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Carotid stenosis degree in CT angiography: assessment based on luminal area versus luminal diameter measurements

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Abstract The aim of this study was to investigate CT angiography (CTA) luminal area measurements in the assessment of carotid artery stenosis compared with the current clinically used criteria based on lumen diameter measurements. Seventy-two vessels in 36 patients were evaluated by CTA and digital subtraction angiography (DSA). Two observers measured area and diameter stenosis degrees using automated 3D CTA analysis software. The ratio of the largest/smallest luminal diameter at the level of maximal stenosis (L/S ratio) was used to describe lumen morphology. Diagnostic agreement between CTA and DSA was calculated. For the assessment of area stenosis, interobserver and intraobserver correlation coefficients were 0.898 and 0.906 (p<0.001). The correlation coefficient between the diameter stenosis and area stenosis was lower in stenoses with extremely noncircular lumen (L/S ratio ≥1.5) (r=0.797, p<0.001) compared with stenoses with circular lumen (LS ratio <1.2) (r=0.978, p<0.001). Only satisfactory agreement (κ 0.54-0.77, p<0.001) was obtained between area stenosis on CTA and diameter stenosis on DSA. Assessment of stenosis degree with area measurements on 3D CTA proved to be reproducible. Area stenosis provides a less-severe estimate of the degree of carotid stenosis but might theoretically express the real hemodynamic significance of the lesion better than diameter stenosis, especially in stenoses with noncircular lumen.

Keywords CT angiography · Carotid stenosis · Spiral CT

Introduction

Carotid artery atherosclerosis is an important etiological factor for ischemic stroke. Conventional digital subtraction angiography (DSA) and the assessment of the degree of stenosis according to the criteria from the North American Symptomatic Carotid Endarterectomy Trial (NASCET) are based on lumen diameter measurements [1]. These techniques have been used as the standards for clinical evaluation of carotid stenosis [2–5]. However, the amount of flow in a tubular structure (vessel) is directly related to the cross-sectional area, and thus measurements based on two-dimensional diameter values inevitably represent only an approximation of the actual flow.

Therefore, evaluation of stenosis degree with true luminal area measurements would be theoretically a more accurate method in any evaluation of real flow through a stenosed carotid segment, vessels that often exhibit irregular lesion morphologies. CT angiography (CTA) noninvasively can provide three-dimensional information of the vessel morphology, and new automated analysis software programs calculate quantitative data on cross-sectional luminal area values.

The purposes of the present study were (1) to investigate the reproducibility of luminal area measurements performed with an automated 3D CTA analysis method in carotid atherosclerotic lesions, (2) to study the relationship between the stenosis degrees based on luminal diameter and luminal area measurements, and (3) to assess the diagnostic agreement between area stenosis degrees measured by 3D CTA and the corresponding diameter stenosis values calculated by the current clinically used DSA criteria.

Materials and methods

Patients

Thirty-six consecutive patients (21 men, 15 women) with symptomatic carotid stenosis confirmed by DSA were included. Neurological symptoms included transient ischemic attacks (n=15), amaurosis fugax (n=10), and minor stroke (n=11). Mean patient age was 68 (range 50–83) years. The study protocol was approved by the ethical committee of our institute. Informed consent was obtained from the patients.

Evaluation and measurements on imaging studies

Biplane DSA (Siemens Neurostar Plus, Forchheim, Germany) (Fig. 1a) was conducted selectively in 72 carotid arteries of 36 patients using frontal, lateral, and two oblique views. Each carotid artery was imaged with 5–6 ml of nonionic contrast media (Visipaque 270 mg/ml, Nycomed, Oslo, Norway) per injection and a flow rate of 8 ml/s. The images were displayed and processed on a monitor with a 1,024×1,024 matrix. The degree of stenosis was measured by an experienced neuroradiologist according to the NASCET criteria based on lumen diameter values.

Multislice CT (Siemens Volume Zoom, Forchheim, Germany) was performed for all patients before or after the DSA examination. The CT scans covered the range between the sixth cervical vertebra and the level of circle of Willis. A slice thickness of 1.5 mm (1 mm collimation, feed 5 mm/s) and a reconstruction interval of 1.0 mm were used. The bolus tracking technique was used to ensure optimal intravascular contrast media density. The contrast agent (Ultravist 300 mgI/ml, Schering AG, Berlin, Germany) volume for CT angiography was 80 ml with a saline chaser bolus of 30 ml using a flow rate of 3 ml/s via a 1.3 mm (18G) cannula through the antecubital vein.

A separate workstation (ADW 4.0, GE, Medical systems, Milwaukee, WI, USA) was used for analysis of CTA images (Fig. 1). Two observers independently performed the measurements of luminal diameters and luminal areas to assess stenosis degree on CTA [6]. One observer repeated the measurements again at a 1-month interval for the determination of intraobserver reproducibility.

An automated 3D CTA analysis method was used. One disadvantage of CTA is that it cannot always accurately delineate the atherosclerotic plaque and the intraluminal contrast density. To avoid errors based on inaccurate vessel-wall recognition by the analysis program, each observer visually checked the estimated lumen areas and made manual corrections, if necessary. Manually corrected measurements facilitate avoidance of the interfering factors, such as ulcerations, calcifications, and adjacent vessels, and thus increase the anatomical accuracy of arterial delineation by automated CT angiography [6].

On 3D CTA, luminal cross-sectional area and smallest diameter were measured from the level of maximal stenosis and from the level of reference distal to the carotid bulb.

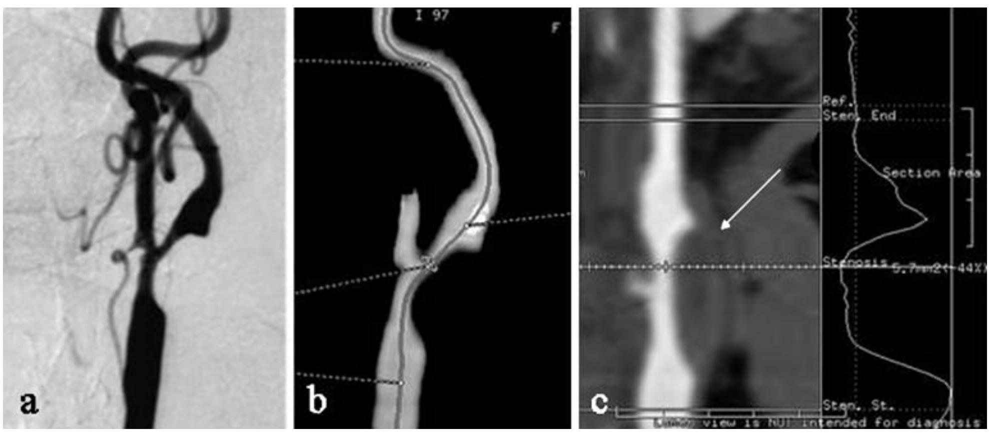

Fig. 1 Conventional digital subtraction angiography (DSA) (**a**) demonstrates stenosis at the left carotid bifurcation. The same lesion was excellently revealed on CT angiography (CTA) with 3D image (**b**) and lumen image (**c**) produced by 3D CTA analysis software. The lumen image (**c**) also shows the plaque (*arrow*). The analysis software also automatically defines the level of maximal stenosis. Regular cross-sectional area (not shown) with the largest/smallest luminal diameter at the level of maximal stenosis (L/S) ratio of 1.0 at the maximal stenosis level was demonstrated. Stenosis degree on conventional DSA was 44%. Measurements on 3D CTA showed minimal lumen area 3.2 mm^2, reference lumen area 8.5 mm^2, and the degree of stenosis based on area measurements was 62%

The stenosis degree based on luminal area values was obtained by the following equation:

$$100 \times \left(\text{area}^{\text{reference level}} - \text{area}^{\text{maximal stenosis level}}\right) \Big/ \text{area}^{\text{reference level}}.$$

The luminal areas in carotid arteries without a visible lumen at the level of the maximal stenosis were considered to be zero. Stenosis degree was, however, estimated to be 95% with both luminal diameter and luminal area assessment methods if no lumen was visible at the level of stenosis but contrast media filling was seen in the internal carotid artery distal to the stenosis, indicative of near-occlusion rather than total occlusion.

Registration of lumen morphology

On 3D CTA, the largest (L) and smallest (S) diameters of the lumen at the level of the stenosis were registered to obtain the L/S ratio, a parameter that describes the morphological features of the carotid lumen, i.e., whether the lesion is concentric or eccentric. To investigate the impact of the L/S ratio on the assessment of carotid stenosis, cut-off points of 1.2 and 1.5 of L/S ratio were chosen to divide the carotids into subgroups.

Statistical analysis

Pearson correlation coefficients between the measured luminal area values at the level of maximal stenosis level, the obtained stenosis degrees based on luminal area measurements and stenosis degrees based on DSA diameter measurements, were calculated. Theoretically, when a carotid lumen is circular in shape (L/S ratio=1.0), as in cases of concentric stenoses, the diameter stenosis degrees of 70%, 50%, and 30% correspond to area stenosis degrees of 91%, 75%, and 51%, respectively (Appendix). In the present study material with complex atherosclerotic lesions, the thresholds of area stenosis degrees that actually corresponded to diameter stenosis degrees of 70%, 50%, and 30% were calculated from polynomial regression equations by establishing curve regression models (Appendix). The diagnostic performance of CTA was assessed with sensitivity, specificity, overall accuracy, and kappa values with reference to conventional DSA. A p value less than 0.05 was considered to be statistically significant.

Results

CTA measurements in normal carotid bifurcations

Five carotid arteries contralateral to the symptomatic side that were visually estimated to be normal both in CTA and DSA were evaluated to obtain a range of luminal diameter and area values in CTA of normal carotid bifurcations. The mean minimal luminal diameters were 6.5 (5.6–7.4) mm at the common carotid arteries, 8.4 (6.5–10.8) mm at the carotid bulbs, and 4.6 (3.6–5.7) mm at the distal internal carotid arteries. The mean minimal luminal area values were 37.3 (26.6–50.1) mm^2 at the common carotid arteries, 67.6 (36.9–120.0) mm^2 at the carotid bulbs, and 18.4 (10.6–28.7) mm^2 at the distal internal carotid arteries, re-

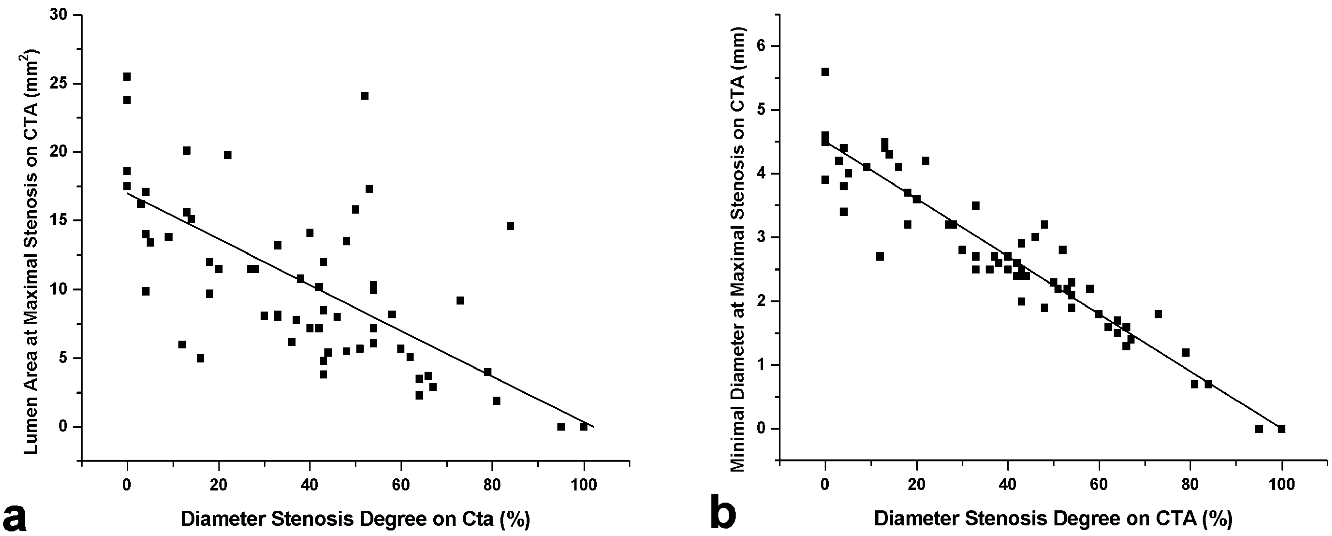

Fig. 2 Linear regression analysis reveals the poor correlation between lumen area at the maximal stenosis level and diameter stenosis in 3D CT angiography (CTA) (**a**). Higher correlation is demonstrated between minimal lumen diameter at the maximal stenosis level and diameter stenosis values of 3D CTA, as expected (**b**)

Table 1 Correlation of the CT angiography (CTA) diameter stenosis degrees with luminal area measurements at the level of maximal stenosis and calculated area stenosis degrees. *L/S ratio* largest/smallest luminal diameter at the maximal stenosis level

		Luminal area versus diameter stenosis		Area stenosis versus diameter stenosis	
		r	*p*	*r*	*p*
All carotid bifurcations	(n=72)	−0.767	<0.001	0.922	<0.001
L/S ratio <1.2	(0=27)	−0.920	<0.001	0.978	<0.001
1.2 ≤L/S ratio <1.5	(n=17)	−0.508	0.037	0.976	<0.001
L/S ratio ≥1.5	(n=28)	−0.641	<0.001	0.797	<0.001

spectively. As expected, the mean L/S ratios of the carotid segments were below 1.2, with only minimal variability, which indicates a circular shape of a normal artery.

Reproducibility of lumen area measurements on CTA

The interobserver and intraobserver correlation coefficients of the measurements of luminal area at the level of maximal stenosis on 3D CTA were 0.716 and 0.821 (p<0.001). The interobserver and intraobserver correlation coefficients of 3D CTA for the area stenosis assessment were 0.898 and 0.906 (p<0.001), respectively.

Relationship between 3D CTA luminal area and diameter measurements

Luminal area on 3D CTA at the level of maximal stenosis significantly inversely correlated with the diameter stenosis (r= −0.767, p<0.001) (Fig. 2) and the area ste- nosis (r= −0.806, p<0.001). The mean value of the L/S ratio in carotid arteries was 1.6 (± SD 0.9, range 1.0–6.8). Table 1 reveals that when one divides the carotid stenoses into three subgroups according to the luminal morphology using the L/S-ratio values, the correlation coefficients between the luminal area at the level of maximal stenosis and diameter stenosis was excellent (r= −0.920, p<0.001) in cases of concentric stenoses where the value of the L/S ratio was below 1.2. However, in cases where there were more eccentric stenoses, then the correlation coefficient was lower (0.508–0.641). There was also a statistically significant correlation between area stenosis and diameter stenosis in all subgroups, but the correlation was lower in the arteries with extremely noncircular lumens.

To graphically illustrate their relationship (Fig. 3), the calculated stenosis degrees based on luminal diameter versus luminal area measurements were plotted with a standard polynomial curve for stenoses with circular lumen (Appendix, Eq. 1) and fitted polynomial curve (Appendix, Eq. 2). This diagram reveals an inconsistency in our results with the standard curve. Especially in the category of moderate stenosis of 30–69%, if one examines the diameter measurements, one can observe a wide dispersion in the stenosis degrees based on area measurements. The scatter plot also reveals that most of the calculated stenosis degrees that were based on diameter measurements were considerably under the standard curve. This finding can be interpreted as a trend toward overestimation of the hemodynamic significance of the carotid stenosis degree when the calculation is based on diameter measurements.

Calculated with regression analysis from the actual area stenosis values of the study material (Appendix, Eq. 2), the threshold value of 74% area stenosis corresponded to the clinically important threshold of 70% diameter stenosis. The threshold of 56% area stenosis corresponded to the threshold of 50% diameter stenosis, and the threshold of 36% area stenosis corresponded to 30% diameter stenosis in this study, respectively. Correspondingly, the thresholds of 5 mm^2, 8 mm^2, and 12 mm^2 for the luminal area at the level of maximal stenosis corresponded to the thresholds of 70%, 50%, and 30% diameter stenosis.

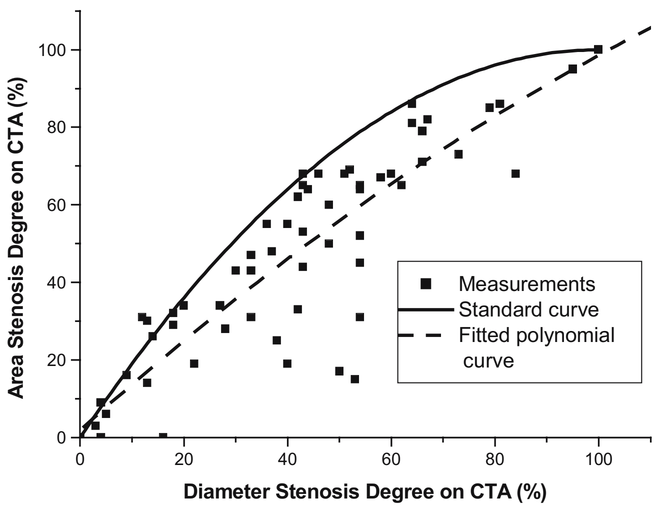

Fig. 3 The correspondence of the stenosis degrees based on the diameter measurements and area measurements in CT angiography (CTA). The standard curve is the polynomial regression curve from the equation A=2N−N^2, where A: area stenosis; N: diameter stenosis. This equation is valid if the lumen of the artery is entirely concentric, i.e., largest/smallest luminal diameter at the level of maximal stenosis (L/S) ratio=1.0

Table 2 Diagnostic performance of CT angiography (CTA) using different thresholds of the degree of area stenosis (n=72) with reference to diameter stenosis on digital subtraction angiography (DSA)

	Sensitivity % (n)	Specificity % (n)	Overall accuracy % (n)	Kappa (95% CI)
70% in DSA				
CTA 76%	61 (14/23)	94 (46/49)	83 (60/72)	0.59 (0.39–0.79)
CTA 80%	61 (14/23)	96 (47/49)	85 (61/72)	0.62 (0.42–0.82)
CTA 84%	52 (12/23)	96 (47/49)	82 (59/72)	0.54 (0.33–0.75)
50% in DSA				
CTA 53%	88 (28/32)	80 (32/40)	83 (60/72)	0.67 (0.50–0.84)
CTA 54%–60%	88 (28/32)	83 (33/40)	85 (61/72)	0.69 (0.52–0.86)
CTA 61%	81 (26/32)	85 (34/40)	83 (60/72)	0.66 (0.49–0.83)
30% in DSA				
CTA 34%	91 (40/44)	79 (22/28)	72 (62/72)	0.70 (0.53–0.87)
CTA 35%–43%	91 (40/44)	86 (24/28)	89 (64/72)	0.77 (0.62–0.92)
CTA 44%	86 (38/44)	86 (24/28)	86 (62/72)	0.71 (0.54–0.88)

Diagnostic performance of lumen area assessments in CTA

Tables 2 and 3 show the diagnostic performance of 3D CTA in the assessment of carotid stenosis in comparison with DSA. High overall accuracy (85%) and excellent specificity (96%) were achieved when a cut-off point of 80% was used as the threshold of area stenosis against the stenosis degree of 70% in DSA. The cut-off point of 4 mm^2 for luminal area at the level of maximal stenosis level exhibited a similar overall accuracy (85%).

Discussion

According to the basic principle of flow dynamics, Poiseuille's Law, the amount of blood flow in a vessel is proportional to the fourth power of the cross-sectional diameter and to the cross-sectional area, assuming there is a constant stenosis length. Cross-sectional imaging obtained with modern three-dimensional imaging can evaluate complex lesion morphology and thus the assessment of area stenosis has become feasible. Quantitative information on cross-sectional luminal area can be easily obtained with new automated 3D CTA analysis software. However, even though this data does appear to provide additional information as an adjunct to stenosis degrees based on diameter values, the clinical impact of this data remains to be clarified.

The first purpose of our study was to assess the reproducibility of 3D CTA area measurements for the assessment of carotid stenosis. The results demonstrated good intraobserver reproducibility and interobserver correlation for area assessment and excellent intra- and interobserver reproducibility for area stenosis assessment.

The eccentricity index has been used as a parameter for assessing the morphological variation in the stenotic artery lumen. [7–9]. The ratio of the luminal diameters is also an effective parameter for that purpose. Hirai et al. [5] used the almost equivalent L/P ratio (L: maximal diameter of measured section; P: perpendicular diameter to the maximal diameter) as the parameter to describe the morphological characteristics of the carotid lumen in CTA. We used the L/S ratio to describe morphological variations of the stenosed lumen cross-section. The L/S ratio is obtained from the result of the largest diameter (L)/smallest diameter (S) at the center of the measured level, and those values are calculated automatically by

Table 3 Diagnostic performance of CT angiography (CTA) using different thresholds of lumen area values (n=72) with reference to diameter stenosis on digital subtraction angiography (DSA)

	Sensitivity % (n)	Specificity % (n)	Overall accuracy % (n)	Kappa (95% CI)
70% in DSA				
Lumen area 3 mm^2	57 (13/23)	98 (48/49)	85 (61/72)	0.61 (0.41–0.81)
Lumen area 4 mm^2	65 (15/23)	94 (46/49)	85 (61/72)	0.63 (0.43–0.83)
Lumen area 5 mm^2	70 (16/23)	90 (44/49)	83 (60/72)	0.61 (0.41–0.81)
50% in DSA				
Lumen area 7 mm^2	72 (23/32)	85 (34/40)	79 (57/72)	0.57 (0.39–0.75)
Lumen area 8 mm^2	81 (26/32)	83 (33/40)	82 (59/72)	0.64 (0.46–0.82)
Lumen area 9 mm^2	88 (28/32)	73 (29/40)	79 (57/72)	0.59 (0.41–0.77)
30% in DSA				
Lumen area 8 mm^2	73 (32/44)	96 (27/28)	82 (59/72)	0.65 (0.48–0.82)
Lumen area 9 mm^2	84 (37/44)	93 (26/28)	88 (63/72)	0.75 (0.59–0.91)
Lumen area 10 mm^2	84 (37/44)	82 (23/28)	83 (60/72)	0.65 (0.47–0.83)

3D CTA analysis software. In the present study, the mean value of the L/S ratio at the level of maximal stenosis was larger than that at the level of reference, reflecting marked lumen irregularity at the level of maximal stenosis. The L/S-ratio values of 1.2 and 1.5 were chosen for cut-off points. Values below 1.2 indicate a circular lumen, values between 1.2 and 1.5 represent a moderately noncircular lumen, and values over 1.5 refer to an extremely noncircular lumen. Our study reveals the impact of the luminal morphology expressed with the L/S ratio on the correlation between the luminal area at the maximal stenosis level and area stenosis with the diameter stenosis (Table 1). In those carotid arteries with L/S ratio of >1.5, i.e., in vessels with obvious eccentric and complex lesions, both the luminal area at the maximal stenosis and the area stenosis degree correlated less well with the diameter stenosis degree than in those carotid arteries with L/S ratio of <1.2, i.e., stenoses with circular lumen. The degree of carotid stenosis calculated with the ratio of vessel diameters does not observe the eccentricity of the stenosed carotid lumen, leading in some cases to an erroneous estimation of the hemodynamic significance of stenosis. This indicates that the calculated stenosis degree based on diameter measurements may not be optimal for the assessment of carotid stenosis in arteries with eccentric or complex plaques.

Since there was no earlier established categorical classification of carotid stenosis degrees based on luminal area measurements, we calculated their sensitivity, specificity, and diagnostic accuracy using DSA as a reference standard and applying a variety of cut-off values. The single measurements of the luminal area, as well as the stenosis degrees based on the luminal area measurements, revealed only moderate diagnostic agreement with the diameter stenosis degree obtained by conventional DSA. An overall accuracy of only 85% was achieved for revealing severe (>70%) diameter stenosis. Cinat et al. [10] detected a similar dispersion between area stenosis and diameter stenosis in their study, which evaluated the use of single-detector CTA in the preoperative evaluation of carotid artery stenosis compared with angiography. The diagnostic performance of CTA was slightly better in their study, i.e., sensitivity of 87 %, specificity of 90 %, and overall accuracy of 89% for the thresholds of >60% for diameter stenosis and >80% for area stenosis.

However, it must be emphasized that compromised diagnostic performance of the area stenosis assessment of CTA with reference to diameter stenosis by DSA should not simply be interpreted as poorer diagnostic ability of the area stenosis assessment. In fact, it may indicate that this new method evaluates a different aspect of those stenotic segments with varying morphologies, which may in fact be more relevant to the accurate recognition of patients at high risk for future stroke, but further studies are warranted to verify this point. It should also be noted that the best diagnostic correlation in our study was obtained by using considerably lower cut-off points than those values deduced from the standard equation for circular stenoses. However, for the evaluation of diagnostic performance, this study compared an area assessment with a diameter assessment. These are already basically two different measurements. Another point is that we have made those different measurements on two-dimensional DSA and from the cross-section of the lumen on CTA to evaluate the diagnostic accuracy of CTA.

Thus far, diameter assessment has been used as the routine method to evaluate the stenosis degree. For example, large randomized clinical trials on the beneficial value of endarterectomy have been carried out on the basis of diameter measurements [11, 12]. One reason this method has achieved such widespread use is at least partly attributable to the fact that, until recently, it has not been possible to assess the cross-sectional area of a vessel by conventional angiography.

With the development of novel imaging technologies, it is now possible to assess the cross-sectional area of vessel lumen with several imaging modalities, such as ultrasound, intravascular ultrasound, magnetic resonance angiography, rotational DSA, and CTA [10, 13–15]. It is possible that diameter measurements alone may lead to a suboptimal evaluation of the hemodynamic significance of the stenosis in those cases where there is irregular sectional morphology of the stenosed artery. The above findings can be considered as advocating the use of luminal area assessment as an adjunct to conventional diameter measurements in the evaluation of the degree of stenosis. For example, this information could help to distinguish patients for carotid endarterectomy or stenting, i.e., if the stenosis degree based on diameter measurements falls into the category of 50–69%, where the beneficial effect of invasive treatment is less-well documented compared with those where stenosis degree is >70%. However, there is still no clinical experience on the advantage of selecting patients for carotid endarterectomy or stenting based on the assessment of area stenosis.

To conclude, the assessment of carotid stenosis degree with area measurements by 3D CTA analysis software proved to be reproducible. Especially in eccentric lesions with noncircular lumens, it does seem that area stenosis often provides a less-severe estimate of the hemodynamic significance of the carotid stenosis than the conventional diameter stenosis. The potential clinical value of the assessment of area stenosis needs to be further evaluated in large clinical trials.

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Appendix

1. The theoretical (standard) equation between area stenosis and where r_2: radius of reference area; r_1: radius of maximal stenosis area; A: area stenosis degree; N: diameter stenosis degree.

The equation $A=2N\text{-}N^2$ is valid when carotid lumens are circular in shape (L/S ratio=1.0) both at the level of maximal stenosis and at the level of reference. Thus for 70%, 50%, and 30% diameter stenosis, the corresponding area stenosis values are 91%, 75%, and 51%, respectively.

2. The regression curve between area stenosis and diameter stenosis by 3D AVA in this study:

$$A = 2.869 + 1.160 * N - 0.002 * N^2$$

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