Unstable Carotid Plaques: Preoperative Identification and Association with Intraoperative Embolisation Detected by Transcranial Doppler

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Objectives: To investigate whether unstable carotid plaque characteristics, as determined by preoperative colour Duplex ultrasonography (CDU) and postoperative histological examination, were associated with particulate embolisation, detected by transcranial Doppler (TCD), during the initial dissection of the carotid bifurcation during carotid endarterectomy (CEA).

Design: A prospective, consecutive study was undertaken of 50 patients undergoing carotid endarterectomy (CEA).

Setting: Leicester Royal Infirmary, Leicester, U.K.

Materials: Carotid plaques were assessed preoperatively using CDU. Intraoperative TCD monitoring of the ipsilateral middle cerebral artery was performed using a Scimed 2 MHz TCD. Carotid plaques removed at operation were processed histologically and multiple sections assessed microscopically.

Chief outcome measures: Plaque composition was classified ultrasonically and histologically according to the Gray-Weale classification and plaque surface characteristics were graded according to a five-point classification. TCD detected emboli were identified and counted during the initial dissection of the artery.

Main results: Particulate embolisation occurred in nine patients. Histologically, embolisation was associated with ulcerated plaque in three cases and ulcerated plaque with associated thrombus in six cases (p = 0.0005). However, the ability of CDU to positively predict embolisation based on the correct identification of an unstable plaque surface was only 25%.

Conclusions: Embolisation during dissection is strongly associated with ulcerated plaque with associated thrombus. CDU is unable to reliably identify these characteristics preoperatively. Intraoperative TCD monitoring can detect potentially harmful embolisation during this stage enabling surgical technique to be modified appropriately.

Key Words: Carotid plaques; Colour Duplex ultrasound; Carotid plaque histology; Intraoperative embolisation; transcranial Doppler; Carotid endarterectomy.

Introduction

Particulate emboli occurring during carotid endarterectomy have been identified as an important cause of perioperative cognitive and neurological deficits. Recent studies have demonstrated that intraoperative embolisation can be detected by continuous transcranial Doppler (TCD) monitoring and that much of this embolisation consist of air and is not associated with any neurological sequelae. However, embolisation occurring during the initial dissection of the artery is particulate, since no air has entered the arterial system, and most probably represents unstable plaque constituents or overlying thrombus dislodged during manipulation of the carotid bifurcation.

The accurate, preoperative identification of unstable carotid plaques prior to carotid endarterectomy (CEA) would enable operative technique to be modified during the dissection of the artery in order to minimise potentially harmful embolisation during this stage.

B-mode ultrasonic imaging of carotid plaques has enabled the identification of certain plaque characteristics associated with a higher incidence of embolic neurological symptoms. These characteristics have been interpreted as representing unstable plaques which are liable to disruption leading to embolisation and the production of symptoms. Some authors have proposed that these characteristics may be used, in
addition to the degree of stenosis, as a basis for selecting patients for CEA. The aims of this study were: (1) to determine whether histologically identified unstable carotid plaques were associated with TCD detected embolisation during the dissection phase of carotid endarterectomy. (2) to determine whether colour Duplex ultrasound imaging could reliably identify these unstable plaques preoperatively.

**Patients and Methods**

A prospective study was undertaken of 50 consecutive patients undergoing CEA. Patients were assessed preoperatively using colour Duplex ultrasonography to identify unstable carotid plaque characteristics. The operations were then monitored with TCD to detect embolisation during the dissection of the artery and the plaques obtained at operation were examined histologically to verify the presence of the high risk features. All patients had symptomatic stenoses greater than 70% using ultrasonic criteria.

**Ultrasound assessment**

All carotid plaques were imaged 1–4 days preoperatively using a Spectra colour Duplex scanner and a combination of 5MHz, 7.5MHz and 10Mhz probes to obtain the clearest possible images. Each scan was performed by an experienced vascular sonographer and classification was based on multiple real-time images. Plaque composition was classified according to the Gray-Weale classification (Fig. 1). Plaque surface characteristics were classified into five types using the criteria illustrated in Fig. 2.

**TCD assessment**

Continuous TCD monitoring of the ipsilateral middle cerebral artery was performed during each operation using a SciMed (Bristol) 2 MHz TCD. All TCD signals were recorded onto digital audio tape for postoperative playback and analysis. During analysis emboli were identified using recognised criteria and all emboli occurring during the dissection phase of the operation were counted. The dissection phase was defined as the time from the start of the operation (i.e. skin cleansing) up to clamping of the internal carotid artery.

**Histological assessment**

At operation the carotid plaque was carefully dissected free of the artery and fixed immediately in 10% formaldehyde. The specimens were then examined macroscopically and microscopically by a single histopathologist (LB) who was unaware of the preoperative ultrasound or intraoperative TCD findings. Multiple sections of the plaque were taken to include the area of maximum stenosis and any other area of interest identified by macroscopic examination. Specimens were processed through graded concentrations of ethanol and xylene before paraffin embedding. Multiple levels of each section were taken and stained with haematoxylin and eosin for microscopic examination. Plaque composition and surface characteristics were classified using the same criteria as the preoperative ultrasound examinations. Ulceration was defined as a break in endothelial continuity. The presence of an associated fibrin layer was used to exclude cases of denudation of the endothelial layer due to operative trauma.

**Data analysis**

The ultrasound and histological classifications of each plaque were compared. The histological classification was used as the "gold standard". The occurrence of embolisation detected by TCD was related to the histological and ultrasonic classifications. The ability of preoperative CDU to correctly identify plaque characteristics was determined by calculating accuracy (true positives + true negatives/total). The ability of preoperative CDU to predict the occurrence of embolisation based on the identification of high risk plaque characteristics was calculated using the positive predictive value (true positives/true positives + false positives). The statistical significance of an association between plaque type and embolisation was calculated using Fisher’s exact test (GraphPAD InStat 1990 software version 1.14). p values less than 0.05 were considered significant for either a positive (+ve) or negative (−ve) association with embolisation.

**Results**

Particulate embolisation during the dissection phase occurred in nine patients (18%).

On histological classification of plaque composition,

### Table 1. Plaque composition

<table>
<thead>
<tr>
<th>Plaque composition</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
<th>Unclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology</td>
<td>24</td>
<td>13</td>
<td>10</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Embolisation</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Histology vs. emboli, p</td>
<td>0.44</td>
<td>0.43</td>
<td>0.41</td>
<td>0.67</td>
<td>0</td>
</tr>
<tr>
<td>Duplex accuracy</td>
<td>60%</td>
<td>52%</td>
<td>74%</td>
<td>88%</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Plaque surface

<table>
<thead>
<tr>
<th>Plaque surface</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
<th>Type 5</th>
<th>Unclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology</td>
<td>2</td>
<td>27</td>
<td>10</td>
<td>9</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Embolisation</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Histology vs. emboli, p</td>
<td>0.67</td>
<td>0.0005</td>
<td>0.25</td>
<td>0.0005</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Duplex accuracy</td>
<td>82%</td>
<td>68%</td>
<td>64%</td>
<td>66%</td>
<td>90%</td>
<td></td>
</tr>
</tbody>
</table>

Emboliation was associated with type 1 plaque in five cases (21%), type 2 plaque in three cases (23%) and type 3 plaque in one case (10%). Therefore, the results for plaque composition (Table 1) show that although there is a trend for emboliation to be associated with plaque types 1 and 2, this is not specific enough to form a basis for the preoperative prediction. In addition, the accuracy of preoperative Duplex in identifying Type 1 and Type 2 plaques was only 60% and 52% respectively.

The results for plaque surface characteristics are more promising (Table 2). On histological classification of plaque surface characteristics emboliation was associated with type 3 plaque (ulcerated) in three cases (30%) and type 4 plaque (ulcerated plaque with associated thrombus) in six cases (66%). Therefore, there is a strong association between type 4 plaque and embolisation during dissection of the artery ($p = 0.0005$). However the accuracy of Duplex scanning to identify either ulceration or ulceration and thrombus is only 64% and 66% respectively. Therefore the ability of Duplex to positively predict emboliation based on the correct identification of the plaque ulceration with associated thrombus is 25%. This is due to a high number of both false positives and false negatives. If just ulceration is considered the positive predictive value is only 30% because of a very high number of false positives.

**Discussion**

Histological examination identified that ulcerated plaques with attached thrombus were significantly associated with TCD detected emboliation during carotid artery dissection ($p = 0.0005$). This would suggest that these plaques are particularly unstable and liable to emboli despite very gentle handling of the artery. Surgical strategies to minimise emboliation might include delaying dissection of the carotid bifurcation until after clamping of the carotid artery or the early clamping of the carotid artery. However these strategies may not be without consequences and would only be justified in patients who were particularly at risk.

The results from this study would suggest that accurate preoperative identification of these surface characteristics by colour Duplex scanning is not possible. Of the nine plaques identified by histology as being ulcerated with attached thrombus, colour Duplex scanning correctly identified only two. This is consistent with the findings of other investigators who have also thrown doubt on the ability of ultrasound to reliably identify surface ulceration or relatively small quantities of intraluminal thrombus.

Histological classification of plaque composition suggested that although emboliation was associated with type 1 and type 2 plaques the majority of plaques in these categories did not emboli and therefore this classification was a poor predictor of emboliation during dissection.

Using the Gray-Weale classification, there was poor agreement between the histological and ultrasound grading of the same plaques. There was particular difficulty in differentiating Type 2 and 3 plaques ultrasonically because of variation within different parts of the same plaque. The use of different angles of insonation and different settings were sometimes sufficient to transfer the same plaque from one category to another. For the purposes of the study, plaques were assigned to the most echolucent category obtained but there was a considerable degree of uncertainty in some cases and this is reflected in the results. However, identification of Type 1 and Type 4 was associated with less uncertainty. Therefore a more reliable classification would consist of a combination of Types 2 and 3 into a single category and have just three levels of differentiation. Ultimately, this disagreement was of little consequence for this study, because even 100% Duplex accuracy on plaque composition would not have been sufficiently specific to justify a change in surgical technique. However, this modified classification may be of use in future studies associating plaque type with clinical symptoms or
embolisation during other procedures such as carotid angioplasty.

In this study the nine patients who experienced embolisation during dissection detected by TCD did not suffer any significant neurological deficits. However, in each case the surgeon was warned as soon as emboli were detected and surgical technique was modified appropriately. In each case embolisation ceased once the carotid artery was clamped. It is possible that if dissection had not been interrupted, continued embolisation in some of these cases may have resulted in neurological deficits.

In conclusion, this study has identified that ulcerated plaques with attached thrombus are associated with intraoperative embolisation. Colour Duplex ultrasound scanning cannot reliably identify these high risk plaques preoperatively. However, TCD monitoring can detect intraoperative embolisation and if surgical technique is modified at the time, the amount of embolisation can be minimised.

References


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