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Duplex Ultrasonography to Predict Internal Carotid Artery Stenoses Exceeding 50% and 70% as Defined by NASCET: The Need for Multiple Criteria

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ABSTRACT

Carotid duplex scanning is being used more frequently as the sole preoperative diagnostic imaging modality for patients considered candidates for carotid endarterectomy. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) has demonstrated the benefit of surgical treatment in patients with carotid stenoses exceeding 70%. The purpose of this study was to determine duplex criteria that accurately predict carotid stenoses exceeding 50% and 70% as defined by NASCET arteriographic criteria. One hundred forty-one patients (264 carotid arteries) considered surgical candidates were prospectively studied over a 2-year period by use of both duplex scanning and digital subtraction cerebral arteriography. Carotid artery stenosis was determined by a single radiologist using NASCET arteriographic criteria. Peak systolic velocity (PSV) and end-diastolic velocity (EDV) were measured in the internal carotid (ICA) and common carotid

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(Abstract continued)
(CCA) arteries by use of duplex scanning. ICA/CCA velocity ratios were calculated for PSV and EDV. Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated. $PSV_{ICA/CCA}$ provided the highest sensitivity, and EDV_{ICA} the highest specificity in this study. Arteriographic stenoses exceeding 50% and 70% were reliably predicted with use of these duplex criteria. It is concluded that duplex criteria can predict carotid stenoses exceeding 50% and 70% as defined by NASCET arteriographic criteria. These criteria should be independently validated by other vascular laboratories.

Introduction

The collaborators of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) recently published results of a randomized multicenter clinical trial of carotid endarterectomy in patients with symptomatic moderate carotid stenoses of 50–69%.[1] A small, but statistically significant, benefit was found for endarterectomy in this group when compared to medical therapy. Also, durable benefits were noted in surgically treated patients with stenoses exceeding 70% at 8 years' follow-up.

Duplex scanning is the most commonly used noninvasive diagnostic imaging modality for evaluation of carotid artery stenosis. Additionally, duplex scanning is being used more frequently as the sole preoperative diagnostic imaging modality before carotid endarterectomy. Commonly used traditional duplex criteria, developed by comparison studies with arteriography, report the carotid bifurcation as normal, 1–15% stenosis, 16–49% stenosis, 50–79% stenosis, 80–99% stenosis, and occluded.[2] These categories are not appropriate for the evaluation of stenoses exceeding 50% and 70%.

Recent North American randomized multicenter trials evaluating carotid endarterectomy include, in addition to NASCET, the Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Veterans Affairs (VA) Cooperative Trial.[1,3,4] These trials measured carotid stenosis by using an arteriographic method comparing the point of maximal stenosis with the distal disease-free internal carotid artery. This arteriographic method differs from those used to establish traditional duplex criteria. The arteriographic techniques used to establish traditional duplex criteria do not provide results equivalent to the methods used in the randomized trials.[5] The purpose of this study was to prospectively develop duplex criteria to reliably predict carotid stenoses exceeding 50% and 70% as defined by the arteriographic method used in NASCET.

Methods

Between March 1996 and June 1998, 141 patients (264 carotid arteries) were prospectively studied with both duplex scanning and carotid arteriography within 30 days of each other. Most of these patients were being evaluated for possible surgical treatment of carotid disease, and this group represents all patients who had technically adequate examinations during the study interval. All duplex studies and carotid arteriographies were performed at St. Joseph Mercy Hospital, Ann Arbor, Michigan.

Digital subtraction percutaneous catheter arteriograms with a $1,024 \times 1,024$ matrix were obtained in all patients. At least two views of each carotid bifurcation, as well as intracranial views, were obtained. The arteriographic stenosis was determined by a single radiologist using NASCET criteria.[5,6] The radiologist was masked to the results of corresponding duplex examinations.

Duplex scanning was performed with an Acuson 128XP10 Duplex Scanner (Mountain View, CA) with a 5-MHz linear array transducer. Peak systolic velocity (PSV) and end-diastolic velocity (EDV) measurements were taken in the distal common carotid artery (CCA) and the internal carotid artery (ICA). All examinations were performed by one of four vascular laboratory technologists using an identical protocol in a lab-

oratory accredited by the Intersocietal Commission for the Accreditation of Vascular Laboratories. In some cases, duplex examination followed arteriography. No attempt was made to mask the technologists to the results of carotid arteriography when it preceded duplex examination.

Maximum PSV and EDV measurements at the carotid bifurcation (PSV_{ICA} and EDV_{ICA}) were compared with the maximum diameter reduction arteriographic stenosis. Additionally, ICA/CCA velocity ratios were calculated for PSV and EDV, respectively ($PSV_{ICA/CCA}$ and $EDV_{ICA/CCA}$). These ratios were also compared with the maximum diameter reduction arteriographic stenosis. Sensitivity (SENS), specificity (SPEC), positive predictive value (PPV), negative predictive value (NPV) and accuracy (ACCUR) were calculated for each criterion (PSV_{ICA}, EDV_{ICA}, $PSV_{ICA/CCA}$ and $EDV_{ICA/CCA}$) at two levels of arteriographic stenosis: 50% or greater and 70% or greater.

Results

Arteriographic occlusion was present in 15 (5%) of the 282 carotid arteries available for comparison. Occluded vessels were excluded from analysis while contralateral vessels were included. Also, three patients had only one artery studied with duplex scanning, thus leaving 264 carotid arteries available for analysis. Stenosis greater than or equal to 50% was present in 134 (51%) arteries. Stenosis greater than or equal to 70% was present in 78 (30%) arteries. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy have been plotted for the measured values of EDV_{ICA} and PSV_{ICA}, and also for the calculated ratios $EDV_{ICA/CCA}$ and $PSV_{ICA/CCA}$.

The performance of EDV_{ICA} as a diagnostic test to determine 50% or greater arteriographic stenosis is shown in Figure 1. Accuracy (87%) was highest at EDV_{ICA} greater than 40 cm/sec. Sensitivity (84%) and specificity (88%) were also high at this point; however, PPV (80%) was somewhat lower. Using EDV_{ICA} greater than 60 cm/sec decreased sensitivity (77%), but accuracy (84%) remained high and PPV (90%) was much higher. Further increases in EDV_{ICA} increased specificity and PPV; however, sensitivity decreased rapidly.

Results from using PSV_{ICA} to predict 50% or greater arteriographic stenosis are shown in Figure 2. Accuracy (86%) was highest at PSV_{ICA} greater than 190 cm/sec. With this PSV_{ICA}, specificity (91%) and PPV (90%) were also high, while sensitivity (82%) and NPV (84%) were somewhat lower. Using PSV_{ICA} greater than 140 cm/sec increased sensitivity (90%) and NPV (89%) with a corresponding decrease in specificity (79%), PPV (80%), and accuracy (84%).

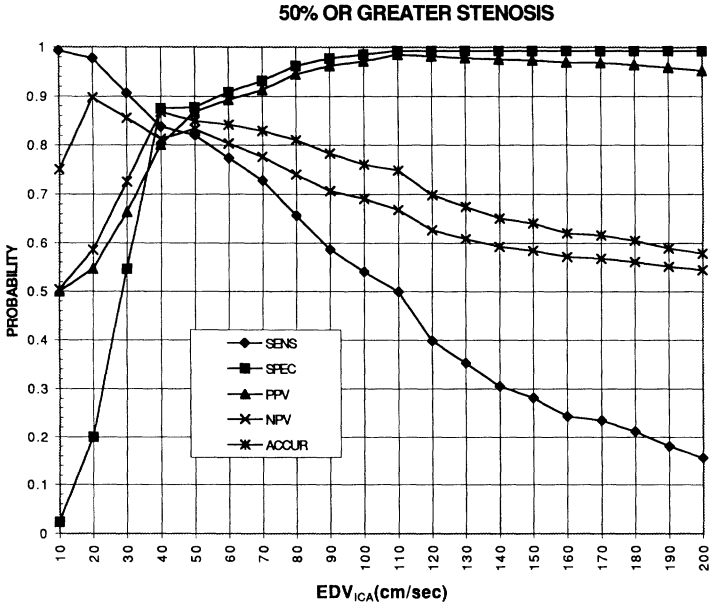

Figure 1. EDV_{ICA} greater than 60 cm/sec provides the high sensitivity (91%) and PPV (89%) needed for use as sole preoperative imaging. Higher velocities provide only small increases in specificity and are associated with large decreases in sensitivity.

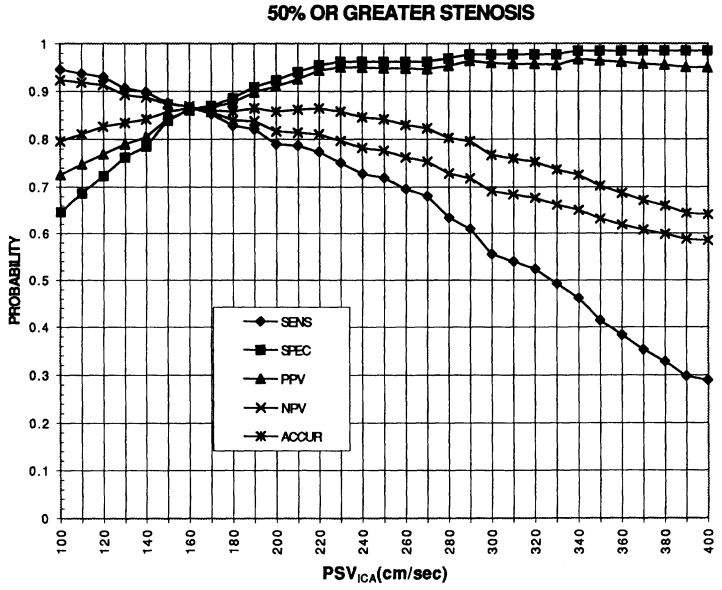

Figure 2. PSV_{ICA} greater than 190 cm/sec provides maximum accuracy (86%) with high specificity (91%) and PPV (90%). Higher velocities are associated with modest increases in specificity and PPV and significant decreases in sensitivity because of the steep slope of the sensitivity curve.

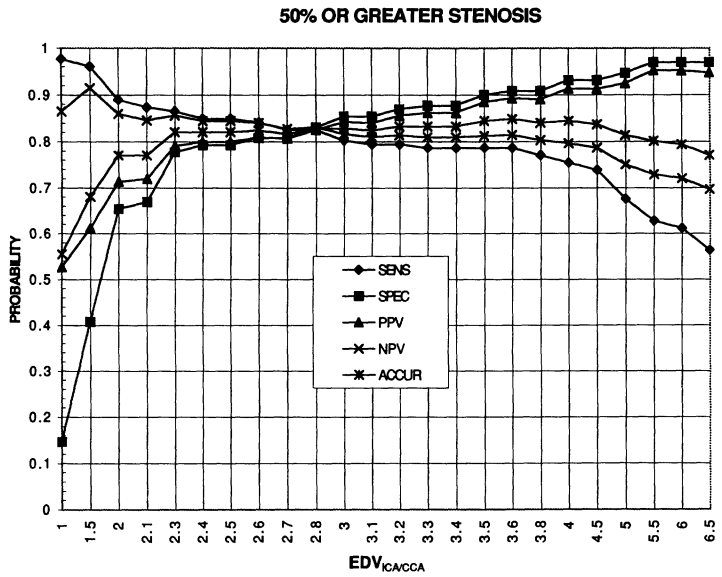

Figure 3. All curves are relatively flat over a wide range of values for $EDV_{ICA/CCA}$. Accuracy (85%) is highest at $EDV_{ICA/CCA}$ greater than 3.6.

Results from using $EDV_{ICA/CCA}$ to predict 50% or greater arteriographic stenosis are shown in Figure 3. A ratio greater than 3.6 provided the highest accuracy (85%). Specificity (91%) and PPV (89%) were also high; however, sensitivity (79%) was lower. A ratio greater than 2.8 increased sensitivity (83%) with associated decreases in specificity (83%) and PPV (83%).

Results from using $PSV_{ICA/CCA}$ to predict 50% or greater arteriographic stenosis are shown in Figure 4. A ratio greater than 1.8 provided high sensitivity (89%) and NPV (88%). Specificity (81%) and PPV (82%) were lower. Accuracy (85%) was maximized at this point. A ratio greater than 2.4 increased specificity (89%) and PPV (87%) at the cost of lower sensitivity (80%) and NPV (82%). Accuracy (84%) was relatively unchanged.

Results from using EDV_{ICA} to predict a 70% or greater arteriographic stenosis are shown in

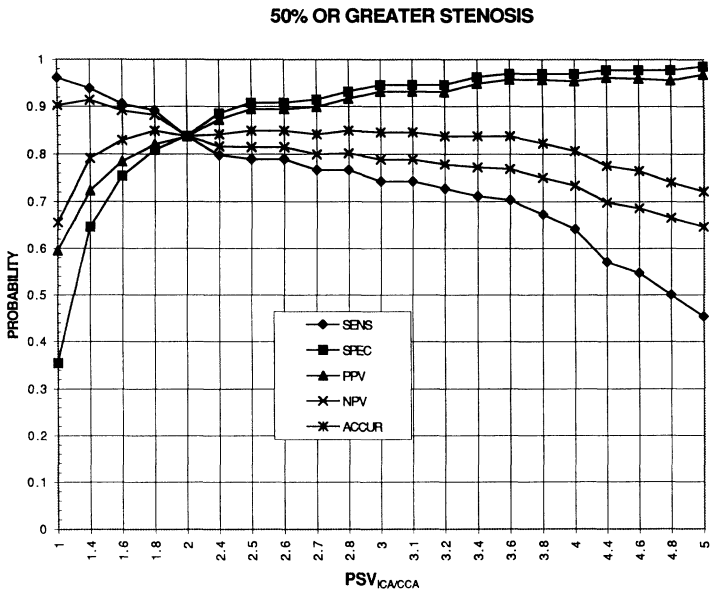

Figure 4. $PSV_{ICA/CCA}$ greater than 1.8 maximizes accuracy (85%) and provides high sensitivity (89%), appropriate for screening.

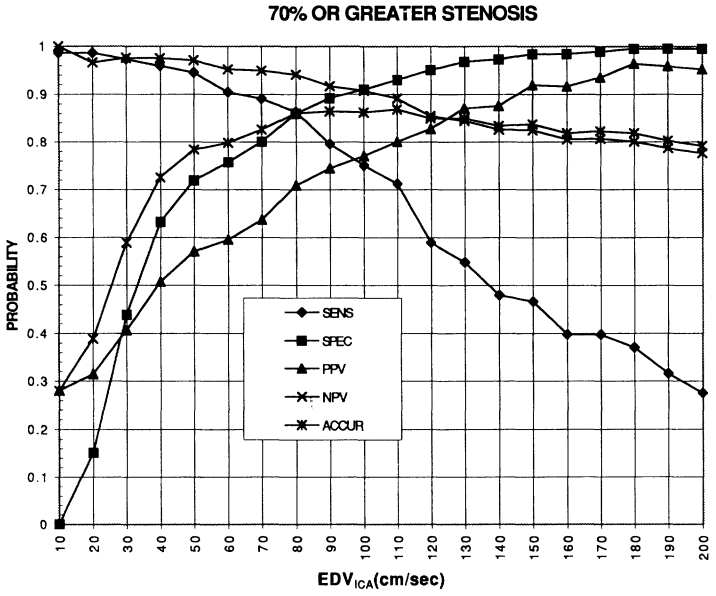

Figure 5. At EDV_{ICA} greater than 150 cm/sec the PPV (92%) is high and this test could be used as sole preoperative imaging. The sensitivity curve is very steep with a corresponding low sensitivity (47%).

Figure 5. Overall accuracy (87%) was highest with EDV_{ICA} greater than 110 cm/sec. Specificity (93%) and NPV (89%) were also high; however, sensitivity (71%) and PPV (80%) were lower. Using EDV_{ICA} greater than 150 cm/sec increased specificity (98%) and PPV (92%) with an accompanying fall in sensitivity (47%) and NPV (83%).

Results from using PSV_{ICA} to predict a 70% or greater arteriographic stenosis are shown in Figure 6. Accuracy (85%) was highest with a PSV_{ICA} greater than 230 cm/sec. Sensitivity (93%) and NPV (97%) were high; however, specificity (82%) and PPV (67%) were considerably lower. Increasing PSV_{ICA} lowered sensitivity without large increases in PPV.

Results from using $EDV_{ICA/CCA}$ to predict a 70% or greater arteriographic stenosis are shown in Figure 7. At $EDV_{ICA/CCA}$ greater than 4.5, sensitivity (97%) and NPV (98%) were high. Specificity (83%) and accuracy (86%) were lower, and

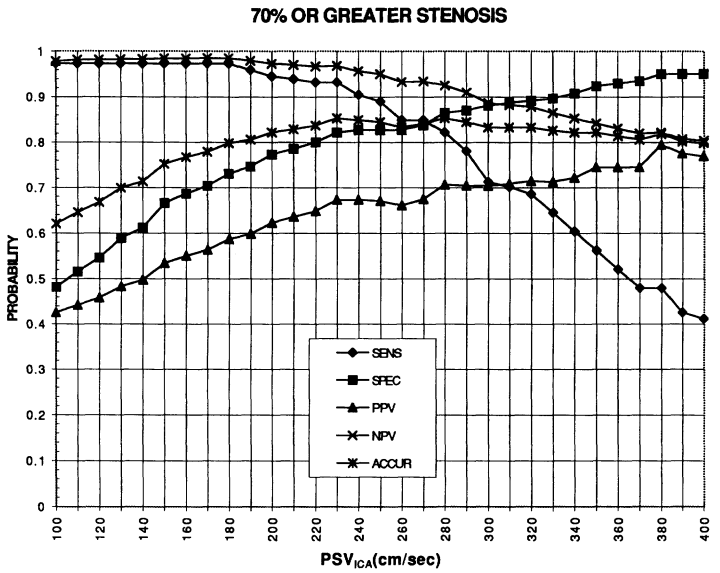

Figure 6. High PPV is never attained with PSV_{ICA}, but sensitivity (93%) is high with PSV_{ICA} greater than 230 cm/sec. This test could be considered for screening.

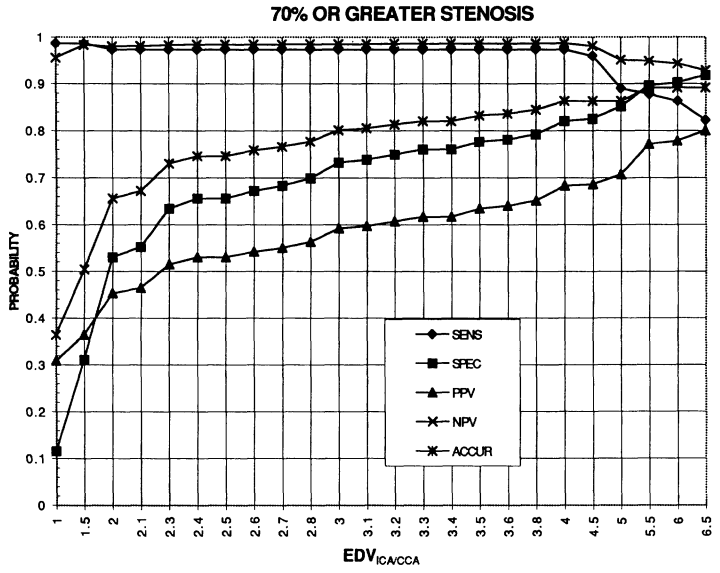

Figure 7. $EDV_{ICA/CCA}$ greater than 4.5 provides high sensitivity (97%). PPV is never high enough to allow use as sole preoperative imaging.

PPV (69%) was considerably lower. Increasing $EDV_{ICA/CCA}$ to 5.5 improved PPV (77%), specificity (90%) and accuracy (89%). Sensitivity (88%) was decreased more than NPV (95%).

Results from using $PSV_{ICA/CCA}$ to predict a 70% or greater arteriographic stenosis are shown in Figure 8. Accuracy (87%) was highest with a $PSV_{ICA/CCA}$ greater than 3.6. This point also gave high sensitivity (92%) and NPV (96%). Specificity (85%) and PPV (71%) were lower. Higher ratios decreased sensitivity without considerable improvement in PPV.

Discussion

The most recent report from the NASCET collaborators verifies the benefits of surgical treatment in patients with symptomatic carotid stenosis ex-

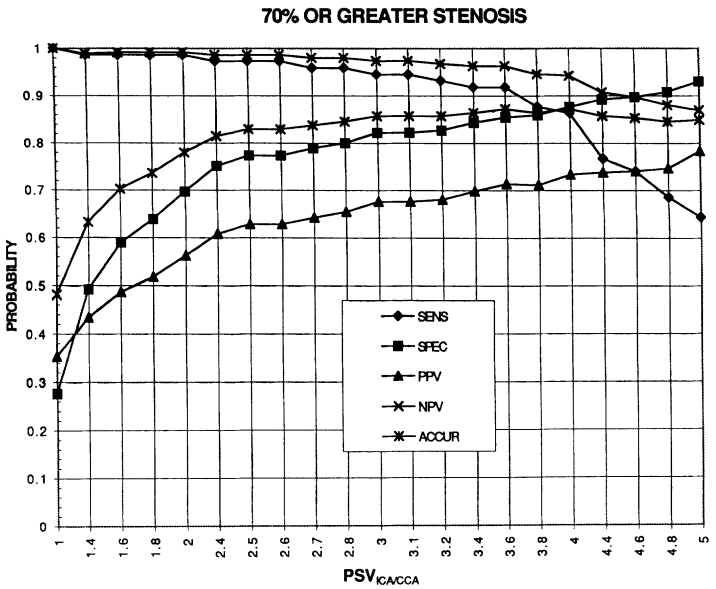

Figure 8. $PSV_{ICA/CCA}$ greater than 3.6 maximizes accuracy (87%) and provides high sensitivity (92%) appropriate for screening. Increasing $PSV_{ICA/CCA}$ decreases sensitivity without significant gains in specificity.

ceeding 70% at 8 years' follow-up.[1] Patients with lesions of 50–69% were found to have a moderate, but statistically significant, benefit from endarterectomy. Specifically, a 29% relative risk reduction for ipsilateral stroke was noted at 5 years' follow-up in the surgically treated group when compared with the medically treated group. Patients with stenoses less than 50% did not experience statistically significant benefits from surgical treatment. The degree of stenosis is arteriographically defined in NASCET by use of a technique comparing the point of maximum stenosis with the distal disease-free ICA. This technique, often referred to as the NASCET method, has also been applied in other multicenter trials. In clinical practice, however, arteriography is expensive, invasive, and associated with potential complications including stroke. Clearly, noninvasive methods to select those patients who will benefit from surgical treatment are desirable.[7] Duplex scanning is the most widely used and thoroughly evaluated noninvasive diagnostic modality.[8]

Duplex criteria for the determination of carotid stenosis have been developed through use of arteriography as the gold standard for carotid stenosis measurement. Several methods have been used to measure carotid stenosis arteriographically. Traditional duplex criteria have been based on arteriographic methods different from those used in NASCET and the other recent randomized prospective studies. The choice of any single arteriographic method to measure stenosis is somewhat arbitrary, and results using the different methods are not equivalent.[9] The method originally used to develop traditional duplex criteria compared residual lumen with estimated normal carotid bulb diameter.[10] This method consistently overestimates the degree of stenosis when compared with NASCET arteriographic criteria. If duplex scans are used to make clinical decisions based on NASCET results, then duplex criteria that are consistent with NASCET methods must be developed.

A useful technique to determine duplex criteria is to plot sensitivity, specificity, PPV, NPV, and accuracy for each duplex criterion. PSV_{ICA}, EDV_{ICA}, $PSV_{ICA/CCA}$, and $EDV_{ICA/CCA}$ have all been evaluated in this manner. The choice of specific criteria is not straightforward. As one moves along the curves it is clear that a higher PPV can be obtained only with the cost of a lower sensitivity and NPV. Similarly, criteria lose specificity as sensitivity increases. Individual vascular laboratory goals and individual clinical circumstances should be considered in choosing duplex criteria. Sensitivity is obviously important if a test is used for general screening where the goal is to find all significant lesions and thus not fail to offer treatment proven to reduce stroke risk. If the goal is to use duplex scanning as the sole preoperative di-

agnostic modality, then criteria providing a high PPV are desirable to avoid operating on patients with lesions not shown to benefit from surgical treatment in randomized trials.[5]

In this study, the most useful criteria to predict carotid stenoses exceeding 50% and 70% were EDV_{ICA} and $PSV_{ICA/CCA}$. Two optimal criteria to predict a 50% or greater stenosis are shown in Table I. If EDV_{ICA} greater than 60 cm/sec was used, specificity (91%) and PPV (89%) were both high. This criterion would be appropriate if duplex scanning was used as the sole preoperative imaging. Unfortunately, sensitivity (77%) was lower with this cut point. A much higher sensitivity (89%) can be obtained by use of $PSV_{ICA/CCA}$ greater than 1.8. Clearly, $PSV_{ICA/CCA}$ is a superior choice for the application of duplex scanning to screening because approximately 90% of all patients with a stenosis of 50% or greater would be identified for further evaluation or treatment through use of this criterion. When both criteria were applied, 99 of 134 carotid stenoses were correctly identified. The PPV (91%) for this group of arteries was high, thus permitting consideration for surgery without additional diagnostic testing. Twenty-one additional arteries meeting only the criterion of $PSV_{ICA/CCA}$ greater than 1.8 could be evaluated further with another diagnostic modality such as magnetic resonance imaging or arteriography. Overall, of the 134 arteries in this study with a 50% or greater stenosis, 120 (90%) were correctly identified for treatment or further diagnostic evaluation. If carotid endarterectomy was deemed appropriate, then 83% of these arteries could potentially be treated without arteriography.

Table I

Optimal Criteria to Predict a 50% or Greater Carotid Stenosis

Criterion	Sensitivity	Specificity	PPV	NPV	Accuracy
$EDV_{ICA} > 60$ cm/sec	77%	91%	89%	80%	84%
$PSV_{ICA/CCA} > 1.8$	89%	81%	82%	88%	85%

PPV, positive predictive value; NPV, negative predictive value; EDV, end-diastolic velocity; PSV, peak systolic velocity; ICA, internal carotid artery; CCA, common carotid artery.

Table II

Optimal Criteria to Predict a 70% or Greater Carotid Stenosis

Criterion	Sensitivity	Specificity	PPV	NPV	Accuracy
$EDV_{ICA} > 150$ cm/sec	47%	98%	92%	82%	84%
$PSV_{ICA/CCA} > 3.6$	92%	85%	71%	96%	87%

PPV, positive predictive value; NPV, negative predictive value; EDV, end-diastolic velocity; PSV, peak systolic velocity; ICA, internal carotid artery; CCA, common carotid artery.

Similarly, Table II shows two optimal criteria to predict a 70% or greater stenosis. Again, EDV_{ICA} proved to be most useful as a potential sole preoperative imaging criterion. When EDV_{ICA} was greater than 150 cm/sec, the PPV (92%) was high, resulting in a low false-positive rate. Specificity (98%) and accuracy (84%) were also high at this cut point; however, sensitivity (47%) was much lower. Unfortunately, the slope of the sensitivity curve is steep (Figure 5), resulting in the exclusion of about half of the diseased arteries if a cut point is chosen to provide a PPV exceeding 90%. Exactly what constitutes an appropriate PPV for sole preoperative imaging is not entirely clear. Investigators in the Asymptomatic Carotid Atherosclerosis Study used a PPV of 95% for entry into the trial with a duplex scan.[3] This PPV corresponds to a false-positive rate of 5%. The importance of a high PPV as an entry criterion for a clinical trial is clear; however, the choice of an appropriate PPV for clinical application to symptomatic and asymptomatic patients with different levels of disease severity is not as straightforward. Individual surgeons will likely have to decide what false-positive rate is acceptable for duplex scanning in the context of sole preoperative imaging and then choose cut points with an appropriate PPV. This type of clinical decision making requires prior validation of vascular laboratory criteria.

Screening for high-grade lesions was more successful in using $PSV_{ICA/CCA}$. Using $PSV_{ICA/CCA}$ greater than 3.6 provided high sensitivity (92%), although the PPV (71%) was considerably lower. Seventy-one of 77 stenoses greater than or equal to 70% were detected by use of this cut point. This performance is clearly more appropriate for a screening criterion. Note that the accuracy (87%) of this test was fairly high, with the broad application of this criterion primarily limited by its low PPV. In this study both carotid arteries in a single patient were considered as independent events, although the influence of a contralateral occlusion on duplex measurements is well documented.[11,12] At the completion of patient enrollment the number of arteries with stenoses exceeding 70% was lower than originally estimated. This circumstance impacted PPV results significantly because false-positive results, mostly due to contralateral occlusions, were more influential in the reduced sample size. The original intent of the study was to develop and validate criteria encompassing the situation of an occluded contralateral artery, occasionally encountered in all busy vascular laboratories. To accomplish this objective, arteries contralateral to occlusions with falsely elevated duplex measurements were kept in the study.

Comparing this study with those of other authors demonstrates similar results. Moneta et al[10] proposed the use of $PSV_{ICA/CCA}$ greater than 4.0 to predict stenoses exceeding 70%. A sensitivity of 91%, specificity of 87%, and accuracy of 88% were reported.[10] Neale et al[13] reported the combination of PSV greater than 270 cm/sec and EDV greater than 110 cm/sec to be 96% sensitive and 91% specific, with an accuracy of 93%. Results from both prior studies are similar to those validated in our study (Figures 5, 6, 8). We are not aware of any comparable studies that evaluate the prediction of stenoses exceeding 50% in a similar prospective manner.

The attractiveness of a single criterion, such as EDV_{ICA} or $PSV_{ICA/CCA}$, to be used for both sole preoperative imaging and screening is obvious. However, an understanding of biologic data analysis, specifically the often inverse relationship between sensitivity and positive predictive value, can spare vascular laboratories from the frequently futile task of forcing a single criterion to function effectively for all clinical purposes. This study supports the use of separate criteria for carotid duplex imaging, depending on the intended use of the study. The use of multiple criteria is both desirable and necessary if individual vascular laboratories seek to maximize the validity of carotid duplex imaging for the dual applications presently utilized.

Duplex scanning can reliably predict carotid stenoses exceeding 50% and 70% as defined by NASCET arteriographic methods. In this study the potential use of duplex scanning for sole preoperative imaging was best accomplished with use of EDV_{ICA}. Alternatively, $PSV_{ICA/CCA}$ was the better criterion for application as a broad screening test. Results from this study are similar to those reported by other authors; however, these similarities do not obviate the process of individual vascular laboratory validation.[10,13,14] Substantial variation between individual vascular laboratories and equipment has been reported in the literature.[15,16] Although the use of registered vascular technologists and accreditation of laboratories by the Intersocietal Commission for the Accreditation of Vascular Laboratories is likely to be helpful in managing the problems of

variation, these measures are not substitutes for the process of validation. The importance of this process is emphasized by the NASCET collaborators, who recommend validation of noninvasive studies at individual centers before arteriography is discarded.[1]

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