Risk of Cerebral Angiography in Patients with Symptomatic Intracranial Atherosclerotic Stenosis

Harry J. Cloft a, Michael J. Lynn b, Edward Feldmann c, Marc Chimowitz d
for the WASID Study Group

a Departments of Radiology and Neurosurgery, Mayo Clinic, Rochester, Minn., b Department of Neurology, Emory University, Atlanta, Ga., c Department of Neurology, Brown University, Providence, R.I., and d Department of Neurology, Medical University of South Carolina, Charleston, S.C., USA

Abstract

Background: A well-defined rate of adverse events following cerebral angiography in patients with symptomatic intracranial atherosclerosis would be useful to physicians making decisions regarding imaging and treatment of these patients. We report the adverse events associated with angiography in patients who underwent single-vessel cerebral angiography as part of the study protocol in the Warfarin-Aspirin for Symptomatic Intracranial Arterial Stenosis trial.

Methods: Single-vessel cerebral angiography was performed to specifically define the degree of stenosis in 196 patients suspected of having intracranial atherosclerotic stenosis on noninvasive tests. Adverse events that occurred within 24 h of cerebral angiography were reported by the sites performing the angiography.

Results: Overall, neurological adverse events occurred in 4 patients (2.0%; 95% CI: 0.6–5.1%), and nonneurological adverse events occurred in 12 patients (6.1%; 95% CI: 3.2–10.5%). All of the neurological adverse events were transient.

Conclusions: The risk of permanent neurological adverse events associated with single-vessel cerebral angiography in patients with symptomatic intracranial atherosclerosis is relatively low. The quantification of the risk of cerebral angiography in patients with intracranial atherosclerosis provides useful information to consider when evaluating noninvasive imaging techniques for their relative value.

Key Words
Cerebral angiography · Intracranial atherosclerotic stenosis, symptomatic

Introduction

The risks of cerebral angiography have been assessed in a number of prospective studies [1–6]. Some of these studies examined adverse event 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. In a meta-analysis of the risk of cerebral angiography in patients with TIA or stroke [7], the risk of transient neurological deficit was 3.0% and the risk of permanent neurological deficit was 0.7%.
Patients with symptomatic intracranial atherosclerotic stenosis are a specific subset of patients with TIA or stroke. Noninvasive identification of intracranial stenosis in these patients by transcranial Doppler (TCD) and magnetic resonance angiography (MRA) sometimes requires catheter angiography for confirmation and measurement of the degree of stenosis [8, 9]. Thus, catheter angiography remains a clinically important technique for patients with intracranial stenosis. The risk of cerebral angiography in this specific subset of patients has not been previously studied. We report the risk of single-vessel cerebral angiography in patients with suspected symptomatic intracranial atherosclerotic stenosis who underwent angiography as part of the study protocol in the Warfarin-Aspirin for Symptomatic Intracranial Arterial Stenosis (WASID) trial.

Methods

Study Design and Patient Eligibility

Details of the WASID study design and results of the comparison of warfarin and aspirin have been published previously [10]. Briefly, the WASID trial was an investigator-initiated, randomized, double-blind, multi-center clinical trial conducted at 59 sites in North America, which was funded by the National Institute of Neurological Disorders and Stroke. The study protocol was approved by the institutional review boards at each site, and all patients gave written informed consent to participate. Patients were enrolled between February 1999 and July 2003.

Inclusion criteria included: TIA or nondisabling stroke within 90 days of randomization that was attributable to angiographically verified 50–99% stenosis of a major intracranial artery (inward carotid, middle cerebral, vertebral or basilar artery); medically verified 50–99% stenosis of a major intracranial artery (in 90 days of randomization that was attributable to angiography in this specific subset of patients has not been previously studied). We report the risk of single-vessel cerebral angiography in patients with suspected symptomatic intracranial atherosclerotic stenosis who underwent angiography as part of the study protocol in the Warfarin-Aspirin for Symptomatic Intracranial Arterial Stenosis (WASID) trial.

Statistical Considerations

We report the percentage of patients experiencing each specific type of adverse event along with a 95% CI calculated using the exact binomial method. We also combined the adverse events into two categories: neurological adverse events (ischemic stroke, TIA, dissection, allergic reaction, groin hematoma, hypotension, congestive heart failure, chest pain, seizure and renal impairment). The numbers and percentages of patients experiencing the other specifically requested adverse events were as follows: TIA – 1 patient (0.5%; 95% CI: 0.01–2.8%); dissection – 1 patient (0.5%; 95% CI: 0.01–2.8%); allergic reaction – 1 patient (0.5%; 95% CI: 0.01–2.8%); and groin hematoma – 8 patients (4.1%; 95% CI: 1.8–7.9%).

Results

For 201 patients, the WASID study provided funds for the cost of a diagnostic single-vessel angiogram. Data on adverse events following the angiogram were not available for 5 patients. Among the remaining 196 patients, 16 (8.2%) experienced at least one adverse event within 24 h after the angiogram (95% CI: 4.7–12.9%).

Among the adverse events for which responses were specifically requested on the CRF, the following did not occur: ischemic stroke, hypotension, congestive heart failure, chest pain, seizure and renal impairment. The numbers and percentages of patients experiencing the other specifically requested adverse events were as follows: TIA – 1 patient (0.5%; 95% CI: 0.01–2.8%); dissection – 1 patient (0.5%; 95% CI: 0.01–2.8%); allergic reaction – 1 patient (0.5%; 95% CI: 0.01–2.8%); and groin hematoma – 8 patients (4.1%; 95% CI: 1.8–7.9%).

For 6 patients (3.1%; 95% CI: 1.1–6.5%), other adverse events were noted. These included 3 neurological events (visual-migrainous phenomenon that resolved in a few hours; headache and nausea; drowsiness requiring hospi-
terial admission following angiogram) and 3 nonneurological events (right common femoral artery dye-injected subintimally; syncope on arising 10 h after angiogram; asymptomatic bradycardia).

Overall, neurological adverse events occurred in 4 patients (2.0%; 95% CI: 0.6–5.1%) and nonneurological adverse events occurred in 12 patients (6.1%; 95% CI: 3.2–10.5%). All of the neurological events were transient. Among the 16 patients with angiographic adverse events, 1 patient had more than one adverse event: groin hematoma and syncope on arising 10 h after the procedure with no residual deficit.

Discussion

We found a very low risk of neurological events within 24 h after single-vessel cerebral angiography was performed for suspected symptomatic intracranial atherosclerotic stenosis in this multicenter trial (59 sites). In particular, there were no ischemic strokes, and only 1 TIA in 196 patients.

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 [1, 3], the total volume of contrast used [1], the length of the procedure [1, 2], the use of more than one catheter [3] and systolic hypertension [2]. One possible reason for the very low rates of neurological adverse events in this study was that angiography was limited to a single vessel.

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 due to the underlying cerebrovascular disease that led to angiography rather than the performance of cerebral angiography itself. Between 24 and 72 h after the performance of cerebral angiography, Dion et al. [2] observed rates of 1.5% for transient ischemic events and 0.3% for development of persistent deficits, rates that were not significantly different from the rates observed in the first 24 h after angiography. These events at 24–72 h following angiography are possibly due to the natural history of a patient’s cerebrovascular disease (especially emboli secondary to atherosclerosis) rather than the performance of angiography. Thus, the neurological adverse event rates in patients with cerebrovascular disease would not be 0 if no angiography, or if ‘perfectly safe’ angiography, could be performed [11].

The overall risk of nonneurological adverse events with angiography in our study was low, which is consistent with other studies [1–3, 7]. In the series by Dion et al. [2], serious nonneurological conditions consisted of 5 large inguinal hematomas requiring fluid replacement or surgery. In the series by Earnest et al. [3], the serious nonneurological adverse events consisted of 2 large inguinal hematomas requiring medical or 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. [1], there were 3 cases of transient hypotension requiring therapy. Minor hematomas occurred in 6.9% of the patients in the series reported by Dion et al. [2], and in 8.1% of the patients in the series reported by Heiserman et al. [1], but they were not reported in the series by Earnest et al. [3]. Dion et al. [2] noted that nonneurological adverse events were significantly related to age of >50 years, hypertension, TIA as an indication, and the presence of a carotid bruit. Since patients with symptomatic intracranial atherosclerotic stenosis share many of these risk factors, their risk of nonneurological adverse events after cerebral angiography would be expected to be higher than in the general population. In our study, 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.

Advances have been made in CT angiography [12], MRA [13–15] and TCD [8] that have led some investigators to suggest that these techniques may soon replace conventional angiography in patients with symptomatic intracranial atherosclerotic stenosis. These techniques are noninvasive and therefore carry a lower adverse event rate than conventional catheter angiography, but diagnostic accuracy is sometimes a problem. For example, in the SONIA (Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis) trial, MRA and TCD identification of 50–99% intracranial stenosis carried a false-positive rate of up to 45% [8].

For accurately identifying the presence and severity of disease and monitoring the effect of stenting, catheter angiography is sometimes required, and it will continue to be required if the SAMMPRIS (Stenting vs. Aggressive Medical Management for the Prevention of Recurrent Stroke) trial shows that stenting is superior to optimal medical therapy in patients with >70% stenosis. Since the risk of cerebral angiography in patients with symptomatic intracranial atherosclerotic stenosis is quite low, the diagnostic accuracy of noninvasive imaging techniques...
will need to be very comparable to conventional angiography if they are to be used as a substitute for conventional angiography. The risk of cerebral angiography in patients with symptomatic intracranial atherosclerotic stenosis defined in this study will be useful to know in deciding the appropriateness of cerebral angiography versus other noninvasive techniques in the evaluation of this high-risk disease.

Acknowledgments

This study was funded by a research grant (IR01 NS36643; principal investigator: M.I. Chimowitz) from the US Public Health Service, National Institute of Neurological Disorders and Stroke.

References


