Flow Separation in the Renal Arteries

Hani N. Sabbah, Earl T. Hawkins, and Paul D. Stein

To determine the nature of the flow in the proximal portion of the renal arteries, a common site for the development of atherosclerosis, we performed pulsatile flow studies in a clear acrylic mold of a normal human aorta and renal arteries. The mold was developed from a cast of the renal arteries prepared in situ during the autopsy of a 27-year-old woman. Flow in the mold was visualized by the illumination of bouyant particles (100 to 300 μ). A range of branch (renal) to trunk (aorta) flow ratios of 0.053 to 0.350 was studied. Flow separation during systole was considered present when particles near the wall reversed direction. Flow separation occurred throughout systole at the superior aspect of the origin of both the left and right renal arteries at a branch-to-trunk flow ratio of 0.053. As the branch-to-trunk flow ratio increased, flow separation occurred during the deceleration phase of right renal flow. At a branch-to-trunk flow ratio of 0.350, flow separation was no longer present. This suggests that flow separation may occur near the renal ostia if renal flow falls appreciably while aortic flow remains elevated. Because flow separation involves low wall shear, mass transfer across the arterial wall may be adversely affected and possibly contribute to the formation of atheroma. (Arteriosclerosis 4:28–33, January/February 1984)

stenosis of the renal artery is most commonly produced by atherosclerosis.1 Within the renal artery the proximal 1 or 2 cm of the main renal artery is typically the site of maximal atherosclerotic involvement.1 In an autopsy study of 500 cases, ranging in age from 0 to 80 years, evidence of atherosclerosis in the renal arteries was first found in the second decade of life in the form of fatty streaks.6 In the second decade of life, 43% of cases showed renal atherosclerosis, and by the sixth decade, 82% of cases showed renal atherosclerosis.2

The predilection of specific locations in the arterial system to develop atherosclerosis has provoked numerous suggestions that mechanical forces related to the dynamics of local blood flow may influence the formation of atheroma. Various fluid dynamic factors including high shear stresses, low shear stresses, turbulence, and flow separation have been implicated. In 1968, Fry demonstrated that exposure of the endothelial surface to shear stresses in excess of 350 to 400 dynes/cm², for periods as short as one hour, resulted in a marked deterioration of the endothelial surface, with endothelial cytoplasmic swelling, cell deformation, cell disintegration, and finally dissolution and erosion of cell substance. Chronic exposure of the arterial endothelial surface to lower shear stresses also caused marked endothelial cell proliferation and distortion of the subjacent fibrillar architecture and occasionally caused subendothelial lipid deposition.4 Postmortem studies by Caro and associates on human arteries led them to propose that the mass transfer of lipids across the arterial wall was adversely affected in regions of low shear. Observations by Caro and Nerem suggested a dependence of the flux of 14C-4-cholesterol across the arterial wall upon the local level of wall shear. The presence of flow separation at branching points and bifurcations is considered to be one form of hydraulic disturbance that contributes to atherogenesis at these sites.7–10 It was suggested that the formation of atheroma in zones where local stasis is produced due to flow separation supports the view that atherogenesis is due to a process of deposition, or thrombosis, from the circulating blood. Although many investigators have described the behavior of flow near branching points using models that simulate the arterial geometry, few studies have been performed with exact molds of human arteries.11,12 The purpose of this investigation was to describe the character of flow in the proximal renal arteries using an exact mold of a human aorta and renal arteries. Special emphasis was placed upon the determination of whether flow separation occurred during pulsatile flow.
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Sabbah et al.

Methods

Preparation of the Renal Mold

A cast of a segment of the abdominal aorta and left and right renal arteries was prepared in situ during the autopsy of a 27-year-old woman who died of bacterial endocarditis. At autopsy, the descending aorta was cross-clamped approximately 10 cm above the renal arteries, divided, and cannulated. The left and right common iliac arteries were also divided and the segment was flushed thoroughly with saline after which the common iliacs were clamped. A liquid casting plastic (Ward's, Rochester, New York) was injected into the segment at a pressure of 100 mm Hg. The perfusion pressure (100 mm Hg) was maintained until the plastic hardened. The segment was then dissected from the body and the plastic replica was removed. The kidneys were removed leaving a 3- to 4-cm length of the renal arteries. A flow-through mold of the renal cast was manufactured commercially (Diversiform, Detroit, Michigan) from clear acrylic resin using a modified method of the lost wax technique. A photograph of the flow through mold is shown in Figure 1.

Pulsatile Flow Studies

The renal mold was incorporated into a pulse duplicating system which we previously described in detail. Using the pulse duplicating system, we were able to reproduce a phasic pattern of renal flow comparable to that observed in dogs and also comparable to renal velocity reported in humans. Flow in both renal arteries and in the aorta proximal to the renal arteries was measured with cannulating electromagnetic flow transducers (Biotronex Laboratories, Incorporated, Kensington, Maryland). Typical phasic patterns of flow in the left and right renal arteries obtained in the pulse duplicating system are shown in Figures 2 and 3. The phasic pattern of aortic flow proximal to the renal arteries (Figure 3) contained a positive component of flow during diastole. This component of flow was introduced into our model to ensure proper physiological division of systolic and diastolic flow in the renal arteries.

Studies were performed at pump rates of 65 to 68 strokes/min (Figure 2) and at a pump rate of 98 strokes/min (Figure 3). Mean flow in each renal artery was varied from 200 to 600 ml/min while maintaining equal flow in both arteries. Proximal aortic flow was varied from 1000 to 3800 ml/min. The magnitude of renal flow was based upon observations in normal subjects by others. In normal subjects, total renal blood flow was determined using the p-aminohippuric acid clearance method. Based upon such measurements, mean total renal flow was 1260 ml/min with a range of 834 to 1605 ml/min.

Flow Visualization

The fluid used in the system was a mixture of glycerin and saline with a viscosity of 0.04 poise. The
density of the test fluid was 1.16 g/cm³. Flow in the renal arteries was visualized by the illumination of bouyant particles added to the test fluid. Amberlite ion exchange resin was screened through a series of sieves to collect particles with a diameter of 100 to 300 μ. The patterns of flow were photographed with a 16 mm motion picture camera at 10 and 100 frames/sec. A camera speed of 10 frames/sec was used to induce "streaking" which defined the path of a given particle over a period of time on a single frame of the film. Timing of the frames of the film with the analog record of renal flow was achieved using a model 628 BX timing pulse generator (Visual Instrumentation Corp., Burbank, California) coupled to both the camera and the analog recorder.

Data Reduction and Analysis

Motion picture films of the pattern of flow in the renal arteries were analyzed with a stop-frame analytic projector. Flow separation was defined based upon the pathline of particles and was considered present when particles near the wall reversed direction during systole (Figure 1). The branch-to-trunk flow ratio was calculated as the ratio of flow in one renal artery to flow in the aorta. For the range of aortic and renal flow studied, the branch-to-trunk flow ratio ranged between 0.053 and 0.350. The Reynolds number was calculated as \( \rho VD/\mu \); where \( \rho \) is the density of the fluid, \( V \) is mean velocity, \( D \) is diameter and \( \mu \) is viscosity of the test fluid. The Reynolds number in the aorta was based upon the aortic diameter measured 2 cm proximal to the renal arteries. In the renal arteries, the Reynolds number was based upon the diameter of the artery measured 0.5 cm distal to the ostium. The frequency parameter \( \alpha \) was calculated as \( R \omega / \nu \); where \( R \) is the radius of the artery at the same location as used to measure the diameter for calculation of the Reynolds number, \( \omega \) is the pulse rate (sec⁻¹) calculated as the (stroke rate × 2π)/60 and \( \nu \) is the kinematic viscosity calculated as \( \mu/\rho \). To assess the presence of flow separation during systole, systolic flow was divided into three phases: an acceleration phase, peak flow, and a deceleration phase as shown in Figure 2.

Results

Secondary flows (spiraling) occurred in both the left and right renal arteries at all levels of flow ratios studied. Secondary flows were very prominent during systole but were markedly diminished or disappeared during diastole. Typical examples of secondary flows in the renal arteries observed during peak renal flow at flow ratios of 0.120 and 0.160 are shown in Figures 4A and B respectively.

Flow separation as it related to the branch-to-trunk ratio, Reynolds number, and the frequency parameter \( \alpha \) is summarized in Table 1. Whenever flow separation occurred, it was always located near or at the origin of the renal arteries at the superior aspect of the wall (Figure 5). Flow separation was present throughout systole at a branch-to-trunk flow ratio of 0.053. As the branch-to-trunk flow ratio increased, flow separation occurred at peak flow and during the deceleration phase of flow in only the right renal artery (Table 1). With a further increment of the branch-to-trunk flow ratio to 0.175, separation occurred only during the deceleration phase in the right renal artery. Flow separation was no longer present when the branch-to-trunk flow ratio reached 0.35. Figure 5 shows a diagrammatic reconstruction of particle pathlines visualized at 100 frames/sec near peak flow at a branch-to-trunk flow ratio of 0.053. The size of the separated region varied only slightly during the various phases of systolic flow. However, it decreased markedly with increasing branch-to-trunk flow ratios.
Increasing the pulse rate from 65 to 98 strokes/min, which increased the frequency parameter \( a \) in the renal arteries from 3.3 to 4.0, had no effect upon flow separation in terms of increasing or decreasing the incidence of its occurrence. The presence or absence of flow separation, instead, appeared to be dependent upon the level of the branch-to-trunk flow ratio (Table 1).

**Discussion**

Observations in this study suggest that flow separation, a fluid dynamic disturbance thought by some to be a factor in atherogenesis, can occur in the renal arteries and is dependent upon the branch-to-trunk flow ratio. Our observations suggest that flow separation is more likely to occur in humans near the renal ostia under conditions where renal flow decreases while aortic flow remains elevated or increases. Exercise might be one such condition, for example, because cardiac output may increase 300% while renal flow may decrease 50% to 80%.17

Flow separation at sites of arterial branching and bifurcations was studied by many investigators using idealized arterial geometries during both steady and pulsatile flow conditions.7-10,18-21 To our knowledge, however, use of arterial molds that duplicate the exact geometry of human arteries is rare.11,12 El Masry et al.18 demonstrated flow separation in models of arterial branches both during steady and pulsatile flows. They suggested that flow separation could be induced through an alteration of the branch-to-trunk flow ratio or by an increase in flow rate. Flow separation throughout the entire cycle in their study occurred at flow ratios of 0.15 and 0.30 in models that simulate the aortic bifurcation.18 LoGerfo et al.,19 using a model of the carotid bifurcation indicated that flow separation during steady flow occurred at a flow ratio of 0.28. Similar observations during pulsatile flow were also made by Ku and Giddens20 using a model of the carotid bifurcation. They observed flow separation throughout the entire cycle at a branch-to-trunk flow ratio of 0.25. Velocity measurements with laser Doppler anemometry and numerical calculation of laminar flow in a plane 90° bifurcation were made by Liepsch and associates22 using an in vitro steady flow system. Flow separation was observed at the superior aspect of the branch for branch-to-

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**Table 1. Relationship of Flow Separation to Flow Ratio, Frequency Parameters \( a \), and Reynolds Number**

<table>
<thead>
<tr>
<th>Stroke rate (min(^{-1}))</th>
<th>Proximal aortic flow (ml/min)</th>
<th>Renal flow (ml/min)</th>
<th>Branch-to-trunk flow ratio</th>
<th>Frequency parameter ( a )</th>
<th>Reynolds number</th>
<th>Flow separation (S)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Right renal</td>
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<tr>
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<td>200</td>
<td>0.053</td>
<td>3.3</td>
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<td>303</td>
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<td>441</td>
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<td>200</td>
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<td>6.8</td>
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<tr>
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<td>350</td>
<td>0.117</td>
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<tr>
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<td>600</td>
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<td>4.0</td>
<td>8.2</td>
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</tbody>
</table>

ACC = acceleration phase of systolic flow; Peak = peak flow during systole; Dec = deceleration phase of systolic flow.

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**Figure 5.** Diagramatic reconstruction of the pathline of particles observed near peak flow at a branch-to-trunk flow ratio of 0.053 indicating sites of flow separation near the origin of the renal arteries along the superior aspect of the wall.
trunk flow ratios ranging from 0.23 to 0.64 and an inlet Reynolds number of 250 to 1130. Even though the site of flow separation is consistent with our observation, prominent differences in methodology exist between the two studies. Liepsch et al. used a two-dimensional model. The branch was exactly 90° to the trunk with sharp corners at the site of branching which may be conducive to flow separation. Steady flow was used, and only a single branch was modelled. In all of these studies, flow separation occurred at higher branch-to-trunk flow ratios than that demonstrated in our study. It should be emphasized, however, that the geometry of the models tested was markedly different, often simulating different arterial segments, so that a direct comparison with our results is not always applicable.

Ku and Giddens showed phasic differences of the size of the separated region in a model of the carotid bifurcation. In their study, flow separation was first observed during the increasing velocity phase (acceleration of flow) along the outer wall. Near peak velocity, the separation zone moved toward the inner wall indicating a growing separation region. The separation zone grew further during the deceleration phase. In our study, flow separation throughout systole was observed only at a flow ratio of 0.053. Only slight variations in the size of the separated region could be identified during the various phases of systole. The variability throughout systole was never as prominent as observed by Ku and Giddens. Again differences in the anatomy of the arterial segments used in both studies may readily account for the observed differences.

Our phasic pattern of aortic flow proximal to the renal arteries was somewhat different during diastole than velocity patterns reported by Mills and associates in humans in that our system contained a positive component of diastolic flow. The higher flow during diastole in the aorta proximal to the renal arteries was introduced in our model to produce physiological diastolic renal flow. Because aortic flow was not physiological during diastole, only observations of flow separation during systole were reported in this study.

The maximal rate of rise of renal flow during systole in our model was lower than that observed in dogs. Whether this difference had an effect upon our observations is uncertain. As we increased the frequency of pulsation from 66 to 98 stroke/min, the peak rate of change of renal flow during systole increased from 26 ml/sec² to 46 ml/sec². The increase in the frequency of pulsation and the concomitant increase in the rate of change of renal flow did not, within this limited range, appear to contribute to or prevent flow separation. This is consistent with observations by others. Guststein and Schneck pointed out, based upon their own observation, that because boundary layer separation is primarily a function of geometry and fluid kinetic energy, the frequency of oscillation is not expected to contribute to or prevent flow separation.

The results of this study indicate the development of localized separated flow at sites with a high predilection for atherosclerosis. The mechanism by which flow separation may contribute to, or initiate atheroma, is not clear. Caro et al. suggested that low wall shear can adversely affect the rate of mass transport of lipids across the arterial wall. Because separated flow regions are inherently low shear areas, the implication would be that an alteration of the near-wall biochemistry may potentially lead to plaque formation. It has been suggested that an adverse effect of low shear on mass transfer results in an accumulation of intimal metabolic products and a deprivation of nutrients at such sites. Regions of flow separation have also been shown in vitro to be sites at which platelet aggregates accumulated. If endothelial injury can occur as a result of the metabolic effects of low shear, then platelet aggregates could adhere to the subendothelium and stimulate smooth muscle proliferation.

We observed prominent secondary flows (spiralising) in the proximal portions of both the left and right renal arteries at all of the branch-to-trunk flow ratios studied. Secondary flows were most prominent during systole, and diminished appreciably or disappeared during the diastolic phase of the cycle, thus suggesting a dependence upon flow rate. Secondary flows have been observed in models of arterial branches and bifurcations. Such secondary flows may result from transverse pressure gradients. Although secondary flows have been observed at arterial branches and at bifurcations, their relevance to atherogenesis, if any, is unknown. It is interesting to note that in an autopsy study of human beings under 40 years of age who died of noncardiovascular causes, Fox et al. demonstrated a spiral distribution of fatty and fibrous plaques in the left anterior descending coronary artery. Whether this observation suggests a role of spiraling of flow in atherogenesis requires further evaluation.

In our study, flow separation was considered to be present when reversal of flow occurred at any time during systole. Because reverse flow may in certain instances, be an integral part of pulsatile flow, some investigators felt it was necessary to distinguish this flow reversal from flow separation. Accordingly, Despard and Miller suggested that for flow separation to be present, flow reversal should occur during the entire cycle. According to such a definition, flow separation would only be present, in our study, at a branch-to-trunk flow ratio of 0.053.

Anatomical variation of geometry at the human renal ostia is certain to play an important role in determining the characteristics of flow at these sites. The renal arteries arise from the sides of the aorta immediately below the superior mesenteric artery. Each is directed outward across the crus of the diaphragm, so as to form nearly a right angle with the aorta. This angle, however, may vary appreciably. We assessed the angle formed between the inferior aspect of the renal artery and the aortic wall from 45...
renal arteriograms illustrated by Bunnell.\textsuperscript{29} The angle varied from 90° to as low as 15° with an average of 60°. In the mold of the renal arteries used in this study, the right renal artery formed a 60° acute angle with the aorta and the left renal artery, a 67° angle. In addition to the angle, other geometric considerations are important in relation to flow separation. In our mold, the superior aspect of the right renal artery arose gradually from the aorta creating an expansion of the aorta at that site; whereas the superior aspect of the left renal artery arose sharply from the aorta (Figure 1). The higher incidence of flow separation at the superior aspect of the right renal artery in comparison with the superior aspect of the left renal artery observed in this study may be attributed to such fine variations of anatomic geometry. Friedman et al.\textsuperscript{30} suggested, on the basis of pulsatile flow studies through molds of human aortic bifurcations of varying geometrical features, that there might be "geometric risk factors" in atherosclerosis. These researchers suggested that variability in the geometric features might contribute to the variability of the focal location and magnitude of fluid dynamic stresses, thus accounting for the variance in arterial disease among individuals. Such a concept of geometric variability is born out to some extent by the differences in the incidence of flow separation observed in our study between the left and right renal arteries. Distinct geometric differences existed between the ostia of both vessels as shown in Figure 1.

In conclusion, in vitro flow visualization in a mold of a normal human aorta and renal arteries showed that flow separation occurred near the renal ostia. The development of flow separation was dependent, in part, upon the branch-to-trunk flow ratio and upon local differences in the anatomical geometric feature present at the renal ostia. The observation of prominent flow separation at low branch-to-trunk flow ratios made in this study, suggest that in humans, conditions which decrease the ratio of renal flow to aortic flow may contribute to flow separation.

References


Index Terms: atherosclerosis • renal arteries • flow separation • secondary flow • shear stress • renal flow
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