The Relevance of Detecting Carotid Artery Calcification on Plain Radiograph

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Background and Purpose: The aim of this study was to determine the potential value of carotid artery calcification observed on plain radiographs in patients referred for carotid angiogram in the diagnosis of carotid artery stenosis.

Methods: One hundred sixty consecutive patients with suspected carotid artery stenosis underwent both plain radiographs of the carotid arteries and digital subtraction angiography of the same vessels. In addition, 108 of these patients also had duplex ultrasound of the same vascular area. The clinical usefulness of the carotid artery calcification was assessed by calculating the likelihood ratios for different test results against results of angiography and duplex ultrasound.

Results: There is a statistically significant association between the degrees of calcification and carotid artery disease as demonstrated by angiography ($P=0.001$), although positive correlation of the degrees of stenosis and calcification was only fair (Spearman correlation coefficient $r=0.4$). The sensitivity of carotid calcification in detecting clinically significant stenosis assuming any calcification is abnormal was 89% with a specificity of 46%. The likelihood ratios for 50% stenosis by angiography varied from 0.24 (no calcification) to 3.9 (level III) and for 50% stenosis by duplex ultrasound varied from 0.21 (no calcification) to more than 5.87 (level III). Assessments of the degree of calcification based on plain radiographs had excellent reproducibility (all intraclass correlation coefficients were greater than 0.9).

Conclusions: In this population with a high prevalence of carotid artery disease, there is an association between the presence of carotid calcification and atheromatous disease. If subsequent studies were to show this to apply in the general population, this could be of value in identifying asymptomatic patients at increased risk. (Stroke. 1993;24:1330-1334.)

Key Words • angiography, digital subtraction • carotid artery diseases • ultrasonics

Cerebrovascular disease is frequently associated with atherosclerotic changes involving the carotid arteries. Atherosclerosis is a gradual progressive disease process in which atheroma may ulcerate through the endothelium, exposing underlying collagen and thereby initiating the process leading to thrombus formation. This thrombus may then act as a source of cerebral emboli. Cerebral ischemia may also occur in the absence of ulceration if the atheroma enlarges and causes stenosis of the carotid artery severe enough to reduce pressure and flow distally in the artery. The yearly risk of cerebral infarction is estimated to be from 1% to 3% in patients with asymptomatic carotid arterial disease and from 5% to 7% in patients with stenotic or ulcerative atherosclerotic lesions of the carotid arteries, with the majority of strokes occurring without preceding transient ischemic attacks. Secondary prevention in the form of reduction of risk factors, pharmacotherapy, or surgical intervention has been shown to reduce the incidence of cerebrovascular accidents in symptomatic patients. One could therefore postulate that the identification of carotid atherosclerosis and/or stenosis, both symptomatic and asymptomatic, may be important in reduction of morbidity and mortality. Such identification may be accomplished (or at least suspected) on the basis of history of symptoms and signs suggestive of a neurologic disease, the finding of carotid artery bruit on clinical examination, or imaging studies including angiography and ultrasound.

We have evaluated the potential role of carotid artery calcification observed on the plain radiograph in the diagnosis of patients with suspected carotid artery stenosis. The starting point is an observation that calcification of the coronary arteries has been found in certain populations to be a useful marker of significant coronary artery disease and to have prognostic significance. Although carotid artery calcification has been described previously, the clinical significance of this finding has not been established. Carotid artery calcification can be identified on radiographs of the cervical spine, skull, facial bones, and chest. In an autopsy study of 25 patients, Bostrom and Hassler found a correlation between the degree of calcification and the occurrence of fibrous plaque at the carotid bifurcation. Imataka et al found that carotid calcification correlated with severe generalized atherosclerosis and found a higher incidence of hypertension, glucose intolerance, and stroke in their study group. Culebras et al studied carotid calcification by computed tomogra-

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phy and discovered an association between the degree of calcification and luminal stenosis. Calcification was more commonly associated with severe stenosis than any other morphological feature of atheroma.

The purpose of our study was to establish the possible relation between carotid artery calcification found on the plain radiographs of the region of carotid arteries and the severity of arterial stenosis. By using intravenous digital subtraction angiography (IVDSA) and duplex ultrasound (DUS) as criterion measures (“gold standards”), the following questions were addressed: (1) What is the association between the degree of carotid artery calcification and the degree of angiographically and ultrasonographically established stenosis? (2) What is the intraobserver and interobserver variability in detecting and classifying the degree of carotid artery calcification? (3) What are the odds that a significant carotid stenosis would be present in a patient with a given level of carotid calcification; in other words, what are the likelihood ratios of carotid artery stenosis associated with different levels of carotid artery calcification?

Subjects and Methods

Population

We studied 160 consecutive patients referred for IVDSA because of clinically suspected extracranial carotid disease. These patients included 111 men with a mean age of 62 years and 49 women with a mean age of 65 years. Patient clinical histories included transient ischemic attack, reversible ischemic neurological deficit, progressive stroke, and completed stroke. Patients younger than age 40 and female patients considered at risk for pregnancy were excluded from the study. The study was approved by the hospital ethics committee, and informed consent was obtained from all patients.

Imaging Methods

The IVDSA studies were all performed using the DV12 system (Philips Medical Systems, Toronto, Ontario, Canada) using an image intensifier of 6 inches and an imaging matrix of 502 pixels. The carotid arterial circulation was imaged from the level of the aortic arch to its intracranial portion. Each angiographic examination was performed by injection of 25 mL of Omnipaque 350 into a peripheral vein. Views were obtained in both the anteroposterior and 30° to 40° oblique projections.

At the time of the angiographic study, a short run (approximately three to five frames) of 105-mm cine film was obtained (without intravenous contrast) at the level of the carotid bifurcation to document the presence and the extent of carotid artery calcification. The positioning of the patient was determined fluoroscopically. The degree of stenosis as assessed by visual interpretation by the radiologist performing the examination was subsequently correlated with the presence and extent of calcification obtained on the 105-mm film.

Although angiography is considered to be the optimal method of estimation of the degree of arterial stenosis, many patients have DUS examination before referral for angiography. We decided to correlate the results of the DUS carotid studies if performed within 3 months of the angiograms. We believed that this would be of value because DUS studies are more likely to be the first line of assessment of symptomatic patients and as a safe noninvasive procedure are more likely to be used in population screening and epidemiological studies. It should be noted, however, that only patients having a stenosis of greater than 50% would be referred for angiography, thereby introducing a bias toward a more severe stenosis in this group of patients. The criterion for stenosis of 50% or greater was an average velocity ratio of 1.5 between the internal and common carotid arteries with spectral broadening in the internal carotid artery systolic wave. The DUS studies were performed using a Diasonics WIDE VUE (St Hilaire, Quebec, Canada) mechanical sector scanner with a frequency of 7.5 to 10 mHz, using a standoff pad. One hundred eight patients who were referred for angiography had had DUS studies performed within 3 months of angiography.

Classification of Calcification

The classification of calcification was based on the morphological appearance on the 105-mm films. The calcifications were either punctate or linear. (Linear was defined as calcified plaque continuous for at least 5 mm as measured directly from the 105-mm film or a series of calcified plaque separated by no more than 1 mm. Estimated minification factor for this equipment was 0.78.) No attempt was made to classify the calcification based on the location of the calcification within the arterial wall.

Grading was based on a system of 0 through 10, with 0 being no calcification, with progression from single and multiple punctate calcification to linear plaque on one side of the artery, on two opposite sides, and continuous across both sides of the artery. In grade 10 the calcification was completely circumferential (Figure). For further statistical analysis we combined calcification grades 1 and 2, 3 through 6, and 7 through 10 into level I, level II, and level III calcification, respectively. Each patient was assigned a single grade of calcification, which was the highest grade of calcification irrespective of the side of calcification. Similarly, the grade of stenosis assigned to the patient was the most severe stenosis, irrespective of side. We have postulated that carotid artery stenosis of 50% or more is clinically significant. The radiologists examining the plain radiographs of the carotid arteries were blinded to the results of the IVDSA or DUS and to patient identification.

Statistical Methods

To test the reproducibility of carotid artery calcification classification, two of the authors (I.D. and A.A.F.) conducted an interobserver and intraobserver study to assess the agreement as to the grade of calcification. The radiologists were blinded to patient identification. The chance-corrected agreement was calculated using an intraclass correlation coefficient (ICC, equivalent to weighted k). This analysis was performed both for 10 grades and for three levels of calcification.

The association between the degree of carotid artery calcification (three levels) and the degree of angiographically established stenosis (no stenosis vs less than 50% stenosis vs 50% to 99% stenosis vs complete occlusion) was measured by χ² and the Spearman correlation coefficient.

To assess the value of carotid artery calcification observed on plain radiograph in the diagnosis of carotid
artery stenosis, we calculated the likelihood ratio for 50% stenosis associated with different levels of carotid artery calcification (using IVDSA and DUS as gold standards). Using likelihood ratios, we then established the posttest probability of significant carotid artery stenosis in patients with given pretest probability and given findings of carotid artery calcification on plain radiograph.

Results

Carotid arterial calcification was identified in 118 (73.8%) of the 160 patients studied. The prevalence of calcification increased with age from 43.7% in the group aged 40 to 49 years to 81.5% in patients aged older than 65 years. None of the patients aged younger than 50 years had a calcification grade of greater than 6; grade 9 and 10 calculations were found exclusively in patients aged older than 65 years.

The ICC quantifying chance-corrected agreement for the 121 radiographs that were interpreted by two radiologists was .92 for 10 grades and .91 for three levels. The chance-corrected agreement for repeated assessment done by the same radiologist was .92 (10 grades) and .91 (three levels) for one radiologist (59 studies) (I.D.) and .94 (10 grades) and .97 (three levels) for the second radiologist (59 studies) (A.A.F.). In each case, ICC was statistically significant (P<.01).

Twenty-nine (18%) of the patients did not have any stenosis detected on IVDSA; 91 (57%) of 160 patients had 50% or more carotid artery stenosis. Table 1 displays the maximum level of calcification compared with the maximum degree of stenosis present on IVDSA. The statistical association between calcification and carotid stenosis was highly significant (χ² = 39.86, df = 9, P = .0001). However, although correlation between the relative disease and calcification was positive, the association was only fair (Spearman correlation coefficient r = .4).

Data showing discrimination between clinically significant carotid artery stenosis (50% or more) and lack of or nonsignificant carotid artery stenosis (less than 50%) are presented in Table 2, which also displays the likelihood ratios associated with different levels of calcification. Likelihood ratios ranged from 0.24 for no calcification to 3.41 for level III.

The corresponding data for 108 patients who underwent DUS evaluation of the carotids are presented in Tables 3 and 4. There was significant correlation between the presence of carotid stenosis established by DUS (χ² = 36.55, df = 9, P = .0001) and only fair correlation between the relative degrees of calcification and stenosis (Spearman correlation coefficient r = .38, P = .0001). The likelihood ratios ranged from 0.21 for no calcification to more than 5.87 for level III calculation.

Analysis of the degree of stenosis on the same side as the calcification showed no statistically valid association.

Discussion

The purpose of this study was to establish whether a reproducible system of grading of calcification could be
designed and if a relation exists between the presence and extent of carotid arterial calcification and the degree of stenosis.

The findings in this study allow several conclusions. First, we have established that the assessment of the degree of carotid arterial calcification is a highly reproducible procedure, with the degree of reproducibility similar to other diagnostic tests.20

We have found that the degree of association between the degree of calcification in carotid disease as assessed by IVDSA and DUS was significant ($P=.0001$), but correlation between the grade of calcification and the degree of stenosis was at best fair ($Spearman$ correlation coefficient $r = .40$ for IVDSA and .38 for DUS). Thus, our findings identify carotid artery calcification on plain radiograph as a marker for significant extracranial carotid disease. The importance of this observation is similar to previously reported significant correlation between coronary artery calcification on plain radiograph (or on autopsy) and presence of coronary artery disease.11

Third, by using IVDSA (and, separately, DUS) as a gold standard we calculated the likelihood ratios characterizing carotid artery calcification observed on plain radiograph as a test and established test properties that do not depend on the prevalence of disease. The clinical usefulness of the likelihood ratios associated with different results of carotid artery calcification on plain radiograph is illustrated in Table 5. This table examines four different scenarios: patients with low (5%), intermediate (25%), and high (75%) pretest probability (or prevalence) of significant carotid artery stenosis, as well as the population of our study (in whom the prevalence of significant stenosis was 57%). Using likelihood ratios established for carotid artery calcification observed on plain radiograph against stenosis demonstrated by IVDSA, data from this table show that in patients with low probability of significant stenosis (5%) the lack of any visible calcification brings the risk of significant stenosis down to 1%. At the same time, a high grade of calcification detected in such patients increases the risk of having significant disease to 15%.

Of note is that calculations presented in Table 5 require the assumption that the properties of the test (likelihood ratios) do not change with different prevalence of the disease in the examined population. Although somewhat controversial, such an assumption is certainly safer for likelihood ratios than for other common descriptors of the usefulness of diagnostic tests, ie, sensitivity and specificity.21

Although the specificity is poor, this may be a reflection of the high prevalence of disease in this patient population. However, in Table 1 several patients with carotid occlusion had low grades of calcification. This may reflect the complex mechanism of production of symptoms in these patients, and this study did not take into account phenomena such as embolism or acute thrombosis in association with minor degrees of stenosis. However, we feel that the results of this study justify a larger prospective study in a group that more accurately reflects the prevalence of disease in the general population. In this respect the study of Loecker et al22 is worthy of comparison. In this study, a significantly increased risk of coronary artery disease in asymptomatic young men was demonstrated in the presence of fluoroscopically visible coronary artery calcification; a negative result for coronary calcification indicated a low risk of coronary disease.

If the relation demonstrated in this study were shown by a prospective study to apply in the asymptomatic population, then it would appear to have potential in identifying individual at-risk patients before the onset of symptoms. Plain radiography of the neck for detection of calcification is inexpensive, quick and easy to perform and interpret, and requires no specialized equipment or training, all of which would be advantages in any potential screening tool. The presence or absence of a significant stenosis could easily and safely be established thereafter by DUS.

Clearly, with readily available and safe methods of assessing carotid stenosis such as DUS and IVDSA, we do not consider detection of carotid artery calcification as being of any relevance or value in symptomatic patients. However, our findings suggest that carotid artery calcification may be useful in identifying asymptomatic at-risk individuals with significant carotid artery stenosis and may be an early marker of evolution of the

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**Table 3. Relation Between Degree of Carotid Artery Stenosis by Digital Ultrasound and Level of Carotid Artery Calcification by Plain Radiograph**

<table>
<thead>
<tr>
<th>Level of calcification</th>
<th>Stenosis of carotid artery (%)</th>
<th>No stenosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100</td>
<td>50-99</td>
<td>&lt;50</td>
</tr>
<tr>
<td>III</td>
<td>3</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>26</td>
<td>5</td>
</tr>
<tr>
<td>I</td>
<td>7</td>
<td>20</td>
<td>9</td>
</tr>
<tr>
<td>No calcification</td>
<td>1</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>66</td>
<td>23</td>
</tr>
</tbody>
</table>

$P=.0001$, $X^2=36.55$, Spearman correlation coefficient $r = .38$.

**Table 4. Relation Between Presence of Significant Carotid Artery Stenosis by Digital Ultrasound and Level of Carotid Artery Calcification by Plain Radiograph**

<table>
<thead>
<tr>
<th>Level of calcification</th>
<th>Stenosis of carotid artery (%)</th>
<th>Likelihood ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥50</td>
<td>&lt;50</td>
</tr>
<tr>
<td>III</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>I</td>
<td>27</td>
<td>10</td>
</tr>
<tr>
<td>No calcification</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
<td>29</td>
</tr>
</tbody>
</table>

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**Table 5. Postest Probability of Significant Carotid Artery Stenosis Given Varying Pretest Probabilities and Different Results of Carotid Artery Calcification on Plain Radiograph (Intravenous Digital Subtraction Angiography as Gold Standard)**

<table>
<thead>
<tr>
<th>Level of calcification</th>
<th>Pretest probability (%)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>25</td>
<td>57</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>15</td>
<td>53</td>
<td>82</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>18</td>
<td>88</td>
<td>68</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>6</td>
<td>53</td>
<td>63</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>No calcification</td>
<td>1</td>
<td>7</td>
<td>24</td>
<td>42</td>
<td></td>
</tr>
</tbody>
</table>

Values are percentages.
disease. We believe that this relation merits a prospective study in an asymptomatic at-risk population.

Finally, how may the risk of stroke be reduced? The role of active medical intervention has not yet been determined. The recent Veterans Affairs Cooperative Study indicates that carotid endarterectomy in asymptomatic patients reduced the incidence of ipsilateral transient ischemic attacks but did not reduce the risk of stroke or death.\(^23\) However, epidemiological studies have identified the major risk factors as hypertension, elevated cholesterol, and smoking. All of these may be reduced either by therapeutic intervention in the higher-risk group or by life-style modification in the general population.\(^24\) Identification of patients in the early stages of carotid atherosomatic disease may aid in effective implementation of such life-style modification and could ultimately assist in reduction of the occurrence of stroke.

Acknowledgment

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References

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