Diagnostic Significance of Flow Separation Within the Carotid Bifurcation Demonstrated by Digital Subtraction Angiography

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The presence of an area of reversed blood flow due to flow separation in the internal carotid artery is a normal finding in Doppler ultrasound studies in vivo as well as in model carotid bifurcations. This flow separation phenomenon is caused by the geometry of the carotid bifurcation and the fluid dynamics of blood. We demonstrated the flow separation phenomenon on lateral-projection intra-arterial digital subtraction angiograms in 99 of 100 carotid bifurcations. The mean duration of flow separation was 5.8 seconds, with values up to 14 seconds in normal carotid bifurcations. The presence of this flow separation phenomenon is almost independent of atherosclerotic lesions and is not correlated with cerebral ischemia. Therefore, the angiographic finding of a flow separation has no diagnostic value. However, our results refer to a factor that may be important in the genesis of atherosclerosis at the carotid bifurcation, namely the duration of the stay of blood and its components within the area of flow separation. (Stroke 1990;21:1674-1679)

The carotid bifurcation, especially the dorsal wall of the proximal internal carotid artery, is the preferred site for atherosclerosis of the supra-aortic arteries.1 There is no conclusive and definite explanation for this distribution pattern; however, the hemodynamics of the carotid bifurcation is considered to be an important factor in the genesis of carotid artery disease. The hemodynamics induce a so-called flow separation phenomenon, an area of reversed blood flow within the proximal internal carotid artery. This flow separation phenomenon has attracted special interest since it is located exactly in that region where formation of atherosclerotic lesions starts.2,3

Undisturbed blood flow in larger arteries is laminar and has a roughly parabolic distribution of flow velocities across the vessel diameter, velocity decreasing toward the periphery due to friction between the moving blood and the vessel wall. The region immediately next to the wall having the lowest flow velocity and kinetic energy is called the boundary layer, which is one prerequisite for the flow separation phenomenon. The other prerequisite is the sudden increase in vascular diameter at the carotid bifurcation. This increase in diameter results in a loss of flow velocity, which is balanced by an increase in pressure (Bernoulli's law) since, omitting frictional forces, the total energy must be constant. Within the boundary layer the resulting pressure gradient induces a region of blood flow reversal,4 which is called the flow separation phenomenon.

Experimental studies with model and cadaver carotid bifurcations have demonstrated this region of reversed blood flow. The presence and extent of the flow separation phenomenon is influenced by the geometry of the bifurcation, rheologic parameters of the flowing blood, properties of the vessel wall, and especially the ratio of the partial flows, which is significantly influenced by the peripheral resistance.5-7 A number of ultrasound studies have proven the existence of this flow separation phenomenon in vivo, and its presence was even considered to indicate the absence of vascular abnormalities.8-11 In contrast to this, there are very few reports on the angiographic demonstration of the flow separation phenomenon.4,11,12

After the installation of a digital subtraction angiography (DSA) unit in our department, we easily demonstrated the flow separation phenomenon, which we had sometimes observed using conventional angiography. Therefore, we decided to test whether this phenomenon is a routine finding on intra-arterial (IA) DSA of the carotid arteries and if there is a correlation between flow separation and the presence of atherosclerotic lesions or cerebral ischemia.
Flow Separation on IA-DSA

Subjects and Methods

We evaluated the lateral series of IA-DSA studies of 65 unselected patients (41 men and 24 women, mean±SD age 46.6±15.0 years). In 35 patients both and in the other 30 patients only one carotid artery were studied, so altogether 100 carotid bifurcations are included in this study.

In 35 patients IA-DSA was performed as part of the diagnostic work-up after cerebral ischemia. These patients had had the acute onset of a reversible or permanent neurologic deficit; hemorrhage had been ruled out by computed tomography (CT).

The other 30 patients had a brain tumor or had undergone a selective intracarotid injection of amobarbital (Wada test) during the preoperative evaluation of epilepsy. In these patients IA-DSA was performed to rule out lesions of the internal carotid artery before its selective catheterization. Patients with high-flow lesions such as arteriovenous malformations or significantly elevated intracranial pressures were excluded from this study.

The DSA unit (Digitron 2, Siemens AG, Erlangen, F.R.G.) with a 512×512 image matrix was connected to a high-resolution image amplifier (Videomed H, Siemens) with a 17 or 29 cm field of view. The acquisition scheme in all studies was 4 frames/sec for the first 6 seconds, 2 frames/sec for the next 8 seconds, and 1 frame/sec until the 30th second, the x-ray dose/frame being 200 μR. The patient lay supine, and the x-ray beam was directed horizontally. Normally 5 ml (in patients with high-grade stenoses 4 ml) of nonionic contrast medium with an iodine content of 300 mg/ml (Ultravist 300, Schering AG, Berlin, F.R.G.) was injected by hand with maximum force into the common carotid artery proximal to the carotid bifurcation. This injection scheme resulted in complete opacification of the vessels in all patients. Run-off of the contrast medium was followed on the instant subtraction monitor, and acquisition was terminated when no more contrast medium was seen in the carotid bifurcation.

For evaluation, the image series was displayed in an endless loop immediately after IA-DSA. This video replay provided the best method for recognizing the flow separation phenomenon since the images are displayed as a movie. The observations were recorded in a standardized protocol. Measurements were made on hard copies since our DSA unit is not equipped with the software for electronic measurement of distances and angles. We determined the bifurcation angle between the internal and external carotid arteries and the diameter of the common, internal, and external carotid arteries. Depending on the image amplifier’s field of view and the patient’s position, the enlargement factor varied widely and could not be determined accurately. Therefore, we computed the ratio of the sum of the diameters of the internal and external carotid arteries to the diameter of the common carotid artery, assuming circular diameters of the vessels.

For this study, each deposit of contrast medium in the carotid bifurcation after passage of the contrast bolus that displayed pulsating variations of position, size, and configuration was defined as a flow separation phenomenon. The duration of flow separation was defined as the interval from the first frame showing the main blood stream of the internal carotid artery free of contrast medium to the last frame with a recognizable contrast medium deposit in the carotid bifurcation. Using the standardized acquisition scheme, this time could easily be determined by the image numbers.

Pathologic changes of the vessel wall that could be seen on lateral angiograms were recorded. Even small plaques resulted in classification of the carotid bifurcation as having atherosclerotic lesions. Therefore, bifurcations classified as being without atherosclerotic lesions had only angiographically inconspicuous lesions. Data on clinical symptoms and the patient’s history were taken from the patient’s neurologic reports. Only carotid bifurcations in patients with a history of a reversible or permanent neurologic deficit of the dependent hemisphere and no evidence of a hemorrhage on CT were included in the group positive for cerebral ischemia.

Statistical analyses were done with the STATGRAPHICS software package (Version 2.6, STSC Inc., Rockville, Maryland) on a personal computer.

Results

The mean±SD age of patients with (55.2±11.8) and without (36.1±11.9 years) atherosclerotic lesions

| Table 1. Duration of Flow Separation and Geometric Parameters in 100 Carotid Bifurcations |
|---------------------------------|-----------------|-----------------|-----------------|
| Total                           | n               | Duration (sec)  | Bifurcation     | Ratio of diameters |
| Atherosclerotic lesions         | 100             | 5.8±3.9         | 32.7±16.0       | 1.14±0.43         |
| With                            | 50              | 5.4±3.3         | 29.6±16.0       | 1.33±0.40         |
| Without                         | 50              | 6.3±4.4         | 35.8±15.4*      | 0.97±0.38†        |
| Cerebral ischemia               |                 |                 |                 |                   |
| With                            | 69              | 5.9±4.0         | 33.0±17.0       | 1.19±0.40         |
| Without                         | 31              | 5.6±3.7         | 32.0±12.6       | 1.04±0.45         |

Data are mean±SD.

*tp≤0.06 (99% confidence level) and ≤0.001, respectively, different from without by unpaired t test.
FIGURE 1. Intra-arterial digital subtraction angiograms showing flow separation phenomenon in normal carotid bifurcation (frame interval 0.25 seconds). Note change of shape of contrast medium deposit and outflow at proximal and distal ends.

of the carotid bifurcation differed significantly ($p \leq 0.001$, 99% confidence level), as did the mean±SD age of patients with and without cerebral ischemia (51.3±13.3 and 42.7±15.4 years, respectively; $p \leq 0.05$). Of 100 carotid bifurcations, an angiographic flow separation phenomenon was found in 99. The only bifurcation without this phenomenon had a high-grade stenosis of the internal carotid
Mean duration of flow separation was 5.8
(range 1.25–22) seconds. There was no significant
difference in duration for carotid bifurcations in
patients with and without atherosclerosis or ischemia
(Table 1). Mean angle of the bifurcation was 32°,
mean ratio of the diameters was 1.14:1. Small but
significant increases in the bifurcation angle and
diameter ratio were found in bifurcations from pa-
tients with atherosclerotic lesions but not cerebral
ischemia (Table 1).

Simple regression analysis showed a moderate
correlation between bifurcation angle and age (cor-
relation coefficient = 0.36, $R^2 = 0.127$) and a moderate
inverse correlation between diameter ratio and age
(correlation coefficient = $-0.38$, $R^2 = 0.146$). No fur-
ther relevant correlations were found; in particular,
there was no correlation between age or geometric
parameters and the duration of flow separation.

Discussion
The flow separation phenomenon is fundamental
at the carotid bifurcation and therefore it is surpris-
ating that, in contrast to ultrasound, there are very few
reports on its angiographic demonstration. Our re-
results show that the flow separation phenomenon can
be a normal finding on IA-DSA (Figure 1) and that it
can be found with angiography using an adequate
technique as often as with ultrasound. We believe
that reasons for this (besides the high frame rate and
the high contrast resolution) are the instant subtrac-
tion feature and the possibility of a movie display
with our DSA unit, which improve the perception of
flow separation significantly, thus making it a routine finding. Furthermore, the high viscosity of the nonionic contrast medium may play a role. However, using the same contrast medium in conventional angiography, we had seen a flow separation phenomenon very rarely.

Evaluation of the flow separation phenomena by DSA is less accurate than by Doppler ultrasound, which allows point measurements of flow velocity. Nevertheless, DSA shows pulsatile variations in the size, shape, and position of contrast medium deposits within the carotid bifurcation. Degree of the flow separation phenomenon varied widely, and (especially in more pronounced cases) outflow of the contrast medium in vortices at the proximal end of the flow separation could be seen (Figure 1, lower left and lower right; Figure 2, right). Sometimes the area of flow separation filled from the distal end after opacification of the main blood stream, leaving a proximal region within the internal carotid artery free of contrast in the first image (Figure 2, left); sometimes inflow of contrast-free blood into the opacified region of the area of flow separation could be observed (Figure 3).

In one patient, who had IA-DSA with the head turned laterally and the x-ray beam directed vertically, the lateral projection of the carotid bifurcation displayed a different flow pattern. In this case a triangular deposit of contrast medium that contracted rhythmically was found. This pattern was seen in a number of standard arteroposterior series of the bifurcation. This finding points to the fact that angiographically demonstrable flow patterns vary with patient positioning under the influence of gravity. Nevertheless, flow separation is not a purely gravitational phenomenon, and all flow patterns observed are consistent with experimental and ultrasound studies.

The presence of a flow separation phenomenon in patients with plaques and even moderate stenoses is partly in contrast to in vivo ultrasound studies. However, Azuma and Fukushima demonstrated flow separation in experiments with model plaques, which supports our findings. In some cases flow separation was found proximal as well as distal to the plaque, resulting in a smooth shape of the main blood stream of the carotid artery (Figure 4, left, center left, and center right). Deposits of contrast medium in shallow ulcerations also showed pulsatile changes in shape and position and can also be considered as a flow separation phenomenon. The absence of any flow separation in one patient with a high-grade stenosis of the internal carotid artery is caused by the extreme acceleration of blood flow velocity found in this patient.

Since the flow separation phenomenon is inherent to flow dividers such as the carotid bifurcation, the finding that its presence is independent of the bifurcation angle and the diameter ratio is no surprise. Furthermore, the flow separation phenomenon was almost independent of the presence of carotid atherosclerotic disease as well as of clinical symptoms of ischemia of the dependent hemisphere. Considering the angiographic diagnosis of carotid artery disease, the demonstration of the flow separation phenomenon is therefore of no diagnostic value. On the other hand, one should not take the presence of the flow separation phenomenon as a sign of an abnormality, especially in the absence of atherosclerotic lesions in symptomatic patients.

The flow separation phenomenon is hypothesized to be the reason for the preferential location of arteriosclerosis at the carotid bifurcation; however,
the mechanism is still a matter of dispute. Mechanical alterations of the endothelium induced by regions of high and low shear stress, an area of abnormal exchange of substrates, or changes in thrombocyte activity within the area of flow separation are considered to be pathogenetic factors.\(^1,5,15,16\)

As mentioned, a number of factors can influence the presence and extent of flow separation (e.g., blood pressure and pressure amplitude, which together with the peripheral resistance define the velocity of the flowing blood, or the blood viscosity, which depends on the number of suspended cells and correlates with the hematocrit). Since even in larger vessels blood behaves as a non-Newtonian fluid, its viscoelastic properties are nonuniform and depend on local variations of flow. Furthermore, it is known from laboratory experiments\(^17\) that elastic walls dampen flow phenomena compared with nonelastic walls. One therefore would expect an increased duration of flow separation in older patients, which we could not confirm.

Since the flow separation phenomenon is very complex, an in vivo study such as ours cannot further elucidate this problem. However, our results reveal an aspect that has so far been somewhat ignored, namely, the duration of stay of the blood and its components within the area of flow separation. A mean duration of the angiographic flow separation phenomenon of \(>5\) seconds, with a range of up to \(14\) seconds even in normal carotid bifurcations, supports theories that alterations of substrate exchange or thrombocyte activity\(^17\) are the driving mechanisms of carotid artery disease.\(^2\)

In patients there is no way to measure the duration of blood stay within the area of flow separation without injecting a dye, which alters the rheologic parameters. Since the contrast medium used is more dense than blood, the blood should actually remain for a shorter time within the area of flow separation. Therefore, in vivo the exact values cannot be determined with radiologic methods due to methodologic constraints, which means that our results can be considered only as a reference for the possible relevance of blood stay within the area of flow separation.

**References**


**Key Words** • angiography, digital subtraction • carotid arteries • hemodynamics
Diagnostic significance of flow separation within the carotid bifurcation demonstrated by digital subtraction angiography.
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*Stroke*. 1990;21:1674-1679
doi: 10.1161/01.STR.21.12.1674

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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/21/12/1674