Carotid Artery Duplex Scanning: Does Plaque Echogenicity Correlate with Patient Symptoms?

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In this study we have investigated the relationship between plaque sonolucency and ipsilateral hemispheric symptoms in 116 patients at risk of cerebrovascular disease (75 symptomatic patients, 41 asymptomatic patients). Our results indicate that plaque sonolucency is significantly associated with the incidence of patient symptoms at presentation. Twice as many symptomatic vessels contained the predominantly sonolucent plaque types (types 1 and 2) compared to contralateral asymptomatic vessels (p = 0.039, odds ratio = 2.9). Vessel stenosis also had a significant association with patient symptoms. No significant interaction was shown between vessel stenosis and plaque sonolucency (p = 0.15, odds ratio = 1.0). A model using vessel stenosis and plaque echogenicity as independent variables showed that degree of vessel stenosis had a closer association with incidence of symptoms (p = 0.03, odds ratio = 1.04) than plaque type (p = 0.13, odds ratio = 0.51).

Introduction

Stroke is one of the commonest causes of severe disability and causes 12% of deaths in England each year. Two-thirds of strokes are related to atherosclerotic disease of the cerebral arteries, and some patients suffer transient ischaemic episodes as a prelude to a major hemispheric stroke. In such patients the risk of stroke can be significantly reduced by appropriate clinical and medical management. The main site of disease is extracranial in the carotid bifurcation, which is amenable to ultrasound imaging and spectral Doppler analysis to detect plaque and determine the degree of any luminal stenosis. Recently the value of detecting patients at high risk of stroke has been emphasised as carotid endarterectomy has been shown to significantly reduce the morbidity and mortality of patients with 70–99% vessel stenosis.

Vessel diameter is not the only risk factor involved. Plaque composition has also been linked to the presence of ipsilateral cerebral hemisphere symptoms. Imperato et al. and Lusby et al. showed a significant association between the pathological finding of intraplaque haemorrhage at carotid endarterectomy and neurological symptoms.

The purpose of this study was to investigate the association between plaque composition as seen sonographically and patient symptoms. The ultrasound characteristics of atheromatous plaques were classified into four types based on the ratio of echolucency to echogenicity. In addition the association between plaque type and the degree of stenosis was investigated with a view to establishing the relative importance of each factor.

Methods

Patients referred for carotid Duplex scanning were entered into a prospective study of cerebrovascular disease. All patients were consecutive referrals to a single vascular technologist and all had risk factors for cerebrovascular disease (Table 1). Two patient groups were identified:

(1) symptomatic: patients with recent (within 4 months) cerebrovascular symptoms referable to the ipsilateral carotid artery territory (n = 75), e.g. amaurosis fugax, hemispheric sensory or motor symptoms.

(2) asymptomatic: patients who had no neurological symptoms (n = 41). Many of these asymptomatic patients were being assessed prior to major surgery such as coronary artery bypass grafting or repair of abdominal aortic aneurysms.
Table 1. The prevalence of cardiovascular risk factors in the symptomatic and asymptomatic patient groups.

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Symptomatic (%)</th>
<th>Asymptomatic (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina/Myocardial infarction</td>
<td>43</td>
<td>44</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>48</td>
<td>22</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>29</td>
<td>24</td>
</tr>
<tr>
<td>Smoker</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Peripheral claudication</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Antiplatelet therapy</td>
<td>12</td>
<td>10</td>
</tr>
</tbody>
</table>

Both patient groups were comparable for risk factors except for a greater number of hypertensives \((p < 0.05)\) and fewer numbers of claudicants \((p < 0.05)\) in the symptomatic group compared to asymptomatic group. Patients were excluded from the study if they were poor historians with uncertain timing of previous cerebrovascular events \((n = 20)\), had poorly localised neurological symptoms such as blackouts or dizziness \((n = 56)\), or had symptoms which were non-hemispheric and could have originated from the vertebro-basilar territory \((n = 14)\). A total of 90 patients were excluded.

The two patient groups provided three groups of vessel for analysis: (i) symptomatic vessels in symptomatic patients; (ii) contralateral asymptomatic vessels in symptomatic patients; (iii) asymptomatic vessels in asymptomatic patients. The cervical carotid arteries on both sides were scanned using a Toshiba SS A 270A Duplex ultrasound scanner with colour Doppler and a 5 MHz and 7.5 MHz transducer. Records of plaque echogenicity and the degree of vessel stenosis were made for each vessel. The Duplex appearance in transverse and longitudinal planes was made with Doppler analysis of peak systolic velocity. Colour Doppler was used to image in both transverse and longitudinal planes and helped distinguish echolucent plaque from vessel lumen. The gain settings were carefully calibrated between examinations to give a standard anechoic appearance to free-flowing blood in the vessel lumens.

Ultrasound plaque appearance was classified according to the ratio of echolucency to echogenicity. This classification system is similar to that used in previous studies \(^7,8\) and defines four types:

1. dominantly echolucent plaques (Fig. 1);
2. substantially echoluent plaques with areas of echolucency greater than 50% (Fig. 2);
3. dominantly echogenic with areas of echolucency less than 50% (Fig. 3);
4. uniformly echogenic plaques (Fig. 4).

In addition, vessels containing no detectable plaque are labelled as “N” and occluded vessels as “Z”.

Vessel stenosis was determined using Duplex sonography according to criteria described previously. The principal measurement was of peak systolic velocity in the narrowed portion of the carotid lumen and based on this velocity the vessels were grouped into three categories: group 1: <40%, (<1.2 m/s); group 2: 40–69%, (1.2–2.0 m/s); group 3: >69%, <100%, (>2.0 m/s and non-occluded).

Fig. 1. Longitudinal section of the carotid bulb demonstrating a plaque type 1. The plaque is outlined by flow within the lumen demonstrated by the use of colour Doppler (shown here as a black and white image).

Fig. 2. Longitudinal section of the carotid bulb demonstrating a type 2 plaque.
Results

Of the 116 patients included in the study 75 patients were in the symptomatic group (53 male, 22 female, mean age 65 years) and 41 patients in the asymptomatic group (32 male, 9 female, mean age 66 years). The distribution of plaque type and degree of vessel stenosis for all patients are shown in Fig. 5 and Fig. 6, respectively.

The predominant plaque type in all three groups was type 4, the most echogenic plaque.

In asymptomatic vessels there was a pronounced step-wise increase in the frequency of the more echogenic plaques, from type 1 through to type 4 (only 2% vessels were of type 1, with 45% being type 4), as shown in Fig. 7. The same trend was also seen within the contralateral asymptomatic vessels in symptomatic patients (Fig. 8) (6.6% vessels showed type 1 plaque and 28% type 4).

Within the symptomatic vessels there was a significant difference in the distribution of plaque types. We combined plaque groups 1 and 2, and plaque groups 3 and 4, to increase our sample size for analysis, and also for comparison with the results of Steffan et al. (8) who used the same combined groups.

![Fig. 3](image1)
Fig. 3. Longitudinal section of the carotid bulb demonstrating a type 3 plaque.

![Fig. 4](image2)
Fig. 4. Longitudinal section of the carotid bulb demonstrating a type 4 plaque.

![Fig. 5](image3)
Fig. 5. Histogram demonstrating the distribution of plaque types for all patients. N vessels free of plaque; Z occluded vessels.

![Fig. 6](image4)
Fig. 6. Histogram demonstrating the distribution of degree of stenosis in all vessels for each of the three vessel groups.

![Fig. 7](image5)
Fig. 7. Histogram demonstrating the distribution of plaque types 1-4, in the asymptomatic vessels in the asymptomatic patient group.
Both plaque types 1 and 2 were observed more frequently in the symptomatic vessels with more than twice as many type 1 and 2 plaques in symptomatic vessels (n = 27) compared to the contralateral vessels in the same patients (n = 11). This was shown to be significant by conditional logistic regression (p = 0.039, odds ratio = 2.9).

The symptomatic patient group was further analysed to see if there was a relationship between (i) plaque type and symptoms, (ii) vessel stenosis and symptoms and (iii) plaque type and stenosis. Conditional logistic regression analysis showed that as plaque echolucency increased so did the likelihood of symptoms. Patients with a carotid artery containing either plaque type 1 or 2 were almost three times more likely (p = 0.012, odds ratio = 2.81) to have ipsilateral symptoms than patients with a vessel containing plaque type 3 or 4.

Using the same method of conditional logistic regression, vessel stenosis was shown to be significantly associated with symptoms especially in the vessels with greater than 69% stenosis (p < 0.03, odds ratio = 2.9). We expected that vessel stenosis and plaque type would be associated. We examined this interaction but found it to be statistically unimportant (p = 0.15, odds ratio = 1.0).

Stenosis and plaque type were then considered as independent variables and each studied to see which was more closely linked with symptoms. Using conditional logistic regression, vessel stenosis in the symptomatic group was shown to have a larger effect on the incidence of symptoms (p = 0.03, odds ratio 1.04) than plaque type (p = 0.13, odds ratio = 0.51).

**Discussion**

These results indicate that plaques that are predominantly echolucent are more likely to be associated with ipsilateral hemispheric symptoms at presentation.

Histopathological evidence correlates echolucent areas with intraplaque soft haemorrhage, lipid or surface ulceration found at operation. Reilly *et al.* conducted the first of several studies that support this. She compared histology with ultrasound appearances in 50 symptomatic and asymptomatic patients. Plaques were described as being either heterogenous echolucent lesions or homogenous echogenic lesions. Thirty of the 36 patients with heterogenous echolucent lesions had intraplaque haemorrhage and the other six had large amounts of lipid, cholesterol or loose proteinaceous deposits. Of 14 plaques seen as echogenic, 11 were smooth fibrous plaques without haemorrhage and three had minute foci of old haemorrhage.

Subsequently, several researchers have shown similar results suggesting that echolucent plaques are more likely to contain recent haemorrhage. However, this is controversial as both Leen *et al.* and Bassiony *et al.* have failed to correlate plaque haemorrhage with symptoms. Indeed both researchers showed that haemorrhage constituted only a very minor component of plaque area, (less than 2.5%), in both asymptomatic and symptomatic plaques. Leen *et al.* found an amorphous granular material mixed with cholesterol as the predominant constituent of symptomatic plaques. He could not identify this material as a chemically known substance. appearances may have deceived previous workers as histologically this substance appeared similar to old haemorrhage. Unfortunately his study did not have ultrasound correlation.

It is interesting that lipids including cholesterol as well as haemorrhage can give an echolucent appearance on ultrasound analysis. Lipids, especially cholesterol, have been implicated as causing neurological deficit by embolisation. The fact that intraplaque haemorrhage and lipid deposits have similar ultrasound appearances and that both represent soft, friable and probably unstable lesions have led investigators, including ourselves, to look very carefully at plaque echolucency.

Intraplaque haemorrhage has been suggested to cause an acute reduction in luminal diameter, resulting in thrombosis and/or intimal ulceration and embolisation of plaque contents. If this were the underlying mechanism for symptom production, one might expect vessel stenosis and plaque echolucency to be linked. Our study, however, showed that vessel stenosis and echolucency appeared to act independently in showing a significant association with symptoms.
Similar results to our study have been reported by Steffan et al. and Langsfield et al., who both used a similar plaque classification system to ourselves. They showed a statistically significant increased number of echolucent plaques in symptomatic vessels. Of note, they reported echolucent plaques as the most common plaque type in symptomatic vessels. Our study, however, showed that echogenic plaques predominated in all vessel groups, with plaque type 4 being the most common. Causes for these differences between studies are not entirely clear, but may be due to different patient selection criteria and plaque characterisation.

It certainly appears that plaque structure and the evolution to produce unstable symptomatic lesions is a complex process that, as yet, is poorly understood.

Langsfield et al. in a longitudinal study showed that in two high-risk but initially asymptomatic vessel groups, approximately 10% gave rise to subsequent ipsilateral symptoms over a 4-year period. Of these new symptomatic vessels, 16% in one group and 35% in the other showed an increase in plaque echolucency. Increased vessel stenosis occurred in 20% of one group and 28% of the second group.

Our study is in agreement with his findings suggesting that both increasing echolucency and degree of vessel stenosis are important factors associated with the incidence of symptoms. In addition, our results show that plaque echolucency and vessel stenosis act independently and that vessel stenosis has a closer association with symptoms at presentation than plaque echolucency.

Conclusion

It is now known that outcome in patients with greater than 70% vessel stenosis is improved with surgery. In patients with moderate degrees of vessel stenosis (30–69%) it is at present unclear whether surgical treatment will give overall eventual benefit. There may be particular patients within this group or even within the mild stenosis group, who are at an increased risk of developing symptoms due to a special type of carotid lesion.

Our results show that both plaque echolucency and stenosis are associated with patient symptoms at presentation. Analysis of plaque echolucency may prove to be an important indicator of a more friable symptom producing lesion and multicentre trials should include plaque type as well as degree of stenosis in their observations.

The underlying pathogenic mechanisms for T.I.A.s and strokes are poorly understood. Further studies with larger patient numbers and monitoring plaque changes over time are necessary to help elucidate the underlying natural history of cerebrovascular disease and the importance of plaque sonolucent in stroke prognosis.

References

3 European Carotid Surgery Trialists' Collaboration Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70 - 90%) or with mild stenosis (0 - 29%) carotid stenosis. Lancet 1991; 337: 1235-1243.

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