The value of repeat pan-angiography in cases of unexplained subarachnoid hemorrhage

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Four-vessel angiography was repeated in 56 patients with confirmed subarachnoid hemorrhage in whom the initial investigation was negative. Only one aneurysm was demonstrated. The results suggest that, with good technique, careful observation, and a complete four-vessel cerebral angiography, a false negative rate of less than 2% can be achieved. It is suggested that to repeat pan-angiography is seldom justified unless further bleeding episodes occur.

KEY WORDS • subarachnoid hemorrhage • intracranial aneurysm • vasospasm • repeat cerebral angiography • pan-angiography

An accurate and reliable diagnosis after subarachnoid hemorrhage (SAH) is necessary if surgery is to be undertaken to prevent rebleeding from arterial aneurysms. In most centers bilateral carotid angiography is carried out routinely and in many clinics a four-vessel, or pan-angiographic study, is performed because of the occurrence of aneurysms in the posterior fossa and the high incidence of multiple aneurysms.

Aneurysms may be missed at angiography. Perret and Nishioka posed four questions, the answers to which might indicate the reliability of angiography in this context:

1. Is there a relationship between the frequency of single- or multiple-aneurysm diagnosis and the extent of angiographic studies?
2. Is there a difference in the incidence of single and multiple aneurysms discovered by angiography and by autopsy?
3. When initial angiographic studies are negative, how often are aneurysms visualized by subsequent studies?
4. How often are aneurysms discovered at autopsy that were missed in angiographic studies?

Several papers have been published that investigate the correlation between angiographic studies and autopsy findings, and Perret and Nishioka themselves made an analysis of the frequency of single or multiple aneurysms and the extent of angiography in the patients with SAH included in the Cooperative Aneurysm Study. In that series, of the 1251 patients whose initial investigations were negative (of whom all had bilateral carotid angiography but not all had vertebral angiography), 207 had further angiography, and 47 previously undetected aneurysms of the anterior circle of Willis were found. At best, if there were no missed aneurysms in the remaining 1050 patients, this would rep-
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TABLE 1
Results of pan-angiography studies in 529 patients with subarachnoid hemorrhage seen 1967–1972

<table>
<thead>
<tr>
<th>Finding</th>
<th>Cases</th>
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<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>arterial aneurysms</td>
<td>339</td>
</tr>
<tr>
<td>arteriovenous malformations</td>
<td>40</td>
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<tr>
<td>negative studies</td>
<td>150</td>
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represent a false negative rate of 3.8% (47 of 1251). However, if the same proportion had been missed in the remainder, it would represent a false negative rate of 23%. The possibility of having an aneurysm after negative angiography in Odom's series of 40 patients was 18%; in that series, repeat angiography revealed four anterior communicating, two internal carotid, and one middle cerebral artery aneurysms in seven patients. These are disturbingly high figures.

The third of Perret and Nishioka's questions has never been fully investigated. It was decided therefore at the Karolinska Hospital to repeat pan-angiography systematically in patients referred with a confirmed SAH in whom the initial angiography was negative, unless there were medical contraindications such as cardiovascular disease, a bleeding diathesis, or extreme age. This paper presents the results of this study.

Clinical Material and Methods

Between 1967 and 1972, 529 patients presented with spontaneous SAH, confirmed by the presence of bloodstained and xanthochromic lumbar cerebrospinal fluid (CSF). Pan-angiography was negative in 150 of these patients (Table 1). In the series, 339 patients had arterial aneurysms (Table 2). Subarachnoid hemorrhages associated with trauma, classical intracerebral hematomas, or tumors were not included. For the purpose of the study, no infundibular dilatation or swelling of a vessel wall less than 2 mm in diameter was regarded as an aneurysm.

All patients with negative initial angiographic findings who were young and healthy enough to be considered for intracranial surgery in the event of an aneurysm being discovered were regarded as suitable for repeat angiography. The very old, those with severe arteriosclerosis or other severe medical conditions, and a number who refused further investigation were, therefore, excluded. In addition, patients seen early in the period whose initial angiographic investigation was incomplete were excluded.

The findings presented are those in 56 patients (34 men and 22 women). One was in the second decade of life, seven in the third, eight in the fourth, 10 in the fifth, 26 in the sixth, and four in the seventh. All had undergone two complete pan-angiographic studies. Pan-angiography is taken to mean three- or four-vessel angiography demonstrating all the major intracranial vessels and both posterior inferior cerebellar arteries.

All patients had multiple serial angiography with Isopaque (meelumine and calcium metrizoates) in at least three projections with automatic injection and standardized timing. In the majority of cases all the major intracranial vessels were demonstrated in one session by the Seldinger femoral route (76 of 112 pan-angiograms). In the remainder, additional percutaneous or brachial injections were required to demonstrate individual carotid or vertebral arteries.

TABLE 2
Site and year distribution of all intracranial arterial aneurysms in 339 patients

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<tbody>
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<td></td>
<td>No.</td>
<td>No.</td>
<td>No.</td>
<td>No.</td>
<td>No.</td>
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<td>12</td>
<td>13</td>
<td>16</td>
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<td>96</td>
</tr>
<tr>
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<td>13</td>
<td>9</td>
<td>16</td>
<td>21</td>
<td>17</td>
<td>90</td>
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<tr>
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<td>12</td>
<td>19</td>
<td>10</td>
<td>12</td>
<td>20</td>
<td>18</td>
<td>91</td>
</tr>
<tr>
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<td>4</td>
<td>6</td>
<td>6</td>
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<td>20</td>
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<tr>
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<td>4</td>
<td>7</td>
<td>5</td>
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<tr>
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<td>50</td>
<td>42</td>
<td>52</td>
<td>68</td>
<td>75</td>
<td>339</td>
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General anesthesia was used in 11 patients for the initial study and in six for the repeat study. There were no complications from angiography or anesthesia in this series apart from some minor bruising at the site of arterial puncture and some transient allergic skin reactions to the contrast medium.

The mean interval between SAH and the initial angiography was 3 days and between SAH and the second investigation 30 days. Early in the study a number of patients were re-admitted some time after discharge for the second investigation. Later patients were kept in hospital and the examination repeated after about 4 weeks when the risk of spasm was less. During the study the time interval between investigations was reduced to between 2 and 3 weeks when it was found that spasm did little to mask an aneurysm.

Summary of Cases

The time interval between SAH and the first and second pan-angiography as well as the degree of vasospasm encountered is depicted in Fig. 1. Vasospasm, as judged by radiological signs of luminal narrowing, was present in an increasing proportion of cases toward the end of the first week. Only two patients had moderate or severe spasm after 3 weeks. One proved to have an anterior communicating aneurysm, and the other a very atypical anterior communicating artery of irregular vessel caliber.

In this series of 56 patients, one aneurism was discovered at the second pan-angiography which had not been seen at the first study, making a false negative rate of 1.8%. This patient was a man of 59 years (Fig. 2). There was no spasm on the day of bleeding when the first angiography was performed. The aneurism was not demonstrated despite technically satisfactory films and projections and a high level of suspicion. The aneurism was easily visualized despite severe spasm when the second investigation was carried out on Day 20. At subsequent craniotomy a very large anterior communicating aneurism was found almost completely thrombosed.

During the period of this study, a total of 150 patients with proven SAH but negative pan-angiography were investigated (Table 1). Among the 94 patients who were not included in the series of 56 patients with repeat pan-angiographic studies, three aneurysms were missed. In one case, an anterior communicating aneurysm with intracerebral clot was overlooked because a frontal abscess was suspected clinically. In another patient, a posterior inferior cerebellar aneurysm was overlooked because at that time subtraction films were not made routinely. The third aneurysm was on the carotid siphon and did not fill with contrast on the second day after the SAH despite films of good quality and no spasm, but did fill and was easily seen (9 mm long) when angiography was repeated on Day 7.
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29, 1 day after a rebleed had occurred. Five patients in the series had small infundibular widenings at the origin of the posterior communicating artery, and in one further case there was a small dilatation less than 2 mm in diameter opposite the ophthalmic artery at the beginning of the intradural portion of the internal carotid, possibly at the origin of a small dural vessel.

Up to the time of writing, only two of the 56 patients in the trial have rebled and died. Autopsy revealed no aneurysms. The cause of death and the source of bleeding was a malignant astrocytoma in one, and multiple cerebral metastases in the other.

Discussion

If the need to establish the source of an SAH is accepted, the question arises of whether a single full angiographic study demonstrating all the major intracranial vessels is sufficient, if negative, to exclude the presence of a surgically treatable lesion. An aneurysm may fail to fill with contrast at angiography; the mechanisms suggested include vasospasm, narrowing of the neck, and alterations in blood flow. Also spontaneous thrombosis is known to occur, although “spontaneous healing” of an intracranial aneurysm is rare. Other possible explanations for the failure to demonstrate the source of the bleeding include the disintegration of the aneurysm at the time of the hemorrhage or the presence of a lesion so small that its significance is overlooked. The aneurysm may lie in the spinal arachnoid space but this occurrence is too unusual to justify the routine use of selective spinal angiography, and this investigation should be reserved for patients with repeated unexplained hemorrhages or those with a suggestive clinical picture.

In this study we were mainly interested in aneurysms of a size sufficient to warrant direct surgical intervention, that is, aneurysms more than 2 mm in diameter. For the significance of smaller aneurysms or infundibular widenings, the reader is directed to articles by Epstein, et al. and Hassler and Saltzman. In the present series, six patients had infundibular widenings. No conclusions can be drawn from our material about their significance. None of these patients have rebled.

Perrett and Bull reviewed the literature and analyzed the discrepancies between the angiographic and autopsy findings in 219 patients who died after SAH. Nine patients in whom the angiographic studies were incomplete were excluded. The aneurysm was accurately diagnosed in 187 (89%) of the remaining 210 patients. The causes of diagnostic error in the 23 patients (11%) left were divided into the following five groups: 1) arterial spasm (five cases); 2) observer error (six cases); 3) inadequate examination (four
cases); 4) normal arteriograms, even in retrospect (four cases); 5) intact aneurysm observed while a second aneurysm (ruptured) was not observed (four cases). The fifth category is really a subdivision of the second group as it represents a form of observer error. They concluded that the potential accuracy of radiological diagnosis should approach 96% if adequate projections of the cerebral vessels are obtained and observer error minimized.

In this series, the diagnostic accuracy predicted by Perrett and Bull exceeded in practice. Among the 56 patients whose pan-angiogram was repeated because they were subjects in the trial, there was one false negative (1.8%). Among all the 150 patients with negative pan-angiograms, four aneurysms were missed (2.7%), two as a result of observer error and two (1.3%) because even in retrospect the recently ruptured aneurysm failed to fill with contrast material at the first angiography. Counter to expectation, there were no examples of failure to detect an aneurysm due to vasospasm. On the contrary, the aneurysm depicted here (Fig. 2) was visible in the presence of vasospasm but did not fill with contrast material at the initial examination when no spasm was present.

Conclusions

These results suggest that with good radiological technique, adequate projections, and subtraction films, a false negative rate below 2% can be achieved if the pictures are conscientiously reviewed by competent and interested observers.

Although in this series only minor and transient complications were encountered, angiography is a serious undertaking and we conclude that repeating a complete pan-angiographic study is seldom justified unless further bleeding episodes occur. On the other hand, angiography of specific vessels should be repeated if they have been inadequately demonstrated at the first study, assuming that the patient is a suitable subject for surgery in the event of discovery of an aneurysm.

References


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