter was calibrated by passing a known volume of blood through a segment of the artery at the end of the experiment. The zero flow was obtained during the experiment by occluding the artery distal to the flow probe. The cutoff frequency for the flow signal throughout the experiments was set at 10 Hz, which reduced the amplitude of the flow signal by 30% at this frequency (12).

**DETERMINATION OF THE PRESSURE-RADIUS FUNCTION**

Both the arterial wall taper and the pressure radius data were obtained in vitro. At the end of each in vivo experiment, the segment of coronary artery under study was marked off with two suture lines 2 cm apart. The segment was checked for leaks and then excised. The unstressed length \( l_s \) between the two suture marks was measured. This procedure provided the necessary information for normalizing all longitudinal extensions, \( \lambda_l = l/l_s \). In most cases, the in vivo \( \lambda_l \) had a value close to 1.4. The segment of the coronary artery was then mounted on

**FIGURE 1**

Physical setup for pressure and pressure-gradient measure-
ments in the left circumflex coronary artery. The pressure transducers, \( p_1 \) and \( p_2 \) with purging valves and the duplex three-way valve are shown on the left and right sides of the heart, respectively. An electromagnetic flow probe was placed proximal to the proximal pressure tap, \( p_p \).

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The overall range of mean pressure and flow encountered in the eight dogs studied varied from 100 to 130 mm Hg and 58 to 427 ml/min, respectively. We selected a few representative cases from four dogs to demonstrate the wide range of flows and shear stresses encountered in the coronary arteries of open-chest dogs. These four dogs henceforth will be identified as dogs A-D.

The pressure-radius functions of the left circumflex coronary artery of these four dogs are shown in Figure 2. The arterial pressure is shown as the ordinate and the circumferential extension ratio, $\lambda_2$, is shown as the abscissa. Here $\lambda_2$ is the ratio of the inner radius $R$ to the undeformed inner radius $R_0$ of the artery. It can be seen that the pressure-radius function is nonlinear within the pulse pressure range of the in vivo experiment.

The complete flow field for the left circumflex coronary artery of dog A is shown in Figure 3. The dog had a mean left circumflex flow of 75 ml/min, a mean pressure of 120 mm Hg, and a pulse pressure of 15 mm Hg. The computed velocity profiles for this dog are shown in Figure 3a, where $T = 0.41$ seconds is the cardiac period and $\tau = t/T$ represents the normalized time. The radial distance $r$ is normalized by the instantaneous inside radius $R(\tau)$, and the axial velocity $w$ is normalized by the maximum center-line velocity $w_m = 53.9$ cm/sec.

Results and Discussion

The overall range of mean pressure and flow encountered in the eight dogs studied varied from

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The velocity profiles at peak flow are almost parabolic in form. At end-systole the velocity near the wall becomes negative. The associated centerline velocity wave is shown in Figure 3b. The profiles of radial velocity $u$ are shown in Figure 3c. They have relatively large negative peaks at $r/R = 0.7$, thus indicating a transfer of momentum away from the wall. The radial velocity of the arterial wall is plotted in Figure 3d; except for a few large spikes, the magnitude of this velocity is very small throughout the cardiac cycle. The pressure-gradient wave is shown in Figure 3f. It has a mean value of -0.254 mm Hg/cm. The circumferential extension ratio, $\lambda_2$, as a function of the cardiac period is depicted in Figure 3g. The dynamic extension of the arterial wall is approximately 4%. The calculated velocity-gradient wave at the wall of the artery is shown in Figure 3h. Throughout diastole it maintains an average value of 800/sec, which when multiplied by the viscosity of blood, 0.04 poise, develops a wall shear of 32 dynes/cm². This behavior of the shear wave is different from that of other
arteries in which the peak shear stress occurs only for a short period during systole. Thus, even under normal flow conditions the coronary intima is subjected to a longer period of relatively high shear stresses. The value of the mean pressure gradient contributed by the wall shear can be obtained from the fact that the frictional force acting over a unit length of the arterial wall, \(2\pi \mu R \left( \frac{\partial w}{\partial r} \right)\), has to be balanced by a pressure-gradient force of \(\pi R^2 \frac{\partial p}{\partial z}\). Hence, the mean pressure gradient contributed by the wall friction can be expressed as \(2\mu R \left( \frac{\partial w}{\partial r} \right)\). For the present case, the value of the mean pressure gradient contributed by wall shear stress is \(-0.204\) mm Hg/cm, which is very close to the total mean pressure gradient shown in Figure 3f. This fact indicates that the major part of the pressure gradient, in this particular case, is used to overcome the wall friction; only a minor part goes to balance the convective accelerations. This behavior is opposite to what is observed in the thoracic aorta (8) and can be explained by the fact that the left circumflex coronary artery is both smaller and stiffer than the aorta. The computed flow wave, \(q\), is shown in Figure 3i. It produces a net flow of \(Q = 0.51\) ml/stroke. The corresponding flow wave measured by an electromagnetic flowmeter is also shown in the figure as the dotted curve. The agreement between the two flow curves is reasonable; however, because of the low frequency response of the flowmeter, the electromagnetic flow signal lacks the dynamic details.

Results from dog B are shown in Figure 4. This

\[ r = 0.97 \]
\[ T = 0.47 \text{ sec} \]
\[ w = 196 \text{ cm/sec} \]
\[ T = 0.01 \]

\[ R = 0.09 \text{ cm} \]
\[ \lambda = 0.97 \text{ mm Hg/cm} \]
\[ Q = 0.95 \text{ ml/stroke} \]
case demonstrates the effect of moderate vascular dilation produced by intravenous infusion of dipyridamole at a rate of 160 μg/min. The mean left circumflex coronary artery flow is 120 ml/min, the mean pressure $p$ is 126 mm Hg, and the pulse pressure is 42 mm Hg (Fig. 4e). The average value of the velocity gradient at the wall during diastole is approximately 4000/sec (Fig. 4h), which is equivalent to a wall shear stress of 160 dynes/cm². This finding shows that even with a moderate mean flow it is possible to have large wall shear stresses which are sustained through diastole. Finally, note that the flow wave, as shown in Figure 4i, is independently verified by an electromagnetic flowmeter measurement, and the agreement between the two flow curves is reasonable except for dynamic details.

Results from dog C are shown in Figure 5. This dog was a large German shepherd (31.6 kg) with a large left circumflex flow of 427 ml/min induced during intravenous infusion of dipyridamole (200 μg/min). This flow represents the highest flow encountered in our study. The mean pressure $p$ during dipyridamole administration was 111 mm Hg, and the pulse pressure was 31 mm Hg (Fig. 5e). As can be seen in Figure 5a, the axial velocity profiles for this dog are more blunt than those for

![Figure 5](http://circres.ahajournals.org/)

**FIGURE 5**

Complete flow field in the left circumflex coronary artery of dog C with large flow rate due to intravenous infusion of dipyridamole. See Figure 3 for explanations. The dotted curve in b represents the measured center-line velocity. The dashed curves in e, h, and i represent the control state prior to infusion of dipyridamole.

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dog A. The center-line velocity wave is shown in Figure 5b; it was independently verified using a hot-film anemometer as indicated by the dotted curve, and the agreement between the two velocity curves is good. The pressure gradient of this dog, as shown in Figure 5f, is large and always negative. It has a mean value of $-4.532 \text{ mm Hg/cm}$, which is approximately 18 times that of dog A. The calculated velocity-gradient wave at the wall is shown in Figure 5h. It has a peak value of $9000/\text{sec}$, which corresponds to a peak wall shear stress of 360 dynes/cm$^2$. This shear stress is within the range of yield stress, approximately 400 dynes/cm$^2$, of endothelial cells determined by Fry (1). The mean pressure gradient computed for the wall-friction effect is approximately one-half of the total mean pressure gradient shown in Figure 5f. Therefore, the remaining half of the pressure gradient is used to balance the convective accelerations.

Before the infusion of dipyridamole, the mean left circumflex coronary artery flow of dog C was $0.87 \text{ ml/stroke}$ or $141 \text{ ml/min}$ and the mean pressure was $127 \text{ mm Hg}$ with a pulse pressure of $19 \text{ mm Hg}$, as can be seen from the dashed curves in...
Figure 5e and i. Also, the magnitudes of both the shear wave and the flow wave indicated by the dashed curves in Figure 5h and i during the control state were much smaller than those obtained during the infusion of dipyridamole.

Results from dog D are shown in Figure 6. As indicated in Figure 2, this dog has the stiffest arterial wall. The mean pressure under the control state was 129 mm Hg and the pulse pressure was 15 mm Hg (Fig. 6e). There is a large dicrotic notch on this pressure wave. The corresponding pressure wave after intravenous infusion of dipyridamole (200 μg/min) is also shown as the dashed curve in Figure 6e. The mean pressure was reduced to 118 mm Hg and the pulse pressure was increased to 25 mm Hg. The dynamic circumferential extension of the arterial wall is only 1.2% (Fig. 6g). Because of the low distensibility of this artery, the flow waves are modified from their usual form, as indicated by the peaking flows, during systole and diastole (Fig. 6i). In view of the large retrograde flow, the velocity profiles, as shown in Figure 6a, are blunter than those in the previous cases. Again due to stiffness of the vessel wall, the value of the mean pressure gradient due to wall shear stress (Fig. 6h) is very close to the total mean pressure gradient shown in Figure 6f. With infusion of dipyridamole, both the wall shear and the flow were greatly increased (dashed curves in Figure 6h and i). The increased flow wave was measured with an electromagnetic flowmeter. This wave is shown by the dotted curve in Figure 6i. The lack of dynamic similarity between the measured and the calculated flow waves is partly due to the low frequency response of the flowmeter and partly due to the fact that the electromagnetic flow probe was applied subsequent to the pressure-gradient measurement. In any case, the mean value of the calculated flow (0.90 ml/stroke) is close to the mean value of the measured flow (1.06 ml/stroke).

It is of interest to consider whether these flow fields could have been accurately computed using the linear theory of blood flow (13, 14). In the linear theory, the force due to the mean longitudinal pressure gradient is balanced solely by the mean frictional forces at the wall, since the force due to convective acceleration is neglected. To the extent that these two forces are not equal, as in dogs B and C, the use of linear theory is not justified. For instance, for dog B the value of the average flow as determined by the linear theory would be 2.29 ml/stroke, but the corresponding values determined by the nonlinear theory and by the electromagnetic flowmeter are 0.95 and 0.72 ml/stroke, respectively. In contrast, for dog A in which most of the average pressure gradient is used to overcome wall friction, the discrepancy between the flows calculated by the linear theory (0.73 ml/stroke) and the nonlinear theory (0.51 ml/stroke) is not so pronounced.

Comparison of the velocity-gradient waves with the corresponding flow waves for each dog shows a definite similarity of form between these two sets of curves. This observation led us to plot Figure 7. In this figure \( \frac{q_{ave}}{R_{ave}^3} \) is plotted against \( S_{ave} \) for all cases studied. Here \( q_{ave} \) and \( R_{ave} \) represent the mean values of left circumflex coronary artery flow and radius, respectively, during a cardiac cycle, and \( S_{ave} \) represents the mean diastolic wall shear. The "consistency parameter," \( \frac{q_{ave}}{R_{ave}^3} \), is commonly used in rheological studies and is proportional to the wall shear for Poiseuille flow (14, 15). Although the flow in the present study was pulsatile, we used this parameter to normalize the effect of various radii among dogs. The straight line in the figure represents the linear regression line for the data. Since the mean coronary flow and the radius can be estimated in man, this figure could be used to predict, to a first approximation, the average diastolic wall shear in man.

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