Correlation of Common Carotid Flow Volume Measured by Ultrasonic Quantitative Flowmeter With Pathological Findings

Takashi Wada, MD; Kuniyasu Kodaira, MD; Kentaro Fujishiro, MD; and Tetsuo Okamura, MD

To evaluate the possibility of quantitatively diagnosing carotid and cerebral atherosclerosis noninvasively, we measured common carotid flow volume in 60 sides (30 patients), using an ultrasonic quantitative flowmeter, and then compared these findings to the severity score of carotid and cerebral atherosclerosis as determined at autopsy. Stenosis decreased common carotid flow volume in the carotid and cerebral arteries. Increases in the severity score varied inversely with reduced flow volume, which was high in inverse correlation ($r = -0.696$). Patients with flow volumes of 8.5 ml/sec or greater did not have stenosis greater than or equal to 75%, whereas all patients with flow volumes of 6.4 ml/sec or less had stenosis greater than or equal to 50%, with 45% of these having stenosis greater than or equal to 75%. These pathological findings confirm that the common carotid flow volume reflects the degree of carotid and cerebral atherosclerosis present and that the lower limit of common carotid flow volume in healthy subjects is 6.5 ml/sec. (Stroke 1991;22:319–323)

Ultrasound has advanced the noninvasive diagnosis of carotid and cerebral atherosclerosis, but quantitative measurement only recently has been possible. Our ultrasonic quantitative flow measurement system has made it possible to measure noninvasively and quantitatively the absolute blood flow volume in the common carotid artery that constitutes the input end of the cerebral arteries.1-2 We have used an ultrasonic quantitative flow measurement system with 3,000 cases and found that common carotid artery blood flow volume ranges from 6.9 to 10.4 ml/sec in normal subjects.3'4 Several authors5-8 have reported similar data, using the same ultrasonic quantitative flow measurement system (Table 1). In these reports, the 95% confidence interval of blood flow volume ranges from 6.5 to 11.4 ml/sec and coincides well with our data. Lower limits of blood flow volume were 6.5 to 7.1 ml/sec. These values are considered a borderline flow to differentiate normal from abnormally decreased flow. Decreased flow is often due to atherosclerosis of the carotid–cerebral arterial system, although other causes may have this effect.

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Few researchers have tried to use angiography to prove clinical data as an index of the grade of cerebral atherosclerosis4-6,8-13 or to document flow data pathologically. This study examines the relationship between common carotid artery blood flow volume and morphological severity of stenosis of the carotid and cerebral arteries. We try to prove the validity of clinical flow measurement in the carotid artery and to establish the measurement range of normal blood flow volumes.

Subjects and Methods

We measured common carotid artery flow volume noninvasively using an ultrasonic quantitative flow measurement system (QFM-2000, Hayashi-Denki Co., Ltd., Kawasaki-shi, Japan).1 The system consists of a component that uses ultrasonic echo tracking to measure vessel diameter and a component that uses a continuous Doppler independent of incident angles to measure absolute blood flow velocity. The absolute blood flow volume is computed from a vessel cross-sectional area calculated by vessel diameter and the absolute blood flow velocity. The error rate in blood flow volume measurements was less than 7% compared to that found with the use of an electromagnetic flowmeter.1

We used current patients at Jikei University Hospital for this study. Measurements were made with 465 patients resting in a supine position, and the average values of blood flow volume were calculated.
TABLE 1. Studies Using Ultrasonic Quantitative Flow Measurement Systems

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Age</th>
<th>Flow volume (ml/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fujishiro and Yoshimura (1982)</td>
<td>140</td>
<td>10–79</td>
<td>6.9–10.4</td>
</tr>
<tr>
<td>Uematsu et al (1983)</td>
<td>120</td>
<td>21–60</td>
<td>6.5–8.7</td>
</tr>
<tr>
<td>Obara and Kodaira (1984)</td>
<td>140</td>
<td>10–79</td>
<td>6.9–10.4</td>
</tr>
<tr>
<td>Sugihara (1985)</td>
<td>60</td>
<td>21–69</td>
<td>6.8–9.9</td>
</tr>
<tr>
<td>Sawai (1987)</td>
<td>108</td>
<td>30–79</td>
<td>6.6–11.4</td>
</tr>
</tbody>
</table>

Flow volume figures represent calculations of 95% confidence intervals of common carotid artery blood flow volume.

At autopsy, the entire common and internal carotid artery, the origin of the external carotid artery, and the basal cerebral arteries (the circle of Willis) with their main branches were removed. The materials were fixed in 10% formalin. As seen in Figure 1, 10 different segments on a single side were processed: two segments of common carotid artery, one segment of external carotid artery, three segments of internal carotid artery, two segments of anterior cerebral artery, and two segments of middle cerebral artery. As for the divided segments of the intracranial arteries, they are the same as in the study of Baker et al. The tissue sections were crosscut at the most severe stenosis site in each segment and were processed routinely and embedded in paraffin. They were also routinely stained with Elastica–van Gieson and Masson’s trichrome. The specimens were magnified with a projector and a light microscope. The circumferences of the residual lumen and the internal elastic lamina, as well as outer circumferences, were traced, and a microcomputer determined the arcs of each. The stenosis ratio was calculated from the ratio of the area enclosed by the intima to that enclosed by the internal elastic lamina. According to the degree of stenosis, each specimen was graded as 0 (0–24%), +1 (25–49%), +2 (50–74%), or +3 (75–100%). Each of 10 segments was scored, and the overall score was the sum of these.

Figure 1. Carotid artery system (A–E) and basal cerebral artery system (a–e) obtained at autopsy. A, Common carotid artery (from the middle to sinus); B, common carotid artery (sinus); C, external carotid artery (origin); D, internal carotid artery (to siphon); E, internal carotid artery (siphon); a, internal carotid artery (to and including trifurcation); b, anterior cerebral artery (anterior to anterior communicating artery); c, anterior cerebral artery (posterolateral communicating artery); d, middle cerebral artery (to first branch); and e, middle cerebral artery (at or behind first branch).
The correlation between blood flow volume and severity score was calculated. Four groups were set according to the value of blood flow volume: 1) greater than or equal to 8.5 ml/sec, 2) 7.5–8.4 ml/sec, 3) 6.5–7.4 ml/sec, and 4) less than or equal to 6.4 ml/sec. In each group, the incidence of grade +2 (stenosis of 50–74%) and of grade +3 (stenosis ≥75%) was studied.

All blood flow volume values were averaged and expressed as mean±SD. Ninety-five percent confidence intervals were calculated from total number, mean value, and SD with a t distribution table. Correlation coefficients were calculated by standard statistical methods. Differences in means were assessed by unpaired t tests.

**Results**

The 60 blood flow volumes ranged from 5.4 to 13.1 ml/sec (mean, 7.88±1.61 ml/sec). Brachial mean blood pressure was 88.8±14.4 mm Hg. Severity scores ranged from 0 to 17 (mean, 6.1±4.2). In 10 segments (Figure 1), the incidence of grade +2 (stenosis of 50–74%) and of grade +3 (stenosis ≥75%) was studied (Table 2). Segment e (middle cerebral artery at or behind the first branch) contained the highest combined incidence of grade +2 (13) and grade +3 (4). There were 15 lesions of grade +2 in segment a (internal carotid artery to and including trifurcation). Overall, larger proportions of the grade +2 and grade +3 lesions were intracranial.

Two typical cases are presented for comparison. Case 1 was an 86-year-old man with carcinoma of the sigmoid colon who had normal blood flow volume on the right side of 8.6 ml/sec. Brachial mean blood pressure was 85.6 mm Hg. Severity score was 1 (grade 0). The severity score for this case was 1, which was extremely low.

Case 2 was an 83-year-old woman with carcinoma of the lung who had reduced blood flow volume of 5.5 ml/sec on the left side. Brachial mean blood pressure was 86.8±14.4 mm Hg. Severity scores ranged from 0 to 17 (mean, 6.1±4.2). In 10 segments (Figure 1), the incidence of grade +2 (stenosis of 50–74%) and of grade +3 (stenosis ≥75%) was studied (Table 2). Segment e (middle cerebral artery at or behind the first branch) contained the highest combined incidence of grade +2 (13) and grade +3 (4). There were 15 lesions of grade +2 in segment a (internal carotid artery to and including trifurcation). Overall, larger proportions of the grade +2 and grade +3 lesions were intracranial.

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The correlation between blood flow volume and severity score was close ($r = -0.696, p < 0.0001$), as shown in Figure 3. We studied the relationship between blood flow volume and the incidence of stenotic lesions of greater than or equal to 50% (grades +2 and +3) in 10 areas on a single side (Table 3). Only two of 18 cases had one stenosis lesion of greater than or equal to 50% in the group with blood flow volume of 8.5 ml/sec or greater; neither of these stenoses was greater than or equal to 75% (Table 4). Thus, flow rates of 8.5 ml/sec or more excluded stenosis of 75% or more anywhere on the side. On the other hand, all cases with blood flow volumes of 6.4 ml/sec or less had stenotic lesions of 50% or more (grades +2 and +3) (Table 3). The mean frequency of stenosis of greater than or equal to 50% for a given side was 3.5±1.7 ($p < 0.01$), which was significantly higher compared with the other groups. Frequency of stenotic lesions was as high as four lesions (four cases), five lesions (two cases), and six lesions (one case) in this group. Five of 11 cases (45%) in this group had stenotic lesions greater than or equal to 75% (grade +3) (Table 4).

**Discussion**

Extracranial and intracranial atherosclerosis is a principal etiologic factor in ischemic cerebrovascular disorders. Therefore, quantitative clinical detection
TABLE 4. Correlation Between Common Carotid Artery Blood Flow Volume and Frequency of Stenotic Lesions of 50% or Greater

<table>
<thead>
<tr>
<th>Blood flow volume (ml/sec)</th>
<th>Frequency of stenosis</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8.5 (n=18)</td>
<td>0 1 2 3 4 5 6</td>
<td>0.1±0.3</td>
</tr>
<tr>
<td>7.5-8.4 (n=14)</td>
<td>5 5 2 2 1 0 0</td>
<td>1.1±1.0*</td>
</tr>
<tr>
<td>6.5-7.4 (n=17)</td>
<td>5 4 4 1 2 1 0</td>
<td>1.6±1.5*</td>
</tr>
<tr>
<td>≤6.4 (n=11)</td>
<td>3 1 4 2 1 0 0</td>
<td>3.5±1.7*</td>
</tr>
</tbody>
</table>

*p<0.01 compared with ≥8.5 ml/sec group.

would be an extremely valuable tool in the treatment of these disorders and the prevention of ischemic cerebrovascular attacks. Angiography is a prominent method for diagnosing atherosclerosis today, but the information it provides is morphological rather than quantitative in any true sense. Furthermore, angiography is invasive. At present, most of our hopes for improving quantitative measurement of atherosclerosis focus on ultrasound.

Since Yoshimura et al1 developed the ultrasonic quantitative flow measurement system, absolute blood flow volume can be measured independently of the ultrasonic beam incident angle. The error rate of blood flow volume measured by this system is less than 7% compared to that found with the use of an electromagnetic flowmeter. Müller et al15 reported that the correlation between the real pulsatile flow as measured by time collection and the flow values measured by ultrasonic quantitative flow measurement system was excellent (r=1.00, p<0.001). Uematsu et al5 reported that the correlation coefficient between the values of the ultrasonic quantitative flow measurement system and those of the electromagnetic flowmeter was 0.94.

The ultrasonic quantitative flow measurement system is one of the most accurate among Doppler flowmeters.10,15 In this study, blood flow volume was measured in the common carotid artery because of the following reasons. 1) It is easier to measure flow volume here as compared to the internal carotid artery because the position of carotid artery bifurcation in the Japanese population is more peripheral than in the Caucasian population. 2) The measurements at the origin of the internal carotid artery have more potential error because of turbulence produced by the carotid bulb and bifurcation. 3) Prior studies have shown high correlations between common carotid artery flow volume and mean cerebral blood flow volume measured by the xenon-133 intra-arterial method (r=0.73).17

Several investigators9-8 have reported common carotid blood flow volume in healthy adult subjects measured by the ultrasonic quantitative flow measurement system (Table 1). The wide range of normal values in these studies is at least partly attributable to cerebrovascular collateral reserve and to variations in the collateral circulation via the circle of Willis.10 The development of carotid–cerebral atherosclerosis may increase circulatory resistance,18 thus reducing common carotid artery blood flow volume. Thus, the lower limits may correspond to the borderline values between the healthy and carotid–cerebral atherosclerosis groups. None of the prior studies defined the extent of vascular disease with autopsy findings or correlated blood flow volume measurements with these findings.

Kameyama19 reported carotid and cerebral atherosclerosis in Japanese autopsy cases. As to stenosis of 50% or more (grades +2 and +3), the order of incidence in the divided areas in his study was almost equal to that in our study. Kieffer et al20 reported the angiographic findings that the most frequent site for severe stenosis was the distal part of the basal cerebral arteries. In our study, the incidence of stenotic lesions (grades +2 and +3) was highest at the distal part of the middle cerebral artery (area e). This result was in accordance with the report of Kieffer et al.20

Uematsu et al5 showed that blood flow volume measured by the ultrasonic quantitative flow measurement system, with the degree of carotid and cerebral atherosclerosis determined by cerebral angiography, was expressed as r=−0.73 (p<0.01), a finding consistent with the results of our study. Imamura13 also reported a significant negative correlation of r=−0.77 (p<0.01).

There have been several reports in which blood flow volume measured by the ultrasonic quantitative flow measurement system was contrasted with cerebral angiography in ischemic cerebrovascular disorders.8,9,11,12 We investigated the highest values at 95% confidence interval in each report. Mizukami et al8 demonstrated that blood flow volume was less than 5.3 ml/sec on the involved side in internal artery occlusion and less than 7.7 ml/sec in middle cerebral stem occlusion. According to the study by Uematsu et al,3 41–70% stenosis of the internal carotid artery gave a value of less than 8.0 ml/sec, 71–90% stenosis gave a value of less than 7.0 ml/sec, and 91–100% stenosis, less than 4.5 ml/sec. Cerebral atherosclerosis gave a value of less than 7.1 ml/sec. Hassam et al12 reported the abnormal cutoff value of blood flow volume as 6.37 ml/sec obtained from comparative study with digital subtraction angiography. From the above data, the highest values of blood flow volume on the involved side of stenosis or occlusion in the carotid and cerebral arteries are 4.5–8.0 ml/sec.
In the relationship between blood flow volume and the average frequency of stenotic lesions greater than or equal to 50% (grades 2 and 3), there was an incidence value of 0.1±0.3 in the group with blood flow volume greater than or equal to 8.5 ml/sec. On the other hand, the frequency in the group with blood flow volume less than or equal to 6.4 ml/sec was significantly as high as 3.5±1.7 (p<0.01). All the cases with blood flow volumes less than or equal to 6.4 ml/sec possessed stenotic lesions of 50% or more. However, it is important to note that blood flow reduction is not always due to atherosclerosis but may also be seen in Alzheimer's disease, severe low-output heart failure, and other conditions.

In conclusion, carotid and cerebral atherosclerosis is nil to slight in cases with blood flow volumes greater than or equal to 8.5 ml/sec, slight to moderate in those with blood flow volumes from 6.5 to 8.4 ml/sec, and severe in those with blood flow volumes less than or equal to 6.4 ml/sec. These results provide a more precise classification scheme than previously published reports, which defined the healthy group as having blood flow volumes of more than 6.5–7.1 ml/sec and the carotid–cerebral atherosclerosis group as having blood flow volumes of less than 4.5–8.0 ml/sec. A quantitative standard for measuring the severity of carotid and cerebral atherosclerosis was confirmed by histopathologic findings in our study.

Hemodynamic examination with the ultrasonic quantitative flow measurement system is very useful in screening patients with symptoms of cerebrovascular disease and asymptomatic patients at risk for atherosclerosis before angiography. It is inexpensive and noninvasive, and it is quickly and easily performed. It may someday replace invasive studies as the best choice for early detection of atherosclerosis.

References
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