Standardization of Carotid Ultrasound
A Hemodynamic Method to Normalize for Interindividual and Interequipment Variability

Carsten Ranke, MD; Andreas Creutzig, MD; Hartmut Becker, MD; Hans-Joachim Trappe, MD

Background and Purpose—Accurate carotid Doppler examination is an important issue in the light of large endarterectomy trials, but recommended cutoff values for detection of >70% stenosis vary widely. Standardization of diagnostic criteria should consider patient variation and instrument variability.

Methods—We prospectively analyzed various Doppler parameters in 44 patients undergoing carotid angiography to evaluate whether normalization through individual reference measurements from the common carotid artery or the distal internal carotid artery could improve accuracy. For assessment of interindividual and interequipment variability, we performed repeated measurements of 40 carotid arteries in 21 patients. Two color-coded duplex ultrasound systems were compared for machine variability estimation: Hewlett Packard SONOS 2500 and ATL Ultramark 9 HDI.

Results—Intrastenotic divided by distally recorded mean blood flow velocity (mean velocity ratio) showed the closest correlation with angiography: $R^2=0.93$. Mean velocity ratio >5 was 97% sensitive and 98% specific for detection of >70% carotid stenosis. Intrastenotic blood flow velocities were significantly different between the 2 duplex systems ($0.22\pm0.16$ versus $0.17\pm0.11$ m/s; $P<0.001$), whereas mean velocity ratio values did not differ significantly. Interobserver variation expressed as 95% CI for predicted stenosis between 2 observers was 13.6% (peak systolic velocity) and 15.4% (mean velocity ratio).

Conclusions—A mean velocity ratio using distal reference measurement in the internal carotid artery can normalize for interindividual and interequipment variability. (Stroke. 1999;30:402-406.)

Key Words: blood flow • carotid artery diseases • diagnostic imaging • hemodynamics • ultrasonography

Two randomized clinical trials, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST), have clearly shown the benefit of endarterectomy in symptomatic patients with >70% carotid stenosis. Contrast angiography, the “gold standard” for preoperative evaluation, is associated with a small but significant risk of stroke. Doppler ultrasound, as a noninvasive screening modality for severe carotid stenosis, allows angiography to be used more selectively. Because of significant instrument variability, individual centers have to validate their device-specific cut-off values angiographically. The ratio of the internal carotid artery to common carotid artery velocity (ICA/CCA ratio) should normalize for patient variation and instrument variability. This ratio is not clearly superior to absolute flow velocities, probably due to CCA diameter variation and variable collateral flow conditions. It was our aim to investigate whether ICA velocity ratio measurement would achieve more accurate stenosis estimation compared with other Doppler criteria currently used.

Subjects and Methods
All patients with a continuous-wave Doppler examination indicating carotid stenosis were eligible for the study. Eighty consecutive patients underwent continuous-wave Doppler and color-coded duplex ultrasound examination in our Doppler laboratory, as specified later in this section. Three of these patients (4%) had to be excluded because of inadequate visualization of the high cervical ICA (2 cases) or distal stenosis (1 case). Forty-four patients underwent both Doppler studies and carotid angiography (23 men and 21 women, aged 54 to 81 years [mean, 69 years]).

Continuous-wave Doppler examination was performed with a 4-MHz probe (Spectradop 2, Delalande). Peak systolic frequency was measured with spectral analysis in the ICA proximally, distally, and in the CCA. The lowest frequency from the high cervical carotid was used as distal reference to exclude false high values from the poststenotic jet or from low insonation angles far cranially.

Color-coded duplex ultrasound was performed on an ATL Ultramark 9 HDI system (Advanced Technology Laboratories) with four transducers: C7-4 curved array, L7-4 and L10-5 linear array, and P5-3 sector probe, as appropriate. The scanhead was applied longitudinally for blood flow velocity measurements. Peak systolic velocity, end-diastolic velocity, and mean blood flow velocity were measured in the ICA proximally and distally, and in the CCA 2 cm proximal to the bifurcation. The highest value of at least 3 measure-
ments was recorded. Doppler angle correction was performed meticulously by use of the color-coded velocity vector,10 with an angle approximately 60° in the CCA and proximal ICA, and <60° for distal measurements in the ICA. Because of poststenotic turbulences, distal reference measurements have to be performed in a vessel site at least 5 diameters beyond the stenosis.11 The high cervical ICA was examined with a lateral or posterolateral probe position with use of color-flow imaging to aid velocity measurement 40 to 50 mm off the bifurcation. Mean blood flow velocity was estimated from the spectral outline as velocity time integral with the trackball and integrated software. Intra-stenotic frequency and velocity values as well as their ratios with corresponding prestenotic and poststenotic values were used for correlation with angiography (in terms of percent stenosis1,13 and minimum lumen diameter12). A correlation was also made with the ratio of ICA peak systolic velocity to CCA end-diastolic velocity.9

Twenty-one patients with carotid stenosis entered the reproducibility study (mean age, 67 years; range, 48 to 81 years). Mean angiographic diameter stenosis was 56±24% (range, 7% to 92%). For assessment of interequipment variability, 20 ICAs in 10 patients (7 men and 3 women, mean age 69 [range, 54 to 81] years) were measured twice: Patients underwent examinations with the ATL machine (linear 10-5 MHz, sector 3-2 MHz probe) and a Hewlett-Packard SONOS 2500 color-coded duplex ultrasound system (linear 7.5 MHz, sector 2.5 MHz probe) on the same day in random sequence by 1 investigator. Transducer, scan direction, and Doppler angle were matched to the previous measurement with the other system.

Twenty ICAs in 11 patients (2 occlusions; 8 men and 3 women, mean age 66 [range, 48 to 80] years) were measured twice for interobserver variation estimation. For this study, the ATL ultrasound system was used with 1 of 4 probes at the investigator’s discretion: C7-4 curved array, L7-4 and L10-5 linear array, and P5-3 sector probe, as appropriate. Each patient was examined twice on the same day: 2 experienced investigators measured peak and mean flow velocity in the stenosis and distally 4 to 5 cm off the stenosis in succession. No arrangement of transducer selection, scan direction, or Doppler angle was made between the investigators. The investigators were unaware of their respective control values until the end of the study.

Selective digital subtraction angiography was performed with a biplane NeuroStar unit (Siemens). Angiographic stenosis was defined as maximal percent diameter reduction, 1−(S/R)%×100%, where S is the narrowest stenosis diameter and R is the normal reference diameter). ICA reference diameter was measured distally and proximally to calculate stenosis according to NASCET1,13 and ECST criteria,2 angiographic area reduction was calculated as 1−[(S1×S2)/ (R1×R2)]×100%, where S1 and S2 are the stenosis diameter from biplane views and R1 and R2 represent both normal reference diameter measurements of the ICA. Reading of angiograms was performed by investigators blinded to the results of the noninvasive study.

Correlation of angiographic stenosis with Doppler measurements was estimated by nonlinear regression analysis, with the coefficient of determination R² as an expression of the proportion of variance accounted for in the model. The standard error of estimate was calculated as a measure of dispersion of the observed values about the regression line. Doppler threshold values for detection of >70% stenosis were determined using the receiver operating characteristic method.14

Interequipment or interobserver correlation of velocities and velocity ratios was expressed by linear regression analysis with Pearson’s product moment correlation coefficient r as measure for goodness of fit. Interequipment or interobserver differences were reported as mean with 95% CI and statistical significance was evaluated by Student’s t-test (2-tailed). By use of nonlinear correlations with angiographic stenosis, peak velocity and mean velocity ratio values were converted into percent diameter stenosis. On the basis of these calculated stenosis values, the 95% CI for interobserver variation was calculated as CI=1.96∗SD. The SD was calculated as follows from the mean variance of the 2 predicted values xi and yi:

\[ SD = \sqrt{\frac{\sum(i-x)(y-i)^2}{n}} \]

Results

Of the 88 carotid bifurcations studied, 48 (55%) had ICA stenosis of ≤70% and 31 (35%) had stenoses of >70% according to NASCET stenosis definition, and 9 (10%) were angiographically occluded. Intra-stenotic divided by distally recorded mean blood flow velocity (mean velocity ratio) showed the closest correlation with angiography (see Figures 1 and 2). Results for blood flow velocity and peak systolic frequency measurements, their respective ICA-based and CCA-based ratios, and the ratio of ICA peak systolic velocity to CCA end-diastolic velocitya are summarized in Table 1.

Mean velocity ratio >5 was 97% sensitive and 98% specific for detection of >70% stenosis based on NASCET criteria, and mean velocity ratio >3 indicated a >70% stenosis according to ECST criteria, with 100% sensitivity and 94% specificity (Table 2).

A severely reduced minimal angiographic stenosis diameter <1 mm12 was indicated by a peak systolic velocity >3.7
m/s (92% sensitivity, 89% specificity), a peak systolic frequency 10.4 kHz (92% sensitivity, 92% specificity), and a mean velocity ratio 7.4 (92% sensitivity, 98% specificity). The minimal angiographic stenosis diameter correlated closely with mean velocity ratio values (Figure 3).

Correlation of the mean velocity ratio with angiographic area reduction was close to the mathematical correlation derived from the continuity equation (Figure 4).

Intrastenotic peak flow velocity values were significantly higher in the ATL series compared with the HP system (2.2 ± 1.6 versus 1.7 ± 1.1 m/s; P < 0.001). Mean interequipment difference was 0.49 m/s (CI, 0.24 to 0.74 m/s). Mean velocity ratio values did not differ significantly between the two systems: 3.9 ± 3.3 versus 3.7 ± 3.3, mean difference 0.1 (CI, −0.1 to 0.3). Interobserver correlation was close for predicted stenosis from peak systolic velocity (r = 0.92) and mean velocity ratio (r = 0.94). Interobserver variation expressed as 95% CI for predicted stenosis between 2 observers was 13.6% (peak systolic velocity) and 15.4% (mean velocity ratio).

**Discussion**

Carotid Doppler should be as accurate as possible, because the decision to perform carotid endarterectomy is based mainly on the degree of stenosis. Intrastenotic peak systolic velocity, the most widely used Doppler parameter, has recommended cut-off values for detection of 70% stenosis between 1.25 m/s and 3.25 m/s. Until now, ultrasound laboratories had to validate their velocity criteria angiographically on an individual basis to normalize for interequipment variability. The ratio of internal to common carotid artery peak velocity was proposed for compensation of interindividual and interequipment variability. Our data (Table 1) and that

### Table 1. Correlation of Doppler Measurements With Angiography

<table>
<thead>
<tr>
<th>Doppler Parameter</th>
<th>NASCET Stenosis</th>
<th>ECST Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R²</td>
<td>SEE, %</td>
</tr>
<tr>
<td>Intrastenotic mean velocity</td>
<td>0.93</td>
<td>9.2</td>
</tr>
<tr>
<td>Poststenotic mean velocity</td>
<td>0.92</td>
<td>10.0</td>
</tr>
<tr>
<td>Intrastenotic peak systolic velocity</td>
<td>0.89</td>
<td>11.8</td>
</tr>
<tr>
<td>Poststenotic peak systolic velocity</td>
<td>0.84</td>
<td>14.5</td>
</tr>
<tr>
<td>Intrastenotic peak systolic frequency</td>
<td>0.79</td>
<td>16.8</td>
</tr>
<tr>
<td>Prestenotic peak systolic frequency</td>
<td>0.76</td>
<td>18.0</td>
</tr>
<tr>
<td>Intrastenotic peak systolic frequency</td>
<td>0.75</td>
<td>18.0</td>
</tr>
<tr>
<td>Prestenotic peak systolic frequency</td>
<td>0.55</td>
<td>24.3</td>
</tr>
</tbody>
</table>

SEE indicates standard error of the estimate.

*Coefficient of determination, as defined by nonlinear regression analysis.

### Table 2. Mean Velocity Ratio Cut-Off Values for Angiographic Diameter Reduction

<table>
<thead>
<tr>
<th>Degree of Stenosis</th>
<th>Cut-Off Value (MVR)</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>NASCET criteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;50%</td>
<td>&gt;3</td>
<td>96</td>
<td>97</td>
<td>98</td>
<td>94</td>
</tr>
<tr>
<td>&gt;60%</td>
<td>&gt;4</td>
<td>93</td>
<td>90</td>
<td>90</td>
<td>92</td>
</tr>
<tr>
<td>&gt;70%</td>
<td>&gt;5</td>
<td>97</td>
<td>98</td>
<td>97</td>
<td>98</td>
</tr>
<tr>
<td>&gt;80%</td>
<td>&gt;10</td>
<td>95</td>
<td>95</td>
<td>85</td>
<td>98</td>
</tr>
<tr>
<td>&gt;90%</td>
<td>&gt;20</td>
<td>67</td>
<td>100</td>
<td>100</td>
<td>98</td>
</tr>
<tr>
<td>ECST criteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;50%</td>
<td>&gt;1.3</td>
<td>91</td>
<td>81</td>
<td>95</td>
<td>68</td>
</tr>
<tr>
<td>&gt;60%</td>
<td>&gt;2.1</td>
<td>90</td>
<td>93</td>
<td>96</td>
<td>82</td>
</tr>
<tr>
<td>&gt;70%</td>
<td>&gt;3</td>
<td>100</td>
<td>94</td>
<td>96</td>
<td>100</td>
</tr>
<tr>
<td>&gt;80%</td>
<td>&gt;5</td>
<td>81</td>
<td>89</td>
<td>84</td>
<td>88</td>
</tr>
<tr>
<td>&gt;90%</td>
<td>&gt;10.5</td>
<td>94</td>
<td>94</td>
<td>79</td>
<td>98</td>
</tr>
</tbody>
</table>

MVR indicates mean velocity ratio (intrastenotic mean velocity divided by the distal cervical internal carotid mean velocity); PPV, positive predictive value; and NPV, negative predictive value.
from previous studies indicate that the CCA is probably not the ideal reference segment for velocity normalization. In high-grade ICA stenosis, flow velocities are reduced in the CCA, with wide variation.

Individual reference measurements from the distal ICA should be superior to CCA-based velocity ratios for 2 reasons. First, because of its extracranial course without branches, the ICA meets the requirements of the continuity equation. Second, velocity measurements for ICA-based ratios are performed proximally and distally, corresponding to angiographic diameter ratio measurements with NASCET criteria.

Our results indicate that the mean velocity ratio (ratio of intrastenotic to distal mean velocity in the ICA) predicts carotid stenosis most precisely. It compensates for patient variation and machine variability simultaneously according to the principle of continuity of flow in the unbranching ICA. Mathematical correlation and Doppler measurements were nearly congruent, indicating that Doppler-derived area reduction comes close to anatomic stenosis (Figure 4).

Because of angle correction, ICA velocity ratios give more favorable results than the frequency ratio originally proposed by Spencer and Reid for the ICA (Table 1). Velocity ratios using distal carotid velocity values as the reference have not been validated until now, probably because velocity measurements were difficult to obtain distally. With sensitive color-flow imaging, the ICA can be traced 40 to 50 mm distally in >95% of all patients, in our experience.

There is a controversy over whether the proximal or the distal portion of the ICA should be the denominator for angiographic stenosis measurement. Because the mean velocity ratio is based on the distal normal portion of the ICA, mean velocity ratio values correlate closely with NASCET angiographic stenosis (Figure 1, Table 1). Because of the wider carotid bulb dimensions, stenosis values based on ECST criteria are higher than NASCET stenosis values: a 70% “local” diameter reduction equals 40% to 50% “distal” stenosis. Small amounts of atheroma do not cause an increase in blood flow velocity with respect to distally recorded velocity because the carotid bulb residual lumen area is larger than the cross-sectional area of the distal carotid artery in minor ECST stenosis. In severe stenosis based on ECST criteria, intrastenotic blood flow velocity is increased with respect to the distal ICA (Figure 2), and a mean velocity ratio of >3 indicates >70% stenosis with high sensitivity and specificity.

Both NASCET and ECST investigators reported a strong benefit for surgery over medical treatment for symptomatic patients with >70% stenosis. Stroke risk from preoperative contrast angiography adds to the overall surgical risk, which is especially important in asymptomatic patients. Duplex ultrasound is safe and cost effective, but as a stand-alone method for preoperative evaluation, ultrasound technique and Doppler criteria have to be standardized. The mean velocity ratio is the most accurate Doppler method because distal velocity normalizes for both interindividual and interequipment variability.

References
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