Vascular and Endovascular Surgery
44(6) 483-488

DOI: 10.1177/1538574410374128
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Importance of Validation of Accuracy of Duplex Ultrasonography in Identifying Moderate and Severe Carotid Artery Stenosis

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Abstract

Background and Purpose: The accuracy of carotid duplex ultrasonography (CDU) in detecting moderate and severe carotid artery disease was evaluated in comparison with arteriography. **Methods**: Accuracy of CDU was correlated with arteriographic findings using North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria in 147 internal carotid arteries. The duplex measurements consisted of peak systolic velocities (PSVs), end diastolic velocities (EDVs), and internal carotid PSV to common carotid artery PSV ratios (ICA/CCA). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy (OA) using the 3 parameters were determined. Receiver operating characteristic (ROC) curves were constructed from the ultrasonographic data for detection of 50% or greater stenosis (moderate disease) and 70% or greater stenosis (severe disease). **Results**: CDU for detecting ≥50% stenosis had a sensitivity of 100%, specificity of 87.8%, and accuracy of 96.6%. The area under the ROC curves for PSV was 0.86 (95% confidence interval [CI] 0.80-0.93), for EDV was 0.86 (95% CI 0.80-0.92), and for ICA:CCA ratio was 0.95 (CI 0.91-0.99). CDU for detecting ≥70% stenosis had a sensitivity of 100%, specificity of 87.1%, and accuracy of 94.5%. The area under the ROC curves for PSV was 0.76 (95% CI 0.68-0.84), for EDV was 0.74 (95% CI of 0.65-0.82), and for ICA/CCA ratio was 0.89 (0.84-0.94). **Conclusions**: We conclude that ≥50% stenosis and ≥70% stenosis can be reliably determined by CDU in our vascular laboratory. Each vascular laboratory must validate their own criteria against the current gold standard of carotid arteriography. A high degree of confidence in CDU is critical before any institution uses the test as the sole diagnostic method prior to carotid intervention.

Keywords
duplex ultrasonography, carotid stenosis, carotid arteriography

Introduction

In the past two decades, carotid duplex ultrasonography (CDU) has become the diagnostic modality of choice to screen patients for the presence of carotid disease. Most centers also use CDU to follow postoperative patients, follow progression of the disease in asymptomatic patients, and to detect extracranial disease in symptomatic patients. Recent large meta-analysis of CDU has demonstrated a sensitivity of 98%, a specificity of 88% for detecting ≥50% stenosis as well as 90% sensitivity and 94% specificity for detecting ≥70% stenosis.[1]

In a time of emphasis on cost control and quality assessment, many investigators advocate eliminating arteriography with its potential complications and use CDU alone, or in combination with magnetic resonance angiography (MRA) or computed tomographic arteriography (CTA) prior to surgical intervention.[2-6] Therefore, continuous internal validation of the accuracy of CDU becomes important for each vascular laboratory.

In this report, we describe validation of our existing criteria (Table 1) and evaluation of each of the 3 common parameters for detecting moderate (≥50%) and severe (≥70%) internal carotid artery (ICA) stenosis.

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Patients and Methods

From January 1, 2006 through December 31, 2008, a total of 82 patients with 147 carotid arteries had complete ultrasonographic and arteriographic data analyzed for correlation. We excluded patients who had arteriography done >30 days after CDU, arteriograms performed outside of our institution, patients with carotid restenosis or previous carotid endarterectomy or stenting, technically inadequate CDU examinations, and inability to accurately measure percentage stenosis on arteriography.

Carotid duplex ultrasonography examinations were performed using Philips iU22 (Philips Biomedical Systems, Bothell, Washington), Logiq 9E (General Electric, Milwaukee, Wisconsin), and Zonare (Zonare Inc, Mountain View, California) scanners with a 7.5-mHz linear array transducer and 5-mHz Doppler frequency. The examinations were performed by 8 registered vascular sonographers and interpreted by 4 vascular surgeons in an Intersocietal Commission for the Accreditation of Vascular Laboratories (ICAVL) accredited vascular laboratory at the Ross Heart Hospital, a part of The Ohio State University Heart & Vascular Center. Examinations included both longitudinal and transverse views of the ICA, common carotid artery (CCA), and the external carotid artery bilaterally with gray scale images, color and Doppler flow being recorded for later interpretation. Standard techniques were used as part of our protocol including aligning the cursor parallel to the vessel wall, obtaining waveforms using a small sample volume ideally placed in the center of the flow, and attempting to keep the Doppler angle at 60° or less. Peak ICA systolic velocities (PSVs), end diastolic ICA velocities (EDVs), and internal to common carotid artery PSV ratios (ICA/CCA ratio) were recorded. Our institutional criteria are shown in Table 1. These criteria have been previously developed as a result of an internal validation process based on correlating CDU with arteriograms.

Percutaneous arteriograms were performed using intra-arterial digital subtraction techniques with at least 2 views in addition to intracranial views. Contrast arteriography findings were viewed in a blinded fashion, by one of the authors (B.S.) on a monthly basis as a routine quality assurance function in the vascular laboratory. The diameter of the lumen at the most severely stenotic site of the ICA was measured to a fraction of a millimeter and used to calculate percentage diameter stenosis based on North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria:[7]

$$\%\,\text{ICA stenosis} = 1 - (\text{ICA stenosis diameter}/\text{normal distal ICA diameter}) \times 100$$

Statistical Analyses

Microsoft Excel (MS Office 2003) program was used to collect all data and create scatter graphs. Two-by-two tables for ≥50% stenosis criteria and ≥70% stenosis criteria were created. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy (OA) were calculated.

Receiver operating characteristic (ROC) curves were constructed to assess the accuracy of ultrasonographic criteria for detecting ≥50% stenosis and ≥70% angiographic defined stenosis. The OA of a CDU was expressed in terms of the area under the ROC curve, ranging from 0.5 (*poor*) to 1.0 (*perfect*). STATA 10.1 software for Macintosh (StataCorp LP, College Station, Texas) was used to generate the fitted curves, the areas under the curves, and to calculate corresponding 2-sided 95% confidence interval [CI].

Table 1. Duplex Ultrasound Criteria for Internal Carotid Artery Stenosis

Stenosis Category, %	PSV, cm/s	EDV, cm/s	ICA/CCA Ratio
<50	<135	<40	
50-69	135-284	>40	2-4
70-99	>285	>85	>4
Preocclusive	Minimal flow		
Occlusion	No detectable flow		

Abbreviations: PSVs, peak systolic velocities; EDVs, end diastolic velocities; ICA/CCA ratio, internal carotid artery−common carotid artery PSV ratio.

Table 2. Accuracy of Carotid Duplex Ultrasonography for 50% Stenosis or Greater (Top) and for 70%or Greater Stenosis (Bottom)

	≥50%
Sensitivity	100%
Specificity	87.8%
False negative	0.00%
False positive	12.2%
Positive predictive value	95.5%
Negative predictive value	100%
Accuracy	96.6%
	≥70%
Sensitivity	100%
Specificity	87.1%
False negative	0.00%
False positive	12.9%
Positive predictive value	91.4%
Negative predictive value	100%
Accuracy	94.5%

Results

A total of 82 patients with 147 eligible carotid arteries had complete ultrasonographic data and corresponding arteriography within 30 days of each other (Table 2). Scatter grams of arteriographic stenosis versus the 3 parameters (PSV, EDV, and ICA/CCA ratio) were generated to demonstrate the distribution of severity of ICA disease (Figure 1). Arteriographic stenosis ranged from 0% stenosis to total occlusions (9), with a mean of 66.8% (SD 21.74). Peak systolic velocities ranged from 0 to 650 cm/s (mean 276.78, SD 173.59) and EDVs from

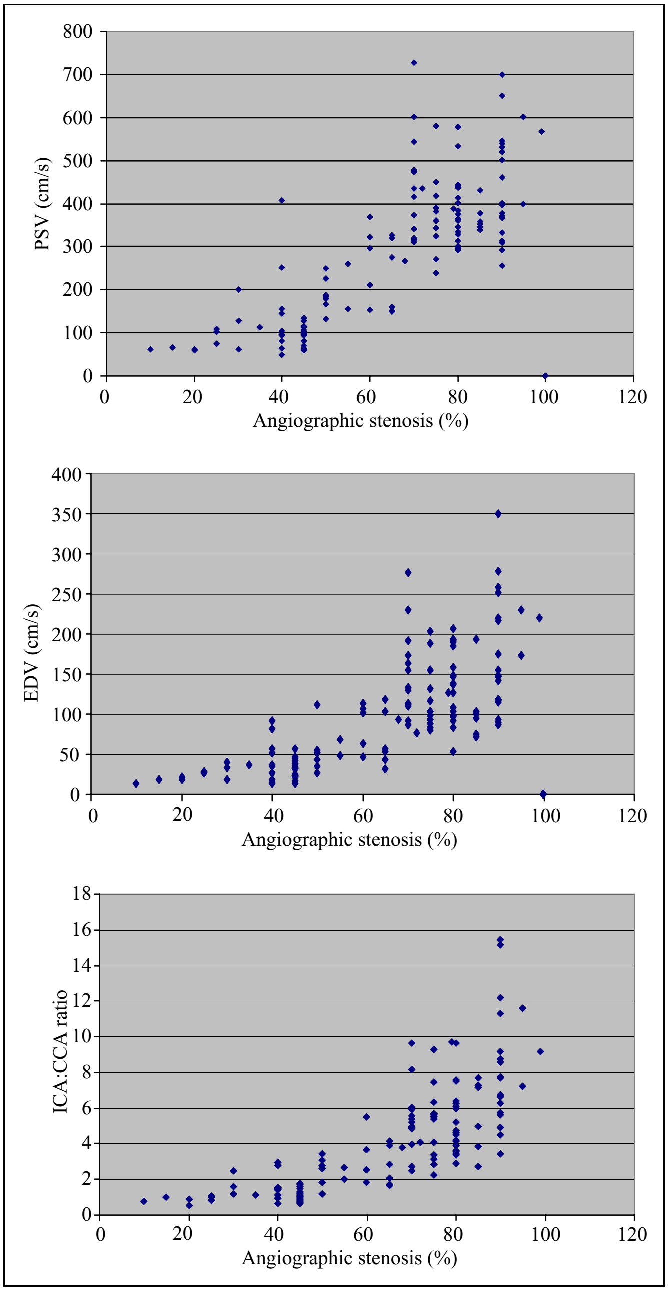

Figure 1. Scatter grams of internal carotid peak systolic velocity (PSV; top), internal carotid end diastolic velocity (EDV; middle), and ratio of internal carotid PSV to common carotid PSV (ICA/CCA) (bottom).

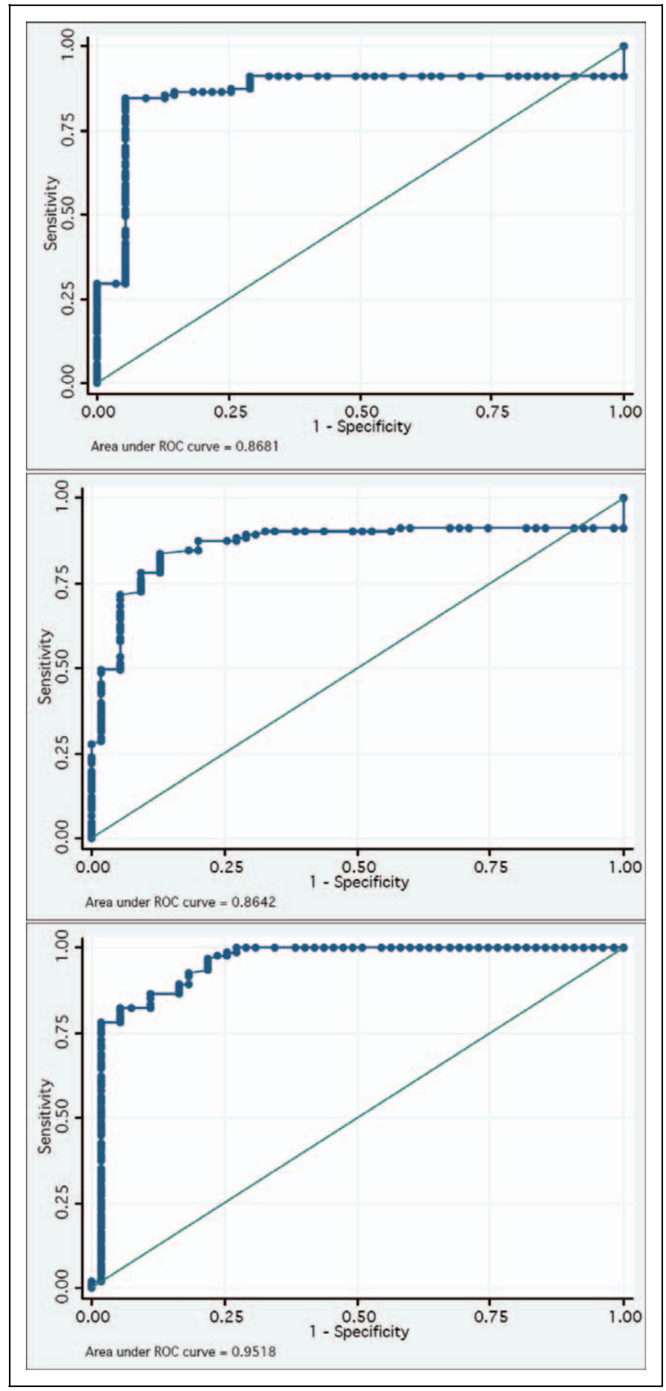

Figure 2. Receiver operating characteristic (ROC) curves illustrating the accuracy with which our ultrasonogrphy criteria are able to detect angiographic stenosis of 50% or greater: top, peak systolic velocity (PSV); middle, end diastolic velocity (EDV), and bottom, ICA/CCA ratio. ICA/CCA indicates the ratio of internal carotid PSV to common carotid PSV.

0 to 350 cm/s (mean 93.53, SD 70.28). After excluding totally occluded ICAs, the ICA/CCA ratios varied from 0.55 to 15.48 (mean 4.16, SD 3.03).

Table 2 depicts the sensitivity, specificity, NPV, PPV, and OA for detecting carotid stenosis $\geq$50% and carotid stenosis $\geq$70%. The threshold of PSV $\geq$ 135 m/s, EDV $\geq$ 40, and an ICA/CCA ratio between 2 and 4 are associated with a sensitivity and NPV approaching 100%, a specificity of 87.8%, a PPV of 95.5%, and an OA of 96.6% in identifying angiographic stenosis $\geq$50%. Our criteria for identifying a $\geq$70% stenosis (PSV $\geq$ 285, EDV $\geq$ 85, and an ICA/CCA ratio > 4) shows sensitivity and NPV of 100%, a specificity of 87%, a PPV of 91.4 % and an OA of 94.5%.

The ROC curves for each of 3 CDU parameters are shown in Figure 2 for $\geq$50% stenosis and in Figure 3 for $\geq$70% stenosis.

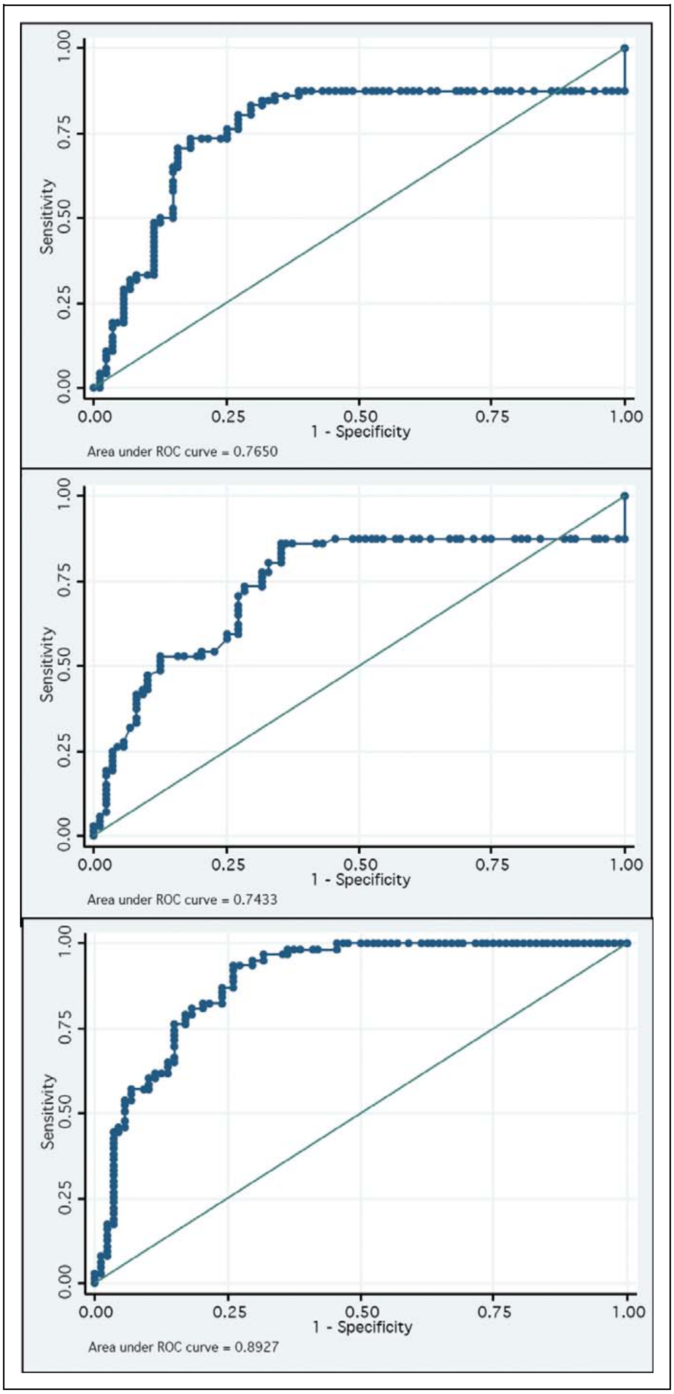

Figure 3. Receiver operating characteristic (ROC) curves illustrating the accuracy with which our ultrasonogrphy criteria are able to detect angiographic stenosis of 70% or greater: top, peak systolic velocity (PSV); middle, end diastolic velocity (EDV) and bottom, ICA/CC ratio. ICA/CCA indicates the ratio of internal carotid PSV to common carotid PSV.

The ROC curve analysis indicated that the accuracy of CDU for $\geq$50% ranges from 0.86 to 0.95 across all 3 parameters (Table 3). The accuracy for $\geq$70% ranges from 0.74 to 0.89 across all 3 parameters (Table 4).

Table 3. Areas Under the Receiver Operating Characteristic (ROC) Curves for 50% Stenosis or Greater

CDU Criteria	Area	Standard Error	95% CI
PSV	0.86	0.03	0.80-0.95
EDV	0.86	0.03	0.80-0.92
Ratio	0.95	0.02	0.91-0.99

Abbreviations: CDU, carotid duplex ultrasonography; PSVs, peak systolic velocities; EDVs, end diastolic velocities; CI, confidence interval.

Table 4. Areas Under the Receiver Operating Characteristic Curves for 70% Stenosis or Greater

CDU Criteria	Area	Standard Error	95% CI
PSV	0.74	0.04	0.68-0.84
EDV	0.74	0.04	0.65-0.82
ratio	0.89	0.02	0.84-0.94

Abbreviations: CDU, carotid duplex ultrasonography; PSVs, peak systolic velocities; EDVs, end diastolic velocities; CI, confidence interval.

Discussion

Carotid duplex ultrasonography is the primary screening modality used to detect carotid artery stenosis in asymptomatic patients and to confirm the presence of extracranial carotid disease in symptomatic patients. The traditional practice has been to use arteriography to confirm the presence of severe carotid stenosis prior to carotid intervention. However, conventional angiography is an expensive and invasive test with known risk of stroke. In a recent retrospective review that included 19,826 patients undergoing cerebral angiography, neurologic complications occurred in 2.63% with 0.14% of strokes resulting in permanent disability.[8] Many investigators have advocated carotid interventions based on CDU findings alone or in combination with MRA or CTA.[2-6] Elimination of arteriography prior to carotid intervention requires compulsive quality assurance and near perfect correlation between CDU and the gold standard. In practice, studies have shown that CDU accuracy can vary widely between laboratories and the magnitude of the variation is clinically significant.[9-11] Therefore, each vascular laboratory must perform a critical comparison of CDU with angiographic data. Deficiencies that are identified during this analysis must be addressed as a part of internal validation process.[1,12]

In reviewing the literature, the 4 most common variables accounting for the variation in OA are equipment, sonographer experience, technical protocols in place, and the interpreting physician. There is evidence that criteria should be validated separately for each piece of equipment.[13] In the Asymptomatic Carotid Artery Stenosis (ACAS) study, 4 manufacturers were used with at least 8 different devices. In their analyses, no factors were identified that predicted reliability of the device.[14] To remedy the situation, Jahromi et al suggest adopting polynomial regression to minimize such errors.[1] This would permit a device-specific CDU report to include a predicted stenosis that is based on a complex relationship between velocities and

Table 5. Correlation Between Contrast Arteriography and Carotid Duplex Ultrasonography (CDU) at the Ohio State University Vascular Laboratory[a]

Arteriography CDU	<50%	50-69%	70-99%	100%
<50%	36	0	0	0
50-69%	**4**	14	0	0
70-99%	**1**	**7**	76	0
100%	0	0	0	9

[a] False-positive values are given in boldface. There were 4 false positives in the >50% stenosis group and 8 false positives in the >70% stenosis group. There were no false-negative values.

degree of stenosis. Based on this data, the devices can be calibrated to improve the validity of the measurement. Our studies were performed on 3 different manufacturers of ultrasound scanners, and our data was not subjected to linear regression by equipment.

False-positive errors, or overestimation of stenosis, and false-negative errors, or underestimation of stenosis, can be attributed to patient's pathophysiology (such as contralateral carotid artery occlusion, hypertensive, or hypotensive patient) or operator technique (such as incorrect Doppler angle placement).[15-17] In our study, using a PSV of 285 cm/s alone to determine ≥70%, we recorded 6 false-positive studies. Of the 6 false positives, 5 had 60% to 65% diameter stenosis by arteriography with only a single vessel shown to have a 40% stenosis. Using an EDV of >85 cm/s alone, 6 of the 8 false-positive vessels demonstrated 60% to 68% stenosis on arteriography. Using the ICA/CCA ratio of >4 alone, there were 2 false positives with arteriograms showing 60% and 65% stenosis, respectively. We had 3 false negatives using a PSV ≥285 cm/s alone and all 3 vessels showed PSVs between 239 and 271 cm/s. Of the 5 false negatives, 4 were associated with EDV between 72 and 80 cm/s. In addition, there were 8 false negatives (ratios <4) with stenosis between 70% and 90% on arteriography. Across all of the 3 parameters (PSV, EDV, and ICA/CCA ratio), there were a total of 12 false positives and no false negatives (Table 5).

Following the publication of the NASCET trial, vascular laboratories rushed to validate and report their accuracy rates with CDU for identifying 70% lesions by arteriography.[18] The 3 most common parameters used to quantify the degree of hemodynamic ICA stenosis are PSV, EDV, and ICA/ CCA ratios. Strandness et al published the most widely used criteria for determining the severity of carotid stenosis based on these parameters.[19] Recently, a multispecialty consensus conference published criteria using all 3 parameters in addition to a plaque percentage estimate.[12] This consensus recommended stratifying stenosis by CDU into 5 main categories: normal (PSV < 125 cm/s with no plaque), <50% stenosis (systolic PSV < 125 cm/s with plaque or intimal thickening), 50% to 69% stenosis (ICA systolic PSV between 125 and 230 cm/s and visible plaque), >70% to near total occlusion (ICA systolic PSV > 230 cm/s and visible plaque and luminal narrowing), and total occlusion. Using the same categories but with our own cutoff points, we have demonstrated a sensitivity of 100% and NPV of 100%, making CDU an excellent tool to detect both moderate and severe carotid disease. In addition, a specificity of 87.1% and 87.8% and PPV of 91.4% to 95.5% for >50% and >70%, respectively, makes the test a good tool to select candidates for surgical intervention. Using similar thresholds (PSV > 290 cm/s and EDV > 80 cm/s), the Strandness group also reported a specificity of 96% and a PPV of 95%.[20]

Most investigators choose the 70% threshold because it is used as a cutoff for recommending intervention in asymptomatic patients. As a screening test, CDU needs to have a high degree of sensitivity and an excellent NPV. However, when evaluating patients for carotid interventions, based on a decision analysis, Clase et al have recommended that specificity and the high PPV remain a critical component of any strategy that looks at risk/benefit ratio.[21] Therefore, when relying on CDU for interventions without contrast studies, it is imperative to err on the side of high specificity and PPV of at least 90% if not greater.[20]

Our study has several limitations. We have previously mentioned the lack of validation for each of the 3 scanners, multiple technologists, and interpreting physicians in our laboratory. The fact that patients in this study were "self-selected" with only those with moderate or severe carotid disease receiving arteriography may have resulted in overestimating true positives and true negatives (specificity and sensitivity).[18] Intraobserver variability is a possible limitation although the agreement rate is reported to be 95.9% at >0% stenosis, 90.4% for >50% stenosis, and 96.8% for total occlusion.[22]

Finally, like with most studies, only a small number of vessels undergoing arteriography were subjected to ROC analyses, possibly biasing the accuracy of the test upward. Using ROC analysis for only highly diseased arteries may make the analysis less reliable for those with milder degrees of stenosis. However, for identifying >70% stenosis, we had no false negatives and an OA of 94.56% (Table 2).

In conclusion, this study re-demonstrates the importance of laboratory-specific validation of criteria for CDU against gold standard of arteriography. Our results show that the use of CDU has excellent sensitivity and NPV for diagnosis of moderate and severe carotid stenosis. In addition, most severely stenosed arteries can be diagnosed with CDU with high specificity and PPV. When a laboratory has established and validated its own diagnostic criteria, CDU is a great noninvasive tool for diagnosing and grading severe carotid stenosis. Yet, a high degree of confidence in CDU is critical before any institution uses the test as the sole diagnostic method prior to carotid intervention.

Acknowledgment

We would like to thank Ioannis Hatzaras for his help with statistical analysis.

Declaration of Conflicting Interests

The author(s) declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The author(s) received no financial support for the research and/or authorship of this article.

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