INACCURACY OF ANGIOGRAPHY IN THE DIAGNOSIS OF CAROTID ULCERATION

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SUMMARY It is generally stated that ulceration of the carotid bifurcation plaque may give rise to embolization and symptoms of cerebral ischemia. It has been suggested that prophylactic carotid endarterectomy is indicated in asymptomatic patients if the angiogram is interpreted as showing ulceration. We therefore determined the accuracy of the radiologic diagnosis of ulceration by comparing the radiologic and morphologic findings in 155 carotid endarterectomies. Ulceration was diagnosed in 54% of the angiograms and 47% of the surgical specimens and was not related to the degree of stenosis. Angiography had a sensitivity of 73%, a specificity of 62% and an overall accuracy of 67%. For the non-flow-restrictive lesions these figures were 65%, 66%, and 66%. If surgery were based on the angiographic diagnosis of ulceration in plaques with less than 50% stenosis, 16 out of 42 operations (38%) would have been done unnecessarily. Variability of the angiographic diagnosis of ulceration is also shown by a high interobserver variability; two sets of two authors read the angiograms independently and disagreed in 24% of the cases. The decision to operate should not depend entirely upon the angiographic diagnosis of ulceration.

THERE HAS BEEN CONVINCING DOCUMENTATION of the relationship between ischemic stroke syndromes and carotid bifurcation atherosclerotic changes and it is generally recognized that symptoms may occur either from embolization from the carotid bifurcation or from flow restriction due to either stenosis or thrombosis of the carotid arteries. Thrombosis resulting in total carotid occlusion is usually easily recognized. Estimation of degrees of flow restricting stenoses however is more difficult and there is a high incidence of inter and intraobserver variability in the interpretation of angiograms. Diagnoses of plaque ulceration may be subject to even wider variability since often subtle pathologic changes are not easily recorded on the radiograms which, usually taken in only two views, offer a very limited portion of the entire circumference of the vessel for study. The decision to operate or not in either symptomatic or asymptomatic patients may often rest solely upon the angiographic appearance of the carotid bifurcation. In instances in which the degree of stenosis viewed on the angiogram exceeds 50-70% of the transverse diameter and cerebral hemispheric symptoms appropriate to that vessel are present the indication for surgical intervention seems clearer than when stenosis is not so evident whereupon the radiographic interpretation of "Ulceration" may be the determining factor.

Because of the great clinical importance of the radiographic diagnosis of ulceration in decision making regarding operative intervention upon carotid lesions, a control study was made comparing the radiographic and gross morphologic findings in carotid artery plaques to determine the accuracy with which this diagnosis compared with the gross morphologic findings in 155 carotid artery plaques retrieved surgically.

Patients and Methods

Comparisons between angiograms and surgical specimens were made for 155 carotid artery plaques...
derived from 124 patients. Angiography was performed generally by transfemoral selective common carotid catheterization with visualization of the carotid bifurcation in frontal and lateral views. Angiograms were reviewed by two experienced neuroradiologists with a composite experience of 30 years in neuroradiology who were unaware of the operative findings and who had to reach agreement on the characteristics of the carotid bifurcations. Degrees of stenosis were measured by comparing the residual lumen within the plaque to the lumen of the carotid artery distal to the bulb. Ulceration was diagnosed when there was irregularity of the vessel wall or a well circumscribed double density superimposed on the artery. Other characteristics that were recorded were sharply margined rounded filling defects in the vessel wall (diagnosed intraplaque hemorrhage), and intraluminal thrombus. Carotid occlusions were excluded from the study. The gross characteristics of carotid plaques were described by the surgeons after the arteriotomy was made, before removing the plaque. Photographs were made while the plaque was in situ as well as after its removal. Ulcerations were diagnosed when there were either clear cut breaks in the lining of plaques over areas of hemorrhage or atheromatous debris, (usually encountered at the very origins of the internal carotid arteries) or if there were pits and depressions in plaques often with sharply delineated margins of color differences between the base of the pit and the adjacent luminal surface of the plaques. Such areas, though their depths might be quite smooth, were interpreted as areas from which embolization of the arterial wall had occurred and a smooth lining had been restored. In other instances deep depressions in the plaque were partially filled with adherent pink thrombus. Correlations were then made with the angiographic findings. No attempts were made to correlate either the light microscopic or electron microscopic findings of lack of continuity of luminal lining cells with the radiographic findings since it could not be expected that such small morphologic features could be recorded radiographically.

Results

The incidence of the different gross plaque characteristics on angiography and surgery is given in table 1. As more than one characteristic could be found in a single plaque, the total numbers exceed the number of plaques that were available for comparison. Ulceration was the most common gross characteristic as it was seen on 54% (84/155) of the angiograms and 47% (73/155) of the surgical specimens. Hemorrhage was diagnosed in only 14% of the x-rays, while gross hemorrhage was seen in 32% of the cases. Thrombus was an infrequent finding on angiography (4%) as well as during surgery (8%).

The incidence of ulceration was then determined for the four different degrees of stenosis as determined on angiography: 0–24%, 25–49%, 50–74% and 75–99% (table 2). Ulceration proved to be almost equally present in all categories, both on angiography and in the surgical specimens.

The diagnostic accuracy of angiography with regard to ulceration was determined from the numbers in table 3. Of the 73 times that ulceration was seen in the surgical specimens, it was so diagnosed 53 times and not 20 times on angiography. This resulted in a sensitivity of angiography of 73% (53/73). No ulceration was seen grossly in the other 82 specimens; of these, 51 angiograms were negative for ulceration while 31 positive, giving a specificity of 62% (51/82). The overall accuracy was 67% (104/155), the predictive value of a positive angiogram 63% (53/84) and the predictive value of a negative angiogram 72% (51/71). When the same calculations were made for only non-flow restrictive lesions, i.e. for stenosis less than 50%, the sensitivity was 65% (26/40), the specificity 66% (31/47), the overall accuracy 66% (57/87), the positive predictive value 62% (26/42) and the negative predictive value 69% (31/45) (table 4).

Discussion

A number of gross morphologic changes are encountered in patients who are experiencing cerebral ischemic symptoms. Ulceration is usually prominently mentioned as being a source of emboli and in its absence on the angiograms carotid lesions are thought to be less apt to result in subsequent strokes. It had

Table 1 Incidence of Different Plaque Characteristics on Angiography and Surgery in 155 Carotid Arteries

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Radiology</th>
<th>Surgery</th>
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<tbody>
<tr>
<td>Ulceration</td>
<td>63 (41%)</td>
<td>38 (25%)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>84 (54%)</td>
<td>73 (47%)</td>
</tr>
<tr>
<td>Thrombus</td>
<td>6 (4%)</td>
<td>50 (32%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (4%)</td>
<td>13 (8%)</td>
</tr>
</tbody>
</table>

Table 2 Incidence of Ulceration on Angiography and Surgery for Different Degrees of Stenosis on Angiography

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>Ulceration present</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Angiography</td>
</tr>
<tr>
<td>0–24%</td>
<td>24 (41%)</td>
</tr>
<tr>
<td>25–49%</td>
<td>18 (62%)</td>
</tr>
<tr>
<td>50–74%</td>
<td>14 (71%)</td>
</tr>
<tr>
<td>75–99%</td>
<td>28 (62%)</td>
</tr>
<tr>
<td>Total</td>
<td>84 (54%)</td>
</tr>
</tbody>
</table>

Table 3 Presence or Absence of Ulceration on Angiography Compared to Surgical Findings

<table>
<thead>
<tr>
<th>Ulceration in surgical specimen</th>
<th>Ulceration on Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>53</td>
</tr>
<tr>
<td>–</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>73</td>
</tr>
</tbody>
</table>

Sensitivity 73% (53/73), specificity 62% (51/81) overall accuracy 67% (104/155), positive predictive value 63% (53/84), negative predictive value 72% (51/71).
previously been documented\(^3\) that ulceration when seen grossly had a poor correlation with symptoms since 40.6% of 101 asymptomatic plaques had ulceration compared to 48% of 275 symptomatic plaques studied (p 0.05). Indeed grossly apparent intraplaque hemorrhage, found in 15/3 of all symptomatic patients had a higher correlation with symptoms than did ulceration. If one accepts the broad definition of gross ulceration previously described, there being a variety of configurations, ranging from minimal disruptions of the laminar lining to deep protrusions into plaque thickened by intramural hemorrhage or collections of atheromatous debris, to shallow pits presenting a smooth lining, to deeper pits containing pink laminated thrombus, suggesting that these are sites from which previous embolization had occurred and then healed,\(^4\) then gross ulceration was the most frequent finding in this study being present in 47% of the specimens. As in other studies\(^5-8\) the pressure of ulceration was not related to degrees of stenosis as its prevalence was almost equal in the four different stenosis categories. The variety of frequently subtle structural changes in carotid plaques which can be interpreted as ulceration render accurate radiographic diagnosis difficult. The relatively low sensitivity, specificity and overall accuracy with predictive values which range between 62 and 72% regardless of the stenosis category be it greater or lesser than 50% confirms the difficulties encountered by other groups\(^1,7\) culminating in the statements of Julian\(^8\) and Bartinsky\(^9\) that the angiographic diagnosis of ulceration is impossible. Coupled with the inherent difficulty of attempting to diagnose subtle surface characteristics of carotid plaques from a limited number of views of the outline of the lumen\(^10-12\) is the high observer variability encountered. In this study angiograms were re-read for ulceration by two of the authors, both experienced neuroradiologists who were unaware of the original classification. This resulted in disagreement in 37 of the 155 cases (24%); on 18 of these the original classification was right and in the other 19 the second classification was correct.

Moore\(^1\) has developed a system of classification of the angiographic appearance of the carotid artery based upon the degree of irregularity diagnosed on the standard angiogram. Although no description is given of the pathologic findings in those patients whose plaques were removed surgically and their correlation with angiographic findings, he concluded that surgical intervention is justified for large and compound ulcerations in non stenotic plaques while smaller types of irregularity do not warrant surgical intervention since in a period of follow-up such relatively minor lesions were infrequently associated with strokes. The natural history of carotid ulceration was also studied by Kroener,\(^14\) who found a cumulative stroke rate by life-table analysis of 1% at seven years and concluded that prophylactic endarterectomy is not justified for asymptomatic ulceration. From our own investigation into carotid plaque pathology one would suspect that in those patients who Moore considered to be surgical candidates there was a very high incidence of intraplaque hemorrhage. When the data were analyzed for the ability of the angiographic study to delineate intraplaque hemorrhage\(^15\) the correlation was discouragingly low. Two of the six times that hemorrhage was diagnosed on the angiogram it was present and grossly apparent in the surgical specimen.

One can only conclude from the present studies that the angiographic appearance of carotid bifurcation plaques is not sufficiently diagnostic of the pathologic changes encountered in the arteries of asymptomatic patients to permit final decisions regarding surgical intervention to rest solely upon the angiogram. In this series, if surgery were based on the angiographic appearance of ulceration in plaques with less than 50% stenosis, 16 out of 42 operations (38%) would have been performed in spite of the minimal pathologic changes at the carotid bifurcations. Rather, the decision to operate should rest upon a variety of factors including the patterns of symptoms, degrees of stenosis, degrees of irregularity on the angiogram and in selected instances, failure of medical therapy. Indeed there were times when even minimal angiographic distortions were associated with advanced pathologic changes including intramural hemorrhage and ulceration discovered when the indication for surgical intervention was the repetitive, stereotyped recurrent attacks of transient cerebral or ocular ischemia which has come to be associated with microembolization from the carotid arteries.

References
Observer Variability in Evaluating Extracranial Carotid Artery Stenosis

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SUMMARY One hundred twenty eight cervical carotid arteriograms were twice viewed by three readers for the evaluation of atherosclerotic disease at the carotid bifurcation. Stenoses were estimated using calipers to the nearest 5 % and lesions were qualitatively characterized as smooth, irregular, or ulcerated. The intraobserver correlation coefficient between estimates of percent stenosis was .94 overall and .98 for the internal carotid artery. The average intraobserver variability in estimating percent stenosis was 5.23 % for all vessels and 6.04 % with a standard deviation of 8.09 % for the internal carotid artery. The intraobserver percent agreement at a fixed stenosis is defined as the percent of the time one reader on two readings would read at least the fixed percent stenosis among cases that might be read as having the fixed percent stenosis. The intraobserver percent agreement rate for the internal carotid artery was 95.9 % at > 0 % stenosis, 90.4 % for 50 % or greater stenosis, and 96.8 % for 100 % stenosis (total occlusion). The interobserver correlation coefficient between readers was .92 overall and .97 for the internal carotid artery. The absolute difference in percent stenosis between readers was 7.21 % for all vessels and 8.64 % for the internal carotid artery with a standard deviation of 9.5 %. The interobserver agreement rate for the internal carotid artery at > 0 % stenosis was 93.0 %, 85.4 % for 50 % or greater stenosis, and 96.8 % at 100 % stenosis. The addition of oblique views had no statistical effect on estimates of percent stenosis but increased the frequency with which irregularity and ulceration were diagnosed in the internal carotid artery.

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