Original Contributions

Diagnostic Significance of Flow Separation in the Carotid Bulb

Stephen C. Nicholls, MD, David J. Phillips, PhD, Jean F. Primozich, BS, Ramona L. Lawrence, BS, Ted R. Kohler, MD, Thomas G. Rudd, MD, and D. Eugene Strandness Jr., MD

Pulsatile blood flow within the normal carotid sinus involves at least two distinct components. That near the flow divider is laminar and antegrade, whereas a boundary layer separation zone in the posterolateral aspect exhibits transient blood flow reversal. It is now possible to document these flow velocity components using pulsed Doppler ultrasound methods. When atherosclerosis develops, it preferentially involves the posterolateral bulb region, obliterating the normal configuration of the sinus with consequent loss of the flow separation zone. It was therefore hypothesized that if flow separation could be detected, it should be predictive of a normal angiogram. To assess this, we evaluated 20 symptomatic patients and two with only bruits found by duplex scanning to have flow separation in either one or both carotid bulbs and who also underwent cerebral angiography. Initial diagnoses were stroke in seven, reversible ischemic neurologic deficit in one, transient ischemic attack in 12, and bruit in two. Flow separation was bilateral in 13 patients (59%). There were 15 patients with symptoms in the territory of a carotid bulb exhibiting flow separation. By angiography, of the 35 bulbs with boundary layer separation, 27 (77%) were normal, with the remainder showing lesions that reduced the diameter of the vessel by 20% or less. Final diagnoses of the 15 patients with symptoms ipsilateral to a carotid sinus exhibiting flow separation were fibromuscular disease in two, lacunar stroke in three, dissection in two, subclavian steal in one, cardiogenic embolus in three, migraine in one, hyperventilation syndrome in one, kink of the mid-internal carotid artery in one, and no diagnosis in one. A normal ultrasound image coupled with flow separation in the carotid bulb in patients presenting with presumptive extracranial carotid disease is therefore shown to be associated with minimal or no carotid atherosclerotic disease on angiography and to reliably predict etiology other than carotid artery disease for the symptoms. (Stroke 1989;20:175-182)

Carotid bifurcation disease has been previously quantified by identifying features of blood flow velocity patterns obtained with ultrasound from the proximal internal carotid artery (ICA) and correlating them with the "gold standard" of contrast arteriography. Specifically, peak frequencies and spectral broadening of pulsed Doppler velocity waveforms obtained from center-stream sites in the ICA are features that have been found to accurately predict disease states when compared with angiography. Previous studies have shown that an increase in spectral broadening during systole without a concomitant increase in peak systolic frequency is a useful feature to predict disease states of <50% diameter reduction by arteriography. Peak systolic flow velocities of >120 cm/sec in the proximal ICA correlate well with disease of >50% diameter reduction. This threshold value was empirically obtained using a 5-MHz ultrasound duplex system at a Doppler angle of 60° in the proximal ICA while assuming an axial direction for the flow velocity vector. Thus, we now have the capability of relating the extent of involvement to the presenting clinical events.

Recent ultrasound studies, however, have documented complex secondary flow velocity patterns at the carotid bifurcations in young, presumed normal subjects. These secondary flows consist of helical patterns, flow separation, and transient flow reversals (Figure 1). These flow patterns have now also been demonstrated in pulsatile flow model studies. Figure 2 illustrates the common carotid artery (CCA) and...
ICA with the relative geometric scaling used for a flow model representing an "average" adult human carotid bifurcation. The CCA-ICA branch is shown with a prominent sinus region on the proximal segment of the ICA. Flow patterns in late diastole are schematically shown in Figure 2A. Laminar unidirectional flows are shown across the sinus except for a small flow separation zone (dotted line) along the outer wall opposite the flow divider. During systole, the Reynolds number greatly increases and the local flow patterns are markedly different, as shown in Figure 2B. The size of the flow separation zone changes and can extend three-quarters of the way across the sinus. A transient flow reversal also occurs within the flow separation zone along the wall opposite the flow divider.

The dynamic character of the flow separation zone and the transient flow reversal during systole result from a pulsatile waveform and are not seen in model studies employing continuous flow. A flow separation zone of constant size is found under conditions of continuous flow since the separation zone is produced by a sufficiently high Reynolds number coupled with a flow lumen of changing caliber and curvature. In addition, a circumferential helical secondary flow pattern is generated due to the branch angle imposing a circumferential force on the fluid components to change the direction of the flow (Figure 3). Antegrade unidirectional flow is seen along and near the apical divider during systole, providing the majority of volume flow to the brain. Such secondary flow patterns are complicated and difficult to interpret unless an understanding of their origin is appreciated. The "Subjects and Methods" section will describe a procedure to
acquire flow velocity waveforms within the sinus region to associate these types of flow patterns and when they occur with secondary flow patterns caused by changes in the vascular geometry in an otherwise normal artery.

The complicated flow patterns at a normal carotid bifurcation result from the presence of a branch point, the pulsatile flow character, the fusiform dilation in the proximal ICA at its origin from the CCA, and the differing resistances in the runoff beds of the ICA and the external carotid artery (ECA). It has been observed that the presence of such flow patterns (boundary layer separation resulting in low and/or oscillatory shear rates) correspond to sites where there is a predilection for atheroma formation (primarily the posterolateral aspect of the bulb), the site of maximum convexity. It is hypothesized that progressive deposition of atheroma alters the luminal geometry of the bulb, initially filling in the sinus and converting it to a tube of uniform caliber and later, with further disease progression, encroaching further into the lumen with generation of vortices and flow disturbances characteristic of stenotic vessels (Figure 4). Loss of the fusiform geometry results in loss of the flow separation zone. It is further hypothesized that the presence of flow separation indicates an absence of disease and should therefore be highly correlated with anatomic and clinical disease-free states.

Until now, the detection and quantification of carotid bifurcation disease has been based on anatomic criteria obtained by angiography, which thus constitutes the gold standard against which all subsequent diagnostic methods must be measured. In this study, therefore, we compared flow patterns according to radiologic criteria.

Subjects and Methods

Between June 1983 and March 1985, 20 patients with symptoms and two with bruits had boundary layer separation detected by duplex scanning; angiography was also performed in these 22 patients. The initial diagnoses are shown in Table 1. The angiograms were read independently and classified as normal or abnormal by a radiologist who classified the carotid bifurcation by degree of involvement; in the latter case luminal disease was quantified as diameter reduction in 10% increments. Several methods of quantifying severity of stenosis by angiographic measurements are currently employed. The most commonly used method compares the residual diameter at the site of disease with the distal extracranial ICA diameter from the same arteriographic view (Figure 5); we used this method. Its major advantage is its wide use, enabling comparison of our results with those of other studies; it may not, however, be the optimum method from a theoretical point of view. The two other most accurate and reproducible methods involve measuring the minimum residual lumen diameter (which has the advantage of being simple and reproducible) and estimating the cross-sectional area of the stenosis with other cross-sectional vessel areas.

The hospital course, results of other diagnostic tests, and the final diagnosis for each patient were evaluated. Correlation was sought between the hemodynamic (flow separation), anatomic (angiographic), and clinical (final diagnosis) evaluations. We used a 5-MHz ultrasound duplex system (Mark V ultrasound duplex scanner, Advanced Technology Laboratories, Bothell, Washington) to document the blood flow velocity patterns across the carotid bifurcation. Since we became aware of the phenomenon of flow separation in the normal carotid bulb several years ago, these secondary flow phenomena have been documented by two methods, audible interpretation of the pulsed Doppler signal and gray-scale spectral analysis of the velocity waveform. Both methods rely upon placing the sample volume at

Figure 4. Schematic diagram of hypothesized primary blood flow patterns as function of plaque deposition. A: normal carotid sinus with unidirectional antegrade flow along apical divider, flow separation zone occupying sinus region opposite flow divider, circumferential or helical flow within sinus, and transient flow reversal along outside wall of sinus. Undiseased carotid bulb probably has the most complicated flow patterns of all. B: with minimal to moderate disease, flow separation zone is partially filled, resulting in marked attenuation of secondary flow patterns caused by branch angle and dilated segment of sinus. C: further narrowing reduces effective cross-sectional area within sinus region to less than that of distal internal carotid artery (ICA). This produces increased peak velocities at site of narrowing and small vortices distal to narrowed segment, which are typical of poststenotic secondary flow patterns. ECA, external carotid artery; CCA, common carotid artery; p, proximal; m, mid.
TABLE 1. Clinical Characteristics and Diagnoses in 22 Patients With Boundary Layer Separation Detected by Duplex Scanning

<table>
<thead>
<tr>
<th>Flow separation</th>
<th>Diagnosis</th>
<th>Angiography</th>
<th>Symptoms in territory of FS bulb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>R ICA</td>
</tr>
<tr>
<td>Bilateral flow separation</td>
<td>Stroke</td>
<td>Lacunar stroke</td>
<td></td>
</tr>
<tr>
<td>1/M/42</td>
<td>Stroke</td>
<td>Lacunar stroke</td>
<td></td>
</tr>
<tr>
<td>2/M/67</td>
<td>Stroke</td>
<td>Dissection</td>
<td></td>
</tr>
<tr>
<td>3/M/55</td>
<td>Bruit</td>
<td>Fibromuscular dysplasia</td>
<td></td>
</tr>
<tr>
<td>4/F/45</td>
<td>Bruit</td>
<td>Fibromuscular dysplasia</td>
<td></td>
</tr>
<tr>
<td>5/F/62</td>
<td>Bruit</td>
<td>Fibromuscular dysplasia</td>
<td></td>
</tr>
<tr>
<td>6/M/37</td>
<td>TIA*</td>
<td>Subclavian steal</td>
<td>10-20%</td>
</tr>
<tr>
<td>7/F/61</td>
<td>TIA*</td>
<td>Kink of ICA</td>
<td>10-20% (ECA)</td>
</tr>
<tr>
<td>8/M/61</td>
<td>Stroke</td>
<td>Dissection</td>
<td></td>
</tr>
<tr>
<td>9/M/37</td>
<td>TIA†</td>
<td>Cardiogenic embolus</td>
<td></td>
</tr>
<tr>
<td>10/M/46</td>
<td>Stroke‡</td>
<td>Cardiogenic embolus</td>
<td></td>
</tr>
<tr>
<td>11/F/46</td>
<td>TIA§</td>
<td>Cardiogenic embolus</td>
<td></td>
</tr>
<tr>
<td>12/M/68</td>
<td>TIA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13/F/58</td>
<td>Stroke</td>
<td>Migraine</td>
<td>10-20%</td>
</tr>
<tr>
<td>Unilateral flow separation</td>
<td>TIA* Hyperventilation syndrome</td>
<td>10-20%</td>
<td></td>
</tr>
<tr>
<td>14/M/73</td>
<td>TIA</td>
<td>Not visualized</td>
<td>Not visualized</td>
</tr>
<tr>
<td>15/M/55</td>
<td>TIA</td>
<td>Not visualized</td>
<td>Not visualized</td>
</tr>
<tr>
<td>16/M/59</td>
<td>Stroke</td>
<td>Cardiogenic embolus</td>
<td></td>
</tr>
<tr>
<td>17/M/54</td>
<td>TIA</td>
<td>Lacunar stroke</td>
<td>Not visualized</td>
</tr>
<tr>
<td>18/M/66</td>
<td>TIA</td>
<td>Cardiogenic embolus</td>
<td>70%</td>
</tr>
<tr>
<td>19/M/71</td>
<td>TIA</td>
<td>Cardiogenic embolus</td>
<td>50%</td>
</tr>
<tr>
<td>20/F/49</td>
<td>TIA</td>
<td>Tension headache</td>
<td>10-20%</td>
</tr>
<tr>
<td>21/M/57</td>
<td>TIA</td>
<td>No diagnosis</td>
<td>10-20%</td>
</tr>
<tr>
<td>22/M/67</td>
<td>RIND</td>
<td>No diagnosis</td>
<td>10-20%</td>
</tr>
</tbody>
</table>

Pt, patient; M, male; F, female; age in years; R, right; L, left; TIA, transient ischemic attack; ICA, internal carotid artery; ECA, external carotid artery; symptoms referable to territory of carotid bulb exhibiting flow separation; Angiography, disease as % reduction of lumen diameter; FS, flow separation.

*Vertebrobasilar TIAS.
†Amaurosis fugax.
‡Retinal artery occlusion.
§Aphasia.
||Sensorimotor loss.

Specific anatomic locations within the sinus region to assess the flow velocity character.

Figure 6 schematically illustrates the human carotid bifurcation. The CCA bifurcates and provides flow to the high-impedance vascular bed of the ECA and to the relatively low-impedance bed of the ICA. The proximal 1–2-cm segment of the ICA is usually characterized by a dilatation of the sinus region, where atherosclerotic disease tends to develop. The ECA is shown in Figure 6 by dashed lines to point out that the parent vessel and its two daughter branches do not generally lie in the same plane. The dotted lines in the CCA and ICA represent the central axes of these arteries. Since two intersecting lines in a three-dimensional space define a plane, it is convenient to define the bifurcation plane by the axes of the CCA and ICA. This plane serves as an anatomic reference by which the pulsed Doppler sample volume can be placed to assess the flow velocity character in the proximal ICA.

As demonstrated in Figure 7, the technologist surveys the bifurcation and then adjusts the ultrasound scanning plane to include the axes of the CCA and ICA (and thus the bifurcation plane as previously defined). Assuming that the ICA is in the bifurcation plane, Location 1 represents flow along the apical divider and is 2 mm from the vessel wall to eliminate velocity gradients within the boundary...
layer; Location 2 represents a center-stream site within the proximal ICA or bulb and is equidistant between the walls of the sinus as defined by the tissue image; Location 3 is opposite the flow divider along the outside wall of the bifurcation but 2 mm or so from the vessel wall to reduce boundary layer effects. The technologist records flow velocities from these three locations to characterize blood flow in the proximal segment of the ICA.

Typical flow separation velocity waveforms used to document patients in this study are shown in Figure 7. The flow waveform from a center-stream site in the CCA proximal to the bifurcation is shown on the left. The flow velocity profile is very blunt across this relatively straight portion of the CCA and exhibits spectral broadening only near the vessel walls, where a boundary layer is present. At Location 1, unidirectional flow is seen along the apical divider. At Location 2, the direction of flow abruptly reverses during systole, generally returns to an antegrade flow during the latter phase of systole, and extends throughout diastole. At Location 3, flow reversal occurs during the acceleration phase of systole and persists throughout systole before returning to low or reversed diastolic flow. The flow velocity waveforms obtained from the sinus in Figure 7 document the essential distinguishing features of the flow separation zone and associated secondary flow patterns.

These flow phenomena define patients with flow separation as documented by gray-scale spectral analysis. It is relatively easy for the technologist to survey the carotid bifurcation and to obtain a view containing the bifurcation plane. The sample volume is then positioned at Locations 1, 2, and 3 within the sinus region using the B-mode image as a reference. Several heart cycles are recorded at each anatomic site for spectral analysis and gray-scale printout.

In some patient studies an audible assessment was also employed. Unidirectional continuous flow was noted along the apical divider. At Location 2 a low-frequency "thumping" was noted during systole, with a continuous nonzero flow in diastole. At Location 3, a "thump" of longer duration was present and little or no diastolic flow was heard. The presence of flow separation in the carotid sinus was documented by one or both methods for all patients presented in this study.

The above methods apply to assessment of the proximal ICA, where the sinus region is clear of intraluminal disease as documented by the ultrasound image. Figure 8 shows a longitudinal section of the bifurcation; an intraluminal lesion is clearly evident in the sinus region. Peak flow velocities do not increase at Location 2, indicating that the effective cross-sectional area of the lumen at the level of the sinus is the same as that of the diseased ICA segment distal to the sinus region. Depending on plaque location and geometry, flow separation is possible distal to a plaque for the same reasons outlined earlier. The flow velocity signal obtained at Point A in Figure 8 is downstream (distal) to the lesion, has a broad spectrum throughout systole, and is not in a region of separated flow; at Point B, flow separation eddies occur during systole because of the sudden increase in effective cross-sectional area distal to the lesion coupled with favorable hemodynamic conditions. Thus, it is possible to have flow separation in the presence of disease. However, all three flow velocity waveforms across the sinus (as shown in Figure 7) are not obtained under these circumstances.

Results

In the 22 patients having angiography, flow separation was noted by duplex scan in both carotid sinuses in 13 (59%); nine patients had flow separation confined to one sinus (Table 1). The symptoms in seven (78%) of these nine were referable to the territory of the contralateral carotid artery; that is, symptoms were referable to the territory of a sinus exhibiting flow separation in only two patients. Of the 22 patients, therefore, only 15 had focal symptoms referable to the territory of a carotid sinus exhibiting flow separation (Table 1).

Of the 13 patients demonstrating bilateral flow separation, 10 (77%) showed no atherosclerotic disease as demonstrated by angiography in the arch, bulb, ECA, siphon, or intracranial circulation.
FIGURE 7. Typical blood flow velocity waveforms are shown for proximal center-stream common carotid artery (CCA) site and for three sites across undiseased sinus (proximal internal carotid artery [ICA]). Along apical wall of ICA (Location 1), blood flow is unidirectional and antegrade (similar to CCA waveform). Transient flow reversal during systole is seen at ICA center-stream site (Location 2), along with diastolic blood flow well above baseline. Along outer wall of ICA (Location 3), diastolic blood flow tends toward zero, along with transient flow reversal during systole.

Of the other three patients, one demonstrated 10–20% narrowing in an ECA but had a normal arch, siphon, and intracranial circulation. The other two demonstrated 10–20% narrowing in the carotid sinus but had normal siphons and intracranial circulations; one of these two patients demonstrated a mild (10–20%) subclavian stenosis.

In the nine patients with unilateral flow separation, the angiograms demonstrated increased distribution and severity of disease compared with the patients with bilateral flow separation. The bifurcation displaying flow separation was normal in six of the nine patients and contained lesions of 10–20% diameter reduction in two (both on the posterolateral aspect); the other patient had disease extending into the mid-ICA, where it caused a 10–20% narrowing. The opposite bifurcation was normal in three of the nine patients; in three a 10–20% diameter reduction was noted, and in the other three diameter reductions of 50%, 60%, and 70% of the lumen were noted. One of these three patients had a 10–20% lesion in the innominate artery and a similar lesion in the siphon. No siphon disease was seen in six of the nine (in two the siphon was not

FIGURE 8. Flow separation can also occur in vicinity of intraluminal disease. At such sites, transient blood flow reversals (bottom) are seen during systole along with reduction in diastolic flow. Point B is within flow separation zone just distal to atherosclerotic plaque. Point A is 2–3 mm distal to or downstream from Point B and is out of flow separation zone. Flow patterns can change markedly over short distances. Imaging capability of ultrasound scanner (top) is essential to distinguish flow separation caused by intraluminal disease from that caused by changes in vascular geometry.
visualized). Of the seven arches visualized, six were normal (Table 1).

The final clinical diagnoses of the 15 patients with symptoms on the side of a carotid sinus exhibiting flow separation were made on the basis of cardiologic and neurologic consultation, electrocardiography, computed tomography, echocardiography, and angiography. The final diagnoses were fibromuscular disease in two patients (in one there was a dissection of the mid-ICA causing complete occlusion), lacunar stroke in three, dissection in two, subclavian steal in one, cardiogenic embolus in three, migraine in one, hyperventilation syndrome in one, kink of the mid-ICA in one, and no diagnosis in one (Table 1).

**Discussion**

As blood passes over the luminal surface of an artery, the frictional forces exerted by the wall surface retard the flow velocities in the adjacent layer. The region in which these forces are active is defined as the boundary layer. Fluid elements at a distance from the surface and outside the boundary layer are not affected by these viscous forces. Due to viscous effects, the momentum of blood within the boundary layer is low but increases toward the apical divider. Changes in the geometry of the artery can result in blood moving against the pressure gradient, from low- to high-pressure regions, due to momentum. Blood with relatively low momentum, such as that within a boundary layer, may become stationary or may reverse flow direction when subjected to gradient reversals. Thus, an area of flow separation results and local regions of stagnant and reversed flow can develop. The predilection of atheroma to form at certain sites in the arterial tree has long been noted. Hugh and Fox 10 and Fox and Hugh 11 noted that atheroma occurred principally at curves and the origins of branch vessels, where boundary layer separation occurs. These authors hypothesized that areas of stasis occurring in regions of flow separation permitted the aggregation and interaction of blood components, resulting in local plaque formation.

These static zones may be demonstrated radiographically. In late films of carotid angiograms in undiseased individuals, dye may be seen remaining in the posterolateral aspect of the bulb (Figure 9). The underlying fluid dynamics have been documented in vitro using models with geometry derived from arteriographed carotid arteries, first with steady 6-7 and later with pulsatile 4 flow. Flow profiles were evaluated with rigid scale models using a hydrogen bubble technique and laser Doppler anemometry. Pulsed Doppler ultrasound has now been employed to demonstrate the presence of similar flow patterns generated in humans. Although the pathophysiologic mechanisms remain to be defined, recent evidence suggests that low and/or oscillating shear forces combined with a prolonged residence time of blood components adjacent to the endothelium show high correlation with the sites of maximum disease. 8 In the carotid bifurcation, this corresponds to the posterolateral aspect of the bulb. Disease progression in the carotid bulb appears as a preferential deposition of atheroma in the fusiform portion of the artery. It would appear, therefore, that at a certain stage of disease the effective area of the residual sinus lumen is reduced to the same caliber as the adjacent artery, with a concomitant loss of the separation zone. Further atheroma deposition encroaching on the lumen results in increased velocities and classic poststenotic flow disturbances (Figure 10). Loss of flow separation might therefore be considered an early sign of disease.

The preeminent place that carotid bifurcation disease has assumed in the etiology of focal neurologic deficits has not lessened the necessity for careful evaluation and differential diagnosis of such symptoms. In most symptomatic patients this requires angiography, which has been the accepted standard for defining disease in the carotid bifurca-
Correlation between angiograms and flow velocity signals as function of disease progression in carotid sinus. Top: flow separation with transient reversal in systole and low diastolic flow is associated with prominent sinus region seen by angiography. Middle: proximal segment of internal carotid artery does not show prominent sinus; corresponding flow velocity waveform does not show transient reversal or reduced diastolic flow (i.e., no flow separation zone is present). Bottom: tight stenosis documented by arteriography correlates with high blood flows and marked spectral broadening. This figure should be compared with schematic representation of Figure 4.

tion, and any alternative testing method must demonstrate a high degree of correlation with it. The accuracy of flow separation in predicting the absence of disease as defined by angiography indicates its usefulness in this regard. It should be noted that all our patients proceeded to angiography on the basis of symptoms thought to represent focal neurologic deficits of possible carotid etiology.

Of particular significance is the relation that flow separation has to eventual diagnosis and management. No patient exhibiting flow separation in a carotid sinus was subsequently diagnosed as having carotid bifurcation disease as the etiology of their symptoms, and none was therefore a candidate for endarterectomy.

The documentation of a flow separation zone in the proximal ICA serves as a marker of normality and suggests other mechanisms as the basis for the patient's symptoms. The clinical evaluation of such patients may therefore be expedited, and the need for a carotid angiogram with its attendant morbidity and mortality may be eliminated.

In addition to the benefits of a noninvasive test, the use of flow patterns in determining the presence or absence of disease offers the ability to detect minor or early disease that may nonetheless be biologically or clinically significant. Angiography has been shown to have significant limitations in this regard. Prospective evaluation of patients exhibiting carotid flow separation will be required to demonstrate whether the parameter also predicts a favorable outcome with respect to neurologic events.

References

Key Words • blood flow velocity • carotid sinus • carotid artery diseases
Diagnostic significance of flow separation in the carotid bulb.
S C Nicholls, D J Phillips, J F Primozich, R L Lawrence, T R Kohler, T G Rudd and D E Strandness, Jr

Stroke. 1989;20:175-182
doi: 10.1161/01.STR.20.2.175

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/20/2/175

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/