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Correlation between carotid bifurcation calcium burden on non-enhanced CT and percentage stenosis, as confirmed by digital subtraction angiography

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Objectives: Previous evidence supports a direct relationship between the calcium burden (volume) on post-contrast CT with the percent internal carotid artery (ICA) stenosis at the carotid bifurcation. We sought to further investigate this relationship by comparing non-enhanced CT (NECT) and digital subtraction angiography (DSA).
Methods: 50 patients (aged 41–82 years) were retrospectively identified who had undergone cervical NECT and DSA. A 64-multidetector array CT (MDCT) scanner was utilised and the images reviewed using preset window widths/levels (30/300) optimised to calcium, with the volumes measured *via* three-dimensional reconstructive software. Stenosis measurements were performed on DSA and luminal diameter stenoses $>40\%$ were considered ''significant''. Volume thresholds of 0.01, 0.03, 0.06, 0.09 and 0.12 cm^3 were utilised and Pearson's correlation coefficient (r) was calculated to correlate the calcium volume with percent stenosis.
Results: Of 100 carotid bifurcations, 88 were available and of these 7 were significantly stenotic. The NECT calcium volume moderately correlated with percent stenosis on DSA $r=0.53$ ($p<0.01$). A moderate–strong correlation was found between the square root of calcium volume on NECT with percent stenosis on DSA ($r=0.60$, $p<0.01$). Via a receiver operating characteristic curve, 0.06 cm^3 was determined to be the best threshold (sensitivity 100%, specificity 90.1%, negative predictive value 100% and positive predictive value 46.7%) for detecting significant stenoses.
Conclusion: This preliminary investigation confirms a correlation between carotid bifurcation calcium volume and percent ICA stenosis and is promising for the optimal threshold for stenosis detection. Future studies could utilise calcium volumes to create a ''score'' that could predict high grade stenosis.

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Coronary calcium scoring is a well-established diagnostic tool as it has been shown to correlate with the degree of coronary atherosclerosis and with future cardiovascular risk [1–3]. The Agatston method of calculating the coronary calcium score is the most widely used methodology; it is based on a combination of measuring the maximum radiodensity and the area of calcium deposition [1]. However, there is limited knowledge regarding the clinical significance of measuring the amount of atherosclerotic calcification in the carotid arteries due to a relatively limited number of publications on this subject compared with the amount of literature on coronary calcium scoring. Interestingly, there is a growing body of recent evidence showing a correlation between the calcium burden at the carotid bifurcation with the degree of angiographically proven stenosis [4–6]. However, potential significant differences in methodology between carotid *vs* coronary calcium scoring are that carotid bifurcation calcium typically consists of a much larger volume and only one primary vessel arises from the carotid bifurcation to supply the brain *vs* three for the heart. In this regard, early works using Agatston-like calcium scores that were not volume-based found a positive correlation between the calcium score and degree of stenosis, but the score was not predictive of future stroke risk; however, preliminary scoring utilising calcium volumes has shown a correlation with both the degree of stenosis and the stroke risk [4–7]. Also, newer data using volume-based coronary calcium scoring have shown a correlation between the score with the degree of stenosis, similar to that obtained via traditional non-volume-based coronary scoring; some have proposed that such volume-based coronary scoring may be applicable to other vascular territories [8].

The authors of this study have previously published preliminary findings regarding the correlation and performance of various calcium volume thresholds for detecting internal carotid artery (ICA) stenosis near the carotid bifurcation [6]. However, one limitation was that post-contrast multidetector CT angiography (MDCTA) source data were utilised to calculate the calcium volume burden.

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Thus, manual manipulation of window/level settings was required to differentiate calcium from contrast within the lumen, which could have theoretically affected measurement objectivity. A second limitation was that MDCTA was the method implemented to document ICA stenosis. Despite recent breakthroughs in MDCTA technology, catheter digital subtraction angiography (DSA) still remains the gold standard for evaluating carotid stenosis [9]. Finally, there may have been a selection bias in that study as the majority of the patients were undergoing evaluation for head and neck cancer [6], which shares some risk factors with atherosclerotic disease (*e.g.* male gender, age, smoking). Selecting a different population with a relatively lower risk of atherosclerosis, as well as a higher rate of true negatives, could better evaluate a potential screening test.

In the current study, we set out to determine the correlation between calcium burden at the carotid bifurcation on non-enhanced CT (NECT) and percent luminal stenosis on catheter DSA in order to confirm our previous preliminary results by evaluating a somewhat random population that should not have an increased risk for atherosclerotic narrowing. In this study, we set out to test the performance of different calcium volumes as predefined thresholds for detecting a ''significant stenosis''. Similar to the previous study, these thresholds were utilised in order to detect lesions before they become haemodynamically ''significant''. As a haemodynamically significant stenosis is traditionally defined as $\geq$50%, we set the threshold for calcium volume to detect stenoses of $\geq$40% [6]. To the best of our knowledge, no previous study comparing calcium burden calculated on cervical NECT scans with the percent ICA stenosis near the bifurcation on the catheter DSA exists.

Methods and materials

Patients

Internal review board approval was obtained and 50 patients were enrolled in this study over a period of 3 years via a retrospective search within the radiology information system (RIS). The inclusion criterion for this study was that patients had undergone both a NECT of the neck (CT of the cervical spine) and DSA of the carotid arteries within a relatively short interval between the two imaging methods (less than 3 months). We sought to implement DSA as the vascular imaging method in this study because of its ability to exclude traumatic vascular narrowing [10, 11]. Patients aged under 40 years and with non-atherosclerotic narrowing of the carotid arteries (such as radiation, cancer, traumatic dissection, etc) were excluded from this study. The reason for imaging was trauma to the skull base or vertebra in 47 of these patients with or without subarachnoid haemorrhage. Of the remaining three patients, one was imaged for altered mental status (thought to be related to trauma), one for malignancy (not near the ICA or supplied by the ICA) and one for severe neck pain.

Included and excluded carotid bifurcations

Of the total 100 carotid bifurcations in these 50 patients, 88 were available for further analysis and were reviewed. In 12 patients, the analysis was carried out unilaterally, thereby yielding 88 carotid bifurcations for further analysis and review. Regarding those 12 patients evaluated unilaterally, DSA data of the carotid bifurcation were lacking on one side due to the lack of a dedicated carotid injection on that side. In 2 of these 12 patients, a DSA had been performed but 1 side was excluded from analysis owing to exclusion criteria: 1 had arterial compression caused by a neck tumour and the other had a carotid stent. Regarding the remaining 10 unilaterally evaluated patients, DSA was only performed on 1 side to exclude vascular injury in 8 patients while in the other 2 DSA was performed for a unilateral workup of subarachnoid haemorrhage. Each patient's DSA was screened to evaluate for the presence of an intramural defect indicative of dissection such as an intimal tear in order to exclude them. However, no such patients with evidence of cervical vascular injury on DSA were found and thus no patients were excluded. Additionally, if there was evidence of an occlusion (n=1), the patient's records were reviewed to evaluate for long-standing occlusion and NECT images were evaluated for the presence of overlying mid-lower cervical soft tissue injury as theoretically cervical blunt trauma could affect the lower ICA near the bifurcation.

Multidetector CT

All NECT scans were performed on a 64-array MDCT system (Brilliance CT; Philips Medical Systems, Best, the Netherlands) located in the emergency department. Scanning was performed per routine cervical spine CT protocol, using 140 kVp with a maximum tube current of 300 mA (adjustable effective current depending on patient body habitus), with a 64 × 0.625 mm collimation, 0.5-mm slice thickness, 0.5-mm reconstruction overlap, pitch of 0.392 and gantry rotation time 0.75 s. Axial source images were reconstructed at 0.5 mm using a dedicated convolution kernel for bone and soft tissues separately and contiguous sections were fused to yield 3-mm slice thickness for review and storage on a picture archiving and communications system workstation. Scanning time was approximately 13 s and the images were obtained during a single breath hold. Scans were performed in a caudal–cranial direction from the the level of T_1 up to the skull base. Source images were displayed with a 20–24 cm field of view (FOV) depending on patient body habitus with a matrix of 512 × 512. The source images were transferred to the three-dimensional (3D) workstation for volume measurements.

Measurement of calcium burden

Calcium volume measurements were performed on a commercially available workstation utilising Vitrea 2 software (Vitrea, Vital Images, Minnetonka, MN). The measurements were performed jointly by a neuroradiology fellow and a neuroradiology staff member with more than 5 years of experience using Vitrea software. For the purpose of carotid bifurcation calcium burden measurement, a volume was manually ''sculpted'' from 2 cm above to 2 cm below the carotid bifurcation while taking care not to include thyroid cartilage, cricoid cartilage or styloid process calcifications. This sculpting consisted of drawing the area intended for inclusion on serial axial images so that other sources of calcification/bone (*e.g.* thyroid/cricoid cartilage and vertebra) were outside of the drawn area and hence excluded from the resulting sculpted volume. A set window/level of 30/300 HU was used (based on results from the previous study) after sculpting and this windowing was performed prior to volume measurement [6]. Solely calcium and bone were visible at that point. Clicking a button labelled ''measurement'' enabled a volume measurement of the visualised densities based on the resultant sculpted and windowed volume. We did not attempt to separate the external carotid or common carotid calcium near the bifurcation from that in the ICA while sculpting. The volume measurement of the plaque burden was automatically calculated in terms of cubic centimetres by the software. The smallest plaque volume that could be calculated by the software was $0.01\ \text{cm}^3$. Figure 1a–c illustrates the aforementioned steps taken to extract the plaque volume.

Digital subtraction angiography

Catheter DSA was performed with femoral catheterisation using a biplane DSA unit (Integris Allura; Philips Medical Systems). In all patients a right groin puncture was performed utilising single-wall technique with a 19-gauge needle. A 5 F introducer sheath (Cordis, Miami Lakes, FL) was placed into the common femoral artery through which the common carotid arteries were catheterised employing a 100-cm angled diagnostic cerebral catheter (H1 Head Hunter catheter; Cook, Bloomington, IN) over an angled hydrophilic glidewire (Glidewire; Terumo Medical Corporation, Somerset, NJ). After a manual test injection, typically 6–9 ml of non-ionic contrast (Iodixanol 320 Visipaque; Amersham Health AS, Oslo, Norway) was used per run. Images in anterior-posterior and lateral projections were obtained for each injection in all patients, with additional oblique projections using the same injector settings if required or if a stenosis was suspected. The runs consisted of a 38 cm FOV (AP), 30 cm FOV (lateral and

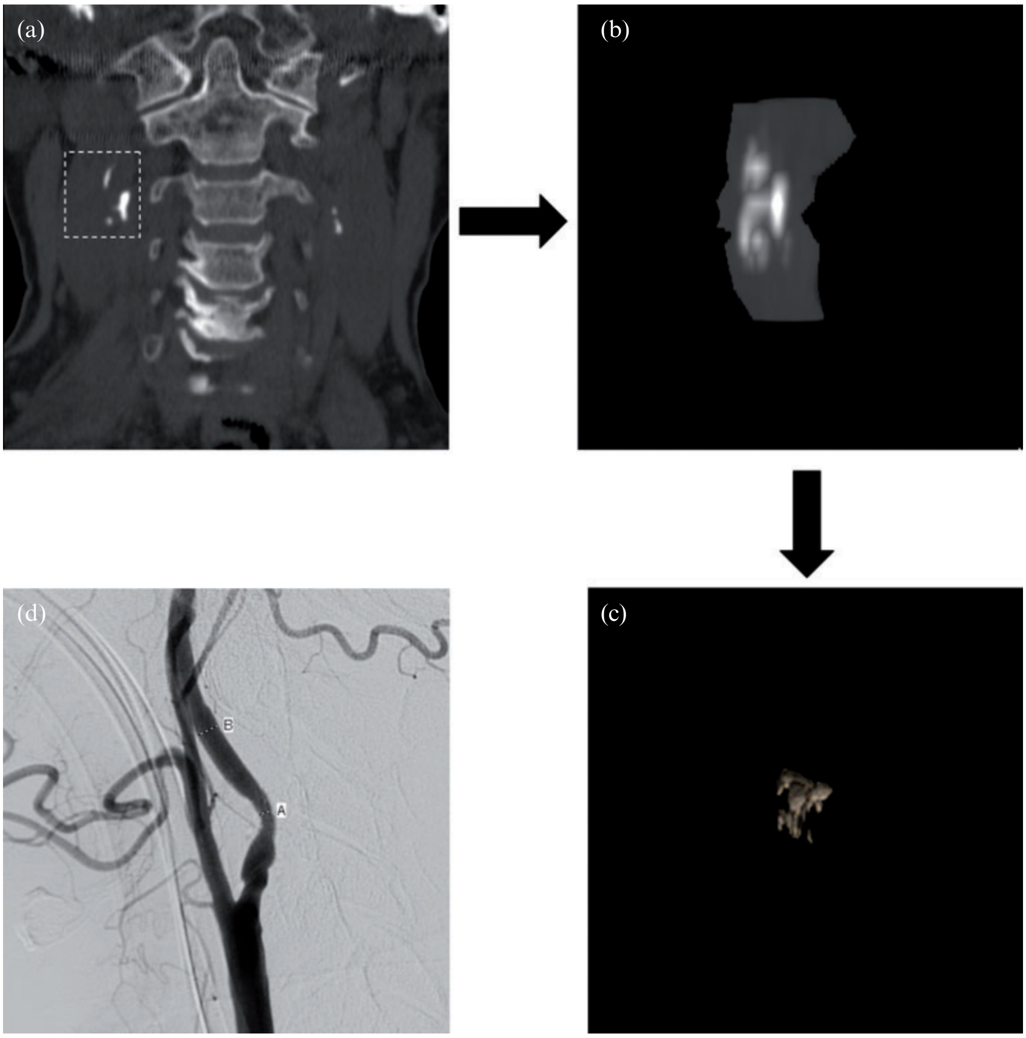

Figure 1. Calculation of plaque volume in a step-by-step fashion using the software and measurement of percent stenosis is demonstrated. (a) Manually drawn region of interest for sculpting is depicted on the coronal maximum intensity projection (MIP) image. (b) Calcified plaque on the sculpted MIP. (c) Volume rendered appearance of the plaque with automatic calculation of calcified plaque volume with a single button click, calculated to be $0.25\ \text{cm}^3$ in this patient. (d) Calculation of percent stenosis on lateral view of carotid digital subtraction angiography. The luminal diameter was measured at the narrowest part (A), which was a post-bulbar location for this particular case; B corresponds to the luminal diameter in the distal cervical internal carotid artery with percent stenosis and was calculated using the following formula: Percent stenosis=(B–A)/B, yielding a 55% stenosis for this patient.

oblique) and a 1024 × 1024 matrix. The spatial resolution was 0.32 × 0.32 mm.

Measurement of percent stenosis

Images were reviewed on the workstation and percent stenosis was measured by using North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria. These measurements were performed more than 3 months after the volume calculations with the interpreters blinded to the calcium volumes. The luminal diameter was measured at the narrowest location and at least 2 cm above the narrowing (Figure 1d). The measurements were performed jointly by a neuroradiology fellow and a neuroradiology staff physician who had more than 5 years of experience performing catheter DSA.

Statistical analysis of the data

Pearson's correlation coefficient (r) was calculated to assess for the degree of correlation between calcium volume on NECT and percent stenosis on DSA. Based on the information obtained from our previous study, r was also calculated for the square root of the calcium volume *vs* percent stenosis as that study found a more linear relationship using the square root [6]. Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were calculated separately for calcium volumes of 0.01, 0.03, 0.06, 0.09 and 0.12 cm^3 using thresholds based on preliminary results from the previous study, and again defining a luminal diameter stenosis of >40% as a "significant stenosis", in order to detect a stenotic lesion prior to the stenosis reaching 50% [6]. A receiver operating characteristic (ROC) curve was plotted for each predefined threshold value of measured calcium volume.

Results

Patients and carotid bifurcations studied

Of the 50 included patients, 34 were male and 16 were female with an age range of 41–82 years (average 59.3 ± 10.8 years). Regarding the 12 patients evaluated unilaterally, 8 were male and 4 were female. Therefore, there were a total of 60 bifurcations analysed in males and 28 bifurcations in females. Again, the indication for the NECT of the cervical region was to evaluate for trauma in all but three of these patients. None of the patients had evidence of carotid vascular injury at any level on the included side of DSA analysis.

Calcium volume as a predictor of calcium burden

Calcium was detected in 34 of the total 88 bifurcations studied (range 0.01–0.35 $\text{cm}^3 \pm 0.11\ \text{cm}^3$). In 54 bifurcations, calcium was found to be negative or below the minimum volume that could be detected by the software. The most commonly detected volume value was 0.01 cm^3 in nine bifurcations, which is the smallest amount of calcium the 3D software is able to detect

Percent stenosis by NASCET criteria and significant stenosis

Varying degrees of ICA stenosis were found in a total of 19 carotid bifurcations with an average of 34.2% ± 25.4%. In 4 of these 19 bifurcations, the degree of stenosis was <10%. There were 7 carotid bifurcations that demonstrated a significant stenosis of >40%, with 1 being totally occluded (tabulated as 100% stenosis). The remaining 8 bifurcations consisted of stenoses ranging from 10% to 40%.

Pearson's correlation coefficient

A significant and moderate correlation was found between the carotid bifurcation calcium volume on NECT (measured in cm^3) and the percent proximal ICA stenosis on DSA (calculated according to NASCET criteria). The correlation coefficient r was calculated to be 0.53 ($p<0.01$). A scatter plot demonstrating the moderate correlation between the calcium volume and the percent stenosis is shown in Figure 2.

A moderate to strong correlation was found between the square root of the calcium volume (in cm^3) and the percent ICA stenosis on DSA. The correlation coefficient r was calculated to be 0.60 ($p<0.01$). A scatter plot demonstrating the moderate–strong correlation between the square root of calcium volume and the percent stenosis is shown in Figure 3.

Statistical measures of performance and receiver operating characteristic

Sensitivity, specificity, NVP and PPV were calculated for the five arbitrarily set threshold values of calcium volume, as summarised in Table 1. Statistically, the square roots of these five thresholds provided the same sensitivity, specificity, PPV and NVP; therefore a duplicate table was not included for purposes of brevity. A ROC curve was plotted for these five thresholds (Figure 4), which demonstrated that the calcium volume threshold of 0.06 cm^3 provided the best combination of sensitivity (100%) and specificity (90.1%) to detect a significant (>40%) proximal ICA stenosis.

Discussion

Stroke is the third leading cause of death in the USA, where at the age of 40 years the remaining life-time risk of developing a stroke is one in five for males and one in six for females [12]. Atherosclerotic changes in the carotid, abdominal and peripheral vasculature places these patients at a considerably higher risk than the general population. Although most believe that the risk of stroke increases with the degree of carotid calcium burden, controversy exists regarding the association between the presence of carotid calcification and stroke [3, 4, 7]. For example, one study attempted to correlate the amount of carotid bifurcation calcium (in a semi quantitative fashion) with white matter changes on CT and concluded that carotid calcium did not independently

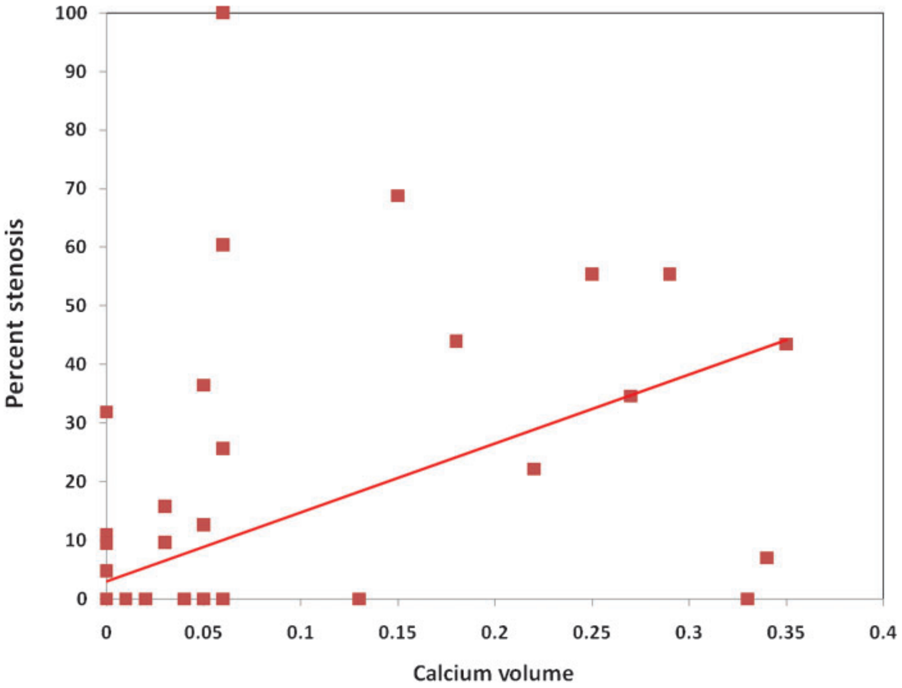

Figure 2. Scatter plot demonstrating the correlation between the percent internal carotid artery stenosis and the calcium volume (in cubic centimetres) at the carotid bifurcation.

serve as a predictor of the severity of white matter ischaemia [7]. However, another study found that volume-based calcium scores of the cervical carotid arteries were likely to represent an independent marker for luminal stenosis and ischaemic symptoms [4]. Also, a more recent study based on a density and area scoring system (akin to coronary scoring) found a moderate correlation between the carotid scores and 10-year stroke risks in males [3]. Similar controversy exists regarding intracranial ICAs calcifications. Although angiographic changes of the intracranial ICA have been shown to correlate with calcium scores, one study found no correlation with the occurrence of future cerebral stroke, while another study found a correlation between ''high grade'' ICA calcification (per visual assessment) and small vessel infarcts [5, 13]. Nevertheless, although there is controversy as to the stroke risk based on various forms of calcium scoring, almost a total consensus exists in recently published literature that a correlation does exist between the calcium burden and angiographically-proven stenosis [4–6]. Hence, some measurement of the calcium burden could be utilised to screen for high grade stenoses. Thus, we set out to confirm the correlation between the carotid bifurcation calcium burden on NECT and percent luminal stenosis on DSA.

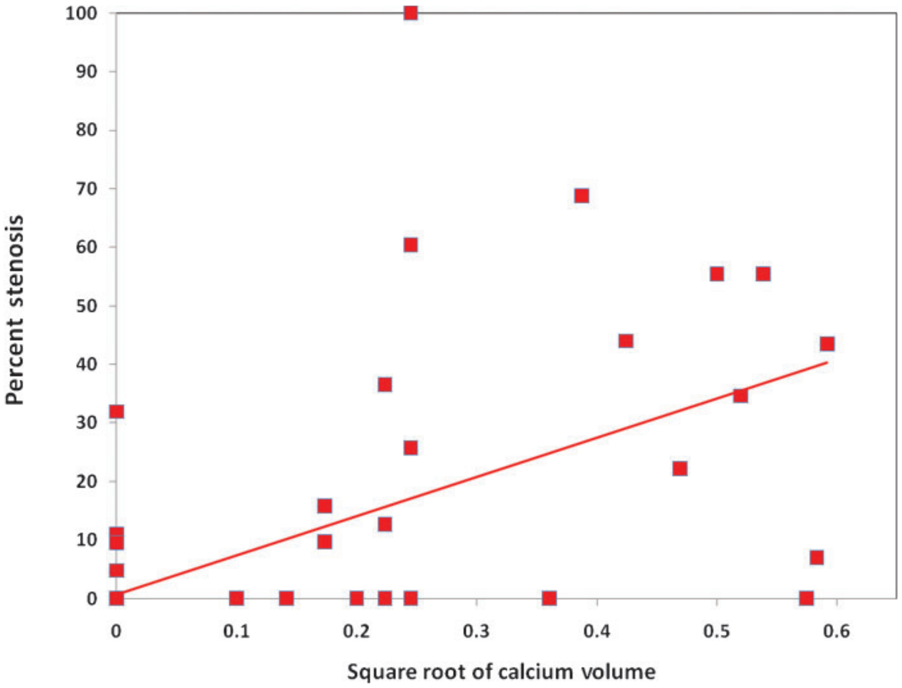

Figure 3. Scatter plot demonstrating the correlation between the percent internal carotid artery stenosis and the square root of the calcium volume (in cubic centimetres) at the carotid bifurcation.

Table 1. Statistical measures of performance for different calcium volume thresholds

Calcium volume (cm^3)	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
0.01	100% (7/7)	66.7% (54/81)	100% (54/54)	20.5% (7/34)
0.03	100% (7/7)	82.7% (67/81)	100% (67/67)	33.3% (7/21)
0.06	100% (7/7)	90.1% (73/81)	100% (73/73)	46.7% (7/15)
0.09	71.4% (5/7)	93.8% (76/81)	97.4% (76/78)	50% (5/10)
0.12	71.4% (5/7)	93.8% (76/81)	97.4% (76/78)	50% (5/10)

NPV, negative predictive value; PPV, positive predictive value.

Currently, luminal narrowing expressed as a percent stenosis is the only standard measure implemented to report the extent and severity of carotid artery stenosis owing to atherosclerotic disease. The widespread use of this measure is based primarily on the results of several well-known randomised clinical trials that have demonstrated a reduction in the risk for ischaemic stroke in patients with luminal stenosis of 50% (assessed by catheter angiograms) after carotid endarterectomy compared with conservative medical treatment alone [14–18]. However, it is important to mention that plaque morphology and composition have also been suggested to complement measurements of luminal dimension for assessing carotid atherosclerotic disease leading to the concept of imaging ''vulnerable plaque'', which may be susceptible to rupture and embolisation despite relatively spared luminal size [19–22]. CT imaging, especially after the advent of MDCT technology, has been shown to be promising in demonstrating detailed plaque morphology and depicting the plaque contents either as the proportion of one to the other or as a percentage of the total plaque volume [23–26]. Several other modalities such as ultrasound (B-mode) and MRI or even positive emission tomography have also been found to be effective for characterisation of plaque contents [27–29].

The main initiative behind the above-mentioned efforts of characterisation of plaque morphology is based on the fact that a carotid stenosis of $\geq$70% occurs in $<$10% of patients with stroke, whereas a carotid stenosis of $<$70% is extremely frequent in the asymptomatic population (70% in males and 60% in females by 64 years of age) [25]. Also notable is that most symptomatic patients have only mild stenoses [30]. Such a phenomenon may be explained by the accumulation of atherosclerotic plaque in the carotid artery causing a phenomenon termed ''positive remodelling'', in which the artery eventually enlarges, preserving the luminal area [31]. In addition, a substantial amount of atherosclerosis is usually present in the carotid bulb before it causes a significant luminal stenosis [26]. Therefore, plaque volume has been suggested as another important feature in addition to percent stenosis and plaque morphology. In a recent article by Rozie et al [26], the authors found a moderate correlation between the total plaque volume (including calcium, lipid and fibrous components) and percent stenosis. In that study, the contribution by lipid increased with increasing total plaque volume (r=0.62, p<0.001), while the contribution by calcium also increased slightly (r=0.42, p=0.001) with an increase in the total plaque volume. Calculating the other components of the plaque volume is a more robust technique but also more complicated, whereas solely measuring the calcium volume could be an easier and potentially a more standardised and reproducible method of detecting the disease burden.

In our previous preliminary study using MDCTA for calcium volume and stenosis determination, we demonstrated a sensitivity of 94% and 88% at 0.03 and 0.06 volumes and specificity of 76% and 87%, respectively, for significant (>40%) luminal stenosis [6]. That study demonstrated a strong correlation between the calcium

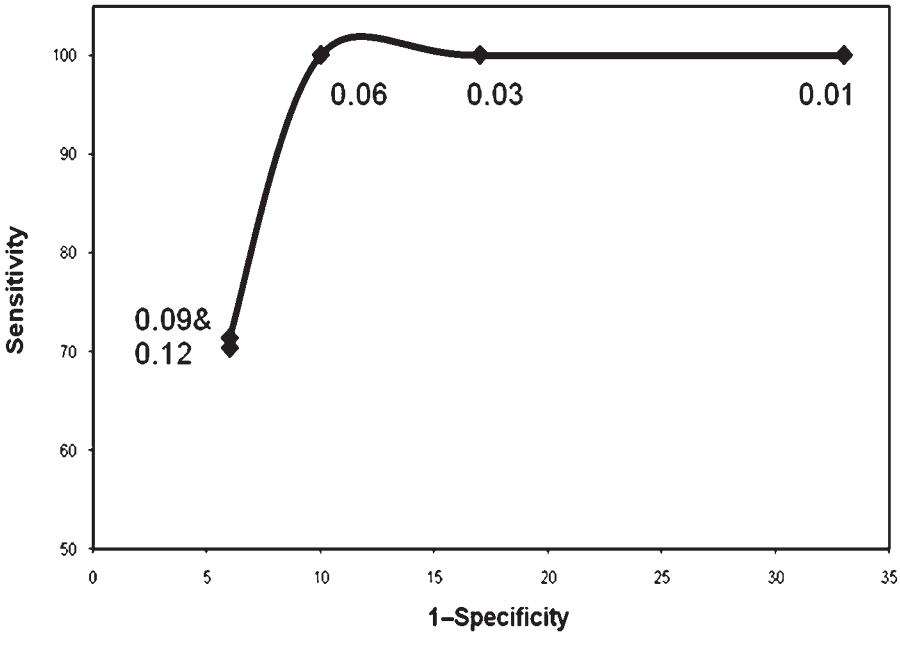

Figure 4. Receiver operating characteristic curve of five calcium volume thresholds.

volume and the percent stenosis of the proximal ICA (r=0.65), with an even stronger association found when the square root of the calcium volume was used to correlate linearly (r=0.77). On the basis of that initial study, the use of the calcium volume as a threshold to evaluate luminal stenosis appeared as sensitive or even more sensitive and more specific in detection of significant internal carotid luminal stenosis near the bifurcation compared with scans utilising helical CT or electron beam CT (EBCT) for coronary scoring to detect significant coronary stenoses. In the literature, there has been a strong correlation between coronary calcium scoring positives on EBCT (using a radiodensity threshold) and the degree of coronary stenosis in the involved vessel on autopsy (r=0.66) [32]. However, in the current study the correlations between the calcium volume and percent ICA stenosis (r=0.53) and between the square root of the calcium volume and percent stenosis (r=0.60) were slightly less than the previous study. This difference is likely to be owing to two factors. First, this study utilised trauma patients (a relatively random occurrence) whereas the previous study likely incorporated some selection bias owing primarily to inclusion of head and neck cancer patients who typically have an inherently higher risk of having atherosclerotic disease. Second, a slight inaccuracy in separating calcium from contrast in the previous study could have overestimated the calcium volumes.

The two largest randomised trials of carotid endarterectomy in newly symptomatic carotid stenosis are NASCET and the European Carotid Surgery Trial (ECST) [14, 15]. Both trials imaged the carotid circulation by using conventional catheter DSA, which was and still is considered to be the gold-standard in evaluating the degree of carotid stenoses. For this reason, DSA was used as the reference imaging standard of the carotid circulation in this study. Current clinical practice in North America relies on guidelines from NASCET, particularly regarding the quantification of ICA percent stenosis, which is why NASCET rather than ECST criteria were implemented for this study. We utilised DSA for luminal diameter measurement implementing the original NASCET criteria, instead of the NASCET-like quantification of stenosis used in our previous preliminary study. Also, we defined a significant stenosis as >40% as opposed to the conventional definition of >50% since our aim was again to detect preclinical lesions before they cause haemodynamic obstruction. There is precedent for using the level of >40% stenosis based on previous reports that have implemented ultrasound for early detection of ICA stenoses [33–35].

In order to determine the accuracy of calcium volume to detect degree of stenosis we used five volume thresholds, 0.01, 0.03, 0.06, 0.09 and 0.12 cm^3, which were the same arbitrarily-set threshold levels that we used in our previous study [6]. The same thresholds were used in order to compare to the previous study. Interestingly, the current study actually found a higher sensitivity (100%), specificity (90.1%) and NPV (100%) at the optimum calcium threshold of 0.06 cm^3 compared with the previously calculated sensitivity (87.5%), specificity (86.7%) and NPV of (95.1%) at the same 0.06 cm^3 calcium volume threshold.

Calcium scoring is often used in coronary vasculature evaluation for plaque detection. Various methods have been employed for this purpose including Agatston scoring, volume-based scoring and modified Agatston scoring [1, 32]. Although a point of debate, some current data suggest that elevated carotid calcium scores may be predictive of future cerebrovascular events [4]. Despite there being promising studies initially that involved the use of EBCT and MDCT for carotid calcium measurement, there is an ongoing debate as to whether calcium scoring is a reliable indicator of cerebrovascular risk detection and in determining the course of management [3, 7, 36]. One controversy arises from the substantial measurement variability (up to 30%) of the conventional Agatson score if applied to the carotid bifurcation [37]. Another potential limitation is that helical CT is well known to be sensitive (88%) but not very specific (52%) in detecting a >50% coronary stenosis [38]. Nonetheless, recent articles in the cardiology literature strongly suggest that there is additive diagnostic value of the coronary calcium score to the coronary angiogram, presumably owing to the limitation of percent stenosis in reflecting the severity of the atherosclerotic disease process, especially during the early stages of the vessel wall changes and positive remodelling [39, 40]. Hence, it has yet to be prospectively studied as to whether carotid calcium volume or other scoring methods will have similar measurement variability between observers and if the specificity will be higher than that of coronary calcium.

There are several notable improvements in the current study. First, the previous study predominantly consisted of patients with head and neck cancer, whereas in the current study the majority of the patients included were admitted for trauma management, theoretically decreasing the selection bias as trauma is a relatively random phenomenon. Second, our NECT evaluation utilised an automated window width/level, which turned out to be less time consuming (less than 1 min) and was likely to be a more reproducible form of measurement, as opposed to the previous contrast-enhanced study that involved a significantly greater amount of time (typically 2–5 min per side) solely on segmenting vascular contrast enhancement from calcified plaque. Third, and probably the most significant improvement, there could have been overlapping of calcium and contrast densities in the previous study which could have resulted in overestimation of the calcium burden and that factor may account for the differences in calculated correlation coefficients between the two studies. Fourth, as DSA [rather than CT angiography (CTA)] was utilised for stenosis measurements, our calculations of percent ICA stenosis should theoretically be at least as accurate as the previous study. Therefore, by replacing CTA with NECT and utilising a standard window width/level when measuring calcium volumes, we theoretically eliminated many of the previous limiting factors and thus the results should be more reproducible. Also, since random trauma patients rather than head and neck cancer patients were the majority of the included patients, these factors may account for the higher sensitivity (100%) and specificity (91%) encountered in this study for significant stenosis detection at the optimal 0.06 cm^3 calcium volume threshold. Hence, our opinion is that if the results previously obtained by CTA in a large cancer population are reproducible thus far, and similar to those obtained by NECT and DSA in a relatively random population, then it would seem that our observations in that previous study were valid and that the use of calcium thresholds could be accurate.

There are several limitations of this study, the most notable being that this was a retrospective analysis. A limited number of subjects (n=50) were studied with only 7 significant stenoses included. Another potential limitation of our study is that only total calcium volumes from the ''tri-vessel area'' (common carotid artery, external carotid artery and ICA) were included, where the uncommon inferior common carotid artery or upper ICA calcified plaques or non-calcified plaques could be missed. Also, although trauma is a random phenomenon and we took great care not to include blunt traumatic injury (the indication for evaluation in the vast majority of the DSA cases), there is a theoretical possibility that patients with traumatic vascular injury would be included as DSA may be inconclusive in cases of mild, non-stenosing wall alterations [41]. However, this did not occur in our study, where including traumatic injuries that lacked calcium deposition would most likely have lowered the sensitivity by creating false negatives; yet, the sensitivity for stenosis detection at the 0.03 and 0.06 cm^3 thresholds was 100%. Finally, it would have been optimal to obtain 2–3 year follow-up clinical data to assess stroke risk as well. We did review such records on available patients but we discovered that, as this study was carried out in a Level 1 trauma hospital and the majority of our patients were referred from the emergency department, some of them had sustained traumatic brain injury and others did not have long-term clinical follow-up within our system. Thus, most patients with clinical follow-up also had serious injuries with neurological impairment and as such it was not feasible to determine long-term stroke risk in this cohort due to such confounding factors.

Although there is a need for screening methods to detect patients at risk for higher grade stenoses, controversy will exist as to which patients to screen and the question will inevitably arise as to why not simply perform CTA or MR angiography in patients with cardiovascular risk factors. In our understanding, the intention of a screening test is to identify patients who are at a high risk in a lower risk, larger population to prevent the larger population from undergoing unnecessary or invasive, riskier examinations (*e.g.* catheter DSA). We note that three commonly accepted elements of screening are (1) outreach to populations with no previous medical attention for the condition, (2) the identification of persons likely to be at high risk for a specific disorder to make further testing and preventive actions possible and (3) follow-up and intervention of the screened population [42]. Hence, it would seem that our random population presenting for trauma would fit criterion (1) and our study identified patients who met criterion (2), whereas we acknowledge that criterion (3) needs to be determined by a prospective, longitudinal study. Theoretically, such studies could evaluate the use of NECT as a screening tool by using a lower radiation dose optimised to the energy of calcium for the purpose of measuring calcium volume; this could theoretically be a quick screening tool or even used in conjunction with duplex imaging. Also, similar to what has been described in recent cardiology literature, the carotid calcium volume could be utilised as part of a scoring system or as an adjunct with additive diagnostic value to the CTA [39, 40]. This study also raises the possibility that, in theory, a relatively simple, semi-automated technique could be developed whereby computer software could help measure calcified plaque that is not obscured by intravascular contrast. We note that the use of calcium volumes is preliminary and as such the utilisation for the purposes of ''scoring'' could be augmented by future methods that also take into account other important factors, such as maximum plaque density and number of vessels involved or even plaque morphology, which were not factors evaluated by this study.

Acknowledgment

Presented in preliminary form at the 46th Annual American Society of Neuroradiology meeting on Thursday 5 June 2008.

Conflict of interest

Dr AM McKinney has a research agreement with Vital Images, Inc. (Minnetonka, MN) enabling him to receive hardware and software for research purposes, but no monetary benefit.

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