Reference Values for Vertebral Artery Flow Volume by Duplex Sonography in Young and Elderly Adults

E. Seidel, MD; B.M. Eicke, MD; B. Tettenborn, MD; F. Krummenauer, PhD

Background and Purpose—Vertebrobasilar ischemia has been attributed to a reduction of net vertebral artery flow volume, the product of mean flow velocity and the cross-sectional area of the vessel. It can be determined by duplex sonography. There are no reference values for vertebral artery flow volume in an age group representative of patients with cerebrovascular disease.

Methods—We examined 50 nonvascular neurological patients (age 55.8 ± 14.0 years). Flow velocities and vessel diameters were recorded in the intertransverse (V2) segments bilaterally, and the flow volume was calculated according to the following equations: (1) Q1 = time-averaged mean velocity × area and (2) Q2 = (time-averaged maximum velocity/2) × area.

Results—Flow velocities and vessel diameters tended to be lower on the right side, resulting in a lower flow volume. Flow volumes (according to Equation 1) were 77.2 ± 29.8 mL/min on the right side, 105.3 ± 46.4 mL/min on the left side, and 182.0 ± 56.0 mL/min net. Side-to-side differences were not significant. Flow volumes calculated with the 2 equations did not differ significantly. An age dependence could not be shown, but vessel diameters and net vertebral artery flow volumes were significantly lower in women than in men. The normal range for net vertebral artery flow volume defined by the 5th to 95th percentiles is between 102.4 and 301.0 mL/min. This wide range is due to the high interindividual variability of the parameters.

Conclusions—On the basis of the reference values presented here, the association of decreased vertebral artery flow volume and vertebrobasilar ischemia should be reevaluated. Additional areas for investigation include the quantification of collateral flow in the vertebral arteries in carotid artery occlusive disease and their contribution to overall cerebral blood flow volume. (Stroke. 1999;30:2692-2696.)

Key Words: blood flow velocity ■ blood flow volume ■ ultrasonography, Doppler, duplex ■ vertebral artery

The mechanism of vertebrobasilar ischemia is discussed controversially in the literature; whereas some authors are convinced embolism is the major cause, as is the case in internal carotid disease, others believe it is primarily a hemodynamic phenomenon due to a reduction in net vertebral artery flow volume. Hemodynamic data obtained by ultrasound investigations of extracranial and intracranial vessels include blood flow velocities and calculated pulsatility indices. Additionally, morphological data can be obtained by B-mode imaging. A potentially important parameter that combines morphological and hemodynamic data is the volume flow rate, a parameter of brain perfusion. The "gold standard" for flow-volume measurements is invasive electromagnetic flowmeters. Noninvasive assessment of flow volume is possible by various ultrasound approaches. First is the so-called QFM flowmeter, which integrates Doppler and A-mode information. Second, duplex ultrasound systems calculate the flow volume as the product of mean flow velocity and the cross-sectional area of the vessel. Conventionally, the time-averaged mean velocity (TAV) is used. This is the intensity-weighted mean velocity integrated over time, obtained with a sample volume that covers the entire vessel diameter. The cross-sectional area of the vessel is usually calculated from a static vessel diameter measured in a B-mode image at the location of the Doppler sample volume, which assumes a circular vessel configuration. A third, more recently developed and highly accurate method uses a color M-mode approach with simultaneous determination of local flow velocities with a time-domain–based color duplex system and functional vessel diameter. Its application to the vertebral arteries is technically limited. Reference data obtained by conventional duplex sonography for young adults (mean age 35 years, range 20 to 63 years) and children have been published previously. Flow volume peaked at the age of 6.5 years, followed by a decline until the age of 18. Possible changes in the elderly have not yet been investigated, and normal values for an age group more representative of cerebrovascular disease patients are lacking.
TABLE 1. Values for Flow Velocities and Diameters in the Right and Left Vertebral Arteries

<table>
<thead>
<tr>
<th></th>
<th>Vs Right, cm/s</th>
<th>Vd Right, cm/s</th>
<th>TAV Right, cm/s</th>
<th>TAMX Right, cm/s</th>
<th>Right diameter, cm</th>
<th>Vs Left, cm/s</th>
<th>Vd Left, cm/s</th>
<th>TAV Left, cm/s</th>
<th>TAMX Left, cm/s</th>
<th>Left Diameter, cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>45.9</td>
<td>13.8</td>
<td>13.6</td>
<td>24.1</td>
<td>0.344</td>
<td>51.5</td>
<td>16.1</td>
<td>15.8</td>
<td>27.6</td>
<td>0.371</td>
</tr>
<tr>
<td>SD</td>
<td>11.1</td>
<td>4.6</td>
<td>3.8</td>
<td>6.7</td>
<td>0.059</td>
<td>13.3</td>
<td>5.8</td>
<td>5.3</td>
<td>8.0</td>
<td>0.058</td>
</tr>
<tr>
<td>Median</td>
<td>43.2</td>
<td>13.3</td>
<td>13.2</td>
<td>23.1</td>
<td>0.345</td>
<td>49.6</td>
<td>14.4</td>
<td>14.5</td>
<td>25.9</td>
<td>0.363</td>
</tr>
<tr>
<td>25% Quartile</td>
<td>37.8</td>
<td>10.2</td>
<td>11.1</td>
<td>19.5</td>
<td>0.298</td>
<td>41.2</td>
<td>11.9</td>
<td>11.8</td>
<td>21.3</td>
<td>0.328</td>
</tr>
<tr>
<td>75% Quartile</td>
<td>52.2</td>
<td>16.2</td>
<td>15.9</td>
<td>28.7</td>
<td>0.381</td>
<td>57.9</td>
<td>17.7</td>
<td>18.6</td>
<td>31.4</td>
<td>0.398</td>
</tr>
</tbody>
</table>

Vs indicates peak systolic velocity; Vd, peak end-diastolic velocity.

The aim of this work was to obtain normal values for flow volumes in the vertebral arteries in an older population, to analyze side-to-side differences, as well as age and sex dependencies.

Subjects and Methods
We examined 50 patients (26 men, 24 women) aged 55.8±14.0 years (range 31 to 84 years) hospitalized in the neurological department for nonvascular diagnoses and without history or signs of cerebrovascular disease or hemodynamically relevant internal carotid stenosis on color duplex sonography. A 7.5-MHz linear transducer of a Philips SD 800 system was used. Before volume-flow measurement was performed in the vertebral arteries, a routine examination of the vertebral artery was performed to document atherosclerosis and to exclude relevant internal carotid stenosis. The patients rested in the supine position for ~15 minutes before the first data were obtained. Both sides were examined. The patient’s head was turned slightly to the opposite side each time. The intertransverse (V2) segment of the vertebral artery was visualized by rotation of the probe posteriorly from the carotid plane. Duplex measurement of angle-corrected flow velocities was done with the sample volume expanded over the entire vessel diameter. The peak systolic and end-diastolic velocities, TAV, and time-averaged maximum velocity (TAMX) were recorded. Angle correction could be done by 1° increments. The vessel diameter (d) was measured in a magnified B-mode image for better accuracy at the site of the Doppler sample volume; adjustment of diameter measurement could be done by 0.1-mm increments. All measurements were documented by black-and-white video printer. All measurements were performed twice, and an average was calculated.

We used 2 different equations for flow volume:

1. \( Q(1) = TAV \times A \)
2. \( Q(2) = (TAMX/2) \times A \)

with area \( A = (d/2)^2 \times \pi \).

TAV is an intensity-based assumption of the mean spatial velocity over the entire cross-sectional area of the vessel (Equation 1, which has been used by previous authors). If parabolic flow is assumed, the mean spatial velocity is half the maximum velocity measured in the center of the vessel; as such, a selective measurement is not feasible in narrow vessels such as the vertebral arteries, and therefore we used half the mean of peak velocities obtained over the entire vessel instead (Equation 2).

Flow-volume measurement with duplex ultrasound is vulnerable to minor errors in angle correction and diameter measurement and is based on the assumption of a circular vessel. Angle correction is essential for flow velocity determination. The error that occurs with a given error in angle correction rises with the angle of insonation, which therefore must be kept small. Errors in angle correction can lead to overestimation or underestimation of flow velocity and can be reduced by the averaging of repeated measurements.

Statistical Analysis
All parameters are represented as mean±SD or median with 25% and 75% quartiles; to derive reference ranges for parameters of interest and cutoffs for normal values, the 5th and 95th percentiles are given. Intrainsdividual comparisons (eg, side-to-side differences) were described with the 95% CI of the intrainsdividual mean difference and tested for significance with the signed rank test (paired Wilcoxon test). The age and sex dependence of parameters were tested for significance with the 2-sample Wilcoxon test. Correlation between age and vertebral artery flow volumes and correlation between flow volumes calculated with Equations 1 and 2 were assessed with Spearman correlation coefficients. A linear regression analysis was performed between flow volumes calculated with Equations 1 and 2. Because of the exploratory character of these analyses, results were not adjusted for multiplicity, ie, probability values resulting from intrainsdividual comparisons (left/right, Equation 1/2) must be regarded as descriptive rather than confirmatory. Local statistical significance was assumed for \( P<0.05 \) for all parameters. Graphical representation of the data was performed by use of box-and-whisker plots for intrainsdividual comparisons and group comparisons; scatterplots were used to illustrate the existence or absence of (linear) association between continuous parameters. All computations were performed with the SAS system (version 6.12.

TABLE 2. Right, Left, and Net Vertebral Artery Flow Volumes Calculated According to Equation 1 and 2

<table>
<thead>
<tr>
<th></th>
<th>Q(1) Right, mL/min</th>
<th>Q(2) Right, mL/min</th>
<th>Q(1) Left, mL/min</th>
<th>Q(2) Left, mL/min</th>
<th>Q(1) Net, mL/min</th>
<th>Q(2) Net, mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>77.2</td>
<td>68.1</td>
<td>105.3</td>
<td>92.2</td>
<td>182.0</td>
<td>159.9</td>
</tr>
<tr>
<td>SD</td>
<td>29.8</td>
<td>26.4</td>
<td>46.4</td>
<td>39.4</td>
<td>56.0</td>
<td>47.7</td>
</tr>
<tr>
<td>Median</td>
<td>74.2</td>
<td>65.7</td>
<td>98.6</td>
<td>83.2</td>
<td>182.5</td>
<td>158.2</td>
</tr>
<tr>
<td>25% Quartile</td>
<td>57.3</td>
<td>53.0</td>
<td>69.7</td>
<td>60.7</td>
<td>141.0</td>
<td>126.0</td>
</tr>
<tr>
<td>75% Quartile</td>
<td>96.5</td>
<td>85.4</td>
<td>130.6</td>
<td>114.3</td>
<td>208.5</td>
<td>180.2</td>
</tr>
<tr>
<td>5% Percentile</td>
<td>31.2</td>
<td>26.2</td>
<td>42.2</td>
<td>39.2</td>
<td>102.4</td>
<td>91.4</td>
</tr>
<tr>
<td>95% Percentile</td>
<td>135.3</td>
<td>112.6</td>
<td>196.1</td>
<td>161.7</td>
<td>301.0</td>
<td>259.8</td>
</tr>
</tbody>
</table>

Q(1) and Q(2) indicate flow volume calculates according to Equation 1 or Equation 2, respectively; 5th and 95th percentiles indicate normal range.
for Windows), and graphics were generated with the SPSS system (version 6.13 for Windows).

Results
In 49 patients, insonation was successfully performed on both sides. In 1 patient, only the left side could be investigated, whereas the right intertransverse segment remained inaccessible. The angle of insonation was 62° ± 6° (range 45° to 75°).

Results for systolic, diastolic, and mean flow velocities, as well as vessel diameters for both sides, are shown in Table 1, and the calculated flow volumes are shown in Table 2 and illustrated in Figure 2.

Flow velocities and vessel diameters tended to be lower on the right side, which resulted in a lower flow volume on that side. Because of a high interindividual variability, side-to-side differences were not statistically significant.

The flow volumes as calculated with Equation 2 were systematically lower than with Equation 1, but results were not significantly different (CI = 0.018 to 0.029). They were highly correlated (r = 0.98 for the right side and 0.99 for the left side), and regression analysis showed only negligible linear deviation.

There were no significant differences in vessel diameter, flow velocities, or flow volumes between younger (<55 years) and older (>55 years) subjects (P = 0.2 to 0.9 for different parameters), and no correlation between age and flow volumes was found (r < 0.1) (Figure 1). Vertebral artery diameters were significantly smaller in women (P = 0.01 for the right and 0.05 for the left side), and net vertebral artery flow volumes were lower in women (P = 0.02; Figure 3). The normal ranges defined by the 5th to 95th percentiles based on our collective data are shown in Table 2. For net vertebral artery flow volume, normal ranges were between 102.4 and 301.0 mL/min or 91.4 and 259.8 mL/min with Equation 1 or 2, respectively.

Discussion
Vertebral artery diameters described by other authors9,12–15 agree with our measurements; only 1 study provided larger diameters.2 Our results for systolic and diastolic velocities are also comparable to9,12,13 or slightly lower than15,16 those found in other studies. Reference values for TAV and TAMX thus far exist only for children10 and young adults9; the latter

Figure 1. Net vertebral artery flow volumes (according to Equation 1) related to age (r = 0.06).

Figure 2. Right, left, and net vertebral artery flow volumes. Number in parentheses indicates Equation 1 or Equation 2; horizontal line within the box represents the median; horizontal lines limiting the boxes represent 25% and 75% quartiles; and whiskers indicate minima and maxima.
are in substantial accordance with the values found in the present study. Ranges given for the different parameters in the previous studies\(^9,10\) also showed a high interindividual variability, which is obviously a characteristic of vertebral arteries that results in wide ranges of normal values.

In this work, we compared 2 different approaches for flow-volume calculation based on different assumptions of mean spatial velocity. Both approaches led to very similar results (Figure 2).

Our results for vertebral artery flow volume are in substantial agreement with those published previously for young adults,\(^9\) with flow volumes of 76±32 mL/min on the right side and 94±32 mL/min on the left side and a net vertebral flow volume of 171±42 mL/min. Vertebral artery flow-volume values obtained by color M-mode were lower (61±26.1 on the right side and 62.9±29.5 mL/min on the left side), possibly because of a lower color sensitivity at deeper depths, without a clear tendency of side-to-side difference.\(^8\) Flow volumes obtained by invasive electromagnetic flowmetry in a few patients were even lower (on the right side 25, 40, 44, and 66 mL/min; on the left side 10, 17, and 34 mL/min).\(^17\) which suggests a potential overestimation with ultrasound techniques. However, apart from these data obtained on a few individuals, reference values for electromagnetic flowmetry are lacking.

In young adults, no age dependency for vertebral artery or internal carotid artery flow volumes could be shown.\(^9\) In common carotid arteries, however, a minor but significant decrease of flow volume was found with age\(^7,18\); this decrease was smaller than anticipated from age differences in flow velocity.\(^9\) In the carotid system, the decrease in flow velocities appears to be partially compensated by an increase in vessel diameter.\(^18\) Our data do not reveal a correlation of age and volume flow in the vertebral system. This may be due to the comparable small sample size. However, cortical or subcortical atrophy in the elderly may be more relevant for the carotid volume flow than for the vertebral system, because the brain stem is not so much affected by the aging process. However, this hypothesis would require more pathological data.

There are studies reporting a decrease in basilar artery flow velocities with increasing age.\(^20,21\) No reliable data on age-dependent basilar artery diameter are available, but it may be speculated that as in the carotid system, this decrease is compensated for by an increase in vessel diameter.

In the present study, we found a significantly lower net vertebral artery flow volume in women. The same observation has been made for flow volume in the common carotid artery, which has been attributed to the sex difference in brain volume.\(^7,18\) However, in another study,\(^9\) no significant differences were found. This discrepancy cannot be explained at present.

An arbitrary threshold of 200 mL/min has been proposed for net vertebral artery flow volume by the conventional duplex sonographic method, below which patients are prone to become symptomatic with vertebrobasilar ischemia.\(^2\) Our data, in accordance with those given for young adults,\(^9\) show that values of well below 200 mL/min are within the normal range for net vertebral artery flow volume. A net vertebral artery flow volume of less than \(\approx 100\) mL/min is below the fifth percentile and should be considered an indication of low vertebral artery flow.

Measurement of flow volume may be helpful in defining vertebral hypoplasia. To date, this has been done by diameter (below either 3\(^1/2\) or 2 mm\(^14\)) or qualitatively as a thin string of color by use of maximum sensitivity in color-coded duplex sonography.\(^16\) Given a 2% to 6% hypoplasia rate, unilateral flow below the fifth percentile could be regarded as indicative of a hypoplastic artery, ie, below \(\approx 30\) to 40 mL/min. A similar value has been suggested previously.\(^9\)

Given the reference values presented here, the association of decreased vertebral artery flow volume with vertebrobasilar ischemia suggested by a previous study\(^2\) should be investigated in the future. Additional areas for investigation are the quantification of collateral flow in the vertebral arteries in carotid artery occlusive disease and their contribution to overall cerebral blood flow volume.

References

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