Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Measuring carotid stenosis. Time for a reappraisal.

A V Alexandrov, C F Bladin, R Maggisano and J W Norris

Stroke. 1993;24:1292-1296
doi: 10.1161/01.STR.24.9.1292
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

Original Contributions

Measuring Carotid Stenosis

Time for a Reappraisal

A.V. Alexandrov, MD; C.F. Bladin, MBBS, FRACP; R. Maggisano, MD; J.W. Norris, MD

Background and Purpose: **Data from recent multicenter carotid endarterectomy trials have questioned the validity and reliability of Doppler ultrasound in the assessment of carotid stenosis.**

Methods: **We prospectively analyzed 45 patients undergoing carotid angiography to compare the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST) methods of measuring carotid stenosis with those of direct visualization ("eyeballing") and duplex ultrasound. Linear NASCET and ECST measurements were also converted into area using the πr^2 function and termed "squared NASCET" (N^2) and "squared ECST" (E^2). In 15 of 45 patients undergoing carotid endarterectomy, the carotid plaque was removed intact, sectioned, and photographed for computer measurement of cross-sectional area. Comparison of this "gold standard" was then made to each method of measurement.**

Results: **Comparison between duplex and the various angiographic measurement techniques revealed significant differences between NASCET and duplex ($P<.0001$), ECST and duplex ($P<.01$), and E^2 and duplex ($P<.01$) but not between N^2, eyeballing, and carotid duplex methods. Even the NASCET and ECST methods themselves differed significantly ($P<.006$). When comparison was made with computerized planimetric measurements of the carotid plaque, there were significant differences for both NASCET ($P<.0007$) and ECST ($P<.007$). Correlation was demonstrated only between planimetry and N^2, E^2, and duplex.**

Conclusions: **NASCET and ECST angiographic methods of measurement consistently underestimate the "true" anatomic stenosis. As such, they represent only "indexes" of carotid stenosis severity. Duplex provides a more accurate measurement of carotid stenosis. (*Stroke.* 1993;24:1292-1296.)**

KEY WORDS • **angiography** • **carotid artery diseases** • **ultrasonics**

Two recently published multicenter studies have firmly established carotid endarterectomy as the best prophylaxis against stroke in cases of high-grade carotid atherosclerosis: the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[1] and the European Carotid Surgery Trial (ECST).[2] The results of similar trials in asymptomatic patients have been published,[3,4] and one other large study is in progress.[5]

To minimize the risks associated with carotid angiography, many trialists used Doppler ultrasound methods to screen for the presence and severity of carotid stenosis. In general, the reported accuracy of noninvasive ultrasound methods has been disappointing, often with wide divergence from results of the apparent "gold standard" of angiography. As a result, some authors suggest that ultrasound methods are so unreliable that they are a "dubious presurgical strategy" and should be used only for the diagnosis of minor degrees of carotid stenosis.[6,7] Promulgation of such opinions will undermine confidence in ultrasound data, may cause some to abandon the use of carotid ultrasound technology, and could in effect deny patients access to a valuable and cost-effective diagnostic aid.

See Editorial, page 1281

Angiographic stenoses with 70% to 80% diameter reduction as measured by NASCET and ECST techniques often have pinpoint lumens at surgery (>90% stenosis). This suggests that both these linear methods of measurement consistently underestimate the "true" anatomic stenosis. The aim of this study, therefore, was to evaluate more closely the apparent discrepancies between carotid angiographic imaging and ultrasound and to compare them with the findings at carotid endarterectomy.

Subjects and Methods

We prospectively compared carotid angiographic findings with those of color-flow duplex sonography (duplex) in patients undergoing carotid endarterectomy from June 1992 to March 1993. All patients had previous transient ischemic attacks or minor stroke. Angiography was performed by the intra-arterial digital subtraction technique via the femoral route using selective catheterization of the extracranial arteries. Biplanar images were obtained for each internal carotid artery (ICA). Measurements of ICA diameter reduction were performed by use of the linear-based methods of NASCET[8] and ECST[2] (Fig 1) and by direct visualization

Received April 16, 1993; final revision received May 20, 1993; accepted June 3, 1993.

From the Stroke Research Unit (A.V.A., C.F.B., J.W.N.) and the Department of Vascular Surgery (R.M.), Sunnybrook Health Science Centre, University of Toronto (Canada).

Correspondence to A.V. Alexandrov, MD, Stroke Research Unit, Sunnybrook Health Science Centre, 2075 Bayview Ave, Toronto, Canada, M4N 3M5.

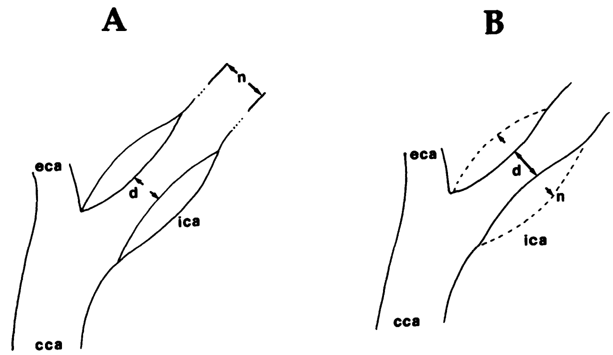

FIG 1. *Diagrams showing methods used by the North American Symptomatic Carotid Endarterectomy Trial (A) and the European Carotid Surgery Trial (B) for estimating diameter reduction of the internal carotid artery (ica) on angiography. The linear formula is $1-(d/n)\times 100$, where d is the diameter of the residual lumen at angiography and n is an estimation of the normal vessel diameter. eca indicates the external carotid artery; cca, the common carotid artery.*

("eyeballing") by an independent neuroradiologist. All measurements were assessed in a blind manner.

To test the difference between linear and area methods of measuring carotid stenosis, we calculated the area luminal reduction from the linear NASCET and ECST formulas using the πr^2 function as outlined in Fig 2. The derived equations were then termed "squared NASCET" (N^2) and "squared ECST" (E^2).

Color-flow duplex sonography of the carotid arteries was performed on a Diasonics Spectra (Diasonics Inc, Milpatas, Calif) using a 7.5-MHz transducer. The highest peak systolic velocity in the stenotic area was documented in each case. Evaluation of the degree of stenosis was based on previously published criteria[9,10] as well as the conversion curve from linear index to area stenosis (Fig 3). This was performed without knowledge of the angiographic findings. In a subgroup of these patients in whom carotid endarterectomy was performed, the plaque was carefully dissected out intact and immediately placed in saline. Plaques that fragmented during surgery were discarded. The plaque was photographed both longitudinally and end-on, placed in formalin followed by decalcification, and photographed again. It was then sectioned manually in approximately 2-mm sections, placed on paper with a 1-mm calibration, and rephotographed (Fig 4).

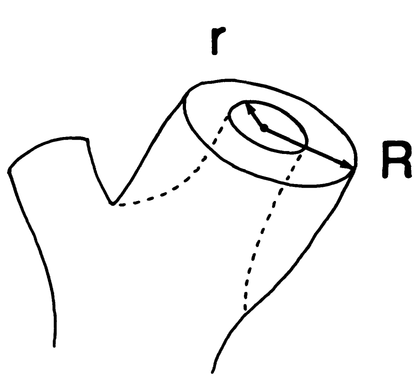

FIG 2. *Diagram showing area luminal reduction of arterial stenosis calculated by the πr^2 formula. Arterial stenosis was calculated as follows: $1-(\pi r^2/\pi R^2)\times 100=1-(r^2/R^2)\times 100=1-(d^2/n^2)\times 100$, where r is the radius of the residual lumen, R is the radius of a normal lumen, d is the diameter of the residual lumen (2r), and n is the diameter of the normal vessel (2R).*

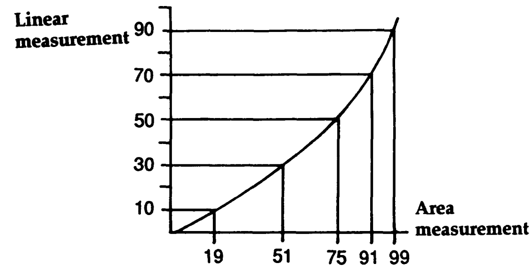

FIG 3. *Mathematical correlation between linear and area-derived measurements.*

The carotid bulb was identified, and the section with the narrowest lumen was selected. Planimetric tracings were taken of these, including the millimeter calibration for references. A computerized program SIGMA SCAN (Jandel Scientific, Corte Madera, Calif) was then used to calculate cross-sectional areas of both carotid bulb and the residual lumen. Percent area stenosis was calculated as $1-(S_r/S_R)\times 100$, where S_r represents the area of the residual lumen and S_R represents the area of the bulb (Fig 2).

To assess the possible influence of plaque shrinkage, measurements of the specimen were made before and after laboratory processing. Processing produced uniform shrinkage of the whole specimen by $13\pm 1.5\%$ which is consistent with previous studies,[11] so that the degree of stenosis was not affected.

Statistical analysis consisted of *t* tests and regression analyses to compare groups.

Results

We evaluated 45 consecutive patients undergoing carotid endarterectomy. When we compared the various linear (NASCET and ECST), eyeballing, and area (N^2 and E^2) methods of angiographic evaluation to carotid ultrasound data, we found significant differences in all, except for N^2 and eyeballing methods (Table 1). Furthermore, when NASCET was compared with ECST, there was also a significant discrepancy ($P<.006$). There were also striking discrepancies when the regression lines were compared (Fig 5). For instance, a NASCET linear stenosis of 55% equaled approximately 70% on ECST, 78% on N^2, and 88% on E^2. Conversely, a duplex stenosis of 80% corresponded to 80% on N^2.

With these discrepancies established, however, the question remains as to which is correct. That is, which method most accurately reflects the anatomic stenosis seen at surgery? We then compared mean ICA stenoses measured by ultrasound and each of the angiographic methods with planimetric measurements taken on the 15 carotid plaques that had been removed intact and evaluated without knowledge of the angiographic or ultrasound findings. NASCET and ECST methods consistently underestimated the planimetric measurements of the surgical specimens, whereas duplex, N^2, and E^2 did not differ significantly (Table 2).

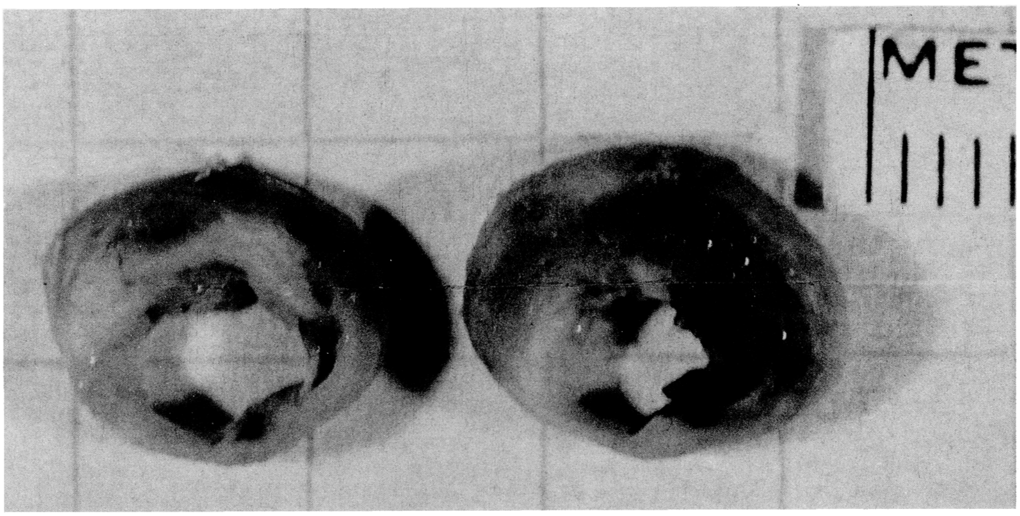

FIG 4. *Photograph of sectioned specimen of carotid plaque with calibrated background for planimetry calculations. The irregular lumen illustrates the difficulty of linear measurements.*

Discussion

Our data indicate that NASCET and ECST methods of angiographic measurement of carotid stenosis differ significantly and that both consistently underestimate the actual "anatomic" stenosis. This reflects the shortcomings of estimating area reduction of the ICA lumen (often asymmetric) by a single linear measurement from angiography. In other words, although mathematically related, what is measured on angiography is not what is seen when looking at the carotid pathology.

The NASCET and ECST "stenoses" in fact represent indexes of severity, and whether they reflect anatomic reality might well be considered irrelevant: the clinical guidelines for carotid surgery have already been established. But it would be equally unrealistic to believe that the world will uniformly adopt either of these two methods of angiographic evaluation, whether it is believed they represent true anatomic stenosis or not. Moreover, the claim that one must read an angiogram and institute management according to the methods and results of one or other of the endarterectomy trials does not do justice to the individual patient. For instance, an 80% ECST stenosis is equivalent to 50% by NASCET[12]; yet, although they are anatomically the same, they will be managed differently. Our data show that the NASCET method is less accurate than the ECST method, but at least it removes the guesswork in predicting the position of the carotid bulb. Only by being aware of the limitations of each technique in predicting the true reduction in lumen diameter can one make an informed decision as to whether a patient warrants operative intervention for a symptomatic carotid stenosis.

There are several problems with the NASCET method. Principally, it depends on finding the first "normal" segment of distal ICA, decided by subjective evaluation of the observer. Also, since the carotid bulb is normally larger than the more distal ICA, minor degrees of stenosis result in a paradoxical "negative" stenosis. For example, an artery with a residual (stenosed) lumen of 5 mm and a normal distal ICA diameter of 4 mm using the NASCET method yields a stenosis of $1-(5/4)\times 100=-25\%$.

This study was limited to analysis of severe carotid stenosis only. In this group, inspection of the linear versus area correlation curve (Fig 3) indicates that there

TABLE 1. Significant Differences (*P*) Between Various Angiographic Measurements and Duplex (82±17%) in 45 Patients

Method	Stenosis (%)	Difference from duplex (*P*)
NASCET	63±18	0.0001
ECST	73±16	0.01
Eyeballing	76±19	NS
N^2	82±17	NS
E^2	90±12	0.01

NASCET, North American Symptomatic Carotid Endarterectomy Trial (linear method); ECST, European Carotid Surgery Trial (linear method); N^2, squared NASCET (area method); E^2, squared ECST (area method); NS, not significant. Values are mean±SD for stenosis.

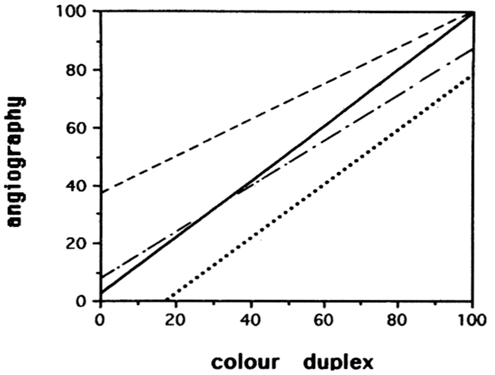

FIG 5. *Simple regression lines demonstrating the correlation between percent stenosis by angiographic measurements of internal carotid artery stenosis and duplex ultrasound in 45 patients. Methods are as follows: · · · , North American Symptomatic Carotid Endarterectomy Trial (NASCET) (r=0.745); —, squared NASCET (r=0.917); — · —, European Carotid Surgery Trial (ECST) (r=0.568); and ---, squared ECST (r=0.634).*

TABLE 2. Percentage of Internal Carotid Artery Stenosis Estimated by Angiography (Linear and Area Derivation), Ultrasound, and Planimetry in 15 Plaques Removed at Carotid Endarterectomy

Patient	NASCET	N^2	ECST	E^2	Duplex	Planimetry
1	70	91	80	97	95	97
2	80	95	75	95	95	93
3	85	99	75	95	95	96
4	50	75	60	84	95	93
5	85	98	95	99	95	94
6	70	91	90	99	95	96
7	95	99	99	99	99	99
8	99	99	99	99	99	99
9	55	80	75	95	95	99
10	55	80	80	97	85	85
11	99	99	99	99	99	99
12	75	95	50	75	99	98
13	85	98	90	99	95	95
14	45	70	60	85	65	65
15	75	95	85	98	95	95
Mean±SD	75±17*	91±10	81±15†	94±7	93±9	94±9

NASCET, North American Symptomatic Carotid Endarterectomy Trial (linear method); N^2, squared NASCET (area method); ECST, European Carotid Surgery Trial (linear method); E^2, squared ECST (area method); duplex, color-flow duplex sonography; planimetry, planimetry of the intact removed plaques.

**P*=.0007 vs planimetry; †*P*=.007 vs planimetry.

is little change in area for larger changes in diameter. Toward lesser grades of stenosis, correlation between linear and area parameters becomes increasingly discrepant. Although we did not have the opportunity to document lesser degrees of stenosis, it is clearly even less likely that NASCET, ECST, and squared derivations will correlate with plaque planimetry.

The ECST method relies on a "guesstimate" of the presumed outline of the carotid bulb, but bulb size is variable and sometimes almost insignificant. This may explain the slightly wider discrepancies between E^2 and N^2 data since, by virtue of its subjectivity, the margin of potential error is greater with the ECST technique.

It is less surprising that duplex methods of estimating carotid stenosis showed no significant differences from surgically removed specimens, since the blood flow velocity in the stenosed artery is dependent on area cross section, not on the symmetry of the lumen. Thus, when area stenosis is used, ultrasound continues to be consistent, even in light of Doppler criteria based on diameter stenosis. Data from the N^2 and E^2 methods are also closer to the actual anatomic stenosis because they represent an expression of area, not linear stenosis. By use of these simple measurements derived from existing data in the NASCET and ECST studies, the carotid stenosis is easily calculated and represents values closer to reality.

It is also reassuring that the time-honored technique of eyeballing (direct visual estimation) was closer to duplex results than either NASCET or ECST methods, since this method is used most widely throughout the world.

These observations are not academic but have critical implications in clinical practice. As Bousser[12] indicated, the NASCET method underestimates carotid stenosis compared with the ECST method, so that a NASCET stenosis of 0% equals an ECST stenosis of 57%. Hence, the NASCET study conclusions, in reality, are based on patients with more stenosed carotid lesions. From our data, the NASCET surgical threshold of 70% diameter reduction actually represents 91% area stenosis, whereas the ECST threshold of 70% is equal to 80% area stenosis. The "moderate" (30% to 70%) NASCET group at present being enrolled actually represents area stenoses ranging from 54% to 91%. Indeed, some patients who are at present being randomized to the medical arm of this study will actually have more than 70% ECST stenosis, which is above the recommended threshold for surgery. As attempts are made to evaluate lower and lower degrees of carotid stenosis, the paradoxical NASCET negative stenoses already alluded to will make accurate assessment impossible.

Discrepancies between duplex ultrasound and angiography have been previously documented,[6,13,14] but our data indicate that duplex is more, not less, accurate than either of the NASCET and ECST methods. The apparent discrepancies, in fact, represent the correlation between linear and area functions.

It has been suggested that the discrepancy between angiography and ultrasound methods reflects the unevenness of the ultrasound technique. Duplex technology is operator and interpreter dependent, but so is angiography. The NASCET or ECST criteria cannot be applied unless a clear biplanar angiographic image of the stenotic area is obtained. Furthermore, because these angiographic formulas were not established using a comparison to a gold standard, one cannot then evaluate performance of duplex in carotid atherosclerosis measured by NASCET and ECST methods. It is essential in studies of this kind to have internal validation of Doppler criteria with quality assessment to provide reliable and consistent results. This should include standardization of equipment, uniform sonographic criteria, and validation of all involved ultrasound laboratories before enrollment into the study.

In conclusion, our data indicate that NASCET and ECST linear methods significantly underestimate the degree of underlying carotid stenosis and are actually less accurate than duplex ultrasound. These inaccuracies in measurement of high-grade carotid atherosclerosis can be easily corrected by using area (πr^2) instead of linear derivations. Duplex ultrasound remains the easiest, least expensive, safest, and most accurate screening test for evaluating carotid stenosis.

Acknowledgments

Dr Alexandrov (a postgraduate research fellow from the Institute of Neurology of the Academy of Medical Sciences, Moscow, Russia) is a recipient of a fellowship award from the Sunnybrook Trust for Medical Research. Dr Bladin (a postgraduate research fellow from the University of Melbourne, Australia) is a recipient of a grant from the Sunnybrook Foundation Research Fund, Sunnybrook Health Science Centre, and the Leslie Eric Paddle Scholarship, University of Melbourne. The authors are grateful to Beverley D. Young, RT, Beverley Bowyer, RN, Wendy C. Gibson, BSc, and the technicians of the Carotid Doppler and Peripheral Vascular Laboratories, Sunnybrook Health Science Centre, for their cooperation in obtaining the data.

References

1. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med.* 1991;325:445-453.
2. European Carotid Surgery Trialists' Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) and with mild (0-29%) carotid stenosis. *Lancet.* 1991;337:1235-1243.
3. Hobson RW, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, Wright CB, the Veterans Affairs Cooperative Study Group. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. *N Engl J Med.* 1993;328:221-227.
4. CASANOVA Study Group. Carotid surgery versus medical therapy in asymptomatic carotid stenosis. *Stroke.* 1991;22:1229-1235.
5. The Asymptomatic Carotid Atherosclerosis Study Group. Study design for randomized prospective trial of carotid endarterectomy for asymptomatic atherosclerosis. *Stroke.* 1989;20:844-849.
6. Haynes RB, Taylor DW, Sackett DL, Fox A, Rankin R, Barnett HJM. Poor performance of Doppler in detecting high-grade carotid stenosis. *Clin Res.* 1992;40:184A. Abstract.
7. Barnett HJM, Barnes RW, Robertson JT. The uncertainties surrounding carotid endarterectomy. *JAMA.* 1992;268:3120-3121.
8. North American Symptomatic Carotid Endarterectomy Trial (NASCET) Steering Committee. North American Symptomatic Carotid Endarterectomy Trial: methods, patient characteristics, and progress. *Stroke.* 1991;22:711-720.
9. Beach KW, Lawrence R, Philips DJ, Primozich J, Strandness DE. The systolic velocity criterion in quantifying internal carotid artery stenosis. *J Vasc Technol.* 1989;13:65-68.
10. Bornstein NM, Norris JW. The value of carotid Doppler ultrasound in asymptomatic extracranial disease. *Can J Neurol Sci.* 1988;15:378-383.
11. Schenk EA, Bond MG, Aretz TH, Angelo JN, Choi HY, Tynalski T, Gustafson NF, Berson AS, Ricotta JJ, Goodison MW, Byran FA, Goldberg BB, Toole JF, O'Leary DH. Multicenter validation study of real-time ultrasonography, arteriography, and pathology: pathologic evaluation of carotid endarterectomy specimens. *Stroke.* 1988;19:289-296.
12. Bousser MG. Benefits from carotid surgery? Yes, but ... *Cerebrovasc Dis.* 1992;2:122-126.
13. Veterans Affairs Cooperative Studies Trialist Group. Duplex accuracy compared to angiography in symptomatic carotid stenosis. *Stroke.* 1992;23:142. Abstract.
14. Ranval TJ, Bailey T, Solis ME, McDonald C, Wallace B, Harshfield D, Barnes RW. Overestimation of carotid stenosis: implications for carotid endarterectomy. *Stroke.* 1992;23:142. Abstract.