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Intracranial Carotid Calcification on Cranial Computed Tomography

Visual Scoring Methods, Semiautomated Scores, and Volume Measurements in Patients With Stroke

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Background and Purpose—Intracranial internal carotid artery calcification is associated with cerebrovascular risk factors and stroke, but few quantification methods are available. We tested the reliability of visual scoring, semiautomated Agatston score, and calcium volume measurement in patients with recent stroke.

Methods—We used scans from a prospective hospital stroke registry and included patients with anterior circulation ischemic stroke or transient ischemic stroke whose noncontrast cranial computed tomographic scans were available electronically. Two raters measured semiautomatic quantitative Agatston score, and calcium volume, and performed qualitative visual scoring using the original 4-point Woodcock score and a modified Woodcock score, where each image on which the internal carotid arteries appeared was scored and the slice scores summed.

Results—Intra- and interobserver coefficient of variations were 8.8% and 16.5% for Agatston, 8.8% and 15.5% for calcium volume, and 5.7% and 5.4% for the modified Woodcock visual score, respectively. The modified Woodcock visual score correlated strongly with both Agatston and calcium volume quantitative measures (both R^2=0.84; P<0.0001); calcium volume increased by 0.47-mm/point increase in modified Woodcock visual score. Intracranial internal carotid artery calcification increased with age by all measures (eg, visual score, Spearman ρ=0.4; P=0.005).

Conclusions—Visual scores correlate highly with quantitative intracranial internal carotid artery calcification measures, with excellent observer agreements. Visual intracranial internal carotid artery scores could be a rapid and practical method for epidemiological studies. **(*Stroke*. 2015;46:2504-2509. DOI: 10.1161/STROKEAHA.115.009716.)**

Key Words: calcification, physiologic ■ carotid artery, internal ■ epidemiological studies ■ risk factors ■ stroke

Stroke is the second most common cause of death worldwide and commonest cause of dependency in adults.[1] Atherosclerosis of the cervical carotid arteries is an established cause of ipsilateral ischemic stroke, and vascular calcification is an indicator of advanced atherosclerosis.[2] Vascular calcification can be quantified noninvasively on a computed tomographic (CT) scan.[3–5]

Coronary artery calcification is an established marker of cardiovascular disease and is an independent predictor of future myocardial infarction.[6] Agatston coronary calcium scoring is a screening test that uses computational image analysis to quantify coronary calcium to test for coronary artery disease.[7,8] It has a sensitivity of >90% for detection of significant coronary arterial stenosis.[9,10] The widespread adoption of Agatston coronary artery calcium scoring to screen cardiovascular disease opens the possibility of developing a similar tool for internal carotid artery (ICA) calcium scoring to predict ischemic stroke.

Several methods for assessing intracranial ICA calcium on brain CT have been described (Table 1; Table I in the online-only Data Supplement). Most used visual qualitative or semiquantitative scoring with only a few using specific software to obtain semiautomated quantitative measures. Quantitative methods need to be rapid, relevant, and reliable if they are to be used in large epidemiological studies, eg, to test the independent prognostic value of intracranial ICA calcification in prediction of stroke.

The purpose of this study was to test the inter- and intraobserver reliability and practicality of 2 visual calcium scoring

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methods and 2 semiautomated methods of quantifying ICA calcification in patients with recent stroke.

Methods

Study Population

We used data from prospectively recruited consecutive patients from the Edinburgh Stroke Study (ESS), who presented with anterior circulation stroke or TIA and underwent cranial CT. Briefly, ESS was a prospective, hospital-based register of 2160 stroke and TIA in- and out-patients, recruited between 2002 and 2005. All patients were assessed by stroke physicians to determine diagnosis. Both Lothian Research Ethics Committee and NHS Research and Development Department approved ESS.

To obtain representative data for the present analysis, we identified patients enrolled in the ESS in 2004 and 2005, excluding those with posterior circulation or hemorrhagic stroke. This yielded 499 patients. The most recent 132 of these patients with retrievable cranial CT scans were extracted for the study. Of these 132 patients, 71 had a gantry-tilted CT data set (which could not be used for Agatston scoring) and 7 had incomplete digital data (no posterior fossa images thus omitting the intracranial ICA), leaving 54 patients as the final study population.

CT Protocol

Patients had cranial CT scans at first presentation with stroke or TIA on a Siemens Sensation 16 (16-slice CT scanner) at 120 kV and 294 mAs with sequential acquisition at section width of 3 mm for posterior fossa and 9 mm for the supratentorium. In all cases, the intracranial ICA was imaged at 3-mm section width.

Calcium scoring was done on each ICA separately, from the petrous apex to the terminal bifurcation, using 4 different methods: 2 semiautomated and 2 visual, as described below.

Semiautomated Quantitative Calcium Scoring

The digital image data were transferred to Vitrea 2 workstation (Vital Images Inc, Plymouth, MN), and semiautomated coronary calcium scoring software (VScore) was used to calculate Agatston calcium score and calcium volume.

Agatston Score. To calculate Agatston score, the software identifies calcifications in the arteries within a region of interest (Figure 1A) in every slice as areas with density >130 HU. At least 3 contiguous pixels with HU>130 are registered as calcification. Area of each of these calcifications is multiplied by a cofactor, which depends on the peak density of the individual plaque (130–199 HU=1; 200–299 HU=2; 300–399 HU=3; and >400 HU=4). Thus, Agatston score is a measure of calcification weighted to a cofactor of peak density of individual plaques. Care was taken to draw the region of interest (Figure 1A) around carotid calcifications on bone window setting to exclude bone from the region of interest, and the readers were allowed to manipulate the window level and width to avoid contamination from adjacent bone. Each ICA was assessed from the petrous apex to the terminal bifurcation (cavernous and supraclinoid portions). Agatston scores for right and left intracranial ICA and the combined total of right and left scores were calculated. The petrous portion of ICA was not assessed because of its close proximity to the bone limited the ability to draw a region of interest around calcifications without including the surrounding bone.

Calcium Volume. The software used to calculate Agatston score also provided an isotropically interpolated calcium volume, measured in cubic millimeter, by calculating the products of numbers of voxels with attenuation >130 HU and summing the total voxel volumes. This calcium volume was recorded for both right and left ICAs separately.

Two raters independently and blindly performed Agatston score and calcium volume measurement on each patient. The raters were radiology trainees with a minimum of 4 years of general training that included neuroradiology. Apart from learning to use the software, no additional special training was given. The first rater performed all measurements twice; the second rater performed all measurements once. First rater performed each of the 2 measurements 1 week apart to avoid memory bias. The raters were blinded to each other's scores and all clinical/other data.

Qualitative Visual Calcium Scores

For qualitative visual scoring, we used 2 methods: Woodcock visual scoring and a modified version of the Woodcock visual scoring. The Woodcock Visual Scoring (Table 1)[16] originally characterized the ICA siphon calcification as absent, mild (thin, discontinuous), moderate (thin, continuous or thick, discontinuous), or severe (thick, continuous) on axial CT. Woodcock method has demonstrated excellent inter- and intrarater agreements[16] and is more straightforward and less time consuming than some of the other visual methods previously described (Table 1; Table I online-only Data Supplement). In the Modified Woodcock Visual Scoring (Table 1; Figure 1B), we modified Woodcock's visual scoring method to provide a more detailed assessment of the burden of calcification in each ICA while retaining speed and practicality. In this modification, we assigned a number to the severity of calcification (0 for no calcification; 1 for thin, discontinuous calcification; 2 for thin, continuous or thick, discontinuous calcification; and 3 for thick, continuous calcification) on each axial CT slice. The number assigned for each axial slice was summed to create a total score for each ICA.

Table 1. Calcium Visual Scoring Methods in the Literature

Scale	Studies
Binary (absent or present)	Ptak et al,[11] Chen et al,[12] Bugnicourt et al[13]
3 points (1: thin, discontinuous or punctuate; 2: thin, continuous or thick, discontinuous; 3: thick, continuous or tubular)	Savy et al,[14] Suzuki et al[15]
4 points (absent, mild, moderate, and severe)	Woodcock et al,[16]* Erbay et al,[17] Erbay et al,[18] Bleeker et al[19]
5 points (0: none, 1: stippled, 2: thin, continuous or thick, discontinuous, 3: thick, continuous, and 4: double tracts)	Babiarz et al,[20] Hong et al 2011,[21] Kassab et al[22]
Multiple scales used	Ahn et al[23]

*The Woodcock score considers all slices on which the internal carotid artery is visible and assigns the closest fitting category. The Modified Woodcock score applies the numeric score for each slice and sums the scores to provide a total score per side; both sides can be combined. Additional study details are available in Table I in the online-only Data Supplement.

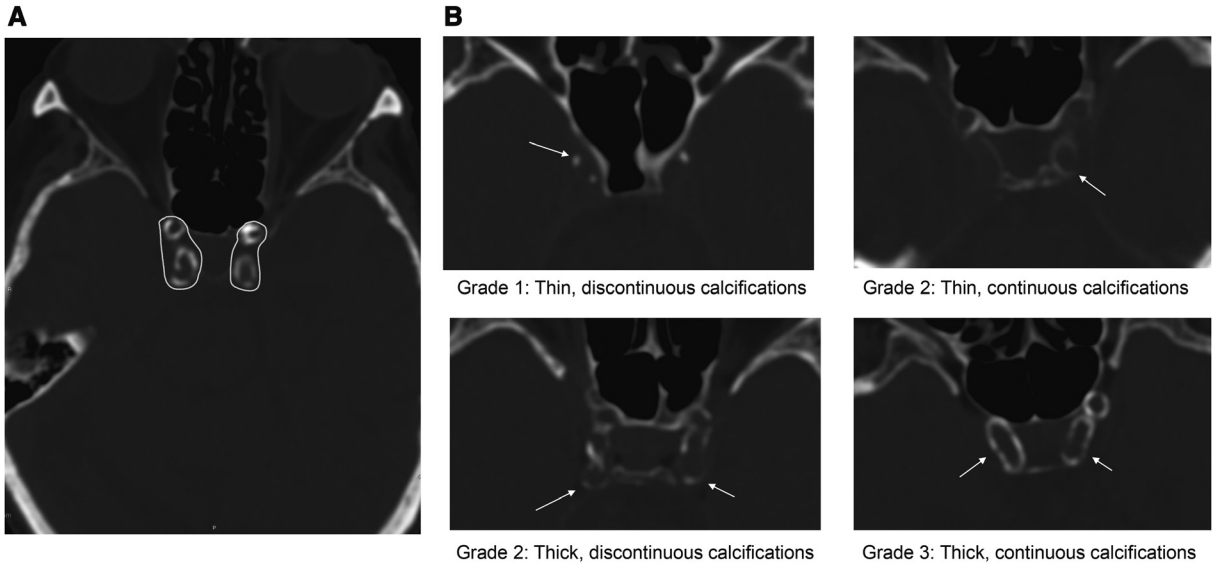

Figure 1. A, Measurement of internal carotid artery (ICA) calcification by semiquantitative methods. A region of interest is drawn around the calcified artery in a wide window setting, from the petrous apex to the internal carotid bifurcation. **B**, Modified Woodcock visual calcium score. Data derived from Woodcock et al.[16] Assessment done per side on each slice and then the slice scores are summed to give an overall calcium grade for each ICA.[16]

For the 2 visual methods, the CT images were viewed on a Carestream PACS workstation (Carestream Health, Rochester, NY), using a fixed bone window setting (window level 800 and window width 2000) without manipulation of the window level or width. As with semiautomated scoring, the segment of each ICA from the petrous apex to the ICA bifurcation was assessed.

Two raters performed both the Woodcock and the modified Woodcock visual calcium scores on each subject. The modified Woodcock score was performed first followed by Woodcock score. The first rater performed the visual scores twice (at least 1 week apart), and second rater performed the visual scores once.

Statistical Analysis

We performed all numeric analyses with SPSS version 14.0. We calculated intra- and interobserver agreement using the coefficient of variation, Bland–Altman method for continuous variables, and κ for categorical variables. We correlated visual scores, Agatston, and calcium volume using Spearman ρ. Plots of Agatston score or calcium volume and modified Woodcock visual score suggested nonlinear relationships. We investigated this nonlinearity with transformations and linear regression, using linear regression model diagnostics (scatter plots, QQ plots, and residual plots) to check for linearity. We used cube root as the transformation for calcium volume and Agatston score because this can be interpreted as a length if the raw data can be interpreted as a volume. All transformations, regression analyses, and graphs used R 2.13.1 (http://cran.r-project.org/)

Results

The sample included 54 CT scans, from 30 men (56%) and 24 women (44%), mean age 76 (range, 45–92) years.

The mean Agatston score was 372 (SD±354) right, 357 (SD±309) left, and 729 (SD±644) combined right left. The mean calcium volume (mm^3) was 298.5 (SD±268) right, 289 (SD±232) left, and 588 (SD±487) combined right left. The median modified Woodcock visual score was 7.0 (range, 0–15) right, 7.0 (range, 0–13) left, and 14.0 (range, 0–28) combined right left. The most frequent Woodcock score was moderate for both right and left.

The intra- and interobserver measures of agreement for Agatston score, calcium volume, and modified and original Woodcock visual scores are presented in Table 2. The absolute difference between observers was low for Agatston score, calcium volume, and modified Woodcock visual score and was not influenced by the amount of calcification, as shown on Bland–Altman plots (Figures I and II in the online-only Data Supplement).

The Woodcock visual score correlated well with (Table 2) the Agatston score (right: Spearman ρ=0.81, P=0.01 and left: Spearman ρ=0.79; P=0.01), calcium volume (right: Spearman ρ=0.81; P=0.01 and left: Spearman ρ=0.80; P=0.01), and modified Woodcock score (Figures I and II in the online-only Data Supplement; right: Spearman ρ=0.81; P=0.01 and left: Spearman ρ=0.83; P=0.01). The total modified Woodcock visual score (combined left and right) also correlated well with total Agatston score and total calcium volume (Figure 2; Spearman ρ=0.89; P=0.01 and Spearman ρ=0.91; P=0.01, respectively). The cube root transformation of Agatston score and calcium volume successfully linearized the relationships with the modified Woodcock visual score (Figure IIIA and IIIB in the online-only Data Supplement). All linear regression model diagnostics were satisfactory. This translated to an increase in calcium volume of 0.476 mm (95% confidence interval, 0.368–0.466; P<0.0001) for each point increase in the modified Woodcock visual score.

Increasing age was associated with higher Agatston score (combined left and right, Spearman ρ=0.31; P=0.05), higher calcium volume (combined left and right: Spearman ρ=0.33; P=0.05), and higher modified Woodcock visual calcium score (combined left and right: Spearman ρ=0.38; P=0.01).

Discussion

We tested an existing, simple visual ICA calcification score against the computational Agatston score, calcium volume,

Table 2. Comparison of Observers: Semiautomated Calcium Measures and Visual Calcium Scores

Measurement	Right ICA	Left ICA	Combined Right and Left ICA
Rater A intraobserver coefficient of variation, %			
Agatston score	9.80	13.80	8.80
Calcium volume	9.10	13.60	8.80
Modified Woodcock visual score	6.90	7.50	5.70
Rater A 1st reading vs rater B, interobserver coefficient of variation, %			
Agatston score	19.80	17.70	16.50
Calcium volume	18.70	15.60	15.50
Modified Woodcock visual score	7.10	7.20	5.40
Rater A 2nd reading vs rater B interobserver coefficient of variation, %			
Agatston score	17.30	19.60	15.60
Calcium volume	17.10	16.00	14.50
Modified Woodcock visual score	8.00	8.50	6.60
Rater A intraobserver κ			
Woodcock visual scoring	0.9 (95% CI, 0.8–1.0); P<0.001	0.8 (95% CI, 0.7–0.9); P<0.001	…
Rater A 1st reading vs rater B interobserver κ			
Woodcock visual scoring	0.7 (95% CI, 0.6 –0.9); P<0.001	0.8 (95% CI, 0.7–0.9); P<0.001	…
Rater A 2nd reading vs rater B interobserver κ			
Woodcock visual scoring	0.8 (95% CI, 0.6–0.9); P<0.001	0.7 (95% CI, 0.6–0.9); P<0.001	…

CI indicates confidence interval; and ICA, internal carotid artery.

and modified visual score in 54 patients presenting with stroke. We demonstrated very good correlation between visual calcium score and both calcium volume and Agatston scores, which were linear once transformed. We have shown that both semiautomated and visual scoring methods are reliable, with good intra- and interobserver agreements. The absolute differences in the values obtained were not dependent on the severity of calcifications. We also demonstrated good to very good inter- and intraobserver agreements for the original and modified Woodcock's visual scores. The modified Woodcock visual score is quick and reliable for quantifying ICA calcifications, translates to an increase of ≈0.5-mm calcium volume per point increase in visual score. Hence, the original and modified Woodcock visual scores are suitable for large studies and can be performed on electronic or printed x-ray film, making existing cohort studies' data accessible for analysis.

The ESS provided a sample of stroke patients representative of stroke in general, large enough for a method comparison study. We calculated intrarater variability by doing paired readings at least 1 week apart to reduce memory bias and inter-rater variability by blinding the 2 raters to each other's scores.

There are strengths and limitations to our study and the Agatston software. Although the software that was originally designed to measure Agatston scores and calcium volumes of coronary arteries can be used to measure intracranial ICA calcifications, it requires the slice thickness to be 3 mm and images acquired without a gantry tilt. The retrospective sample meant that many patients had to be excluded because of gantry tilt. The method also could not be used for the petrous part of the ICA because of its position within a bony canal. Both raters felt that the visual scoring methods, although simpler, posed difficulty in correct differentiation of arterial

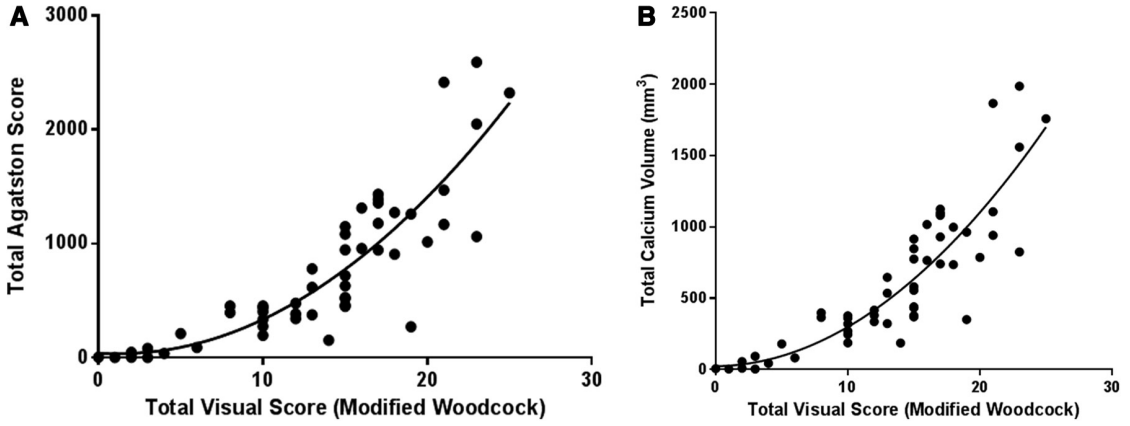

Figure 2. A, Modified Woodcock visual score vs Agatston score: R^2=0.83, P<0.0001 (cube root–transformed linear plot; Figure IIIA in the online-only Data Supplement). **B**, Modified Woodcock visual score vs calcium volume: R^2=0.84, P<0.0001 (cube root–transformed linear plot; Figure IIIB in the online-only Data Supplement).

calcification from adjacent osseous structures even on wide window settings. A larger sample and more raters would be helpful although we note that our study is more comprehensive than other studies to date (Table I in the online-only Data Supplement) by testing 2 visual grading and 2 computational ICA calcium measurement methods in the same patients and provided intra- and interobserver agreements for all methods. Locations of calcification may be as important as total calcium burden; our study did not test location. Further score development could consider incorporating location information.

Several previous studies tested correlations between intracranial calcification and systemic diseases,[11,14,24,25] brain ischemic changes,[13,17,20,21,25–27] and carotid stenosis.[15,16,19,22,28] Only 2 studies compared visual calcium scoring and semiautomatic calcium volume measurement.[19,23] Bleeker et al[19] used CT angiography and categorized intracranial calcification visually into absent, mild, moderate, or severe (similar to Woodcock approach) and found good interobserver agreement for visual calcium score (linear-weighted κ=0.62; 95% confidence interval, 0.54–0.70), excellent interobserver agreement for semiautomatic quantitative calcium volume (Pearson correlation coefficient, 0.99; P<0.01; 95% limit of agreement 0.3±8.5 mm^3). It did not, however, provide data for visual score versus quantitative calcium volume or for intraobserver agreement. The use of CT angiography can lead to more difficulty in delineating carotid calcification from intraluminal contrast and adjacent bone. Ahn et al,[23] using 2 raters, compared 4 visual grading scores (Babiarz [0–4], Kassab [0–4], Erbay [1–4], and Hong [0–4]) to semiautomatic calcium volume measurement, but did not assess interobserver agreement. Spearman correlation coefficients for visual grading scales versus volume measurement were 0.857 for Babiarz, 0.856 for Kassab, 0.849 for Erbay, and 0.881 for Hong scales although the same visual score could have a wide range of volumes. We also found that the modified Woodcock visual score (which scores each axial slice and then creates a total sum score) shows a high correlation with total calcium volume, the association being steeper for higher calcium burdens (Figure 2B); using the cube root of the calcium volume linearizes the relationship, turning the visual score into a reliable quantitative estimate of calcium volume (≈0.5-mm calcium/modified Woodcock score point) while retaining speed and practicality, making it suitable for epidemiology and potentially (with more testing) for clinical practice. Three studies assessed semiautomated quantitative scoring of intracranial ICA, 2 using Agatston scoring[26,28] by a single reader. Neither study assessed inter- or intraobserver agreement. The third study by de Weert et al[25] had 2 observers and used a custom-designed software as a plug-in to the freely downloadable software Image J with 2 observers. The interobserver coefficient of variation was 7%, intraclass correlation coefficient was 0.99, showing excellent interobserver agreement. Although the interobserver agreement appeared better than ours, the method is time consuming and impractical for large epidemiological studies.

More studies are needed to validate the modified Woodcock method of assessment of intracranial ICA calcification in a wide range of subjects (eg, without stroke but without and with vascular risk factors) to determine the contribution of ICA calcium scoring to diagnosing vascular health and predicting future stroke.

Summary

We have shown excellent correlation between both visual and semiautomated computational methods of assessing intracranial ICA calcification with excellent inter- and intraobserver agreements. Furthermore, the modified Woodcock visual score estimates calcium volume. Thus, we conclude that a simple 4-point slice-by-slice overall visual calcium grade can reliably be used to provide a rapid, practical method for large epidemiological studies, eg, to evaluate the strength of association between ICA calcification and stroke risk. Further testing is required before introduction into clinical use.

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Disclosures

None.

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