Original Article

Detection of Internal Carotid Artery Stenosis with Duplex Velocity Criteria Using Receiver Operating Characteristic Analysis

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Abstract

Introduction: Duplex ultrasonography is an excellent non-invasive screening tool for carotid artery stenosis. The aim of this study was to evaluate optimal ultrasonographic criteria for determination of internal carotid artery stenosis with reference to digital subtraction angiography. Materials and Methods: From January 1995 to December 2003, 114 symptomatic patients underwent both duplex ultrasonography and angiography. Seven velocity criteria were compared with angiographic stenosis and receiver operating characteristic curves were used to determine the best cutoff for each criteria. Results: Internal carotid artery/common carotid artery systolic velocity ratios (PSV ICA/PSV CCA) and systolic internal carotid artery/diastolic common carotid artery ratios (PSV ICA/EDV CCA) were superior to other criteria for diagnosing internal carotid artery stenosis. For 50% stenosis, the best criterion of PSV ICA/PSV CCA was 1.5 [sensitivity 100%, specificity 85%, area under the curve (AUC) 99%], and the best criterion of PSV ICA/EDV CCA was 3.5 (sensitivity 100%, specificity 58%, AUC 99%). For 60% stenosis, the best criterion of PSV ICA/PSV CCA was 2.6 (sensitivity 100%, specificity 94%, AUC 99%), and the best criterion of PSV ICA/EDV CCA was 10.3 (sensitivity 100%, specificity 96%, AUC 99%). For 70% stenosis, the best criterion of PSV ICA/PSV CCA was 3.1 (sensitivity 100%, specificity 91%, AUC 99%), and the best criterion of PSV ICA/EDV CCA was 10.3 (sensitivity 100%, specificity 91%, AUC 99%). Conclusion: Our study showed that velocity ratios are superior to other criteria for detecting carotid stenosis. Each laboratory needs to validate its own results.

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Key words: Angiography, Duplex, Extracranial, Internal carotid artery

Introduction

Carotid stenosis is a clear marker of increased stroke risk and is an important parameter in clinical risk stratification. Grading carotid stenosis has a direct impact on management decisions in view of the benefit provided by carotid endarterectomy in symptomatic patients with 70% to 99% stenosis.[1] Patients in this group who underwent endarterectomy had significantly lower stroke risks compared to medically treated patients. Subgroups of patients with 50% to 69% stenosis may expect a smaller benefit from surgery: a larger number of patients must undergo surgery to prevent a stroke at 2 years compared to patients with ≥70% stenosis.[1] The benefit of endarterectomy for asymptomatic patients with ≥60% stenosis has been demonstrated in the Asymptomatic Carotid Atherosclerosis Study.[2]

The diagnostic criteria from both the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[1] and European Carotid Surgery Trial[3] were based on angiography. Although digital subtraction angiography (DSA) is the gold standard for the evaluation of extracranial internal carotid artery (ICA) stenosis, it is an invasive procedure associated with a small but definite 4% risk of transient ischaemic attack and a 1% risk of permanent neurological deficit.[4] Therefore, a suitable non-invasive screening test is required. Screening should be sensitive to detect patients with significant stenosis who require angiography and exclude those with minimal or no disease

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who do not require it. The current method of choice for non-invasive screening of the carotid artery is duplex ultrasonography.[1] Although several criteria are available for diagnosing carotid stenosis, there is no consenus on the ideal criteria. This is due to the operator-dependent nature of ultrasonography, and different equipment, techniques and disease patterns in different populations. Even with similar equipment, criteria used in one vascular laboratory may not have the same validity and predictive value when used in another laboratory. It is hence important to validate ultrasonographic diagnostic criteria using DSA as the gold standard. Validation is part of the accreditation process developed by multidisciplinary groups to assess the performance of vascular laboratories.[5]

The aim of this study was to evaluate optimal ultrasonographic criteria for determination of ICA stenosis of more than or equal to 50%, 60% and 70% with reference to DSA results.

Materials and Methods

From January 1995 to December 2003, 114 patients who presented to our institution within 120 days of the onset of ischaemic symptoms (transient ischaemic attack or nondisabling stroke) were recruited. This study was approved by the Hospital Institutional Review Board NNI-IRB/05/010. Informed consent was obtained from all patients. These patients had undergone both carotid duplex ultrasonography and DSA within 1 month of each other and were being evaluated for carotid endarterectomy. This study does not include consecutive patients. Angiography was only performed after patients were willing to accept the possible risks of angiography. In our study, no patient suffered adverse neurological consequences as a result of this procedure. Of these patients, 20 were excluded from the study because of the occlusion of one or both ICA and atypical flow patterns within vessels, such as low velocities in near-occlusion, and extensive calcified plaques resulting in long segments of acoustic shadowing. The breakdown is as follows: 8 patients had extensive calcified plaques resulting in long segments of acoustic shadowing. In another 8 patients, both carotid duplex and angiography showed complete internal carotid artery occlusion that is angiography collaborated with carotid duplex findings. In the remaining 4 patients, carotid duplex showed total internal carotid artery occlusion. Angiography showed almost total occlusion with a very thin string of contrast in the occluded artery (near-occlusion). All patients with non-large artery aetiologies of stroke and ipsilateral carotid stenosis were included. However, patients with cardiac embolism and prior ipsilateral carotid endarterectomy were excluded, as duplex studies did not show stenosis in these 2 groups. Finally, 94 patients were assembled. Each carotid bifurcation was treated as an independent case in the final analysis; i.e., data from 188 vessels were available for analysis.

Duplex Study

Duplex ultrasonographic studies of the carotid arteries were performed on a Diasonics Spectra (Diasonics Inc, Milpatas, California) using a 7.5-MHz transducer. The cervical ICA, common carotid artery (CCA) and external carotid artery (ECA) were examined in transverse and longitudinal sections using B-mode grey-scale imaging and colour Doppler ultrasound. The colour window was adjusted so that the point of maximal velocity in the ICA was either red or shifting towards white because of aliasing. Velocity waveforms were obtained at the point of greatest mean frequency shift on the colour map. Readings were routinely obtained from the CCA at the base of the neck, just proximal to the carotid bifurcation; the proximal, mid and distal ICA; and the ECA at an incident angle ≤60º. Colour ultrasound was used to aid identification of the residual lumen. Doppler spectrum was obtained from any site of significant stenosis, as detected by either B-mode or colour mapping. The highest peak systolic velocity (PSV) and end diastolic velocity (EDV) were recorded from each location. The entire visible length of the ICA and CCA was examined so that any plaques of low echogenicity would not be overlooked.

Angiogram

DSA was performed via the transfemoral route, with selective catheterisation of the extracranial arteries on a digital angiography system (Advantx LCN/CN +, GE Medical Systems, Wisconsin, MI). DSA runs of selective bilateral CCA injections were obtained in the standard anteroposterior and lateral projections. The measurements were made on a printed hard copy with the N method and expressed as a percentage diameter reduction of the vessel. The diameter of the residual lumen was measured at the most stenotic site. The N denominator was determined at the first segment of the far-distal ICA with parallel walls beyond the post-stenotic dilatation according to NASCET.[1] The degree of stenosis reported by DSA was used as the gold standard. The following velocity criteria were compared with DSA: PSV ICA, PSV CCA, EDV ICA, EDV CCA, PSV ICA/PSV CCA, PSV ICA/EDV CCA, EDV ICA/EDV CCA. The radiologist who interprets the angiography is not blinded to the ultrasound or clinical history.

Statistical Analysis

Sensitivity, specificity and area under the curve (AUC), together with their 95% confidence intervals (CIs) and

Table 1. Area Under the Receiver Operating Curves (and Confidence Interval, CI) of the Velocity Parameters for Diagnosis of Carotid Stenosis

	Carotid stenosis (%)					
Parameter	50		60		70	
PSV ICA/PSV CCA	0.99	(0.986-1)	0.99	(0.98-1)	0.99	(0.97-1)
PSV ICA	0.98	(0.97-1)	0.98	(0.95-1)	0.98	(0.95-1)
PSV CCA	0.29	(0.18-0.4)	0.29	(0.18-0.4)	0.29	(0.18-0.4)
EDV ICA	0.95	(0.92-0.99)	0.96	(0.93-0.99)	0.96	(0.92-0.99)
EDV CCA	0.3	(0.19-0.4)	0.26	(0.16-0.36)	0.27	(0.17-0.38)
EDV ICA/EDV CCA	0.97	(0.94-1)	0.98	(0.96-1)	0.98	(0.95-1)
PSV ICA/EDV CCA	0.99	(0.97-1)	0.998	(0.99-1)	0.99	(0.98-1)

CCA: common carotid artery; EDV: end diastolic velocity; ICA: internal carotid artery; PSV: peak systolic velocity

accuracy, were studied for each criterion. Sensitivity was defined as the number of true-positive studies divided by the sum of true-positive and false-negative studies. Specificity was defined as the number of true-negative studies divided by the sum of false-positive and true-negative studies. We used the receiver operating characteristic (ROC) curve to compare the performance of each of the 7 criteria in classifying patients with more than or equal to 50%, 60% and 70% carotid stenosis. An ROC curve is a graph that displays the relationship between the sensitivity and specificity of a diagnostic tool across a spectrum of cutoffs.[6] The overall accuracy of a diagnostic tool is expressed in terms of AUC, ranging from 0.5 (poor) to 1.0 (perfect). Data analysis was carried out in Stata (V7.0). All tests were conducted at the 5% level of significance.

Results

The ages of the 94 patients ranged from 53 to 76 years (mean, 64; standard deviation, 8.8). The male-to-female sex ratio was 2.9:1. The ethnic proportion in our study was – Chinese:Indian:Malay:Others = 83:6:3:2. Conversely, in the Singapore population, it was – Chinese:Indian: Malay:Others = 77:8:14:1.[7]

70% stenosis

AUCs for 70% stenosis for all criteria are shown in Table 1. AUCs for 70% stenosis indicated that PSV ICA/EDV CCA (AUC, 0.99; 95% CI, 0.98 to 1.00) and PSV ICA/ PSV CCA (AUC, 0.99; 95% CI, 0.97 to 1.00) (Fig. 1) performed relatively better than the other parameters. For predicting stenosis of 70% or more using PSV ICA/PSV CCA criteria, a cutoff of 3.1 provided us with a sensitivity of 100%, a specificity of 91% and an accuracy of 95% (Table 2). Using PSV ICA/EDV CCA criteria to predict more than 70% stenosis, we found that a cutoff of 10.3 gave 100% sensitivity, 91% specificity and 95% accuracy (Table 2).

Table 2. Sensitivity, Specificity, Area Under Curve and Accuracy of PSV ICA/PSV CCA and PSV ICA/EDV CCA, Together with Their Cutoff Values to 50%, 60% and 70% Carotid Stenosis

Carotid stenosis (%)		50	60	70
PSV ICA/PSV CCA	Cutoff	≥1.5	≥2.6	≥3.1
Sensitivity		100	100	100
Specificity		85	94	91
Area under curve		99	99	99
Accuracy		93	97	95
PSV ICA/EDV CCA	Cutoff	≥3.5	≥10.3	≥10.3
Sensitivity		100	100	100
Specificity		58	96	91
Area under curve		99	99	99
Accuracy		79	98	95

CCA: common carotid artery; EDV: end diastolic velocity; ICA: internal carotid artery; PSV: peak systolic velocity

60% stenosis

AUCs for 60% stenosis for all criteria are shown in Table 1. AUCs for 60% stenosis indicated that PSV ICA/EDV CCA (AUC, 0.998; 95% CI, 0.99 to 1.00) and PSV ICA/ PSV CCA (AUC, 0.99; 95% CI, 0.98 to 1.00) (Fig. 2) performed relatively better than the other parameters. For predicting stenosis of 60% or more using PSV ICA/PSV CCA criteria, a cutoff of 2.6 provided us with a sensitivity of 100%, specificity of 94% and an accuracy of 97% (Table 2). Using PSV ICA/EDV CCA criteria to predict more than 60% stenosis, we found that a cutoff of 10.3 gave 100% sensitivity, 96% specificity and 98% accuracy (Table 2).

50% stenosis

AUCs for 50% stenosis for all criteria are shown in Table 1. AUCs for 50% stenosis indicated that PSV ICA/EDV CCA (AUC, 0.99; 95% CI, 0.97 to 1.00) and PSV ICA/ PSV CCA (AUC, 0.99; 95% CI, 0.986 to 1.00) (Fig. 3) performed relatively better than the other parameters. For

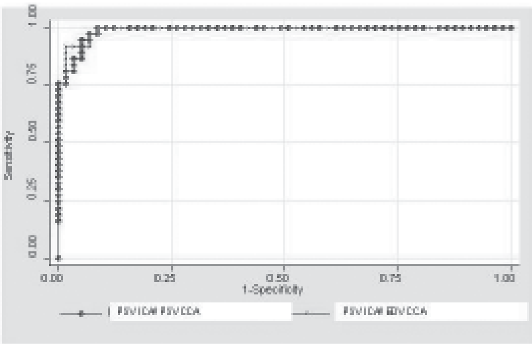

Fig. 1. Receiver operating characteristic curve for 70% stenosis using PSV ICA/PSV CCA and PSV ICA/EDV CCA.

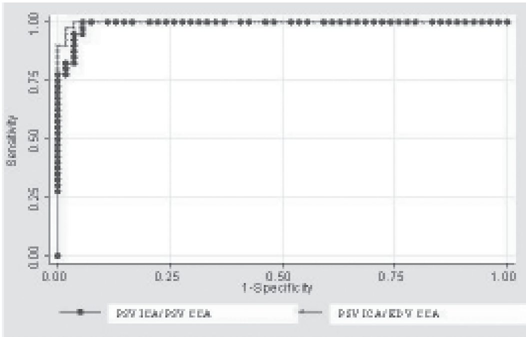

Fig. 2. Receiver operating characteristic curve for 60% stenosis using PSV ICA/PSV CCA and PSV ICA/EDV CCA

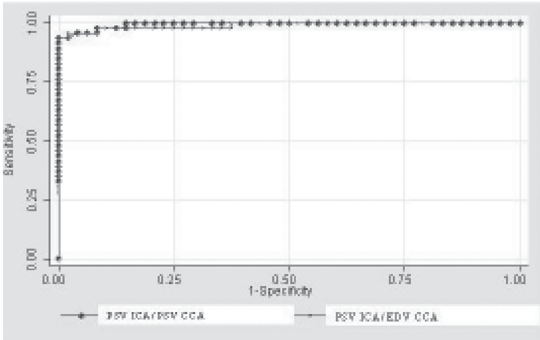

Fig. 3. Receiver operating characteristic curve for 50% stenosis using PSV ICA/PSV CCA and PSV ICA/EDV CCA.

predicting stenosis of 50% or more using PSV ICA/PSV CCA criteria, a cutoff of 1.5 provided us with a sensitivity of 100%, specificity of 85% and accuracy of 93% (Table 2). Using PSV ICA/EDV CCA criteria to predict more than 50% stenosis, we found that a cutoff of 3.5 gave 100% sensitivity, 58% specificity and accuracy of 79% (Table 2).

Discussion

The Chinese formed the majority of the study, as expected from the population ethnic distribution. However, there were comparatively more Indians and less Malays in our study compared to the general population. The higher prevalence in Indians may be due to genetic factors. One of our co-authors recently published a paper on local stroke prevalence.[7] In that study, stroke prevalence was highest among Chinese men and lowest among Malay women. This is comparable to our study.

To date, 7 velocity criteria using duplex ultrasonography have been proposed to detect carotid stenosis.[8-10] Our study showed that among the 7 criteria, velocity ratios are the most accurate. A literature search revealed that systolic velocity ratios of ICA/CCA are useful in diagnosing carotid stenosis.[8-23] Since ultrasonography is used as a screening tool in our laboratory, we selected cutoffs with high sensitivity in order to minimise false-negatives. Accuracy remained high for our chosen values.

For 70% stenosis, our ratio of 3.1 was intermediate (between 2.5 and 4.5) and our sensitivity and specificity were 100% and 91%, respectively. The accuracy of 95% ranks highly among current literature.[11-16]

For 60% stenosis, our ratio of 2.6 was intermediate (between 2 and 3.2-3.5).[17,18] The sensitivity, specificity and accuracy were 100%, 94% and 97%, respectively.

For 50% stenosis, our ratio of 1.5 was intermediate (between 1.3 and 2.5).[15,16,19-23] The sensitivity, specificity and accuracy were 100%, 85% and 93%, respectively.

Few authors evaluated the ratio of PSV ICA/EDV CCA.[10,24] In our study, a cutoff of 3.5 was useful for determining 50% carotid stenosis, with 100% sensitivity and 58% specificity (Table 2). For both 60% and 70% stenosis, a cutoff of 10.3 achieved 100% sensitivity although the specificity differed. Knox et al[24] found a ratio of 7.5 predictive of ≥60% stenosis with high accuracy. There were no published data for 50% and 70% stenosis using PSV ICA/EDV CCA.

PSV has been the most generally accepted single parameter for detecting and quantifying stenosis.[10,15,25-27] PSV increases with narrowing of the artery and is useful for grading carotid stenosis. It is the easiest measurement to obtain, necessitates no additional calculation and shows great sensitivity and specificity. Two recent papers from *Radiology*[8] and *Journal of Vascular Surgery*[9] deserve special comment. The first paper[8] was a consensus statement from an expert panel of radiologists, whereas the second paper[9] was a systematic review and meta-analysis of published studies from 1966 to 2003. Firstly, both papers acknowledged that standard duplex criteria for grading stenosis does not exist, and encourage validation of each laboratory's results. Secondly, although they recommended the use of PSV ICA as grading criteria, they pointed out that PSV ICA may not be reliable under certain circumstances: presence of tandem lesions, contralateral high-grade stenosis, discrepancy between visual assessment of plaque and PSV ICA, elevated CCA velocity, hyperdynamic cardiac state, or low cardiac output. For example in a patient with low cardiac output, the PSV ICA may be disproportionately low when compared with the PSV ICA/PSV CCA. Hence one must be aware of limitations using PSV ICA. Because of this, the authors recommended additional criteria for assessment of carotid stenosis, such as velocity ratios of ICA/CCA. In our study we found that PSV ICA was highly predictive of carotid stenosis: the sensitivity, specificity, accuracy and AUC were high for 70% stenosis (AUC, 0.98; 95% CI, 0.95 to 1), 60% stenosis (AUC, 0.98; 95% CI, 0.95 to 1), and 50% stenosis (AUC, 0.98; 95% CI, 0.97 to 1) (Table 1). We absolutely agree with *Radiology*[8] and *Journal of Vascular Surgery*[9] that PSV ICA is excellent for grading carotid stenosis. However in our study, we found that the ICA/CCA velocity ratios fared slightly better compared to PSV ICA (Table 1).

EDV is useful for high-grade stenosis when aliasing is problematic for measuring PSV. However, it is dependent on outflow resistance and shows greater variability than the PSV.[11,28] PSV CCA reflects the severity of an ICA lesion. A low PSV CCA with increased pulsatility index corresponds to a high-grade ICA stenosis. By itself, this parameter is poorly predictive of ICA disease. This also holds true for EDV CCA.

Although the study was conducted over 9 years, when results were compared between the earlier half and later half of the study, we found that ICA/CCA velocity ratios still remained superior compared to other parameters for diagnosing carotid stenosis.

In summary the 2 major limitations with the use of velocity criteria are:

1) Modification by general circulatory conditions unrelated to the carotid artery lesion. These include haematological disorders (anaemia, haemodilution), proximal haemodynamic disorders (cardiac output, arrhythmia), distal haemodynamic alterations (intracranial stenosis, cerebral arterial venous malformation) and contralateral haemodynamic alterations (subclavin steal, carotid occlusion).[29] To overcome this variability, ICA/CCA systolic and diastolic velocity ratios were recommended. Although diastolic ratios were introduced to detect high-grade stenosis, it is likely to have great variability as EDV CCA can often be so low as to drop below the measurement range of the Doppler spectrum analyser.
2) A smooth plaque lining the bulb has no discernible haemodynamic effects but can be detected by B-mode duplex ultrasonography. On the other hand, increased velocities recorded at a curvature or kinking may result in overestimation of the degree of stenosis. Other factors affecting accuracy include plaque asymmetry and extensive calcified plaques, obscuring the carotid lumen and preventing complete Doppler sampling.

Although ultrasonography is a good screening tool, there are potential limitations:

1) False negatives may result from a failure to identify near-occlusion, mistaking them for mild-to-moderate stenosis due to the lack of turbulence with severely limited flow. Alternatively, they could be misread as occlusion. Recognition of these nearly occluded vessels, however, is usually not a problem because of extensive plaques and/or thrombus evident on B-mode. The use of colour Doppler ultrasound increases the accuracy of stenosis determination since a string of colour may often be seen in a near-occluded artery (carotid string sign). The “normal” or low velocities measured in the tiny residual lumen belies the severity of the disease and are as such misleading.
2) Limited field of view with no information on the intracranial vasculature.
3) Occasionally fails to identify intraluminal thrombus.
4) Technical problems include patient movement, obese patient, short neck, and carotid bifurcation at or above the mandible edge.

Our study showed that duplex ultrasonography is an excellent screening tool for detecting extracranial ICA stenosis. We found PSV ICA/PSV CCA and PSV ICA/EDV CCA ratios superior to other velocity criteria for the diagnosis of more than or equal to 50%, 60% and 70% ICA stenosis. All patients with angiographically confirmed stenosis were detected using our criteria.

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