The Safety of Dedicated-Team Catheter-Based Diagnostic Cerebral Angiography in the Era of Advanced Noninvasive Imaging

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BACKGROUND AND PURPOSE: Given the current high quality and usefulness of noninvasive cerebrovascular imaging, invasive angiographic evaluation of the cerebrovascular system is justified if the procedural risk for a neurologic complication is far below the anticipated benefit. The purpose of this study was to evaluate the safety of diagnostic cerebral angiography provided by a dedicated neurointerventional team in a high-volume university hospital.

MATERIALS AND METHODS: A consecutive cohort of 1715 patients undergoing diagnostic cerebral angiography at our institution from 2000 to 2008 was retrospectively assessed for incidence of stroke or TIA related to cerebral angiography. In the subgroup of patients ($n = 40$) who serendipitously underwent DWI within the first 30 days after cerebral angiography, the presence of new DWI hyperintensities found in territories explored during angiography was tabulated. Complications related to the catheter technique and sheath placement were also studied.

RESULTS: No stroke or permanent neurologic deficit was seen in any of the 1715 patients undergoing diagnostic neuroangiography. One patient experienced a TIA. Nonneurologic complications without long-term sequelae occurred in 9 patients. Two patients had punctate areas of restricted diffusion in territories that had been angiographically explored.

CONCLUSIONS: Within a high-volume neurointerventional practice, the risk for neurologic complications related to catheter-based diagnostic cerebral angiography can approach zero. As the absolute number of invasive diagnostic procedures diminishes with time, diagnostic cerebral angiography remains a useful tool while providing a foundation for neuroendovascular interventions, and should preferably be performed in institutions with high-volume operators also capable of managing unanticipated complicating adverse events.

ABBREVIATIONS: CTA = CT angiography; DSA = digital subtraction angiography; DWI = diffusion-weighted MR imaging; ICA = internal carotid artery; MCA = middle cerebral artery; MRA = MR angiography; TIA = transient neurologic deficit/transient ischemic attack

In the past decade, CTA, MRA, and Doppler ultrasonography have gained increasing importance in the diagnosis of cerebrovascular disease, given their noninvasive nature. Nevertheless, with regard to blood flow characterization as well as to temporal and spatial resolution, catheter-based, state-of-the-art cervicocerebral DSA remains the criterion standard for diagnosis and treatment of patients with cerebrovascular disease. To ensure favorable patient outcomes, technical expertise and an awareness of the risks of angiographic ischemic complications, including temporary and/or permanent deficits, is necessary. The specific indications for requesting catheter-based cerebral angiography vary significantly from institution to institution and are, in part, determined by the perception of procedural risk. The purpose of this study was to evaluate the safety of diagnostic cerebral angiography provided by a dedicated neurointerventional team in a high-volume university hospital.

Materials and Methods

Patient Population

From January 2000 to October 2008, a total of 1715 patients consisting of 1040 females (age range, 6–100 years; mean age, 52.9 ± 15.2 years; median age, 53 years) and 675 males (age range, 15–89 years; mean age, 52.5 ± 16.7 years; median age, 54 years) underwent diagnostic cerebral angiography at our institution. All patients in this consecutive cohort were prospectively entered into a data base tabulating neurologic and nonneurologic angiographic complications. All patient charts were retrospectively evaluated for brain MR imaging performed within the first 30 days after the angiogram to assess for silent emboli potentially related to angiography. In 40 patients consisting of 22 women (mean age, 43.9 ± 11.8 years; median age, 42.5 years) and 18 men (mean age, 49.2 ± 17.2 years; median age, 50.5 years), MR imaging studies including DWI were serendipitously obtained within the first 30 days after cerebral angiography. MR imaging was evaluated for punctate hyperintensities in the distal territory of the cortical, subcortical, or perforating vessels suggesting an ischemic event. The underlying indications leading to diagnostic cerebral angiography included aneurysm ($n = 410$); subarachnoid hemorrhage ($n = 263$); arteriovenous malformation ($n = 155$); arteriovenous fistula ($n = 39$); intracerebral hemorrhage ($n = 120$); arterial occlusive

disease including vasospasm (*n* = 276); vasculitis (*n* = 11); venous occlusive disease (*n* = 13); and other disorders including tumor, developmental venous anomaly, and cavernous malformation (*n* = 428).

Technique

Diagnostic cerebral angiograms were performed by one of the 2 dedicated full-time attending neurointerventionalists at the hospital, predominantly with the assistance of a clinical neurointerventional fellow. Patients were restricted from solid foods for 6 hours before the procedure but were permitted to have sips of clear fluids with medications. Outpatient procedures were performed in the morning, and patients were observed for a minimum of 4 hours before discharge. The vital signs and neurologic signs were monitored in the recovery room by a nurse. In all patients, peripheral intravenous access was secured before angiography. Intravenous conscious sedation was administered by a certified nurse with the patient under continuous monitoring via electrocardiography, pulse oximetry, and vital signs unless medical reasons contraindicated intravenous conscious sedation. Intra-arterial access was obtained in all cases by puncturing the common femoral artery with use of a 5F micropuncture kit (Cook, Bloomington, Indiana).

Using a single-wall puncture technique, a 4F or 5F sheath (Cordis, Miami Lakes, Florida) was placed. This sheath was continuously flushed in an antegrade manner with pressurized degassed heparinized saline (3000 IU of heparin in 1000 mL of normal saline). The same concentration was used for continuous flushing of the diagnostic catheter irrigated through a rotating hemostatic valve connected to a 2-inlet manifold, switchable between heparinized saline and power-injected contrast. All manually used syringes for heparinized saline and contrast were clear polycarbonate syringes (Medallion; Merit Medical OEM, South Jordan, Utah), which facilitate identification of air bubbles and facilitate bubble clearance. A 4F Berenstein II (Cordis), 4F Vertebral (Cordis), or 5F Davis (Cook) diagnostic catheter was used. In cases with tortuous anatomy on the basis of CTA or MRA findings, a 5F Simmons 1 or 2 diagnostic catheter (Cook) was used. An angled hydrophilic 0.035-inch radiofocus glidewire (Terumo, Somerset, New Jersey) was used in all cases. The nonionic contrast media used was Ultravist 240 (Bayer HealthCare, Wayne, New Jersey).

Most angiographic injections were performed with a power injector (Mark V; Medrad, Indianola, Pennsylvania) unless extenuating circumstances warranted hand injections. Standard injection rates and volumes were as follows: 8 mL/s for 12-mL total injectate for the common carotid artery, 6 mL/s for 9-mL total injectate for ICA, 3 mL/s for 6-mL total injectate for external carotid artery, and 4 mL/s for 8-mL total injectate for vertebral artery injections with rise times between 0.1 and 0.3 s. Procedures consisted of biplane DSA (Advantx; GE Healthcare, Milwaukee, Wisconsin) with appropriate angiographic sequences as indicated. At the completion of each procedure, mechanical suture closure (Perclose; Abbott Vascular Devices, Redwood City, California) or collagen plug closure (Vasoseal; Datascope, Mahwah, New Jersey) was used in most patients from 2000 to 2006. In 2006, the preferred method for groin closure reverted to manual compression at the puncture site for 15 minutes until complete hemostasis was achieved. Three patients with arteriotomy site-related complications (see below) in whom closure devices were used prompted this change in the puncture site paradigm. All angiograms performed as part of an intervention, intraoperatively in a surgical suite, or which involved superselective catheterization of the intracranial vasculature

for diagnostic purposes were excluded from consideration for this study.

Analysis

A neurologic complication was defined as any new neurologic sign or symptom, or worsening of a preexisting neurologic deficit occurring either during the procedure or within 24 hours after the procedure. Neurologic complications were classified as transient if they resolved within 24 hours, reversible if they lasted more than 24 hours but less than 7 days, and permanent if they persisted more than 7 days.[1] A nonneurologic complication was defined as any sign or symptom that occurred either at the puncture site or systemically within 24 hours of the procedure. An adverse event was defined as a procedure-related angiographic finding without neurologic signs or symptoms that may or may not require treatment.[2]

Results

Neurologic Complications

No stroke or permanent neurologic deficit was seen in any of the 1715 patients undergoing diagnostic neuroangiography. One patient (0.06%) experienced a TIA during the procedure that consisted of a bilateral visual field cut that completely resolved within minutes. The patient was given aspirin and was monitored overnight. The vascular anatomy in this patient did not pose any specific challenges; a 4F system was used without abnormally prolonged catheterization time.

Silent Emboli on MR Imaging

Two (5%) of the patients in the subgroup undergoing DWI (*n* = 40) after cerebral angiography had punctate areas of restricted diffusion corresponding with angiographically explored territories. The first patient, a 57-year-old man, presented with angionegative subarachnoid hemorrhage and underwent subsequent angiography 7 days postictus for vasospasm check and demonstrated mild vasospasm in the left M1 segment. The patient was neurologically intact, and the vasospasm was treated with intra-arterial infusion of 5 mg verapamil. An MR imaging examination was obtained 7 days after the initial angiography to assess for causes of subarachnoid hemorrhage. Tiny foci of increased signal intensity on DWI ipsilateral to the site of vasospasm were found. Whether these changes reflect ischemic events caused by vasospasm in distal vessels or sequelae of an embolic event caused by angiography is not clear.

The second patient, a 78-year-old man with insulin-dependent diabetes, also presented with subarachnoid hemorrhage and underwent cerebral angiography at 1 day and 11 days postictus. Angiography results were negative for aneurysm, arteriovenous malformation, or arteriovenous fistula. An MR imaging examination was performed to evaluate for other potential causes of subarachnoid hemorrhage 1 day after the angiogram. DWI revealed multiple punctate areas of restricted diffusion in the posterior fossa and the convexities that were not seen on subsequent DWI imaging 25 days later. Markedly tortuous origins of both vertebral arteries and both proximal portion common carotid arteries were noted on subsequent angiography 11 days after the hemorrhage. The initial angiogram report did not make note of difficulties in catheterizing these vessels. Both cases of abnormal DWI findings postangio-

graphically had a common underlying disease (angionegative subarachnoid hemorrhage) and a common comorbidity, hypertension.

Technique-Related Complications
A total of 9 technique-related complications occurred in 8 patients (0.5%).

Vertebral and Carotid Vessels
Extracranial vessel dissections occurred in 4 patients (0.2%), affecting the right vertebral artery in 2 patients and the left common and right ICA in 1 patient each. These dissections were non flow-limiting in 3 patients, prompting conservative management with aspirin. Emergent stent placement was required for a 65-year-old woman with a history of an acute infarct in the left MCA territory and suspected stenosis of the precavernous and cavernous segments of the left ICA diagnosed on MRA. The angiogram revealed a 50% stenosis of the cavernous segment of the left ICA and luminal irregularities of the cervical ICA, consistent with fibromuscular dysplasia. The procedure was complicated by a clinically silent dissection of the left common carotid artery during the second injection from the same catheter position. This dissection seemed to have been caused by the contrast jet. The dissection led to immediate and marked flow limitation; therefore, emergent stent placement with a 10-mm × 30-mm Precise stent (Cordis, Warren, New Jersey) was performed. In addition, 3000 U of heparin and an eptifibatide (Integrilin) bolus were administered before stent deployment, followed by a continuous eptifibatide infusion. The patient remained neurologically intact throughout the procedure.

All patients with dissection were middle-aged women with a primary diagnosis of an intracranial aneurysm; they also showed vascular changes suggestive for fibromuscular dysplasia. Other risk factors were hypertension and smoking in 1 patient each. None of the patients experienced long-term sequelae.

Access Vessels/Sheath Placement
Sheath-related complications occurred in 5 patients (0.3%), 3 of whom required surgery. A 59-year-old female patient with an asymptomatic right vertebral artery dissection also went on to have a multilobed, partially thrombosed pseudoaneurysm of the left superficial femoral artery. After removal of the 5F sheath, a collagen plug device (Vasoseal) had been used for groin closure. A small pseudoaneurysm (0.8-cm diameter on sonography) was diagnosed because of tenderness at the groin puncture site and during the course of 1 week increased in size to 2.8 cm in diameter and was associated with pain and tenderness, as well as skin changes. Vascular surgical exploration was performed on the pseudoaneurysm, and a 2- to 3-mm opening in the left superficial femoral artery was found; the opening was sutured with #5–0 Prolene.

Surgery was also necessary for a second 70-year-old female patient with severe peripheral vascular disease who underwent cerebral angiography for angiographic assessment and potential embolization of the olfactory groove meningioma. When the 6F sheath (Cordis) was placed into the right common femoral artery, it was noted that the J-wire could not be advanced because of presumed atherosclerosis at the common iliac ori-

gin. Therefore, access was gained in the left common femoral artery, and a 6F sheath was inserted. After cerebral angiography, a final pelvic angiogram revealed an occlusion of the right femoral artery requiring surgical repair. The patient recovered and underwent resection of the olfactory groove meningioma 2 days later.

The third surgical patient was a 67-year-old woman with multiple small intracranial aneurysms and stenoses of both proximal ICAs. Angiography was indicated to anatomically delineate the origins of the clinoid and ophthalmic segment aneurysms on the right side. After removal of the 5F sheath in the right groin and closure of the puncture site with the Perclose device, the right-sided pedal pulses initially detectable with Doppler disappeared. Sonography results confirmed occlusion of the right common femoral artery. The patient was transferred to the operating room for surgical exploration. Intraoperatively, the Perclose closure stitch elevated the posterior plaque, occluding the vessel. The Perclose stitch was removed and endarterectomy performed. A good pedal pulse was restored, and the patient was discharged 2 days later.

Endovascular repair of a peripheral complication was performed in a 64-year-old male patient in whom a small gluteal artery branch was angiographically noticed, giving rise to a small region of persistent contrast staining in the right pelvis. A Renegade Hi-Flo microcatheter (Boston Scientific, Natick, Massachusetts) was advanced through a 5F Davis catheter (Cook) over a Transcend (Boston Scientific) 14 soft-tip microwire, and the gluteal branch was embolized with two 2.5 × 20-mm Berenstein liquid coils. Neither a hematoma nor decrease in hematocrit levels occurred. The intraoperative findings confirmed that the left-sided aneurysm was the source of the bleeding.

While the sheath was being upgraded from 5F to 6F, difficulty was encountered in advancing the sheath in an 81-year-old female patient with a partially thrombosed left MCA aneurysm. An angiogram of the right iliac artery showed a 2-cm dissection and an intimal flap in the distal right external iliac artery. Given normal angiographic peripheral runoff, the dissection was not treated.

Four of the 5 patients with sheath-related complications were women, and 4 of the 5 patients had a primary diagnosis of aneurysm. All patients had hypertension and access vessel disease, and 3 of 5 patients had a collagen plug device for closure of the puncture site.

Systemic Complications
Systemic complications were encountered in 2 patients (0.1%). One 49-year-old female patient had a contrast reaction with hypotension and facial swelling, requiring stabilization with intravenous fluids. A second 68-year-old female patient who had ICA occlusion while receiving heparin experienced hypotension because of a groin hematoma and required transfusion with 2 U of packed red blood cells. Both patients recovered and were discharged the day after cerebral angiography.

Discussion
Despite advances in noninvasive diagnostic neuroimaging, diagnostic cervicocerebral angiography remains the criterion standard for the evaluation of patients with cerebrovascular

disease[3,4] and is the foundation for successful endovascular interventions. The spatial detail and temporal hemodynamic information—combined with the ability to physiologically and anatomically assess the filling characteristics of a single injected vessel—provided by modern angiography combined with advanced rotational 3D imaging are unequalled by non-invasive studies. The increasing volume of endovascular treatments with recent technological advances demands acumen and technical skills to assess cerebrovascular circulation.

The increased diagnostic accuracy of DSA compared with CTA and MRA should be balanced against the risks of DSA, most importantly, that of permanent neurologic deficit, which has been reported to range widely from 0.3% to 5.7%.[4] Dedicated neurovascular specialists report complication rates lower than 1%.[5] On the basis of prospective studies looking at more than 1000 procedures, the combined transient and reversible neurologic complication rate of cerebral angiography within the first 24 hours have been reported to widely range as low as 0.3% to as high as 6.8%.[4] Patients with symptomatic atherosclerotic disease have been reported to have a 2- to 3-fold higher risk for stroke (0.5–5.7%) from diagnostic cerebral angiography compared with patients who have asymptomatic atherosclerotic lesions (0.1%–1.2%).[4,6] In our prospective consecutive cohort of 1715 patients undergoing cerebral angiography from January 2000 to October 2008, no permanent neurologic deficits occurred. One patient (0.06%) had a rapidly resolving transient neurologic deficit.

Two (5%) of the 40 patients studied with DWI within 30 days of cerebral angiography had punctate areas of restricted diffusion. This rate of silent emboli compares favorably with previously published data. Several prospective studies[7-10] used DWI before and after intra-arterial cerebral angiography and reported an incidence of silent microemboli ranging from 18.5% to 23%, including both diagnostic and interventional procedures. Excluding interventions because of their inherent higher risk for microemboli, Krings et al[11] in 2006 found silent microemboli in 11.1%. Atherosclerotic vessel wall disease, vasculitis, and hypercoagulable states were shown as risk factors for silent microemboli. These changes, though clinically inapparent, suggest structural ischemic brain damage[7] and may harbor subtle neuropsychological correlates that are only picked up if thoroughly investigated. The low incidence of transient neurologic deficits (0.06%) and silent microemboli (5%) in our patients might in part be explained by a preponderance of patients with aneurysms, arteriovenous malformations, and arteriovenous fistulas (867/1715 patients) compared with the much smaller cohort of patients with symptomatic atherosclerotic cerebrovascular disease (276/1715) in whom one might expect a higher complication rate. Proper technique might be the most important factor to minimize the risk for angiography. Disrupting an ulcerated plaque with the catheter or glidewire may result in a stroke. We advocate routine use of a road-mapping technique to identify potential hazards at "hot spots" for atherosclerotic plaques and tortuosities at the carotid bifurcation or vertebral artery origin before deeper cannulation. In modern angiographic suites, such roadmaps may require no more than a few milliliters of contrast. Thromboembolism from the hardware (catheters, glidewires) introduced into the bloodstream is another causative mechanism for neurologic complications after cerebral

angiography. To prevent stagnation of blood in the deadspace of the catheter when the glidewire is withdrawn, continuous antegrade catheter flushing with pressurized heparinized saline and a manifold system is the standard at our institution. This system remains under constant antegrade flush and can be readied for contrast injection by simply turning a flow-directing stopcock on the manifold without the need for repetitively reconnecting and disconnecting the power injector. Other potential complications include arterial dissections related to the catheter or glidewire, air embolism, platelet activation,[12] and neurotoxicity of contrast agents.[13,14] These concerns led to our use of nonionic contrast material; small catheters; and a closed, continuously antegrade flushing system to prevent air embolism. Arch aortographies are associated with higher neurologic complication rates[14,15] and require a large contrast load (50 mL). Therefore, we very rarely perform such arch aortograms, and none were performed in this series. Information regarding the origins of the great vessels is either gained from the noninvasive imaging or is identified with low-volume contrast hand-injections in the aortic arch when nonroutine anatomy is encountered, such as with bovine common carotid origins or direct origin of the vertebral artery from the arch.

The nonneurologic complication rate for cerebral angiography heavily depends on the broad inclusion of complications and on postangiographic observation. Delayed hematoma at the puncture site is a common complication in patients undergoing systemic administration of heparin[16] and was encountered in one of our patients requiring transfusion. In the earlier prospective studies, local complications such as groin hematoma described by Kerber et al,[17] Jeans et al,[18] and Dion et al[19] varied from 0.6% to 14% in patients suspected of having cerebral ischemia. In the retrospective studies by Swanson et al[20] and Reilly et al,[21] the local complication rate ranged from a low of 4.1% to a high of 20.8%. Asymptomatic adverse events such as dissections occurred in 4 patients (0.2%) in our series, one of whom required stent placement. That percentage is in keeping with the most recently reported incidence of 0.15% iatrogenic dissections by Fifi et al.[22] We believe that detection of features of fibromuscular dysplasia should trigger an especially cautious approach to catheter and guidewire manipulations within the craniocervical circulation. Nonneurologic complications related to sheath placement were found in 5 patients (0.3%), 3 of whom required surgery. Female sex and diagnosis of cerebral aneurysm were identified as predisposing factors for dissection and sheath-related complications. In the series of Fifi et al,[22] arteriotomy site–related complications were found in 0.15% of patients who were evaluated within the first 6 hours after the procedure. The low rate of contrast reactions during cerebral angiography in this series compares favorably with reported rates of such reactions (0.7%) in cross-sectional imaging patients at our institution[23] and is likely related in part to the decreased likelihood of arterial contrast administration triggering such reactions.

Diagnostic angiography performed in the hands of an experienced neurointerventional team also provides the advantage of immediately correcting and intervening in procedural complications. This advantage was well illustrated by one of our own patients requiring immediate stent placement for a technique-related carotid dissection, and another patient re-

quiring immediate repair of a small peripheral pelvic arterial perforation. Other possible interventions could hypothetically include revascularization for thrombolysis or mechanical means in cases of intracranial thromboembolism. The synergistic effect of high-volume physicians and high-volume centers on better patient outcomes has been described in various studies for coronary artery bypass surgery,[24] percutaneous coronary interventions,[25] and carotid endarterectomy.[26]

In a high-volume neurointerventional practice, the risk for neurologic complications related to catheter-based diagnostic cerebral angiography can approach zero. The rate of nonneurologic complications can also be kept at a minimum despite increasingly complex cerebrovascular cases and an increasing population of patients treated with endovascular techniques. Nevertheless, the decision to perform cerebral angiography should be made after careful and thorough consideration of all cross-sectional data including CTA and/or MRA. Operator experience, technique, and procedural volume are key considerations to ensure the safety of diagnostic cerebral angiography.

Conclusions

With the advent of modern noninvasive imaging tools to evaluate cerebral vasculature, the total number of invasive diagnostic procedures will likely diminish. In contrast, the spectrum of neurointerventional and therapeutic catheter-based procedures is continuously increasing, requiring a high level of technical expertise. Diagnostic cerebral angiography is the foundation for safe and successful neuroendovascular intervention and should therefore be performed in institutions with dedicated high-volume neurointerventional operators.

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