Multidimensional Characterization of Carotid Artery Stenosis Using CT Imaging: A Comparison with Ultrasound Grading and Peak Flow Measurement

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Abstract *Purpose:* Clinical decision making for carotid surgery depends largely upon stenosis grade. While digital subtraction angiography remains the gold standard for stenosis grading, many physicians use less invasive modalities. The purpose of this study was to compare the results of multidimensional Computed tomography (CTA) with ultrasound (US) grading and peak flow velocity (PSV).

Methods: 37 stenosed carotid arteries were studied retrospectively in 36 consecutive patients. US grading and PSV were compared to multidimensional CTA analysis (diameter, area and volumetric measurements), performed by a medical software company. Calculations of stenosis percentage on CTA were made using the NASCET and ECST methodology. Diameter measurements were also performed by a neuroradiologist.

Results: All CTA diameter, area and volume measurements had only modest correlation with PSV ($r < 0.5$) and ultrasound grading ($p < 0.5$). There was concordant classification of stenosis grades in only 40—60% of cases. CTA diameter, area and volume measurements had good correlation ($0.69 < r < 0.87$) with one another using ECST methodology. Using NASCET methodology on CTA, correlation between diameter and area was insignificant ($r = 0.32$). CTA volumetric analysis with the NASCET method yielded 27 negative stenosis grades. Repeatability coefficient for selecting the normal distal ICA 20 mm more distally was 20% for diameter and 43% for area. CTA diameter interobserver repeatability coefficients were 22.9% (NASCET) and 17.8% (ECST) and 0.7 mm (lumen) and 1.9 mm (vessel).

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Conclusions: All CTA measurements showed moderate correlation with both ultrasound grading and PSV. Selection of the level of the normal distal ICA influences the NASCET calculations and can produce discrepant stenosis grades. Multidimensional CTA analysis seems to have no additional value for stenosis grading, but provides other useful anatomic information.

Introduction

Clinical decision making regarding intervention for carotid stenosis depends upon the grade (percentage) of stenosis. The large clinical trails on which many physicians rely for this decision used digital subtraction angiography (DSA) to grade the stenosis.[1–4] Measuring according to the NASCET criteria is done by comparing the diameter of the lumen at the most stenotic part of the vessel to the diameter of the normal ICA distal to the stenotic portion. The ECST method compares the lumen diameter of the most stenotic part to the estimated original diameter at the site of the carotid bulb. In clinical practice however, many physicians tend to use less invasive modalities such as duplex ultrasound, computed tomography angiography (CTA) or magnetic resonance angiography (MRA).[3,4]

One of the advantages of CTA and MRA over angiography is the three dimensional and/or multiplanar views that can be generated and reconstructed. The multiplanar views produced with MRA and CTA offer a more complete assessment of luminal narrowing; any asymmetry in luminal morphology which may affect the stenosis measurement when using angiography can be detected with MRA and CTA.[5] In addition, MRA and CTA allow for visualization of the vessel, plaque and surrounding structures. The variety in post-processing techniques for CTA and MRA has made comparison of these imaging modalities difficult.[6,7] With the rapid evolution and development of imaging software it has become possible to perform 3D multidimensional measurements of carotid artery stenosis, based on CTA source data. The value of multidimensional analysis has yet to be established. The purpose of this study was to compare measurement and grading of ICA stenosis with CTA and ultrasound. Furthermore, measurement of stenosis on CTA is currently based on measuring the diameter at the point of maximum stenosis and comparing this with the diameter of the normal portion of the carotid artery distal to the stenosis (NASCET method).[8] Most studies have focused on maximum intensity projection (MIP) images when comparing CTA and MRA to DSA.[9] This assumes NASCET methodology and compares luminal diameters only. In this study, however, we used the axial images on CTA which allows one to visualize the carotid artery and plaque as a whole and to determine percent stenosis based on ECST methodology. While accepted NASCET methodology relies on distal ICA as reference for 'normal' diameter, this may not always be the most accurate estimation of true percent stenosis at the lesion. Indeed, if the ICA measurement is taken too proximal, post-stenotic dilatation may produce exaggerated percent stenosis, while ICA measurement taken too distally when the vessel has tapered on its way intracranially, may underestimate percent stenosis. Comparison of the luminal diameter or area with the diameter or area of the vessel at the stenotic level (ECST method) may give a more accurate measure of the stenosis.

Methods

Thirty-six consecutive patients (24 male, 12 female, mean age 77, range 61–90) underwent a duplex ultrasound and CTA with subsequent 3D reconstruction between August 2005 and September 2006 (Fig. 1). One patient had multidimensional imaging of both left and right carotid arteries. This resulted in a comparison of measurement of 37 carotid arteries in 36 patients.

CTA analysis

CTA scans were performed according to institutional protocol using a 64 (16) slice Siemens Sensation CTA scanner (Siemens Medical Solutions Inc., Malvern, PA, US). The imaging protocol was set at 0.6 (0.75) mm collimation and a pitch of 0.9 (1.0). Radiation exposure parameters were 120 (120) kVp and 270 (200) eff. mAs, resulting in a CT dose index (CTDIvol) of 20.66 (15.60) mGy. Field of View (FOV) of 140 and matrix size (512 × 512) resulting in a voxel size of 0.27 mm × 0.27 mm × 1.0 mm. A dose of 100 ml intravascular non-ionic contrast (Ultravist 300, Bayer, Germany) was injected at a flow rate of 4.0 ml/s. The scan was started using bolus triggering software with a threshold of 70 HU over baseline.

3D reconstructions were made by a commercial medical software company (Medical Metrix Solutions (M2S), West Lebanon, NH, USA) using the raw (DICOM) CTA data provided by our medical center. Reconstructed CTA slides, perpendicular to the ICA, were used to map location of maximum stenosis as well as normal appearing distal internal carotid artery. Diameter and cross-sectional area were measured at both locations. Volume of lesion was calculated for all lesions by straddling the point of maximum stenosis for a distance of 2 mm proximally and 2 mm distally (Figs. 2 and 3). A similar volume of normal distal ICA was also calculated. Calculations were performed using NASCET (equation 1) and ECST methodology (equation 2). All diameter measurements were made by a neuroradiologist as well as by MMS technicians.

$$\text{stenosis grade} = \text{Diameter}_{\text{stenotic lumen}} / \text{Diameter}_{\text{distal normal ICA}}$$

$$\text{stenosis grade} = \text{Area}_{\text{stenotic lumen}} / \text{Area}_{\text{distal normal ICA}} \tag{1}$$
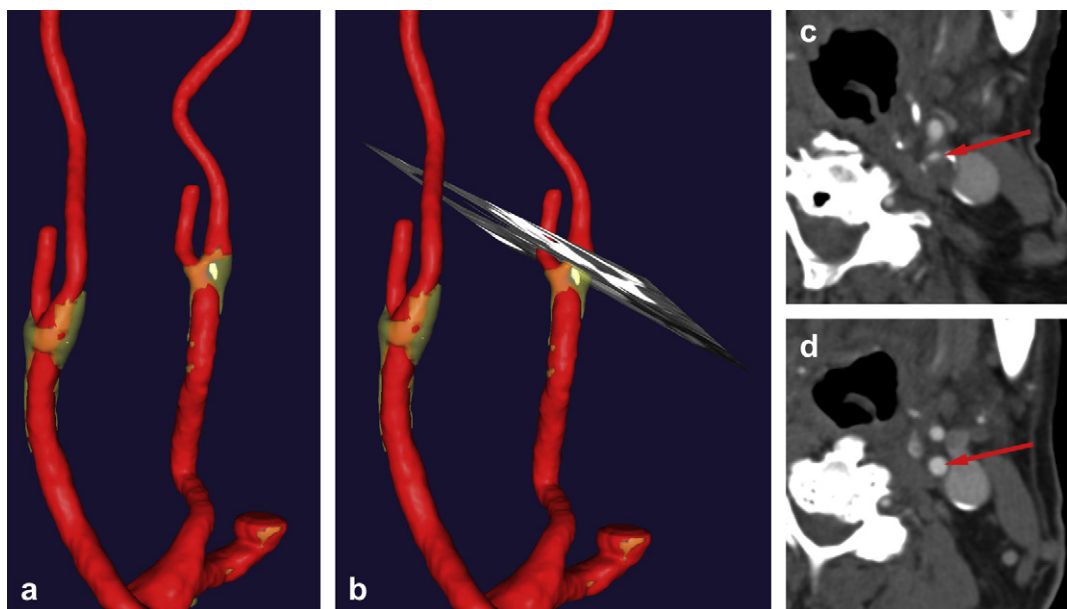
Figure 1 3D reconstruction with (a) and without (b) axial plane perpendicular to lumen of the ICA. Yellow color represents thrombus/non-calcified plaque and white color represents calcification. At the axial slide the red arrows indicates the point of maximal stenosis (c) and the distal normal portion (d) of the ICA.

$$\text{stenosis grade} = \text{Volume}_{\text{stenotic lumen}}/\text{Volume}_{\text{distal normal ICA}}$$

$$\text{stenosis grade} = \text{Diameter}_{\text{stenotic lumen}}/\text{Diameter}_{\text{vessel}}$$

$$\text{stenosis grade} = \text{Area}_{\text{stenotic lumen}}/\text{Area}_{\text{vessel}} \qquad (2)$$

$$\text{stenosis grade} = \text{Volume}_{\text{stenotic lumen}}/\text{Volume}_{\text{vessel}}$$

Duplex ultrasound

Duplex examinations were performed by experienced radiographers at an ICAVAL accredited vascular laboratory with a Philips HDL 5000 ultrasound machine (Philips Medical Systems, Bothell, WA, United States). Duplex was performed with both B-mode imaging (5 MHz) and pulse-wave Doppler frequency (12–20 kHz) measurements with an angle of insonation of 60 degrees. PSV was the maximum systolic velocity recorded on pulsed wave Doppler in the ICA. Measurements were taken from the proximal, mid, and distal ICA. Ultrasound grading was performed according to the University of Washington (Strandness) Criteria as shown in Table 1 and were based on peak systolic velocity (PSV), end diastolic velocity (EDV), the presence of spectral broadening and end-systolic bulb flow reversal.

Stenosis grading

For comparison of ultrasound grading with CTA stenosis grading we used the following scale: 0 = 0–15%, 1 = 16–49%, 2 = 50–79%, 3 = 80–99%. Negative (−1) stenosis grade is only applicable to the NASCET method: when the measurement of the stenotic lumen is larger then the measurement of the distal normal ICA.
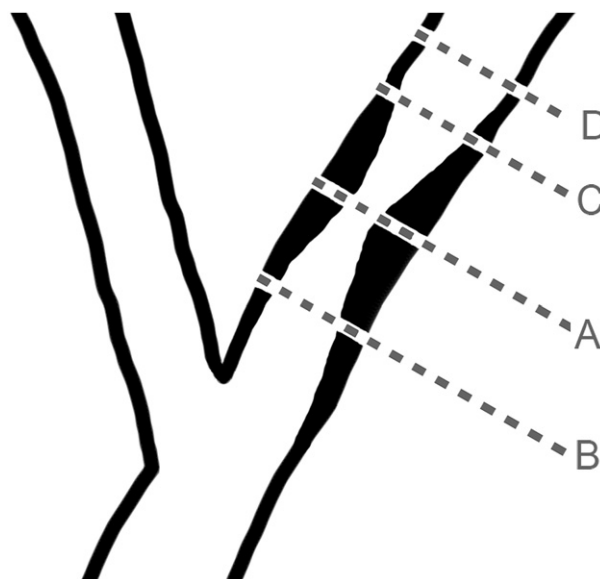
Statistical analysis

Relationship between PSV and CTA stenosis percentage (diameter, area, volume) using NASCET and ECST methodology were compared with Pearson's two-tailed correlation coefficient (r) which is used for the comparison of parametric data. Correlation was considered significant when $p < 0.05$. The relationship in grading (−1 to 3)

Figure 2 Diagram showing relevant landmarks and cut-off points for analysis of the ICA: point of maximum stenosis (A), proximal (B) and distal (C) volume cut-off 2 mm from point of maximum stenosis and normal appearing portion of distal ICA (D). Volumetric analysis is based on the volume between A and C.
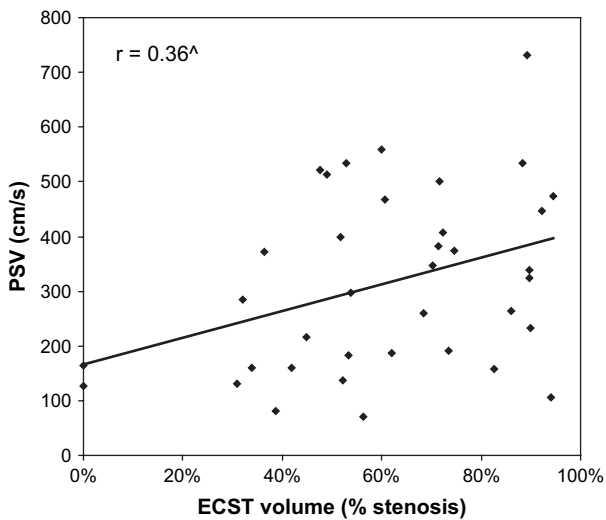
Figure 3 PSV plotted against the percentage stenosis measured with CTA volumetric measurement using the ECST method. ^ = significant correlation.

between Ultrasound and CTA were analyzed with the two-tailed Spearman rank correlation (p) coefficient. Correlation was considered significant when $p < 0.05$. Bland and Altman (interobserver) variability analysis was used for comparison of the NASCET method with selection of the normal distal ICA and selection 20 mm distal to this point and comparison between measurements by the imaging company and the institutional neuroradiologist.[10]

Results

Mean time between duplex and CTA or vice versa was 12 days (range 0–77). Overall correlation between CTA and PSV and ultrasound grading is moderate ($0.17 < r < 0.47$ and $0.23 < p < 0.48$) (Table 2). Exclusion of 7 severe calcificated carotid arteries resulted in similar correlation ($0.17 < r < 0.50$ and $0.25 < p < 0.50$).

Diameter

Ultrasound PSV showed modest correlation with stenosis percentage measured with CTA diameter using the NASCET ($r = 0.45$) and ECST method ($r = 0.47$). Correlation with ultrasound grading was also modest for CTA grading with NASCET ($p = 0.48$) and ECST ($p = 0.36$) methodology. CTA grading with NASCET methodology underestimated ultrasound grading in 19% (7/37) of cases, overestimated in 22% (8/37) of cases and classified the same in 59% (22/37) of cases. CTA grading with ECST methodology

underestimated ultrasound grading in 51% (19/37) cases, overestimated in 5% (2/37) of cases and classified the same in 43% (16/37) of cases.

Area

Area measurement of stenosis on CTA with the ECST method showed only modest correlation with PSV ($r = 0.40$) and ultrasound grading ($p = 0.39$). CTA area measurement with NASCET methodology resulted in 3 negative stenosis percentages and did not showed a significant correlation with PSV ($r = 0.17$; $p = 0.32$) and ultrasound grading ($p = 0.30$; $p = 0.07$). Removing one outlier which indicated a negative stenosis of 120% changed correlation to $r = 0.47$ and $p = 0.37$.

CTA grading with NASCET methodology underestimated ultrasound grading in 51% (19/37) of cases, overestimated in 8% (3/37) of cases and classified the same in 41% (15/37) of cases. CTA grading with ECST methodology underestimated ultrasound grading in 16% (6/37) cases, overestimated in 35% (13/37) of cases and classified the same in 49% (18/37) of cases.

Volume

CTA volumetric measurement with the NASCET method, which divides the luminal volume of the stenotic portion by the volume of the distal normal ICA (with equal length as the stenotic portion) did not seem to be feasible: In 27 cases this calculation yielded a negative stenosis percentage. CTA volumetric analysis with ECST methodology showed modest correlation ($r = 0.36$) with PSV and insignificant correlation with ultrasound grading ($p = 0.23$; $p = 0.17$). CTA grading with ECST methodology underestimated ultrasound grading in 49% (18/37) cases, overestimated in 14% (5/37) of cases and classified the same in 38% (14/37) of cases.

CTA diameter, area and volume

Using ECST methods for measuring stenosis on CTA, diameter, area and volume had good correlation with one another ($0.69 < r < 0.87$). NASCET diameter and area measurements showed insignificant correlation ($r = 0.32$; $p = 0.051$) but when removing the NASCET area outlier of -120% this correlation increases to $r = 0.73$.

NASCET method

When comparing NASCET measurement (on CTA) using different reference distal ICA sites the repeatability coefficient was 20.0% for diameter and 43.4% for area.

Table 1 The University of Washington (Strandness) Criteria for ultrasound stenosis grading

Normal	PSV < 125 cm/s		no spectral broadening	end-systolic bulb flow reversal
1–15%	PSV < 125 cm/s		no or minimal spectral broadening	no end-systolic bulb flow reversal
16–49%	PSV < 125 cm/s		marked spectral broadening	
50–79%	PSV > 125 cm/s	EDV < 140 cm/s		
80–99%	PSV > 125 cm/s	EDV > 140 cm/s		

Table 2 Correlation between CTA measurements and PSV and ultrasound grading

CTA Correlations	PSV (r)	Ultrasound Stenosis grading (p)
Diameter (NASCET)	0.45[a]	0.48[a]
Diameter (ECST)	0.47[a]	0.36[a]
Area (NASCET)	0.17	0.30
Area (ECST)	0.40[a]	0.39[a]
Volume (NASCET)	N/A	N/A
Volume (ECST)	0.36[a]	0.23

[a] Significant correlation.

Imaging company vs. institutional neuroradiologist

The mean diameters that were measured on CTA by the imaging company and the neuroradiologist were 2.6 mm (SD 1.0 range 0.9–5.1) versus 2.4 mm (SD 0.9 range 1.4–4.4) for the lumen at the point of maximum stenosis, 7.3 mm (SD 1.5 range 4.0–4.5) versus 7.4 (SD1.4 range 4.4–10.6) for vessel at this point and 4.6 mm (SD 0.8 range 2.4–6.1) versus 4.7 mm (SD 0.8 range 2.5–6.4) for the distal ICA lumen. Interobserver repeatability coefficients for diameter measurements were 0.7 mm for the lumen at the point of maximum stenosis, 0.7 mm for the luminal diameter at the level of the normal distal ICA and 1.9 mm for the vessel diameter of the normal distal ICA. The interobserver repeatability coefficient for CTA diameter percentage stenosis measurement were 22.9% for NASCET and 17.8% for ECST.

Discussion

CTA measurements showed moderate correlation coefficients compared with PSV and ultrasound grading. We expected the correlation coefficients to be higher, and were surprised by this finding. Clinical decisions regarding the indication for surgery are based primarily on degree of stenosis, and a correlation coefficient of <0.5 and an agreement of 40–60% for stenosis grade is inadequate. Such correlation does not support the notion that CTA can replace US as a sole imaging modality at this time.

Our starting hypothesis was that CTA area measurements would be different from diameter measurements given that area considers asymmetric shapes but diameter varies depending on the projection. Area measurements yielded similar correlation coefficients as diameter measurements allowing us to conclude that diameter is an adequate approximation for area when considering degree of stenosis. Volumetric analysis using the NASCET method was often not feasible, because the majority of the results were negative values ($n = 27$), indicating that the stenotic lumen has more volume than the distal normal lumen of equal length. This may have resulted from a degree of post-stenotic dilatation or perhaps the fact that the normal internal carotid artery has a slightly more bulbous shape in the proximity of the bifurcation and thus has a larger volume when compared with the distal ICA. When using volumetric analysis with the ECST method, this measure shows modest correlation ($r = 0.36$) with PSV and insignificant correlation ($p = 0.23$) with ultrasound stenosis grading. The results may be improved by adjustment of the anatomical cut-off points. For the purpose of standardization, the volume of lesion was calculated for all lesions by straddling the point of maximum stenosis for a distance of 2 mm proximally and 2 mm distally. We acknowledge that we have neglected the fact that in some cases the plaque extended into the common carotid artery, which might have influenced our measurements.

The problem of negative stenosis grades also arose in 3 cases for area analysis with the NASCET method. The NASCET stenosis grade decreases as the distal ICA becomes smaller, leading to underestimation of stenosis grade. When selecting the distal normal ICA 20 mm more distally, the repeatability coefficient of 43% indicates that the NASCET method is highly dependent on selection of the level of the distal ICA, as small discrepancies in diameter or area may severely influence the calculations.

The repeatability coefficients of the actual CTA diameter measurements by the software company and the institutional radiologist were 0.7 mm for luminal diameter and 1.9 mm for vessel diameter. This indicates good repeatability between the observers. The vessel diameter has a lower repeatability coefficient than lumen as a stenosed vessel is obviously more difficult to measure due to lack of contrast. However, the repeatability coefficients for CTA diameter stenosis grading by the software company and the institutional radiologist were between 15% and 23% which is large. When closely examining how stenosis grades are calculated (formula 1 & 2) in relation to the mean diameters that were measured (4.6 vs. 4.7 mm, 2.6 vs. 2.4 mm and 7.3 vs. 7.4), then a slight change (repeatability coefficients: 0.7 mm–1.9 mm) for the numerator and/or the denominator has a major impact on stenosis grade calculation. This seems to be the explanation for the variability of the CTA stenosis grades. Of note, the observer variability we observed for the CT measurements has also been described for DSA by Padayachee et al.[11] Thus observer variability appears not to be restricted to CT and also is problematic for DSA when grading carotid artery stenosis.

Our data suggests a moderate correlation between ultrasound and multidimensional CTA stenosis grading. However, this does not simply mean that CTA multidimensional analysis is inferior to ultrasound. Three dimensional CTA is of particular use for the planning of endovascular treatment and offers valuable information such as carotid tortuosity, aortic arch type, degree of calcification, length of landing zone distal to the lesion for deployment of a protection device, and information regarding the status of the vertebral arteries and circle of Willis. The large trials on which physicians rely for clinical decision making (NASCET, ECST and ACAS) used angiography for stenosis grading.[1,2,8,12] To draw a more definite conclusion about the preferable imaging modality for stenosis grading, the relation between multidimensional CTA, ultrasound and angiography should be further investigated.

Further research is needed to explore the possibilities of multidimensional characterization of stenosed arteries. Technical considerations may also have led to poor correlation. Duplex ultrasound examinations are operator dependent.[13] Although examinations were standardized

according to protocol, some operator induced error may exist. On the other hand, the semi-automated fashion of CTA image segmentation may be a cause for the moderate results. All of the CTA images were processed by the imaging company on a technician guided base. Although standard operating procedures (SOP's) and a protocollized technician review process were used, some error may be induced. Future developments that will use fully automatic image processing will overcome this problem. With advancing technology in CTA and MRA, by means of advanced postprocessing and improved spatial resolution of image acquisition, the results may improve enabling more accurate determination of normal vessels diameters. This is likely to have significant impact on calculations for percent stenosis.

Until that time, multidimensional characterization of carotid artery stenosis by CTA seems to have only modest correlation with ultrasound when determining the degree of stenosis; however it does provide useful information. In the era of carotid stenting, CTA with three dimensional reconstructions provides important anatomic information. We currently view carotid CTA as a complimentary study to carotid ultrasound when contemplating carotid artery endarterectomy or stenting.

Acknowledgements

Conflict of Interest

None.

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