Risk of Cerebral Angiography in Patients With Subarachnoid Hemorrhage, Cerebral Aneurysm, and Arteriovenous Malformation
A Meta-Analysis

Harry J. Cloft, MD, PhD; Gregory J. Joseph, MD; Jacques E. Dion, MD, FRCP(C)

Background and Purpose—A well-defined complication rate of cerebral angiography in patients with subarachnoid hemorrhage (SAH), cerebral aneurysm, and arteriovenous malformation (AVM) would be useful to physicians making decisions regarding the imaging of these patients. We sought to define a statistically significant complication rate through meta-analysis of prospective studies in the literature.

Methods—Meta-analysis of 3 published prospective studies of complications in cerebral angiography was performed to specifically define the risk of cerebral angiography in patients presenting with SAH, cerebral aneurysm, and AVM. The complication rates for cerebral angiography in patients with SAH and AVM/aneurysm without SAH were compared with the complication rates in patients who underwent cerebral angiography for transient ischemic attack (TIA)/ischemic stroke with use of the Fisher exact test.

Results—The combined risk of permanent and transient neurological complication was significantly lower in patients with SAH compared with patients with TIA/stroke (1.8% versus 3.7%; \( P = 0.03 \)). The combined risk of permanent and transient neurological complication was significantly lower in patients with aneurysm/AVM without SAH compared with patients with TIA/stroke (0.3% versus 3.7%; \( P = 0.001 \)). When the patients with SAH and cerebral aneurysm/AVM were combined, the overall risk of permanent and transient neurological complication was significantly lower than for the TIA/stroke patients (0.8% versus 3.0%; \( P = 0.001 \)), as was the risk of permanent neurological complication (0.07% versus 0.7%; \( P = 0.004 \)).

Conclusions—The risk of permanent neurological complication associated with cerebral angiography in patients with SAH, cerebral aneurysm, and AVM is quite low (0.07%). This risk is lower than previously recognized. (Stroke. 1999;30:317-320.)

Key Words: aneurysm ■ cerebral angiography ■ cerebral arteriovenous malformation ■ subarachnoid hemorrhage

The risks of cerebral angiography have been assessed in a number of prospective studies.1–6 Some of these studies examined complication rates in all patients undergoing cerebral angiography,1–4 while others have examined the risk only in patients undergoing angiography for transient ischemic attack (TIA) or ischemic stroke.5,6 The risk in patients with TIA and ischemic stroke has tended to be higher than in patients with other indications for cerebral angiography, but it has not yet been possible to show a statistically significant difference.1–3 It is difficult to show such differences in risk between various populations because the risk of cerebral angiography in any population is rather low, so data from large patient populations must be accumulated to achieve statistical significance. The risk of cerebral angiography in patients with symptoms other than TIA or ischemic stroke, such as those with subarachnoid hemorrhage (SAH), cerebral aneurysm, and arteriovenous malformation (AVM), may actually be significantly lower than the risk of cerebral angiography generally reported in the literature. A well-defined complication rate of cerebral angiography in patients with SAH, cerebral aneurysms, and AVMs could be used by physicians in making patient management decisions, such as (1) whether CTA should be used instead of cerebral angiography in searches for cerebral aneurysm,7,8 (2) whether a second angiogram is justified in patients with SAH when no source for hemorrhage is found on the initial angiogram,9 and (3) whether MRA or cerebral angiography should be used as follow-up imaging in patients with AVMs treated with radiosurgery.10,11

Enough data to show a statistically significant difference in complication rates for various patient subgroups can potentially be accumulated by combining data from several studies through the process of meta-analysis.12 In this study, we use meta-analysis to...
specifically define the risk of cerebral angiography in patients presenting with SAH, cerebral aneurysm, and AVM.

Subjects and Methods

We performed a computerized MEDLINE search of the literature for studies of the complication rates of cerebral angiography using the keywords cerebral angiography, adverse effects, and cerebral angiography, mortality. The studies found in the MEDLINE search were then further evaluated for appropriateness for inclusion in the meta-analysis. The criteria for a study to be included in the meta-analysis were (1) prospective studies of complication rates for transfemoral cerebral angiography; (2) patients with SAH, cerebral aneurysm and AVM without SAH, and TIA/ischemic stroke were included in the patient population; and (3) the breakdown of indications for angiography and the relative complication rate for each indication are reported in the study. Three studies1–3 fulfilling these criteria were found. The number of transient and permanent neurological complications within 24 hours of angiography were tabulated. The number of nonneurological complications were also recorded. Each of the 3 studies used in the meta-analysis was performed at academic institutions where residents and fellows participated in the performance of cerebral angiography. Patients were grouped into the following 4 categories: (1) acute SAH, (2) cerebral aneurysm or AVM without SAH, and TIA/ischemic stroke were included in the patient population; and (3) the breakdown of indications for angiography and the relative complication rate for each indication are reported in the study. Three studies1–3 fulfilling these criteria were found. The number of transient and permanent neurological complications within 24 hours of angiography were tabulated. The number of nonneurological complications were also recorded. Each of the 3 studies used in the meta-analysis was performed at academic institutions where residents and fellows participated in the performance of cerebral angiography. Patients were grouped into the following 4 categories: (1) acute SAH, (2) cerebral aneurysm or AVM without SAH, (3) TIA/ischemic stroke, and (4) other indication for cerebral angiography.

The complication rates for cerebral angiography in patients with SAH and AVM/aneurysm without SAH were compared with the complication rates in patients who underwent cerebral angiography for TIA/ischemic stroke using the Fisher exact test. A value of \( P<0.05 \) was considered statistically significant.

Results

The results are summarized in the Table. The combined risk of permanent and transient neurological complications was significantly lower in patients with SAH compared with patients with TIA/stroke (1.8% versus 3.7%; \( P=0.03 \)). The combined risk of permanent and transient neurological complications was significantly lower in patients with AVM/aneurysm without SAH compared with patients with TIA/stroke (0.3% versus 3.7%; \( P=0.001 \)). The difference in risk of permanent neurological complication in patients with SAH or AVM/aneurysm without SAH compared with patients with TIA/stroke, however, was not statistically significant (0.3% and 0% versus 0.7%; \( P=0.20 \)). When the patients with SAH and cerebral aneurysm/AVM were combined, the overall risk of permanent and transient neurological complications was significantly lower than the TIA/stroke patients (0.8% versus 3.0%; \( P=0.001 \)), as was the risk of permanent neurological complication (0.07% versus 0.7%; \( P=0.004 \)).

One of the 415 patients studied for SAH had a permanent neurological deficit within 24 hours of cerebral angiography. This patient, from the series of Dion et al.,2 became symptomatic when recurrent hemorrhage occurred from the ruptured aneurysm at 24 hours after angiography.

Although all 3 of the studies used in the meta-analysis recorded nonneurological complications, these studies did not state what the indication for angiography was in patients with nonneurological complications. Therefore, it is impossible to compare the rates of nonneurological complications between the various groups of patients. The serious nonneurological conditions consisted of 5 large hematomas requiring fluid replacement or surgery in the series of Dion et al.2 In the series of Earnest et al.,3 the serious nonneurological complications consisted of 2 large hematomas requiring medical or

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients, n</th>
<th>Nonneurological complications</th>
<th>Neurological complications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Serious</td>
<td>Permanent</td>
</tr>
<tr>
<td>Heilserman et al1</td>
<td>1000</td>
<td>3 (0.3)</td>
<td>0</td>
</tr>
<tr>
<td>Dion et al2</td>
<td>1002</td>
<td>5 (0.5)</td>
<td>0</td>
</tr>
<tr>
<td>Earnest et al3</td>
<td>1517</td>
<td>12 (0.8)</td>
<td>1 (0.07)</td>
</tr>
<tr>
<td>Total</td>
<td>3517</td>
<td>20 (0.6)</td>
<td>1 (0.03)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAH patient subtotal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transient</td>
<td>137</td>
<td>0 (0)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Permanent</td>
<td>5 (0.5)</td>
<td>1 (0.1)</td>
<td>5 (0.3)</td>
</tr>
<tr>
<td>Aneurysm/AVM patient subtotal</td>
<td></td>
<td>374</td>
<td>153</td>
</tr>
<tr>
<td>Transient</td>
<td>0 (0)</td>
<td>3 (0.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Permanent</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>TIA/stroke patient subtotal</td>
<td></td>
<td>227</td>
<td>637</td>
</tr>
<tr>
<td>Transient</td>
<td>4 (1.8)</td>
<td>7 (2.5)</td>
<td>23 (3.6)</td>
</tr>
<tr>
<td>Permanent</td>
<td>4 (1.8)</td>
<td>0 (0)</td>
<td>4 (0.6)</td>
</tr>
<tr>
<td>Other patient subtotal</td>
<td>262</td>
<td>66</td>
<td>659</td>
</tr>
<tr>
<td>Transient</td>
<td>1 (0.4)</td>
<td>1 (1.5)</td>
<td>6 (0.6)</td>
</tr>
<tr>
<td>Permanent</td>
<td>1 (0.4)</td>
<td>0 (0)</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.
surgical therapy, 3 incidences of peripheral thromboembolic events, 5 cases of transient hypotension requiring medical therapy, 1 case of transient hypertension requiring medical therapy, and 1 case of infection. In the series by Heiserman et al., there were 3 cases of transient hypotension requiring therapy. Minor hematomas occurred in 6.9% of patients in the series reported by Dion et al., and 8.1% of patients in that reported by Heiserman et al., and were not presented in the series reported by Earnest et al.

Discussion
We found a lower risk of neurological complications with SAH, aneurysm, and AVM than in patients with TIA/stroke. Only 1 permanent neurological deficit occurred within 24 hours of angiography in 1384 patients with SAH, cerebral aneurysm, or AVM, and that was the result of rebleeding of an aneurysm 24 hours after angiography. This rebleeding is not likely to have been causally related to angiography but, rather, due to the natural history of an untreated, ruptured cerebral aneurysm. Therefore, one could argue that the risk of permanent neurological complication may be even less than the value of 0.07% calculated from this data.

Multiple factors have been correlated with the risk of cerebral angiography. The risk of cerebral angiography has been correlated with the age of the patient, total volume of contrast used, length of the procedure, use of more than 1 catheter, and presence of systolic hypertension. Patients with TIA/stroke as an indication for cerebral angiography tend to have more of these risk factors than patients with SAH, cerebral aneurysm, or AVM. The average age of patients with TIA/stroke was approximately 10 years older than the average age of patients with SAH, cerebral aneurysm, or AVM in the series reported by Dion et al. and Earnest et al.

People who undergo cerebral angiography tend to have cerebrovascular disease, which can lead to cerebrovascular events with or without cerebral angiography. Many neurological events attributed to cerebral angiography may be caused by the underlying cerebrovascular disease that led to angiography rather than to the performance of cerebral angiography itself. Between 24 and 72 hours after the performance of cerebral angiography, Dion et al. observed rates of 1.5% for transient ischemic events and 0.3% for development of persistent deficits, rates that were not significantly different from those observed in the first 24 hours after angiography. These events at 24 to 72 hours after angiography probably result from the natural history of the patient’s cerebrovascular disease (especially emboli secondary to atherosclerosis) rather than the performance of angiography. The neurological complication rates in patients with cerebrovascular disease would not be zero if no angiography or if “perfectly safe” angiography could be performed.

A risk of angiography unique to patients with SAH secondary to cerebral aneurysm rupture is a risk of rebleeding during contrast injection. Rebleeding during angiographic injection is quite low, however. No case of rebleeding during angiography occurred in the 415 cases of acute SAH included in this meta-analysis. Because the risk of rebleeding in the first 24 hours following SAH is 4%, and the risk is then 1% to 2% for each day thereafter for the next 4 weeks, some patients will occasionally suffer rebleeding while angiography is being performed. An experimental study in dogs has shown that arterial pressure does increase during contrast injection into the cervical carotid artery, creating a theoretical increase in risk of rebleeding. Rebleeding during contrast injection is, however, apparently quite rare.

The risk of nonneurological complications could not be evaluated for patients with SAH or other indications of cerebral angiography because insufficient data were available in the studies used in the meta-analysis. The overall risk of serious nonneurological complications is low, however (0.6%). Only 1 permanent sequela of a nonneurological complication occurred in 3517 patients in our meta-analysis. Although it was not possible to stratify the risk of nonneurological complications in the various subgroups of patients in our meta-analysis, Dion et al. noted that nonneurological complications were significantly related to age of >50 years, hypertension, TIA as an indication, and the presence of a carotid bruit.

Because this study is a meta-analysis and all of our data come from the 3 published series used, it was not possible to further evaluate the data for important confounding risk factors, such as patient age, length of procedure, and degree of atherosclerosis. Such risk factors are certainly important and may account for much of the increased risk of angiography in patients with TIA/stroke. A patient with SAH who happens to be elderly and have severe atherosclerosis likely has a higher risk for cerebral angiography than the average patient with SAH. However, knowing the risk of cerebral angiography in the typical patient with SAH, cerebral aneurysm, or AVM is still useful in making decisions about how to manage these patients, understanding that the data reflect the whole group of patients with these disorders and that management decisions need to be tailored to each individual patient’s circumstances.

Another limitation of our study is that because the overall complication rate is so low, it is difficult to acquire enough data to accurately characterize the risk of cerebral angiography in various patient subgroups. It was not possible to show a statistically significant difference in the risk of permanent neurological complication between patients with SAH and TIA/stroke, probably because of the overall low risk of permanent neurological deficit in both of these groups. However, there was a statistically significant difference in the rate of combined transient and permanent complication rates between these groups, and it is reasonable to assume that the rates of transient and permanent neurological complications vary proportionally.

Advances have been made in magnetic resonance angiography (MRA) and computed tomographic angiography (CTA) that have led some investigators to suggest that these techniques may soon replace conventional angiography in the search for aneurysms in patients with SAH and in the evaluation for residual AVMs after stereotactic radiosurgery. These techniques are noninvasive and therefore carry a lower complication rate than conventional catheter angiography. The superior spatial resolution of catheter angiography over both MRA and CTA and the lack of
flow-related artifacts that affect MRA are the reasons that catheter angiography remains the current standard diagnostic examination for cerebral aneurysms. The risk of cerebral angiography has also been discussed as a factor in deciding whether a second angiogram is justified in patients with SAH when no source for hemorrhage is found on the initial angiogram.9

Ruptured cerebral aneurysm is a very serious condition requiring prompt, accurate diagnosis and treatment, and misguided surgery can result in significant morbidity and mortality. AVMs are also a serious condition requiring highly accurate diagnosis and treatment. Misguided treatment of cerebral aneurysms and AVMs resulting from inaccurate imaging can potentially result in disastrous consequences. Since the risk of cerebral angiography in patients with SAH, cerebral aneurysm, and AVM is quite low, the diagnostic accuracy of noninvasive imaging techniques such as MRA and CTA must be comparable to that of conventional angiography if they are to be used as a substitute for conventional angiography. The risk of cerebral angiography in patients with SAH, cerebral aneurysm, and AVM defined in this study will be useful in deciding the appropriateness of cerebral angiography versus other noninvasive techniques in the evaluation of these serious conditions.

References
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