Application of Duplex Ultrasound in Conjunction with Computed Topography Angiography to Identify Native Carotid Artery Stenosis

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Abstract

Doppler ultrasound (DUS) examination is used to determine degree of stenosis by comparing patient records to threshold values of peak systolic velocity (PSV) through the internal carotid artery (ICA). DUS often overestimates the severity of stenosis. Computed tomography (CT) angiography (CTA) serves as the standard for diagnosis of stenosis, yet significant discrepancies remain between the DUS threshold values and the degree of stenosis determined by CTA analysis, especially for patients in the 50%–69% stenosis range. Therefore, standardization of stenosis diagnostic criteria between CTA and DUS findings is incomplete. Results from qualifying patients in the Geisinger medical system who underwent CTA and DUS analysis within a 3-month period were reviewed retrospectively by two blinded physicians to assess the concordance between current DUS parameters and degree of stenosis determined by CTA. Our data indicated significantly elevated PSV values as being the appropriate thresholds for determining both 50%–69% and >70% stenosis. The PSV values recorded were greater than 240 and 270, respectively. This study also showed some of the limitations that exist with CTA and DUS analysis in determining the percentage of ICA stenosis. Future studies will examine modified selection criteria to see if a more dependable PSV value can be elucidated.

Introduction

Internal carotid artery (ICA) stenosis is an abnormality often associated with atherosclerosis, the buildup of plaque on the artery walls. The ICA is particularly susceptible to atherosclerosis near its origin due to the bifurcation of the common carotid artery (CCA). At areas of bifurcation, turbulent blood flow allows for greater deposition of calcified residue which, over time, leads to greater luminal narrowing due to shear stress alterations of the arterial walls (1). Due to restricted blood flow or embolic debris traveling to the brain, potentially severe complications may occur. These can range from transient ischemic attacks (TIA) to debilitating strokes. It is estimated that carotid atherosclerosis is responsible for up to 20% of ischemic strokes (2). Primary preventive strategies, close monitoring, and medical and surgical management are all elements of ensuring optimal patient outcomes.

Monitoring of ICA stenosis includes four primary modalities, including carotid duplex ultrasound (CDUS), magnetic resonance angiography (MRA), computed tomography angiography (CTA), and catheter angiography. CDUS uses doppler waves to give a report on both the velocity of the blood through the lumen of the artery as well as some basic information of the morphology of the arterial lumen. CTA and MRA both allow for direct visualization of a substantial amount of vasculature ranging from the aortic arch to the intracranial vessels where the imaging can be used to study direct morphology. These methods are extremely useful tools of measurement, but their specific measurement values in determining the risk of future strokes in asymptomatic patients is uncertain.

Of these modalities, two frequently used in conjunction with one another are CTA and CDUS. CDUS can provide insight into the velocity of blood flow through areas of stenosis. This velocity can then be correlated within a range of the degree of stenosis. CDUS can accomplish this in an inexpensive, noninvasive, and radiation-free manner. There is limited direct imaging from CDUS, however, and its quality depends on the individual recording the test; thus, this is where CTA's application can aid providers. CTA allows for

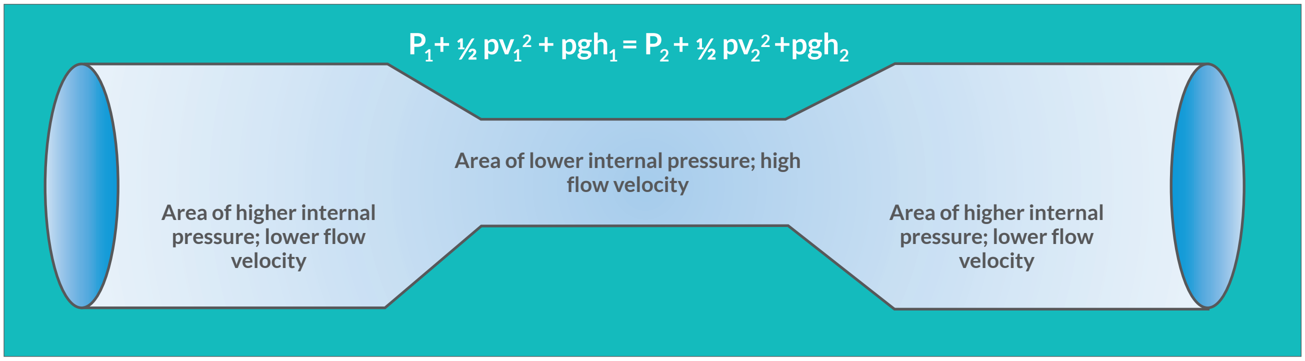

Figure 1. Pictorial representation of Bernoulli's pressure dynamics.

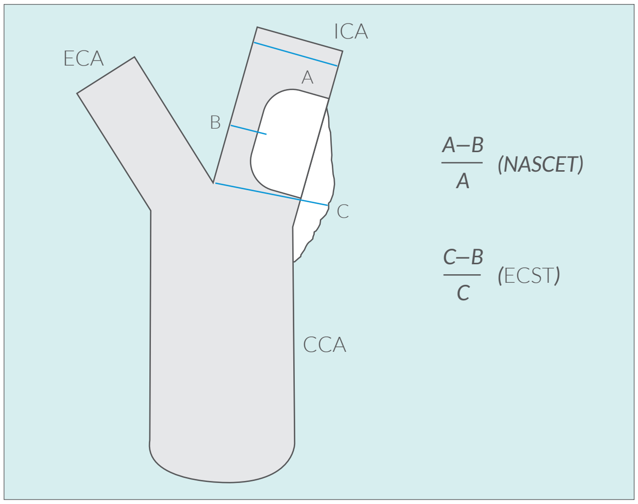

Figure 2. A comparison of the North American Symptomatic Carotid Endarterectomy (NASCET) method and European Carotid Surgery Trial (ECST) measurement methods. NASCET measures the widest portion of the ICA lumen distal to the plaque to the area of greatest stenosis. ECST measures the greatest area of the carotid bulb to the area of greatest stenosis.

visualization of the vasculature, and this can provide more direct measurement of stenosis, albeit with radiation exposure and exposure to iodinated contrast dye (3).

DUS measurements were originally compared to patient angiography records to use the peak systolic velocity (PSV) as a measure of degree of ICA stenosis. The basis for this measurement is Bernoulli's pressure dynamics (Figure 1). Bernoulli's equations show the relationship between the pressure inside the lumen and the result of that pressure on the correlating velocity. As lumen diameter increases, internal pressure increases and fluid velocity decreases. As lumen diameter becomes smaller, such as in the case of carotid atherosclerosis, the internal pressure decreases and fluid velocity increases.

Based on Bernoulli's pressure equations, higher PSV will correlate with a greater degree of stenosis. While CTA and CDUS are sound measurement devices, there exist inconsistencies in certain ranges where CDUS and CTA measurements do not correspond to one another as strongly as would be preferred in patient management. Barlinn et al. demonstrated this in their 2016 study where CTA and DUS measurements strongly correlated with one another in determining the degree of stenosis across all stenosis ranges. To further test these findings, Barlinn et al. conducted Bland-Altman analysis. This is a technique where two modes of measurement in medical settings are compared in a visual manner to assess differences between the averages of the two measurement modalities and interpret an agreement interval. This analysis showed large incongruences between DUS and CTA stenosis measurements. In terms of correlation, there was a difference of 3.57%. While this was an encouraging finding, the Bland-Altman analysis showed a 95% confidence range of -29.26 to 22.84, demonstrating the concerningly high levels of variability between the two measurement types (4, 5). Similarly, in the 2023 study by Simann et al., their findings showed that CTA was the superior measurement device, and there existed substantial differences between the measurements recorded when comparing CTA and DUS. The range of degree of stenosis in which the greatest differences existed was in the patient population that had an ICA stenosis between 50% and 69% (6). This range represents important threshold values for determining whether a patient requires medical or surgical management, especially if they are symptomatic. In addition to these inconsistencies in evaluation, limitations and sources of measurement error exist in each. For example, high degrees of calcified plaque can interfere with CDUS signal and give artificially low-velocity flow volumes. CTA imaging results can be influenced by the angle with which the artery is viewed, the interpretation of the viewer, and the quality of the image itself.

Guidelines for determining the degree of ICA stenosis are detailed in the North American Symptomatic Carotid Endarterectomy Trial and the European Carotid Surgery Trial (7). The NASCET trial based the severity of stenosis off the lumen diameter of the region of greatest disease burden and compared this lumen diameter of the unaffected region distal to the stenosis (Figure 2). When compared to the ECST, which determined stenosis by comparing the most affected region to the carotid bulb, the NASCET guidelines often produce a less severe result. While these guidelines have served as the usual source for interpreting PSV values and concurrent treatment regimens, they have fallen under scrutiny, especially in the determination of stenosis in the 50%–69% range in asymptomatic patients (8).

Currently, treatment guidelines suggest that patients with a history of stroke or TIAs and 50%–69% stenosis may benefit from surgical intervention, such as stenting or CEA. Those with less than 50% stenosis will not benefit from surgery. Older individuals, men, and those with stenosis exceeding 70% are at greatest risk and would most likely benefit from surgery. Ultimately, the decisions on managing patients with 50–69% stenosis are determined by the patient's clinical features, associated comorbidities, and overall health (9). History of a TIA is a useful clinical indicator for the need for intervention, but, per a 1996 study by Hankey, only 15% of stroke victims have a preceding TIA (10). Therefore, many of those patients who ultimately suffer a stroke would be considered to have asymptomatic carotid stenosis. These are the patients for whom intensive medical intervention, as described previously, would be especially beneficial, and medical intervention would be more beneficial to these patients than surgical procedures such as CEA and CAS. Medical management of stenosis would include controlling hypertension, smoking cessation, switching to the Mediterranean diet or other heart-healthy diets, reduced sodium intake, antiplatelet medications, lipid-lowering agents, and ACE inhibitors (11).

Current NASCET guidelines give a PSV value of 125 cm/sec as the threshold value for a stenosis equal to or greater than 50%. This threshold value has been tested with several rigorous trials, and there is significant concern that the value does not appropriately hold up. This can have significant ramifications for the management of ICA stenosis, as patients may undergo unnecessary and invasive procedures such as stenting or carotid endarterectomy (CEA) when medical management may be sufficient. Beach et al., in their 2012 analysis, proposed an even higher value at 165 cm/sec utilizing scatterplot data of 3,000 different data points (12). In their 2021 study, Gornik et al. found that a PSV value of 180 cm/sec was more consistent with a stenosis of 50%–69% than was the value given in the NASCET guidelines (13). In their study, they compared these PSV values to the more robust catheter angiography measurement as opposed to CTA. Given that the 50% stenosis value represents such an important marker for potential intervention strategies in symptomatic patients and potentially the start of more aggressive medical management in asymptomatic patients, it is important to define a value distinguishing this degree of stenosis as thoroughly as possible.

While it is also of high clinical relevance to best distinguish these values in the guidance of treatment for the sake of efficacy in a treatment regimen, it is also just as imperative to use proper guidance in overseeing resource management. In a 2007 study by Pawaskar, it was shown that stenting was significantly more expensive than CEA, most of which was due to procedural cost (14). Even more inexpensive was the ability to medically manage patients with asymptomatic stenosis of 50% or greater. Ultimately, best medical treatment (BMT) is the most optimal approach in management of both asymptomatic and symptomatic stenosis. Whether in using statins for hyperlipidemia, smoking cessation, hypertension management, or antiplatelet therapy, these interventions are significantly less invasive, have less side-effects, and are usually more cost-effective (15). Other factors favoring medical management as opposed to surgical management in terms of financial burden included elderly patients above the age of 75 with lower life expectancy following the procedure, which was noted to be of value as the degree of atherosclerosis increased proportionally to age. While comparisons of demographics and surgical methods does not fall directly under the purview of this study, it is important to note that the monitoring of the degree of ICA stenosis does dictate medical and surgical strategies.

In our study, we looked to find a more robust measurement of PSV that correlates with a stenosis value of 50%–69% as seen in CTA. This was done by comparing the values of PSV to the degree of stenosis determined via CTA by two board-certified vascular surgeons in patients receiving both a CTA and a DUS reading within 3 months of each other prior to any surgical intervention. Furthermore, we explored detailing more robust threshold PSV values for >70% stenosis in a similar manner. From this, we gained better understanding for guiding proper medical and surgical management of these patients with a goal of increased efficacy and decreased financial burden.

Methods

Four board-certified vascular surgeons at Geisinger Medical Center conducted a blinded review of the CTA of patients who had CDUS within a 3-month period from a pool of patients in the Geisinger medical system. Patient data came from a retrospective chart review of patients who had a CTA and DUS within 3 months of each other from January 2021 through May of 2021. Approval for this study was obtained from Geisinger's Institutional Review Board (2020-0119). Patients who were used for measurement could not have a procedure in the intervening time interval between when the CTA and DUS were collected. Furthermore, an artery's data was not used if it was found on the CTA that the region of stenosis had been previously stented, was contained in the common carotid artery, or had any influence from a previous intervention. Patients were disqualified from use if the quality of the image was poor. Examples of where this occurred include CTAs with significant image distortion due to movement or other artifacts and an excessive buildup of calcified atherosclerosis that made measurements difficult and unreliable. These various factors defined our exclusion criteria from the study. From DUS reports, the PSV was recorded for each artery, and if available the end-diastolic velocity (EDV) was recorded as well. If available, a ratio of the ICA to the CCA was recorded. The patient's age, surgical history, medical history, and substance use history, including tobacco and alcohol use, were recorded for demographic analysis.

For direct visualization of the CTA, the three-dimensional Aquarius iNtuition Viewer TeraRecon (TeraRecon, Durham, NC, USA) platform was used. A centerline through the artery under study was created by a member of the research team who was not part of the final measurement process. These centerlines were created using TeraRecon prior to review. Each physician measured an artery using the same centerline to avoid any deviations in the measurement of the lumen due to differences in the centerline itself. Two board-certified vascular surgeons measured the degree of stenosis from the CTA, and if there was a greater than 40% discrepancy between their measurements, a third physician would review the CTA. This reading would replace the values that were most significantly different from the other two. Arteries with 25% stenosis or less were deemed clinically insignificant and treated in a similar fashion to arteries with no evident stenosis. The stenosis values were analyzed in three different categories of measurement that were available on the iNtuition platform: the average area of the residual lumen and stenotic lumen, the diameter of the residual lumen and stenotic lumen, and the minimum and maximum diameters of the arterial lumen. To determine which of these categories provided the most robust measurements, receiver operating characteristics (ROC) and area under the curve (AUC) analysis were performed. ROC-AUC analysis also utilized other variables collected from the patient tests to determine which provided the most reliable measurements. These other variables included peak systolic velocity (PSV), end-diastolic velocity (EDV), common carotid artery to internal carotid artery ratio, PSV + ratio, EDV + ratio, and PSV + EDV + ratio. After finding the most robust predictor of degree stenosis, a PSV value that represented each threshold of clinically relevant stenosis was produced.

Results

The initial data includes 126 patients (252 arteries). Cases were excluded if the difference between two measurements of stenosis on computed topographic angiography (CTA) was 40% or higher, or the absolute difference was 25% or greater if one of the two measurements obtained demonstrated a stenosis of zero. Cases were also excluded if both measurements were zero or if the patient met any exclusion criteria, such as a surgery between the time of the CTA and the duplex ultrasound DUS, poor CTA image, or stenosis of the common carotid artery. Of these, 187 individual arteries from 121 patients met the inclusion criteria and were included in the final analysis.

Table 1 showed the characteristics of the 121 patients. The mean age was 68.2 years and 67.8% of the patients were male. Among the patients, 43.8% received either a CAS, CEA, or both procedures prior to recording a PSV from their DUS. All other comorbidities are detailed in Table 1.

<table>
<tr><th colspan="4">Patient characteristics and demographics</th></tr>
<tr><td colspan="2">Age at imaging (SD)</td><td colspan="2">68.2</td></tr>
<tr><td colspan="2">Gender, n%</td><td colspan="2">Male: 82 (67.8%)</td></tr>
<tr><td colspan="2">Coronary artery disease, n%</td><td colspan="2">Present: 47 (38.8%)</td></tr>
<tr><td colspan="2">Congestive heart failure, n%</td><td colspan="2">Present: 20 (16.5%)</td></tr>
<tr><td colspan="2">Dysrhythmia, n%</td><td colspan="2">Present: 18 (14.9%)</td></tr>
<tr><td colspan="2">Chronic obstructive pulmonary disease, n%</td><td colspan="2">Present: 35 (28.9%)</td></tr>
<tr><td colspan="2">Diabetes, n%</td><td colspan="2">Present: 33 (27 .3%)</td></tr>
<tr><td colspan="2">Hypertension, n%</td><td colspan="2">Present: 110 (90.9%)</td></tr>
<tr><td colspan="2" rowspan="2">Smoking, n%</td><td colspan="2">Prior: 63 (52.1%)</td></tr>
<tr><td colspan="2">Current: 34 (28.9%)</td></tr>
<tr><td colspan="2">Creatinine, mean (SD)</td><td colspan="2">1.0 (0.22)</td></tr>
<tr><td colspan="2">Creatinine, umol/L, mean (SD)</td><td colspan="2">89.9 (19.61)</td></tr>
<tr><td colspan="2">Previous ASA usage</td><td colspan="2">115 (95.0%)</td></tr>
<tr><td colspan="2">Previous antiplatelet drug usage, n%</td><td colspan="2">102 (84.3%)</td></tr>
<tr><td colspan="2">Previous statin use, n%</td><td colspan="2">106 (87.6%)</td></tr>
<tr><td colspan="2">Previous chronic anticoagulant use, n%</td><td colspan="2">7 (5.8%)</td></tr>
<tr><td colspan="2">Previous ACE inhibitor/ARB use, n%</td><td colspan="2">68 (56.2%)</td></tr>
<tr><td colspan="2">Previous beta-blocker use, n%</td><td colspan="2">59 (48.8%)</td></tr>
<tr><td colspan="2">Prior coronary artery bypass graft, n%</td><td colspan="2">26 (21.5%)</td></tr>
<tr><td colspan="2">Prior percutaneous coronary intervention, n%</td><td colspan="2">32 (26.4%)</td></tr>
<tr><td colspan="4">Prior CEA/CAS n%</td></tr>
<tr><td>Both: 5 (4.1%)</td><td>CAS: 17 (14.0%)</td><td>CEA: 31 (25.6%)</td><td>Neither: 68 (56.2%)</td></tr>
<tr><td colspan="2">Prior large arterial bypass, endarterectomy, PVI, n%</td><td colspan="2">8 (6.6%)</td></tr>
<tr><td colspan="2">Prior amputation of leg, foot, or toe,n%</td><td colspan="2">2 (1.7%)</td></tr>
<tr><td colspan="2">Prior TIA or stroke, n%</td><td colspan="2">38 (31.4%)</td></tr>
<tr><td colspan="4">Prior CEA by side, n%</td></tr>
</table>

Table 1. Patient characteristics and demographics.

Table 2 showed the AUC from each ROC analysis. Score ranges are between 0.5 and 1.0, with 0.5 being an uninformative test and 1.0 being a perfect test. Scores of 0.5–0.6 were unsatisfactory, 0.6–0.7 satisfactory, 0.7–0.8 were seen as reliable, 0.8–0.9 were highly reliable, and 0.9–1.0 were ideal. AUC scores were reliable to highly reliable for all velocity parameters for classification of CTA stenosis < 50% vs 50%–69% for average vessel diameter measurement (AUC < 0.8). AUC was reliable for all velocity parameters for classification of CTA stenosis < 50% vs 50-69%, for minimum vs maximum vessel diameter measurement and reduction in vessel lumen area measurement (AUC 0.7-0.8). The AUC was reliable for classification of CTA stenosis 50%–69% vs ≥ 70% when the parameters included EDV for average vessel diameter measurement. When using the minimum vs maximum vessel diameter measurement, the AUC was reliable when then model included PSV only or PSV and ratio combination. The AUC was higher in reliability for classification of CTA stenosis 50%–69% vs ≥ 70% for all parameters except ratio only for reduction in vessel lumen area measurement. None of the parameters, unfortunately, were within the optimum category for reliability.

Of the different modalities the most robust predictor for <50 – 50%–69% stenosis was the average vessel diameter measurement, specifically utilizing the PSV and ratio of the internal carotid artery to the common carotid artery. Overall, average vessel diameter provided the most robust predictors of <50 – 50%–69% stenosis throughout all categories. For predicting degree of stenosis for 50%–69% vs ≥70%, the reduction in vessel lumen area measurement provided the most robust measurements. Specifically, using the PSV and ratio of the ICA to the CCA was the most robust of these measurement modalities.

Given that average vessel diameter provided the most robust measurements, ROC analysis was conducted to determine the threshold PSV values for determining the degree of stenosis. The bolded values in Table 3 represent the optimum cutoff points. Overall, specificity was poor while sensitivity was higher with higher than anticipated cutoff points. There was a greater negative predictive value (NPV) as opposed to positive predictive value (PPV) for these points. Youden's index captures the performance of these values in predicting degree of stenosis. The Youden's index for these threshold values was poor, indicating that a high degree of inaccuracy and false positives and false negatives would occur. Ultimately, the highest-sensitivity cutoff point with the greatest NPV was a PSV of ≥ 240. This value had a concurrent specificity of 71.1%, a PPV of 63.6%, NPV of 92.9%, and a Youden's index of 0.614, indicating one of the highest levels of reliability of our compiled measurement parameters but a lower degree of reliability overall.

Table 4 similarly provided an elevated value for the PSV that was most sensitive and specific for stenosis greater than 70%. The number of patients was low, with only 12 total falling in this range. The suggested PSV value was a velocity greater than or equal to 250 cm/s. This carried a sensitivity of 87.9% and a specificity of 71.4%, a positive predictive value of 90.9%, and negative predictive value of 64.5%. Overall, the reliability of these scores was low, with a Youden's index value of 0.593.

Discussion

The determination of the degree of ICA stenosis is usually done with CTA and CDUS. The PSV gathered from the CDUS is often used in gauging degree of stenosis via the NASCET guidelines. These threshold values, however, may not be optimum in determining management in asymptomatic patients who have a stenosis of 50%–69%. Furthermore, the use of CTA and CDUS have provided unreliable and surprisingly low levels of certainty when determining degree of stenosis when utilizing the values obtained from CDUS in comparison to CTA. CTA remains the most reliable modality for measuring stenosis outside of catheter-based carotid angiography but does come with other risks such as radiation exposure and greater financial burden. A 2021 study by Samarzija et al. showed that CTA measurements showed a positive correlation with PSV values from CDUS studies, however, this correlation coefficient was unable to tell absolute values between the measurements. This study also showed that CTA severely underestimated the degree of stenosis throughout all ranges of stenoses, and that there was a high degree of standard error determined from the measurements (16). Similarly, our study showed that the threshold values determined by average vessel diameter measurements were poor. In Table 2, ROC-AUC comparative analysis determined that average vessel diameter measurements provided the most robust results. When this method was used to determine PSV threshold values most indicative of 50%–69% stenosis, the findings resulted in a PSV of ≥ 240 cm/sec, as shown in Table 3. This was higher than anticipated and while associated with a high degree of sensitivity (90.3%) and high NPV (92.9%), it had a low specificity (71.1%), PPV (63.6%) and a low Youden's index (0.614). This value is therefore effective at ruling out patients who may be thought to have 50%–69% stenosis but will carry with it a high degree of false negatives and false positives. This has poor implications for its use in determining medical and surgical management in patients with 50%–69% stenosis.

	< 50% vs 50-69%	50-69% vs ≥70%
Average vessel diameter measurement		
PSV	0.871	0.615
EDV	0.857	0.708
ratio	0.833	0.584
PSV + ratio	0.899	0.595
PSV + EDV	0.871	0.782
PSV + EDV + ratio	0.898	0.783
Minimum vs maximum vessel diameter measurement		
PSV	0.783	0.705
EDV	0.777	0.679
ratio	0.761	0.642
PSV + ratio	0.799	0.711
PSV + EDV	0.782	0.685
PSV + EDV + ratio	0.800	0.697
Reduction in vessel lumen area measurement		
PSV	0.778	0.849
EDV	0.786	0.821
ratio	0.766	0.787
PSV + ratio	0.798	0.863
PSV + EDV	0.791	0.849
PSV + EDV + ratio	0.807	0.857

Table 2. Area under the curve for ROC analysis of velocity parameters for prediction of CTA stenosis.

Velocity parameter threshold	Sensitivity	Specificity	PPV	NPV	Youden's Index
Gold standard					
PSV ≥ 125 cm/sec	0.984	0.441	0.496	0.980	0.425
Ratio ≥ 2	0.871	0.541	0.514	0.882	0.412
PSV ≥ 125 cm/sec + ratio ≥ 2	0.871	0.568	0.529	0.887	0.439
Modified parameters					
PSV ≥ 140	0.984	0.496	0.521	0.982	0.480
PSV ≥ 160	0.968	0.541	0.541	0.968	0.509
PSV ≥ 170	0.952	0.568	0.551	0.955	0.520
PSV ≥ 180	0.952	0.586	0.562	0.956	0.538
PSV ≥ 190	0.919	0.595	0.559	0.930	0.514
PSV ≥ 140 + ratio ≥ 2	0.871	0.577	0.535	0.889	0.448
PSV ≥ 160 + ratio ≥ 2	0.855	0.613	0.552	0.883	0.468
PSV ≥ 170 + ratio ≥ 2	0.855	0.631	0.564	0.886	0.486
PSV ≥ 180 + ratio ≥ 2	0.855	0.640	0.570	0.888	0.495
PSV ≥ 190 + ratio ≥ 2	0.839	0.649	0.571	0.878	0.488
PSV ≥ 240	**0.903**	**0.711**	**0.636**	**0.929**	**0.614**
PSV ≥ 270	**0.887**	**0.757**	**0.671**	**0.923**	**0.644**
PSV ≥ 240 + ratio ≥ 2	0.823	0.757	0.654	0.884	0.580
PSV ≥ 260 + ratio ≥ 2	0.807	0.784	0.676	0.879	0.591

Table 3. ROC analysis table predicting <50% and 50%–69% stenosis using average vessel diameter measurement.

A similar trend was observed in our values for determining stenosis values greater than 70%. Our PSV value was a velocity greater than or equal to 250 cm/s. This carried a sensitivity of 87.9% and a specificity of 71.4%, a PPV of 90.9%, and NPV of 64.5%. Overall, the reliability of these scores was low, with a Youden's index value of 0.593. Similarly, these scores would not be clinically reliable for use as markers for determining stenosis greater than 70%. The current gold standard is a PSV of 230 cm/s or greater.

Determining degree of stenosis is paramount to managing patients to reduce the risk of ischemic stroke and prepare for worsening of stenosis. A stenosis of 50% is particularly important since patients with a 50% or greater degree of stenosis are at higher risk of stenosis progression and therefore at higher risk of ischemic stroke. Risk of stenosis progression is positively associated with the stenosis grade; higher degrees of stenosis may continue to worsen, and this includes patients who are asymptomatic (17). Once it is determined that a patient has a 50% or greater stenosis, the onus of follow-up becomes much more critical. A 2012 study by Dua et al. showed that out of 288 patients, 26 (9%) developed symptoms or had a severe increase in their stenosis to >75%. The comorbidities most associated with stenosis increase included coronary artery disease (8.1%), hyperlipidemia (7.3%), and hypertension (6.7%) (18). Our study, and others, show that our current methodology for predicting 50%–69% stenosis is unreliable, and this confounds the ability to appropriately gauge the risk of patients for ischemic events, provide appropriate treatment plans, and accurately determine risk of disease progression. Aside from carotid angiography, the gold standard of accurately determining degree of stenosis, albeit invasive, current noninvasive measurement techniques

Velocity parameter threshold	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Youden's Index**
Gold standard					
PSV ≥ 230 cm/sec	0.901	0.679	0.901	0.679	0.580
EDV ≥ 100	0.604	0.857	0.932	0.400	0.461
ratio ≥ 4	0.670	0.857	0.938	0.444	0.527
PSV ≥ 230 + EDV ≥ 100	0.604	0.857	0.932	0.400	0.461
PSV ≥ 230 + ratio + EDV ≥ 100	0.473	0.929	0.956	0.351	0.402
0.0.Modified parameters					
PSV ≥ 250	0.879	0.714	0.909	0.645	0.593
PSV ≥ 270	0.868	0.750	0.918	0.636	0.618
ratio ≥ 3.3	0.769	0.714	0.897	0.488	0.483
EDV ≥ 70	0.868	0.643	0.888	0.600	0.511
EDV ≥ 90	0.714	0.821	0.929	0.469	0.535
PSV ≥ 230 + ratio ≥ 3.3	-	-	-	-	-
PSV ≥ 250 + EDV ≥ 70	0.868	0.714	0.908	0.625	0.582
PSV ≥ 250 + EDV ≥ 90	0.714	0.857	0.942	0.480	0.571
PSV ≥ 250 + EDV ≥ 100	0.604	0.857	0.932	0.400	0.461
PSV ≥ 250 + ratio ≥ 3.3	-	-	-	-	-
PSV ≥ 250 + ratio ≥ 4	0.670	0.893	0.953	0.455	0.563
PSV ≥ 250 + ratio ≥ 3.3 + EDV ≥ 70	0.747	0.750	0.907	0.477	0.497
PSV ≥ 250 + ratio ≥ 3.3 + EDV ≥ 90	0.626	0.857	0.934	0.414	0.483
PSV ≥ 250 + ratio ≥ 3.3 + EDV ≥ 100	0.517	0.857	0.922	0.353	0.374
PSV ≥ 250 + ratio ≥ 4 + EDV ≥ 70	0.670	0.893	0.953	0.455	0.563
PSV ≥ 250 + ratio ≥ 4 + EDV ≥ 90	0.571	0.929	0.963	0.400	0.500
PSV ≥ 250 + ratio ≥ 4 + EDV ≥ 100	0.473	0.929	0.956	0.351	0.402
PSV ≥ 260 + EDV ≥ 70	0.868	0.714	0.908	0.625	0.582
PSV ≥ 260 + EDV ≥ 90	0.714	0.857	0.942	0.480	0.571
PSV ≥ 260 + EDV ≥ 100	0.604	0.857	0.932	0.400	0.461
PSV ≥ 260 + ratio ≥ 4	0.868	0.714	0.908	0.625	0.582
PSV ≥ 260 + ratio ≥ 3.3 + EDV ≥ 70	0.747	0.750	0.907	0.477	0.097
PSV ≥ 260 + ratio ≥ 3.3 + EDV ≥ 90	0.626	0.857	0.934	0.414	0.483
PSV ≥ 260 + ratio ≥ 3.3 + EDV ≥ 100	0.517	0.857	0.922	0.353	0.374
PSV ≥ 260 + ratio ≥ 4 + EDV ≥ 70	0.670	0.893	0.953	0.455	0.563
PSV ≥ 260 + ratio ≥ 4 + EDV ≥ 90	0.571	0.929	0.963	0.400	0.500
PSV ≥ 260 + ratio ≥ 4 + EDV ≥ 100	0.473	0.929	0.956	0.351	0.402

Table 4. ROC analysis – diagnosing a 50%–69% versus > 70% stenosis using reduction in vessel lumen area measurement.

are not sufficiently diagnosing stenosis risk with an acceptable degree of accuracy. Better defining threshold values for PSV is a start, and determining proper follow-up for patients who are asymptomatic and in this vague degree of stenosis of 50%–69% is necessary.

Ischemic events are debilitating and require high degrees of resource utilization. Medical management of patients determined to have 50% stenosis or higher should be aggressive. Current optimal management for patients who are not requiring surgery or are poor candidates is multifactorial. Medically, aspirin daily of 75–325 mg/d, with rivaroxaban at 2.5 mg bid, or Clopidogrel 75 mg OD or ticagrelor 90 mg BID (if ASA-intolerant or allergic to ASA) is beneficial to reducing ischemic events in patients. Lipid lowering therapies with a goal LDL <1.8 mmol/L (70 mg/dL; <1.4 mmol/L [54 mg/dL] for very high risk) via a high-dose statin with ezetimibe or PCSK9 inhibitors is beneficial. Antihypertensives with ACEi/ARBs for a blood pressure goal <130/80 is ideal. Glucose-lowering therapy to a HbgA1c <7% further reduces risk. Finally, and least costly to patients, are lifestyle modifications including smoking cessation, transitioning to a healthier diet such as the Mediterranean diet, and moderate-intensity exercise 4–7 times a week to prevent atherosclerosis (19).

While this may appear to be a great deal of medical intervention, prevention of stroke not only maintains a patient's health and independence, but it also prevents financial burden from hospitalizations and interventional procedures in addition to the medical expenses for necessary follow-up. Data from 2006–2008 showed that the financial burden for patients suffering either a hemorrhagic or ischemic stroke was an average of $20,396 ± $23,256 (20). Further financial burden following a stroke include transportation concerns, household expenses, relocation, property loss, informal and formal home care, and potential disability causing job loss. Furthermore, the cost of inpatient management of a stroke vastly outweighed outpatient preventive measure (21).

Given the health and financial benefits that early detection of ICA stenosis of 50% or greater incurs in better managing patients, it is clearly imperative to better diagnose, monitor, and effectively treat. Of these, diagnosis and accurately gauging the degree of stenosis continues to present challenges. As seen in our study, and others like it, the threshold values outlined in NASCET do not appear to accurately gauge the degree of stenosis, and the current modalities available are flawed. Further studies challenging these thresholds are necessary and determining better ways to determine ICA stenosis in a cost-efficient and non-invasive manner will benefit patients greatly.

Conclusions

In conclusion, our data does not give a reliable PSV value for determining accurately a degree of ICA stenosis. Our data yielded a PSV value of greater than or equal to 240 cm/s for determining 50%–69% stenosis and PSV value of 250 cm/s for stenosis greater than 70%. Our results, along with other studies cited here, however, do indicate that the value for determination of ICA stenosis as put forth by the NASCET is too low in determining the accurate degree of stenosis. We propose that the best PSV value for determining 50%–69% stenosis will be higher than 125 cm/s. Further studies evaluating PSV values to CTA findings are needed to better refine the diagnosis and management of ICA stenosis in a cost-effective and efficient manner.

Disclosures

We have no disclosures.

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References

1. Dhawan SS, Avati Nanjundappa RP, Branch JR, et al. Shear stress and plaque development. *Expert Rev Cardiovasc Ther* 2010;8:545-56.
2. Liu J, Zhu Y, Wu Y, Liu Y, Teng Z, Hao Y. Association of carotid atherosclerosis and recurrent cerebral infarction in the Chinese population: a meta-analysis. *Neuropsychiatr Dis Treat*. 2017 Feb 20;13:527-533.
3. Adla T, Adlova R. Multimodality Imaging of Carotid Stenosis. *Int J Angiol*. 2015 Sep;24(3):179-84.

4. Barlinn K, Floegel T, Kitzler HH, Kepplinger J, Siepmann T, Pallesen LP, Bodechtel U, Reichmann H, Alexandrov AV, Puetz V. Multi-parametric ultrasound criteria for internal carotid artery disease-comparison with CT angiography. *Neuroradiology*. 2016 Sep;58(9):845-51.
5. Giavarina D. Understanding Bland Altman analysis. *Biochem Med* (Zagreb). 2015 Jun 5;25(2):141-51.
6. Simaan N, Jubeh T, Wiegler KB, Sharabi-Nov A, Honig A, Shahien R. Comparison of Doppler Ultrasound and Computerized Tomographic Angiography in Evaluation of Cervical Arteries Stenosis in Stroke Patients, a Retrospective Single-Center Study. *Diagnostics* (Basel). 2023 Jan 26;13(3):459.
7. Ferguson GG, Eliasziw M, Barr HW, Clagett GP, Barnes RW, Wallace MC, Taylor DW, Haynes RB, Finan JW, Hachinski VC, Barnett HJ. The North American Symptomatic Carotid Endarterectomy Trial: surgical results in 1415 patients. *Stroke*. 1999 Sep;30(9):1751-8.
8. Warlow CP. Symptomatic patients: the European Carotid Surgery Trial (ECST). *J Mal Vasc*. 1993;18(3):198-201. PMID: 8254241.
9. Louridas G, Junaid A. Management of carotid artery stenosis. Update for family physicians. *Can Fam Physician*. 2005 Jul;51(7):984-9.
10. Hankey GJ. Impact of treatment of people with transient ischemic attacks on stroke incidence and public health. *Cerebrovasc Dis*. 1996;6(Supp1):26–33.
11. Spence JD. Management of asymptomatic carotid stenosis. *Ann Transl Med*. 2020 Oct;8(19):1262.
12. Beach KW, Leotta DF, Zierler RE. Carotid Doppler velocity measurements and anatomic stenosis: correlation is futile. *Vasc Endovascular Surg*. 2012 Aug;46(6):466-74.
13. Gornik HL, Rundek T, Gardener H, Benenati JF, Dahiya N, Hamburg NM, Kupinski AM, Leers SA, Lilly MP, Lohr JM, Pellerito JS, Rholl KS, Vickery MA, Hutchisson MS, Needleman L. Optimization of duplex velocity criteria for diagnosis of internal carotid artery (ICA) stenosis: A report of the Intersocietal Accreditation Commission (IAC) Vascular Testing Division Carotid Diagnostic Criteria Committee. *Vasc Med*. 2021 Oct;26(5):515-525.
14. Pawaskar M, Satiani B, Balkrishnan R, Starr JE. Economic evaluation of carotid artery stenting versus carotid endarterectomy for the treatment of carotid artery stenosis. *J Am Coll Surg*. 2007 Sep;205(3):413-9.
15. Mohd AB, Alabdallat Y, Mohd OB, Ghannam RA, Sawaqed S, Hasan H, Ellebedy M, Turkmani K, Al-Ezzi S. Medical and Surgical Management of Symptomatic and Asymptomatic Carotid Artery Stenosis: A Comprehensive Literature Review. *Cureus*. 2023 Aug 10;15(8):e43263.
16. Samaržija K, Milošević P, Jurjević Z, Erdeljac E. Comparison of Carotid Stenosis Grading by CT Angiography and Doppler Ultrasonography: How the Statistical Methods Applied Influence the Results. *Acta Clin Croat*. 2022 Feb;60(3):457-466.
17. Ong CT, Wong YS, Sung SF, Wu CS, Hsu YC, Su YH, Hung LC. Progression of Mild to Moderate Stenosis in the Internal Carotid Arteries of Patients with Ischemic Stroke. *Front Neurol*. 2018 Dec 3;9:1043.
18. Dua A, Patel B, Kuy S, Seabrook GR, Tondravi N, Brown KR, Lewis BD, Rossi PJ. Asymptomatic 50% to 75% internal carotid artery stenosis in 288 patients: risk factors for disease progression and ipsilateral neurological symptoms. *Perspect Vasc Surg Endovasc Ther*. 2012 Dec;24(4):165-70.
19. Hackam, Daniel G. Optimal Medical Management of Asymptomatic Carotid Stenosis. AHA Journals. *Stroke*. 2021;52:2191–219
20. Wang G, Zhang Z, Ayala C, Dunet DO, Fang J, George MG. Costs of hospitalization for stroke patients aged 18-64 years in the United States. *J Stroke Cerebrovasc Dis*. 2014 May-Jun;23(5):861-8.
21. Rochmah TN, Rahmawati IT, Dahlui M, Budiarto W, Bilqis N. Economic Burden of Stroke Disease: A Systematic Review. *Int J Environ Res Public Health*. 2021 Jul 15;18(14):7552.