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ORIGINAL RESEARCH

Internal carotid artery stenosis: validation of Doppler velocimetric criteria

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Abstract

Background: Carotid endarterectomy is effective in reducing recurrent stroke in patients with carotid stenosis. Duplex sonography is widely used for diagnosing internal carotid artery (ICA) stenosis. Surgeons often base management decisions solely on this technique. Published velocimetric criteria should be validated in each laboratory. This study aims to validate Doppler velocimetric criteria for different grades of ICA stenosis and evaluate intracranial collateralization circuits.

Methods: Duplex scans from 10,435 consecutive patients routinely referred to our Neurosonology Unit from 2003 to 2011 were reviewed. Cases with ICA stenosis ≥50% (ultrasonographic morphologic criteria) were grouped by percentage of stenosis (ECST method). Mean ICA peak-systolic (PSV) and end-diastolic velocities (EDV), carotid index and presence of collateral flow were recorded. Pearson's coefficient was used to correlate percentage of stenosis and velocity parameters. One-way ANOVA was performed for the presence of collateralization.

Results: Nine-hundred and sixty cases of ICA stenosis ≥50% were identified. The Pearson's correlation values were R=0.802, p<0.001; R=0.724, p<0.001 and R=0.769, p<0.001 for the PSV, EDV and carotid index, respectively. The presence of collateral flow increased significantly for a stenosis ≥70% (p<0.001). For stenosis ≥70%, PSV >182 cm/s showed a sensibility of 80%, specificity of 82% and accuracy of 88%, EDV >61 cm/s showed a sensibility of 76%, specificity of 80% and accuracy of 86%, and carotid index >2.3 showed a sensibility of 82%, specificity of 82% and accuracy of 89%. These velocities were superior to the recently published consensus criteria for diagnosing stenosis ≥70%. Collateral blood flow increased significantly for stenosis ≥70% (p<0.001).

Conclusion: This work defined optimal velocimetric criteria for ICA stenosis in our laboratory, enabling the correct diagnosis when morphological criteria are lacking. The presence of collateralization was important to identify hemodinamically significant stenosis.

Keywords: Internal carotid artery stenosis, Velocimetric criteria, ECST, NASCET; Endarterectomy, Collateral blood flow.

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Introduction

The efficacy of carotid endarterectomy (CEA) in reducing recurrent stroke in patients with carotid stenosis has been well established [1-4] and this technique remains the gold standard for the management of carotid artery disease [5]. The benefits of this intervention, however, are largely dependent on the degree of stenosis [2, 4, 5] and all efforts should be made in order to accurately identify patients who will benefit from this intervention.

Doppler ultrasonography (DUS) is now widely used for the diagnosis of internal carotid artery (ICA) stenosis. The diagnostic accuracy of ultrasonographic duplex imaging has been demonstrated for both moderate and high-grade ICA stenosis, using angiography as a reference [6-11]. This imaging method is commonly the only diagnostic technique performed in patients at risk for atherosclerotic carotid artery disease. DUS has widely replaced preoperative carotid angiography in clinical routine and surgeons often base management decisions solely on this technique [2-4, 8, 10, 12-14]. Patient selection for CEA should be based on a combination of both ultrasound imaging (US) and velocity measurement of carotid stenosis [9]. Several studies have demonstrated the accuracy of B-mode imaging in predicting the grade of stenosis [15-20]. However, in severe disease, adequate B-mode images may be difficult to obtain, as more complex and heavily calcified plaques create shadowing and other artifacts that impair correct plaque measurements. In fact, for severe stenosis hemodynamic criteria are prevailing [9]. The correlation between degree of stenosis and velocity is demonstrated by the "Spencer's curve"[21], which has proven to be a reliable criterion for grading stenosis [9, 12, 22]. Nonetheless, there is considerable variability in published velocimetric criteria for stenosis. This variability is caused, along with other factors, by differences in Doppler protocol and equipment in each laboratory and operator differences in measurement acquisition [9, 23, 24]. Therefore, internal validation of carotid duplex interpretation criteria is essential [10, 25, 26]. The preferred method for validation of Doppler velocimetric criteria would be comparing the grade of stenosis obtained by this method with measurements obtained by arteriography [8, 10, 27-30]. However, it is not always feasible to obtain angiographic correlation for quality assessment of ultrasonography (US) studies especially in centers where US is the main diagnostic technique chosen.

Although DUS is an efficient diagnostic tool to identify moderate to severe (<80% ECST – European Carotid Surgery Trial) stenosis [31], velocity measurements alone are not sufficient to differentiate moderate from severe (≥80% ECST) stenosis [9]. The presence of collateral blood flow may increase post-stenotic blood pressure in the ICA, reducing blood pressure gradients over the stenosis, thus leading to an underestimation of the degree of stenosis and, perhaps, exclusion from surgical treatment. Established collateral blood flow identified by transcranial Doppler can help recognizing stenosis of hemodynamic significance, especially when blood flow velocity criteria combined with plaque morphology are inconclusive [32]. Thus, it is recommended that a search for transcranial collateral flow is made [9].

The purpose of this study was to validate ultrasound velocimetric criteria in our Neurosonology Unit for different grades of ICA stenosis measured by US imaging in our laboratory, as well as to evaluate the presence of intracranial collateralization circuits as a mean of distinguishing moderate and high-grade stenosis.

Methods

From January 2003 through December 2011, a total of 10,435 patients were routinely referred to our laboratory for clinically driven US evaluation of carotid artery disease. Duplex ultrasonography examinations were performed by two experienced neurosonology technicians using a Philips (Bothell, WA) HDI 5000 scanner. Each study was reviewed by neurosonology dedicated neurologists.

Complete examination of the common (CCA), internal (ICA) and external carotid arteries, as well as the vertebral arteries, was performed. Standard techniques were used as part of the examination protocol: aligning the cursor parallel to the vessel wall, obtaining waveforms using a small sample volume ideally placed in the center of the flow, and maintaining the Doppler beam angulated at 60º or less to the blood flow vector. The grade of ICA disease was assessed by analysis of plaque morphology and blood flow velocity measurements, namely peak systolic velocity (PSV) and end-diastolic velocity (EDV) at the point of highest stenosis, and internal carotid artery/common carotid artery peak systolic velocity ratio (carotid index). The maximal diameter reduction, measured morphologically at the most severely stenotic site of the ICA, was recorded by US imaging and used to calculate percentage diameter stenosis according to ECST method [3]. The cerebral basal arterial segments were also examined, using a pulsed 2-4 MHz Doppler transducer: the middle, anterior and posterior cerebral arteries were investigated using the transtemporal approach, whereas the ophthalmic arteries (OA) were insonated through the transorbital window, and intracranial vertebral arteries, as well as basilar artery, through the suboccipital window. Blood flow velocity signals were analyzed to determine direction and velocity. The presence of collateral blood flow through the anterior communicating, posterior communicating and ophthalmic arteries was assessed.

Cases with ICA stenosis ≥50% graded by US imaging morphologic criteria in our Unit were retrospectively selected for analysis. Groups were defined by percentage of stenosis, measured as diameter narrowing, as follows: (1) 50-59%; (2) 60-69%; (3) 70-79%; (4) 80-89% and (5) 90-99%. Patients with occlusion of the ICA, previous carotid endarterectomy or stenting, isolated parietal thrombus, arterial dissection, incomplete or inadequate morphologic imaging were excluded from analysis.

The Pearson's correlation coefficient (R) was used to correlate percentage of stenosis and velocity parameters. Receiver operating characteristic (ROC) curves were constructed to compare DUS stenosis with PSV, EDV and carotid index and to establish optimal criteria for each stenosis range. The overall accuracy of each velocity criterion was expressed in terms of the area under the ROC curve (AUC), ranging from 0.5 (poor) to 1.0 (perfect). The confidence intervals (CI), sensitivity and specificity were calculated. One-way ANOVA followed by Bonferroni's post-hoc comparison tests were performed for the presence of collateralization in each stenosis range. Microsoft Excel (MS Office 2010) was used to collect all data and perform descriptive statistics. SPSS Statistics version 20 (IBM, Armonk, NY, USA) was used to perform the remaining analysis.

Results

Between January 2003 and December 2011, carotid duplex sonography and transcranial Doppler (TCD) were performed in 10,435 consecutive patients. In 783 patients (551 men and 232 women aged 68 ± 11 years) stenosis ≥50% was identified in 977 internal carotid arteries. Data concerning velocity measurements was available for 960 exams (960 for PSV, 946 for EDV, and 929 for the carotid index). For 17 cases, data concerning velocity measurements was not available; 187 patients had bilateral ICA stenosis ≥50%, and 66 patients had contralateral ICA occlusion. TCD flow data was available in 481 arterial systems. Missing collateral TCD flow data were mostly attributable to acoustic difficulties to insonate the temporal bone.

The number of examined ICA in each range of stenosis, as measured by US imaging, is presented in **Figure 1**. In 32% (304 vessels), an ICA stenosis with diameter reductions of ≥70% was found. As expected, exams with less severe stenosis were found more often. There were only 24 ICA with stenosis in the 90-99% stenosis range. Since sample size for the 90-99% range was too small for the ROC curve analysis, the last two ranges (80-89% and 90-99%) were merged.

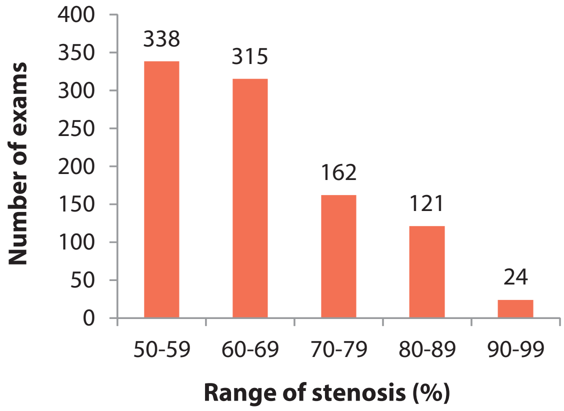

Figure 1. Distribution of the exams by range of stenosis as measured by US imaging (ECST method).
US = Ultrasound imaging; ECST = European Carotid Surgery Trial

Mean velocities and carotid index for the different ranges of stenosis were: for 50-59%, 111/35 cm/s, carotid index: 1.3; for 60-69%, 161/51 cm/s, carotid index: 2.1; for 70-79%, 218/78 cm/s, carotid index: 2.8; for 80-89%, 377/151 cm/s, carotid index: 5.3; for ≥90%, 409/191 cm/s, carotid index: 7.0.

The Pearson's correlation coefficient for the different velocimetric criteria were 0.802 for PSV, 0.724 for EDV and 0.769 for carotid index ($p<0.001$), indicating a strong correlation between these velocity measurements and the range of stenosis (**Table 1**).

Scatterplots of US measured stenosis versus the 3 parameters (PSV, EDV, and carotid index ratio) were generated to demonstrate the distribution of severity of ICA disease (**Figure 2**).

Table 1 depicts the velocimetric criteria for PSV, EDV and carotid index ratio in the different ranges of stenosis, as established by ROC curve analysis, as well as the presence of intracranial collateralization in those ranges. **Figure 3** portrays the ROC curves for the different ranges of stenosis, with the respective sensitivities, specificities and accuracies (represented by the area under the curve—AUC).

As shown in **Figure 4**, the presence of collateral flow increased significantly for stenosis ≥70% ($p<0.001$). For

Table 1. Velocimetric criteria for the different ranges of stenosis.

Range stenosis	PSV	EDV	Carotid index	Collateral flow
50-59%	<152	<50	<1.9	-
60-69%	152-182	50-61	1.9-2.3	-
70-79%	182-251	61-81	2.3-3.3	+
80-99%	>251	>81	>3.3	+
Pearson's correlations	0.802*	0.724*	0.769*	

*p<0.001: + present; - absent.

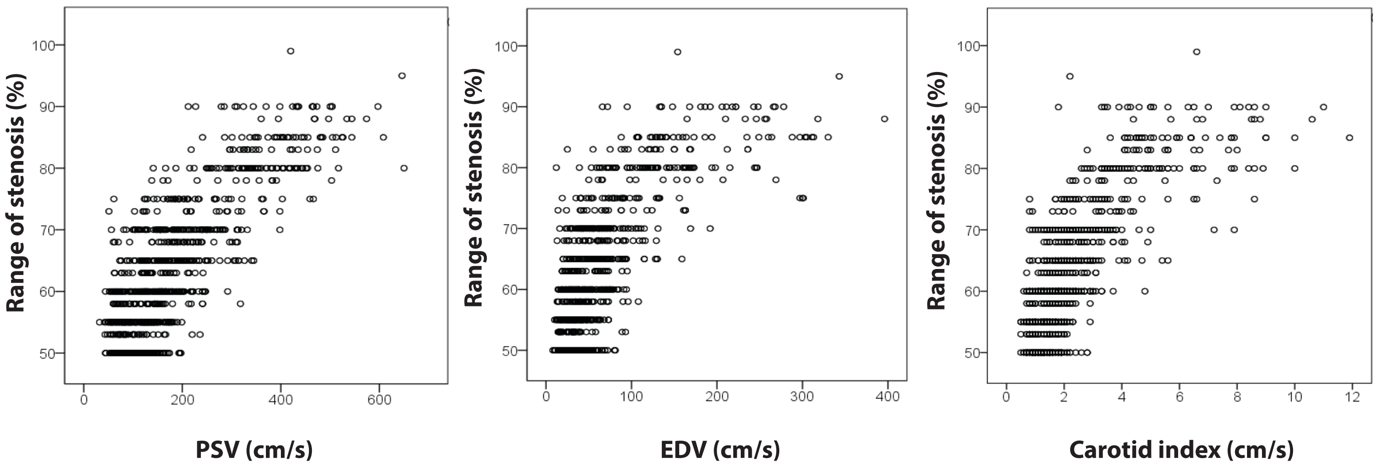

Figure 2. Scatterplots the diameter percentage stenosis measured by B-mode and the internal carotid artery (ICA) peak-systolic velocity (PSV), end-diastolic velocity (EDV) and ICA/common carotid artery PSV ratio.

stenosis 50-59%, no collateral flow was identified and for stenosis 60-69%, 1% of the exams presented collateral flow. For stenosis of 70-79%, 80-89%, and 90-99%, collateral flow was identified in 14%, 61%, and 92% of the exams, respectively. There was high specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for predicting stenosis ≥70%, although sensitivity was low (**Table 2**).

The specificity, sensitivity and overall accuracy using the consensus criteria for diagnosing stenosis ≥70% (PSV >125 cm/s; EDV >40 cm/s and carotid index >2) and ≥80% (PSV >251 cm/s; EDV >81 cm/s and carotid index >3.3) (ECST method)[12] are presented in **Table 3**. Sensitivity, specificity and accuracy of our criteria are also depicted in **Table 3**. As shown in the table, for stenosis ≥70% ECST, sensitivity would be higher, but specificity and overall accuracy would be lower using the consensus criteria. For stenosis ≥80% ECST, sensitivity would be higher for PSV, but specificity and overall accuracy would be lower using the consensus criteria; for EDV and carotid index, on the other hand, sensitivity was lower and specificity and overall accuracy were higher with the consensus criteria.

Considering the criteria defined for our laboratory for stenosis ≥70% ECST, a PSV >182 cm/s would erroneously define 6% of stenosis as <70%, 11.5% of which would be correctly diagnosed by the presence of collateral blood flow on TCD. Similarly, considering EDV >61 cm/s and carotid index >2.3, 8% and 6% would be erroneously defined as having stenosis <70%, 7% and 8% of which, respectively, would be correctly diagnosed by the presence of collateral blood flow on TCD.

Established collateral blood flow was not observed in cases with <70% ICA stenosis, except in 2 patients with stenosis range 60-69%. In one patient, stenosis was defined

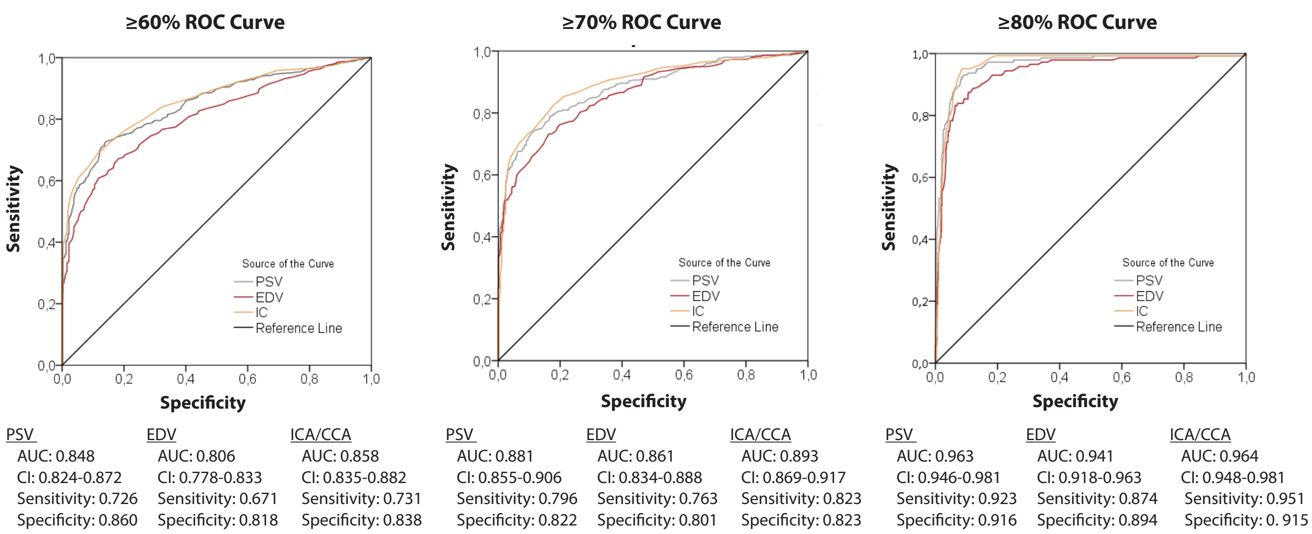

Figure 3. ROC curves comparing PSV, EDV and carotid index for ≥60%, ≥70% and ≥80% stenosis.

AUC = Area under the curve; CI = Confidence interval; EDV = End-diastolic velocity; PSV = Peak systolic velocity; ROC = Receiver operating characteristic

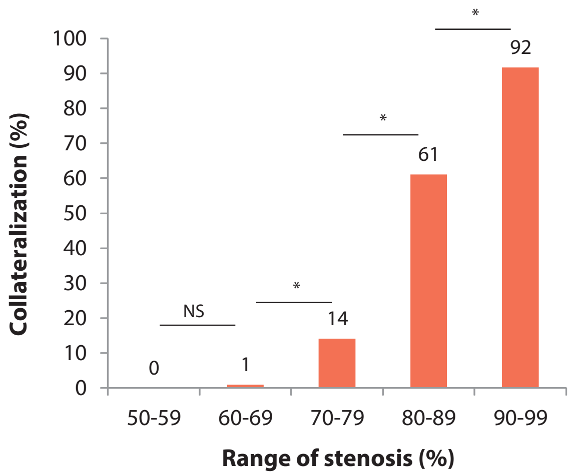

Figure 4. Percentage of cases presenting intracranial collateral flow on transcranial Doppler ultrasonography.
*p<0.001; NS = Not significant (p>0.05)

Table 2. Presence of collateral flow for predicting stenosis ≥70%.

Sensitivity	39.2%
Specificity	99.5%
PPV	97.4%
NPV	78.0%
Accuracy	80.4%

PPV = Positive predictive value; NPV = Negative predictive value

as 68% by morphological criteria, but the established velocimetric criteria enabled the diagnosis of stenosis ≥70% (PSV/EDV: 238/102 cm/s and carotid index 2.5). Absence of collateral blood flow was observed in 18% cases (174 vessels) of high-grade (≥70% stenosis) ICA stenosis.

Discussion

This work aimed to establish the optimal velocimetric criteria for the diagnosis of stenosis grade in our Neurosonology Unit. Our results showed that for diagnosing stenosis ≥70% ECST our criteria were more accurate than the consensus criteria. For stenosis ≥80% ECST, the PSV criterion was superior to the consensus. However, the consensus criteria for EDV and carotid index were superior to our criteria. The presence of collateral blood flow was highly specific for stenosis ≥70% and was helpful in the diagnosis of stenosis is those ranges when velocity criteria pointed to a lower range of stenosis.

Carotid endarterectomy (CEA) guidelines in symptomatic carotid artery stenosis are based on ECST and NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria of ≥70% carotid stenosis as estimated from angiography [3]. A NASCET 50% to 69% stenosis is equivalent to an ECST ≥70%, while a NASCET 70% to 99% stenosis equates to an ECST ≥80% [33]. Morphologic criteria are prevailing in low-degree disease, but for more severe stenosis velocimetric criteria should be used to define stenosis degree, especially when plaque characteristics impair a correct measurement [9]. These criteria

Table 3. Specificity, sensitivity and accuracy of the consensus criteria and our Neurosonology unit criteria for diagnosing stenosis ≥70 and ≥80% (ECST method).

Range stenosis	Criteria	Duplex variable	Sensitivity	Specificity	Accuracy
ECST ≥70% (NASCET ≥50%)	Consensus criteria	PSV	93.3%	43.1%	60.8%
		EDV	92.3%	50.6%	65.6%
		Carotid index	88.6%	70.0%	78.9%
	Local criteria	PSV	79.6%	82.2%	88.1%
		EDV	76.3%	80.1%	86.1%
		Carotid index	82.3%	82.3%	89.3%
ECST ≥80% (NASCET ≥70%)	Consensus criteria	PSV	94.5%	87.6%	88.6%
		EDV	79.2%	94.5%	92.2%
		Carotid index	92.7%	93.0%	93.0%
	Local criteria	PSV	92.4%	91.8%	91.9%
		EDV	93.9%	84.6%	85.4%
		Carotid index	97.6%	87.4%	88.3%

ECST = European Carotid Surgery Trial; EDV = End-diastolic velocity; PSV = Peak systolic velocity; NASCET = North American Symptomatic Carotid Endarterectomy Trial may, however, lead to underestimation of stenosis owing to reduced maximal flow velocities caused by increased resistance or turbulence, serial stenosis or low flow caused by high distal collateral pressure [34]. Without adequate detection of plaque burden, patients with severe stenosis may be excluded from surgical treatment. Overestimation, on the other hand, may occur in the presence of compensatory increase in volume flow owing to contralateral severe stenosis/occlusion [35]. Also, there is considerable overlap in velocity measurements between moderate and high-degree stenosis [9]. TCD can help determine whether stenosis defined to be high grade with DUS has hemodynamic significance more distally. Conversely, signs of established collateral flow indicate a hemodynamically relevant stenosis that can, therefore, be classified as high grade and can help identify patients with severe plaque burden and no significant increase in ICA blood flow velocities [32, 36]. TCD has been demonstrated to accurately detect stenosis ≥70% [9, 32, 37] and is, hence, an invaluable tool, especially when plaque assessment and velocity criteria combined are inconclusive [32]. Nevertheless, a significant discrepancy between cervical ICA stenosis and signs of intracranial collateral flow might be due to intracranial ICA stenosis prior to the emergence of the ophthalmic artery.

Most DUS velocity thresholds were defined using angiography estimates of stenosis and the reliability of these thresholds has been questioned [3, 36]. A wide variability among laboratories was found with regard to the relationship between carotid angiographic stenosis and Doppler velocity [12, 23, 25, 29, 30, 38-43]. This variability is caused not only by intrinsic factors, such as plaque characteristics, but also by differences in operator technique and experience and device related factors [23]. It has been demonstrated that velocimetric criteria should be validated separately for each piece of equipment [38]. Other groups have analyzed the performance of their standard criteria against the consensus criteria, and found theirs to be more accurate in defining the range of stenosis [10, 44, 45].

There is good correlation of both the NASCET and the ECST methods of calculating percentage stenosis with DUS and both have similar sensitivity and specificity [46]. The NASCET method was used to overcome the lack of direct visualization of the contour of the artery at the stenosis in angiographic measurements, as in the ECST this contour is guessed. With US, the residual lumen and the artery diameter can be directly measured at the point of interest. Therefore, the ECST method is favored in our laboratory, since it can better illustrate plaque burden and is less prone to underestimation when severe stenosis and low post-stenotic flow lead to distal segment involution [9, 47].

In this work, PSV was used as the primary parameter in assessing the percentage of carotid stenosis. It has been shown to be reproducible and to have high sensitivity, specificity, and positive predictive value across most studies [10, 12, 45, 48, 49]. EDV and the carotid index were used as secondary criteria, as proposed by the consensus criteria [12]. These criteria have been shown to be accurate in the diagnosis of ≥70% stenosis, but were less so in detecting 50-69% stenosis [10]. In our study, the parameter with the highest Pearson's correlation was the PSV (0.802) in contrast to both the EDV (0.724) and the carotid index (0.769) ($p<0.001$), which is in agreement with findings from other series [10, 12, 44, 45, 49]. The values defined in our Neurosonology Unit were superior when compared to the consensus criteria of PSV >125 cm/s, EDV >40 cm/s and carotid index >2.0 for detecting ≥70% stenosis (ECST method), with overall accuracy of 88%, 86% and 89% versus 60%, 65%, and 79% for the consensus criteria. Although some sensitivity was lost, the specificity of our criteria was higher than the consensus criteria. For diagnosing stenosis ≥80% ECST, however, although our PSV criterion was superior to the consensus, with overall accuracy of 92% vs 88%, the consensus criteria for EDV and carotid index were superior to ours, with overall accuracy of 92% and 93% against 85%, and 88%, respectively. In order to base the decision of a carotid intervention on DUS, it has been recommended that specificity must be high, avoiding performing an invasive technique without sufficient benefit to the patient [50]. Additionally, TCD was invaluable in identifying hemodinamically significant stenosis, enabling the reappraisal and correct diagnosis of a significant percentage of patients defined as having <70% stenosis by velocimetric and morphologic criteria. Established collateral flow to the middle cerebral artery virtually always indicated pre-cerebral vessel disease with stenosis ≥70%.

Using diameter reduction instead of area reduction, the anatomic parameter for the hemodynamic effect, can be considered a limitation of this work. The relation between the two parameters is not linear, since it depends on the shape of the stenosis (concentric or eccentric). Our decision was based on the fact that, diameter reduction was the method chosen for NASCET and ECST and is widely considered to be the gold standard for decision-making [9].

Over the years, the characteristics of the atherosclerotic plaques, namely the approximated stenosis degree, have also been validated against the plaque observed in surgery by the vascular surgeon of our stroke group. This fact has contributed to the choice of ultrasound as the main diagnostic method in our center.

Another potential limitation is the fact that our criteria are derived from DUS only, as angiography was not available to confirm the US measurements and performing carotid angiography in all of our patients did not seem feasible or justified. However, there is evidence that US imaging can accurately measure ICA diameter reductions independent of velocimetric criteria [16-18, 44, 51, 52]. MacKenzie and co-workers have shown that US imaging correlates closely with angiographic measurements [16] and it has been shown that DUS correlates strictly with histological endarterectomy specimens [22, 51, 52]. Moreover, many studies indicate that DUS is sufficient for safely determining the need for surgery in patients being considered for CEA [53-56].

To our knowledge, this is the first work establishing optimal Doppler velocimetric criteria based only on US imaging. Although this study served as an internal validation of velocimetric criteria in our Neurosonology unit, its results may be extrapolated to other neurovascular laboratories. It enabled the definition of the optimal velocimetric criteria for each stenosis range in our laboratory, allowing a better estimation of the stenosis when plaque characteristics prevent an accurate morphological measurement. As only one device was used and there are only two technicians and three interpreting physicians in our laboratory, there was minimal variability in performing the exams and interpreting the results. DUS is a powerful tool for diagnosing and grading severe stenosis, especially when there are established and validated criteria. Experienced technicians and physicians, as well as continuous internal validation of the accuracy of DUS, are critical in any institution that uses DUS as the sole diagnostic method before surgical intervention.

Abbreviations

AUC: Area under the ROC curve; CCA: Common carotid artery; CEA: Carotid endarterectomy; CI: Confidence interval; DUS: Doppler ultrasonography; ECST: European Carotid Surgery Trial; EDV: End-diastolic velocity; ICA: Internal carotid artery; NASCET: North American Symptomatic Carotid Endarterectomy Trial; OA: Ophthalmic arteries; PPV: Positive predictive value; PSV: Peak systolic velocity; NPV: Negative predictive value; ROC: Receiver operating characteristic; TCD: Transcranial Doppler; US: Ultrasound imaging

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Competing interests

The authors declare no conflict of interest.

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