Measurement of CBF and carotid artery pressure compared with cerebral angiography in assessing collateral blood supply after carotid ligation

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Angiographic assessment of collateral circulation to the brain at the circle of Willis was compared with measurements of cerebral blood flow (CBF) and internal carotid artery pressure during temporary carotid clamping in the prediction of tolerance of unilateral carotid ligation as treatment for intracranial carotid aneurysms in 92 patients. From CBF studies it was predicted that a substantial number of patients (27%) would suffer severe cerebral ischemia if carotid ligation were carried out. No single angiographic feature provided this predictive information. Bilateral fetal type of posterior communicating arteries were associated with significantly lower carotid artery back pressure on temporary carotid occlusion, and unilateral absence of posterior communicating arteries was related to lower CBF, but neither feature was associated with a significant reduction in the rate of successful carotid ligation. We believe that preliminary percutaneous digital carotid compression with electroencephalographic monitoring, followed by intraoperative measurement of the change in regional CBF and internal carotid artery pressure during temporary carotid clamping provides a safe method of selecting patients for carotid ligation. Carotid angiography with or without contralateral carotid compression is of little value in this respect.

KEY WORDS □ angiography □ cerebral blood flow □ carotid ligation □ internal carotid artery pressure □ aneurysm

THERAPEUTIC ligation of the carotid artery is followed by focal cerebral ischemia in a proportion of patients ranging from less than 5% to more than 30%, even when carotid occlusion is carried out gradually under local anesthesia. The onset of ischemia may be delayed for hours or even days after the carotid occlusion. Many techniques have been advocated in an endeavor to predict and thus select out those patients who run a high risk of developing hemiplegia following carotid ligation. Although carotid angiography has been held to give a poor indication of tolerance of carotid ligation, several specific factors disclosed during cerebral angiography have been thought by others to indicate a poor collateral blood supply to the brain in the event of unilateral carotid occlusion. These include hypoplasia of the first part of the anterior cerebral artery, failure of cross-filling of the anterior cerebral artery complex,
either spontaneously or despite contralateral carotid artery compression, and wide caliber “fetal” posterior communicating arteries.

Other methods used for the identification of the high-risk patients are trials of carotid compression with testing of neurological function, with electroencephalographic (EEG) monitoring, measurement of carotid artery back pressure, and measurement of jugular venous blood gases. For the past 10 years, it has been the practice in this department to advise carotid ligation for most patients with aneurysms of the carotid artery, and from these to select patients for permanent carotid ligation principally by measuring the change in regional cerebral blood flow (CBF) produced by temporary clamping of the carotid artery after its surgical exposure in the neck. The technique has been progressively refined to reduce the complication rate and yet reject for ligation only the minimum number of patients who it is predicted would develop hemiplegia should permanent carotid ligation be carried out.

Our present methods consist of a preliminary screening by percutaneous digital carotid compression under EEG control followed by operative measurements of CBF and of internal carotid artery pressure (ICAP) and EEG under control conditions and during temporary carotid clamping. In previous studies we have shown that this combination of measurements in the prediction of cerebral ischemia is superior to measurements of EEG or carotid artery pressure alone, or to measurements of jugular venous blood gases during temporary carotid compression.

We now have experience with more than 100 patients in whom measurements have been made of CBF during temporary clamping of the common and/or internal carotid arteries, together with angiographic studies. These data provide a unique opportunity for comparison between various morphological features observed during angiography and the actual changes in CBF and carotid artery pressure recorded during verified temporary carotid occlusion. In addition, the validity of these radiological and hemodynamic predictions can be assessed from the clinical neurological outcome of those patients accepted and rejected for permanent carotid ligation. We believe that this report is the first in which cerebral angiographic features are compared with the hemodynamic response of the intracerebral circulation to occlusion of one of its main trunks of supply.

Clinical Material and Methods

Adequate data from both angiographic and CBF studies were available in 92 patients, all of whom had aneurysms arising from various parts of the intracranial portion of the internal carotid artery. Most patients (83%) were female, and the age range was wide, from 13 to 69 years, at the time of referral for carotid ligation. In 74 cases subarachnoid hemorrhage had occurred; most of the remaining patients presented because of local complications of the aneurysm. Forty-three patients were classified as Grade 1 on the Botterell scale at the time of ligation, 24 were in Grade 2, 11 in Grade 3, and four in Grade 4.

Angiography

All 92 patients underwent bilateral carotid angiography and 55 also had vertebral or subclavian angiograms performed. Thirty-seven of the 92 patients had further carotid angiography performed during contralateral carotid artery compression. All angiographic films were restudied retrospectively for this investigation in order to assess the adequacy of the anterior and posterior communicating links of the circle of Willis, and the caliber of the constituent vessels.

Spontaneous cross-filling was said to be present if one or more of the main branches of one carotid artery filled from an injection of contrast medium into the opposite carotid artery. Cross-filling was described as appropriate if it occurred spontaneously toward the branches of the carotid artery to be ligated, and inappropriate if it occurred only toward branches of the opposite (unligated) carotid artery. Cross-filling occurring during carotid compression was studied in 37 cases.

The anterior cerebral artery was defined as hypoplastic when its diameter was less than 1 mm and the appearances were not attributable to spasm (Fig. 1). The posterior communicating artery was deemed to be fetal in type when its caliber equalled or approached that of the anterior or middle cerebral arteries (Fig. 2).

All carotid angiograms were carried out under general anesthesia with controlled ven-
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tilation; general anesthesia was used also for 69 (75%) of the patients during successful or attempted carotid ligation. Details of the anesthetic technique have been described fully in a previous publication, together with measurements and careful control of other indices, such as body temperature, arterial blood gases and pressure. The remaining 23 patients, all in the early part of the study, were operated on under local anesthesia. During carotid ligation, continuous monitoring of the EEG was carried out using a standard 16-channel display and the records were scrutinized immediately for signs of focal slowing during temporary occlusion of the common or internal carotid artery. In the last 45 patients, ICAP was also monitored continuously with the carotid system patent and during temporary occlusion of common and/or internal carotid arteries.

Cerebral Blood Flow Measurement

Measurements of CBF were performed in all patients in two or three regions of the affected hemisphere. Xenon-133 dissolved in saline was delivered via a Teflon cannula inserted into the internal carotid artery after surgical exposure of the carotid bifurcation. Control measurement of CBF was followed by another with the common or internal carotid artery temporarily clamped proximal to the site of 133Xe injection. Gamma radiation activity was detected by sodium iodide crystals collimated 1 in diameter, and their outputs were subjected to pulse-height analysis to reject gamma ray energies falling outside the range 73 to 89 keV.

Data processing has been refined to a considerable extent during these studies. At first, radiation counts were fed through ratemeters connected to a potentiometric strip chart recorder to plot graphically the curve of isotope washout from the brain, while a scaler connected in parallel recorded total radiation counts during the 10-minute clearance period. The value of CBF was calculated by hand, measuring the half-time of the initial slope of the clearance curve, to obtain a quick preliminary estimate of flow; then after 10 minutes of clearance mean CBF could be calculated by dividing the height of the clearance curve (peak count rate, obtained from the chart record) by the area under the curve (total counts, obtained from the scaler) and correcting for background radiation recorded before and after the flow measurement. It was possible also to obtain values for fast and slow components of CBF by curve stripping, but these were found to be less useful in predicting the effects of carotid ligation than mean (height/area) flow. This is because of shifts in the proportions of fast and slow flow weighting factors which occur in some patients during induced changes of cerebral blood produced by carotid clamping.

Fig. 1. Angiogram showing hypoplastic left anterior cerebral artery; diameter less than 1 mm.

Fig. 2. Angiogram showing fetal type of posterior communicating artery.
In addition, we have found the height/area calculation to be not only more accurate but more reproducible than calculation of slope.29

We now calculate CBF values using on-line data processing by a PDP12 computer connected by a direct cable link between the operating theater and the data processing laboratory. This system permits a graphic display of up to four washout curves with an early estimate of flow by an initial slope calculation (Fig. 3). At the end of the 10-minute clearance period, a tabular display of the height/area CBF values is provided, including data from four channels for up to six runs of consecutive CBF measurement (Fig. 4). These displays on the computer oscilloscope are relayed back to the operating theater by closed-circuit television, providing the operator with almost immediate information on CBF. The early estimate of flow, although less accurate than the height/area value, is of considerable value, since if severe brain ischemia is produced by carotid clamping it can be detected and reversed without the need to wait for the full 10 minutes of isotope clearance. The methods used to compute these flow values have been fully described elsewhere.41

Based on the changes in CBF observed during temporary carotid clamping, a decision was made to ligate the carotid artery, to repeat the control measurement and try the effect of clamping of the other (internal or common) carotid artery, or to abandon the procedure, leaving the carotid system patent, because this appeared safer then ligation even allowing for the risk of recurrent subarachnoid hemorrhage. (In practice, in relatively few of the patients in this study who were rejected for carotid ligation was intracranial surgery a feasible alternative.)

**Criteria for Carotid Ligation**

The criteria used for recommending permanent ligation have been modified during this investigation. In the first 47 patients we did not conduct preliminary screening by digital carotid compression, and only CBF measurements were made. Carotid ligation was carried out if temporary carotid clamping caused less than a 25% reduction in CBF from control. This regimen resulted in 39% total incidence of postligation ischemia, with prolonged deficit in 13%. In addition, a large proportion of patients (34%) were rejected for ligation, some of whom could possibly have been safely ligated. In the light of these findings, the following modified criteria were adopted in the next 45 patients:

1. All patients were first submitted to a minimum of 3 minutes of percutaneous digital carotid compression during continuous EEG monitoring while awake.
Assessment of collateral blood supply

<table>
<thead>
<tr>
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</tr>
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| Permanent ligation of the carotid artery was carried out in 67 (73%) of the 92 patients in the entire series, and was deemed unsafe in the remaining 25 patients (27%). The rejection rate for carotid ligation was 34% in the first 47 cases (Series 1) using the simpler method of calculating blood flow and only the rule of 25% reduction in flow. In the last 45 patients (Series 2), in whom computerized CBF measurements were preceded by digital carotid compression and supplemented by measurements of ICAP, the rejection rate fell to 20% and the rate of complicating cerebral ischemia was lower (Table 1).

Of the 67 patients who underwent ligation, 13 (19%) suffered some temporary ischemia but without lasting sequelae. Four patients (6%), however, suffered more severe cerebral ischemia which in two cases proceeded to massive cerebral infarction and death, and in the remaining two patients to a permanent neurological deficit. All of these four patients were in the early series and there has been no mortality or lasting neurological deficit attributable to carotid ligation in the last 45 patients. Using this technique, we have not seen a case of late postligation hemiplegia.

Of the 25 patients who were deemed unsuitable for permanent ligation because of unacceptable reductions in CBF during temporary carotid clamping, there was still an appreciable incidence of postoperative neurological deficit. This was despite the fact that the carotid system had been left patent, after resolved on long-term follow-up examination, in other patients follow-up studies were incomplete.

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TABLE 2
Filling of contralateral cerebral vessels during carotid angiography

<table>
<thead>
<tr>
<th>Category</th>
<th>Vessels Filling*</th>
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</thead>
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<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td>spontaneous cross-filling</td>
<td></td>
</tr>
<tr>
<td>to appropriate side</td>
<td>32</td>
</tr>
<tr>
<td>to inappropriate side only</td>
<td>—</td>
</tr>
<tr>
<td>cross-filling during contralateral</td>
<td>0</td>
</tr>
<tr>
<td>carotid compression</td>
<td></td>
</tr>
</tbody>
</table>

*ACA = anterior cerebral artery; MCA = middle cerebral artery; PCA = posterior cerebral artery.

being occluded only for one, or at the most two, periods of 15 minutes. Nine of the patients (36%) suffered a temporary neurological deficit and three patients (12%) were left with a prolonged neurological deficit. Thus, nearly half of these patients showed some neurological disturbance following temporary clamping of the carotid artery on one side although this was mild and transient in most cases. This serves to confirm the importance of identifying high-risk patients and the danger which such patients run of developing permanent and possibly fatal cerebral ischemia should the carotid artery be ligated. Although the adoption of the modified CBF criteria served to decrease ischemic complications in the group of patients with completed carotid ligation, the change of protocol did not appear to influence the complication rate in patients rejected for ligation.

Angiographic Cross-Filling

Spontaneous angiographic cross-filling was observed in 60 of the 92 patients, although in nearly all cases this was represented by filling of the opposite distal anterior cerebral artery only. There was filling toward the appropriate hemisphere in 50 cases and in only 10 cases did the spontaneous cross-filling occur solely toward the inappropriate side for the carotid artery to be ligated.

In 37 patients further angiography during compression of the contralateral carotid artery showed some cross-circulation in all cases, consisting of filling of both anterior and middle cerebral arteries on the opposite side and in two instances filling of the posterior cerebral artery also (Table 2). Thus, we never observed failure of cross-filling with carotid compression and assume that this group of patients would be very small indeed.

When the rate of acceptance and rejection for carotid ligation based on the changes in CBF were compared in these subgroups, 68% of patients with spontaneous cross-filling to the appropriate side were able to tolerate carotid ligation with 32% rejected for ligation. Of the patients showing spontaneous cross-filling only to the inappropriate side, 80% were accepted for ligation. These groups can be compared with the patients who showed no spontaneous cross-filling, 78% of whom were accepted for ligation, a rather higher proportion of ligation, in fact, than in those patients with cross-filling. Of the 37 patients who demonstrated cross-filling on contralateral carotid compression, 76% were accepted for ligation. These rates for acceptance and rejection for carotid ligation show no statistically significant difference from each other, nor from the overall rates for acceptance and rejection for a carotid ligation in the entire series or in the two subseries. There was no difference in the incidence of temporary or prolonged cerebral ischemia in patients with and without spontaneous angiographic cross-filling.

Finally, the values of CBF and ICAP that were recorded during temporary clamping of the carotid artery and the percentage reductions were compared in these subgroups and showed no differences (Fig. 5, Table 3). For example, mean CBF in patients with spontaneous cross-filling to the appropriate side was 32 ± 1 ml/100 gm/min, with an ICAP of 60 ± 4 mm Hg during carotid clamping; this can be compared to the patients with no spontaneous cross-filling in whom clamped CBF was 34 ± 3 ml/100 gm/min, and ICAP
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55 ± 3 mm Hg. This has to be contrasted with the highly significant difference in both CBF and ICAP values which occurred between patients accepted and those rejected for ligation (p < 0.001), understandably, since it was on this basis that patients were selected (Table 4).

Hypoplastic Anterior Cerebral Artery

Seven of the 92 patients (8%) had radiological evidence of hypoplastic anterior cerebral artery and of these only three were able to accept permanent carotid ligation. This represents a 43% ligation rate, but because of the small numbers involved this reduced rate is not significantly different from that of the group without this anomaly. In four patients the hypoplastic vessel was on the same side as the carotid artery to be ligated and in three cases it lay on the opposite side. One of the first group and two of the second group of patients underwent ligation, without neurological deficit.

The clamped blood flow values in the patients with hypoplastic anterior cerebral arteries showed no significant difference from those without this anomaly, or even from the patients with successful ligation. Clamped values of ICAP were lower at 50 ± 5 mm Hg than in patients without the anomaly, but the difference just failed to attain statistical significance. It must be assumed that in these patients the posterior communicating artery (PCA) provides adequate collateral flow.

Wide Caliber Posterior Communicating Arteries

In 25 patients a wide caliber (fetal) PCA was present on one side only; 19 (76%) of these patients had successful ligation. In 18 patients the condition was present bilaterally and 14 (78%) of these patients underwent successful ligation. Thus, the ligation and rejection rates for this group of patients were not significantly different from the series as a whole, or from the group of patients without this vascular configuration.

When the clamped values of blood flow and carotid artery pressures were compared, patients with unilateral fetal configuration of a PCA were not significantly different from patients with normal arteries. In patients with bilateral fetal PCA's CBF values during clamping were not different, but there was a significantly lower ICAP of 46 ± 4 mm Hg.

**TABLE 3**

<table>
<thead>
<tr>
<th>Category*</th>
<th>Accepted</th>
<th>Rejected</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cases</td>
<td>%</td>
<td>No. of Cases</td>
</tr>
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</tr>
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<tr>
<td>cross-filling</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>to appropriate</td>
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<td>68</td>
<td>16</td>
</tr>
<tr>
<td>side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>to inappropriate</td>
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<td>80</td>
<td>2</td>
</tr>
<tr>
<td>side only</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>no spontaneous</td>
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<td>78</td>
<td>7</td>
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<td>cross-filling</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>during</td>
<td>28</td>
<td>76</td>
<td>9</td>
</tr>
<tr>
<td>compression</td>
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</tr>
<tr>
<td>unilateral</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>fetal PCA</td>
<td>19</td>
<td>76</td>
<td>6</td>
</tr>
<tr>
<td>bilateral</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>no PCA</td>
<td>14</td>
<td>78</td>
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<tr>
<td>unilateral</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>absent PCB</td>
<td>34</td>
<td>69</td>
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<td>69</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>67</td>
<td>9</td>
</tr>
</tbody>
</table>

*ACA = anterior cerebral artery; PCA = posterior communicating artery.

**FIG. 5.** Mean reductions in cerebral blood flow (CBF) and internal carotid artery pressure (ICAP) expressed in percentage terms produced by temporary carotid clamping in various groups of patients.
TABLE 4

<table>
<thead>
<tr>
<th>Category</th>
<th>Cerebral Blood Flow (ml/100 gm/min)</th>
<th>Internal Carotid Artery Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>all ligated</td>
<td>36 ± 1</td>
<td>63 ± 3</td>
</tr>
<tr>
<td>all rejected for ligation</td>
<td>26 ± 2†</td>
<td>41 ± 3†</td>
</tr>
<tr>
<td>spontaneous cross-filling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>to appropriate side</td>
<td>32 ± 1</td>
<td>60 ± 4</td>
</tr>
<tr>
<td>to inappropriate side only</td>
<td>34 ± 3</td>
<td>59 ± 5</td>
</tr>
<tr>
<td>no spontaneous cross-filling</td>
<td>34 ± 2</td>
<td>55 ± 3</td>
</tr>
<tr>
<td>cross-filling during compression</td>
<td>32 ± 2</td>
<td>55 ± 3</td>
</tr>
<tr>
<td>hypoplastic ACA</td>
<td>32 ± 4</td>
<td>50 ± 5</td>
</tr>
<tr>
<td>unilateral fetal PCA</td>
<td>36 ± 2</td>
<td>58 ± 4</td>
</tr>
<tr>
<td>bilateral fetal PCA</td>
<td>32 ± 2</td>
<td>46 ± 4†</td>
</tr>
<tr>
<td>unilateral absent PCA</td>
<td>29 ± 2†</td>
<td>61 ± 6†</td>
</tr>
<tr>
<td>bilateral absent PCA</td>
<td>33 ± 2</td>
<td>59 ± 2</td>
</tr>
</tbody>
</table>

*Mean values (± standard error of the mean) of cerebral blood flow and internal carotid artery pressure obtained during temporary clamping of the common and/or internal carotid arteries. ACA = anterior cerebral artery; PCA = posterior communicating artery.
†Significant differences (p < 0.02) between the mean values in patients with and without the angiographic anomaly.

(p < 0.02). The incidence of postligation ischemia was not significantly increased however.

Apparent Absence of Posterior Communicating Arteries

In 16 patients the PCA was not visualized during angiography on one side only, and 11 (69%) were successfully ligated. In both of these groups of patients the incidence of cerebral ischemia following acceptance or rejection for ligation was not appreciably different from patients in whom PCA's were seen.

In those patients with unilateral apparent absence of the PCA, the clamped values of CBF were significantly lower than in patients without the anomaly (29 ± 2 ml/100 gm/min; p < 0.02). Curiously, bilateral "absence" of PCA's was not associated with this reduction in blood flow and in both groups of patients the changes in ICAP and the incidence of cerebral ischemia were not different from the remaining patients.

Discussion

It has been asserted that the circle of Willis acts as an important mechanism for the redistribution of blood to the brain in the event of occlusion of a major input vessel, implying that there may be a certain proportion of the total cerebrovascular resistance located at this level. Anomalies of the circle of Willis would on this basis be thought to dispose to focal cerebral ischemia in the event of unilateral carotid artery occlusion. The main evidence for such assertions has come from postmortem studies showing an association between anomalies of the circle of Willis and the incidence of areas of cerebral softening or infarction.1,7 The evidence is not strong, however, and even these studies suggest that a further mechanism or pathological abnormality is required before cerebral ischemia can take place.

Reports that incriminate anomalies of the circle of Willis in the pathogenesis of focal cerebral ischemia must be read against the many reports in the literature showing the high incidence of such anomalies in normal patients (40% to 50%), and in patients with intracranial aneurysms (60%) who have not suffered from cerebral ischemia.1,25,28 Padget26 has even stated that, if minor deviations are included, all patients with intracranial aneurysms will be found to have some anomaly of the circle of Willis. Such reports suggest that the role of these anomalies alone in the production of brain ischemia is a minor one.

Evaluation of the circle of Willis during life presents further difficulties because radiological study has its shortcomings. Posterior communicating arteries that may not opacify on carotid angiography may sometimes do so satisfactorily on vertebral angiography. The anterior communicating artery may never be visualized, its presence and adequacy being inferred from the extent of spontaneous cross-filling on unilateral angiography. Such cross-filling will depend, however, not only on the size of the anterior cerebral and communicating arteries, but also on the size of bolus of contrast medium, the rate and force of injection, and its relationship to cardiac systole.44 Angiography
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performed during compression of the contralateral carotid artery will naturally vary according to the degree of compression applied to the vessel. We have found it extremely useful to apply a pulse meter to the ear lobe on the side of the carotid artery to be compressed as a check on adequate occlusion of the vessel.

There are, therefore, multiple reasons why angiographic assessment of collateral circulation via the circle of Willis may give an incomplete picture of the true physiological situation. This is reflected in divergent opinions expressed in the literature of the value of cross-filling observed during carotid angiography, either spontaneous or during contralateral carotid compression. Several groups have claimed that well visualized cross-filling provides a good index of collateral circulation and when observed is a reliable sign that such patients will tolerate carotid artery occlusion safely. Small, et al., 32 however, considered that such angiographic data alone were unsafe and patients should also be subjected to a trial period of carotid compression before it could safely be used permanently, because exceptions to the rule were not infrequently observed. This is in fact seen in a series of 47 patients reported by Wilkinson, et al., 28 in which two of three patients with "exceptionally complete cross-filling" failed to tolerate carotid ligation, and it has been suggested that such complete cross-filling may make it more likely that a "steal" of blood down the internal carotid will occur during common carotid occlusion. 24 In a later and larger series of patients, Beatty and Richardson 3 concluded that the demonstration of cross-filling on angiography was not a reliable guide to the tolerance of unilateral carotid ligation, and this conclusion must also be drawn from the present study.

Beatty and Richardson 3 found, however, that the presence of bilateral wide caliber PCA's was an indication of poor expected tolerance of carotid ligation. Our study, which contained a larger number of such patients, would provide only limited corroboration of this view, in that patients with this anomaly did have a lower back pressure in the carotid artery after the vessel had been occluded proximally. On the other hand, most of our patients with this abnormality did in fact tolerate carotid ligation satisfactorily without a significantly increased incidence of cerebral ischemia following ligation. We would suggest that the identification of this radiological anomaly in patients in whom carotid ligation is proposed should not act as an absolute contraindication to ligation, but it should certainly be interpreted as a warning to proceed with caution.

The neuroradiological feature that might well carry the greatest adverse significance for the expected tolerance of carotid ligation is the presence of a hypoplastic anterior cerebral artery. 22 The low incidence of this finding in our series, however, diminished the statistical importance of such an observation, so that we were unable to prove the deleterious influence of this anomaly.

The results of this study, in demonstrating that radiological assessments of the cross-circulation at the level of the circle of Willis are unhelpful in determining whether brain ischemia will follow carotid artery occlusion, lead to the conclusion that the crucial vascular resistance that determines collateral supply in the brain lies distal to the circle of Willis. Observations of the intraluminal pressure gradient from the arterial to the venous ends of the cerebrovascular system support this conclusion. 16 The pressure drop occurring from the aorta to the circle of Willis and large distributing vessels immediately distal to it is small, probably less than 30 mm Hg, so that there is a pressure drop of three to four times this magnitude in the vascular bed distal to the circle of Willis. Only a small part of the total resistance resides in the circle vessels proper. 5 This minor resistance is further diminished by the capacity of the component vessels of the circle for vasodilatation in response to increased demand during carotid occlusion as observed by ourselves and others. 20, 22 Our study also suggests that a more important role is played by the other system of collaterals, namely, the leptomeningeal anastomoses. The adaptive capacity of these vessels to sudden hemodynamic stress such as ligation has been shown to be rapid in experimental animals, 33 but its significance in man has not been ascertained.

If measurement of the cerebral circulation is to have a physiological meaning, it must take place within the brain tissue and not simply be a measure of the arterial input in the main extracranial vessels. For this reason the inert gas clearance methods, of which 133Xe is an example, must be considered superior to measurements of blood flow in the
carotid arteries in the neck using electromagnetic flowmeters in the assessment of cerebral circulation and its response to occlusion of the input vessels. In the inert gas clearance methods, tissue blood flow is measured and this is precisely what is required.

This approach may be open to the criticism that it is an "instant" measurement aimed at the prediction of an event (cerebral ischemia) which may be gradual or delayed in onset, and which may be due not to failure of collateral blood supply but to extending thrombosis or embolism from the site of ligation. This is the same criticism that would be leveled at angiographic evaluation of the cerebral circulation. In the case of CBF measurements, however, we believe it can be reasonably answered. We have never observed a case of late postligation hemiplegia in any patient judged by CBF measurements to be able to tolerate carotid occlusion, even though in all cases carotid occlusion has been abrupt. The pattern of postligation hemiplegia seen in our small number of cases has been uniformly that of a deficit evident immediately after surgery, in most cases resolving quickly and completely. The hemodynamic changes which follow carotid occlusion have been shown both clinically and experimentally to persist for at least a week and probably much longer, consisting in reduction in carotid artery back pressure and a reduced capacity of the cerebral circulation to respond to the normally vasodilatory stimuli of hypoxia, hypercarbia, and arterial hypotension. Episodes of late hemiplegia are much more likely to be due, in our opinion, to this documented reduction in the responsiveness of the cerebral circulation to stressful episodes of hypoxia or hypotension. There is scant pathological evidence for the often quoted view that such episodes are due to thrombosis or embolism. Furthermore, the protection that carotid ligation confers against recurrent subarachnoid hemorrhage, the reduction in the size of aneurysms of the internal carotid artery and the amelioration of signs ascribed to local pressure from such aneurysms are all eloquent clinical testimony to the fact that the hemodynamic change initiated by carotid occlusion persists, so that measurements taken at the time do indeed have a predictive value. We find that patients in whom the CBF reductions during temporary clamping are just inside the acceptable limit for ligation are in a correspondingly precarious situation for the first 3 postoperative days, being exquisitely sensitive to even mild hypoxia or hypotension.

The further question that merits discussion is whether a system that utilizes measurements in an anesthetized patient can be safer than the widely practiced method of gradual carotid occlusion in the conscious patient. The variable incidence of postligation hemiplegia in other series mentioned at the onset does in fact consist mainly of patients who were managed in this latter way. Even with gradual carotid occlusion in the awake patient, the physician must await clinically detectable signs of cerebral ischemia or EEG changes before releasing the clamp, and cerebral ischemia of late onset will not be detected at all. It is this late onset ischemia that is most likely to result in a permanent deficit.

Conclusions

We believe that the technique of measuring the change in regional CBF during temporary clamping of the carotid artery provides a sound basis for determining which patients will and will not safely tolerate permanent carotid ligation. By preliminary screening of patients by percutaneous digital compression under EEG control followed by a combination of CBF measurement with ICAP, together with careful control of blood gases, body temperature, and anesthetic depth, the morbidity and mortality of carotid ligation can be reduced to very low levels.

In contrast, examination of carotid and vertebral angiograms is an inefficient way of making predictions of the cerebral collateral blood supply in the event of a unilateral carotid occlusion. Of the several morphological and functional variants in the configuration of the circle of Willis examined in this study, none was found to be associated with a significantly different rate of acceptance and rejection for carotid ligation measured against changes in CBF.

The only items of significance to emerge from this portion of the study were the lower values of ICAP during carotid clamping recorded in patients with bilateral fetal type of PCA's and the lower CBF values in patients in whom the PCA was apparently absent on one side only. The physiological significance of this last observation is not obvious.
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It must be concluded that an accurate forecast as to clinical tolerance of carotid ligation or the cerebral hemodynamic response cannot be made using standard cerebral angiography.

Because the early results of this study were associated with an unacceptably high morbidity and rejection rate for permanent ligation, several safeguards were introduced into the protocol including preliminary digital carotid compression under EEG to try to detect those few patients in whom even brief carotid compressions would produce disastrous cerebral ischemia. To this we have now added the measurement of CBF in both hemispheres by the atraumatic \(^{133}\)Xe inhalation technique with promising early results.\(^{19,40}\) In the operative phase, great stress has been laid on the maintenance of steady-state physiological conditions during CBF measurement. The overall result has been a gratifying low incidence of ischemic complication in those 80% of patients who have a completed ligation but the problem of ischemic complications in the 20% of patients who are unable to tolerate ligation demands continued attention.

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