Safety of Cerebral Digital Subtraction Angiography in Children
Complication Rate Analysis in 241 Consecutive Diagnostic Angiograms
Ingrid M. Burger, BS; Kieran J. Murphy, MD; Lori C. Jordan, MD; Rafael J. Tamargo, MD; Philippe Gailloud, MD

Background and Purpose—Catheter-based cerebral angiography remains an important diagnostic tool in the pediatric population, particularly considering the currently growing interest in diagnosing and treating cerebrovascular disorders in children. There are no recent estimates of the complication rate associated with modern diagnostic digital subtraction angiography (DSA) in the pediatric population. The purpose of this study was to estimate the rate of complications occurring during cerebral angiography in children.

Methods—Data from 241 consecutive pediatric cerebral angiograms performed at a single institution were entered into an institutional review board–approved database. Information on patient demographics, DSA indication, neurovascular diagnosis, and intra procedural and postprocedural complications was collected.

Results—Our population included 115 boys and 90 girls, with age ranging from 1 week to 18 years (mean ± SD, 12 ± 5 years). All angiograms were technically successful. No intraprocedural complication was noted; in particular, there was no occurrence of iatrogenic vessel injury (dissection) and no transient or permanent neurological deficit secondary to a thromboembolic event. One child with a complex dural arteriovenous fistula experienced a fatal intracranial rehemorrhage secondary to a posterior fossa varix rupture 3 hours after completion of an uneventful diagnostic angiogram. The rates of intraprocedural and postprocedural complications were therefore 0.0% (95% CI, 0.0% to 1.4%) and 0.4% (95% CI, 0.012% to 2.29%), respectively.

Conclusions—The rate of immediate complications occurring during diagnostic cerebral angiography in children is very low. No intraprocedural complication was documented in the reported series. DSA performed by experienced angiographers is a safe procedure that can provide critical diagnostic information. (Stroke. 2006;37:2535-2539.)

Key Words: catheter-based angiography ■ children ■ complications

Recent advances in noninvasive neurovascular imaging techniques, including magnetic resonance angiography (MRA) and computed tomography angiography (CTA), have reduced the number of catheter-based cerebral angiograms performed for purely diagnostic reasons. Digital subtraction angiography (DSA) remains, however, the most accurate imaging technique for evaluation of the cerebrovascular system. As such, DSA continues to be widely used to complement partial or questionable information obtained by noninvasive imaging means. In addition, new angiographic techniques, such as 3-dimensional DSA, 3-dimensional digital angiography, and 3-dimensional fusion DSA, have further enhanced the diagnostic accuracy of DSA. In parallel with these technical advancements, constant improvements in angiographic devices, such as wires and catheters, combined with the development of safer contrast agents, have continued to reduce the already low risk of complications associated with catheter-based angiography. The assumption remains, however, that catheter-based angiography is more challenging or dangerous in children. As a result, angiography is frequently delayed—if obtained at all—in this age group, despite the fact that the information it would provide might be invaluable for timely and accurate diagnosis and decision making. The risk of an intraprocedural complication such as stroke is obviously 1 of the principal reasons preventing referring physicians from requesting catheter cerebral angiography for their patients, along with the cost and availability of trained pediatric angiographers. This concern is, of course, legitimate and needs to be addressed by publication of the actual rates and types of complications associated with cerebral DSA in the pediatric population. Availability of such information to both referring physicians and neuroradiologists is particularly important at the time of decision making and parent counseling. Although earlier studies have already reported low complication rates for pe-
TABLE 1. Patient Age Distribution

<table>
<thead>
<tr>
<th>Age Group (in Years)</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 1</td>
<td>12</td>
</tr>
<tr>
<td>1 to 10</td>
<td>70</td>
</tr>
<tr>
<td>&gt;10</td>
<td>123</td>
</tr>
</tbody>
</table>

Pediatric cerebral angiography, no estimation of the complication rate for modern diagnostic cerebral DSA is currently available. This study examined the complication rate observed in a series of 241 consecutive diagnostic cerebral angiograms performed in 205 pediatric patients at a single institution between January 1999 and May 2006.

Patients and Methods

Patient Population

This report is based on analysis of a pediatric neurovascular database approved by our institutional review board (IRB). The data selected for this review consisted of 241 consecutive cerebral angiograms performed in 205 children (age 18 or less) at a single institution (Table 1). This represents ~5% of the total number of diagnostic cerebral angiograms (n=4320) performed at the same institution during the period under investigation. The studies can be subdivided into diagnostic cerebral angiograms per se (n=181) and angiograms performed as part of a WADA test (n=35) or stereotactic treatment (n=25). Cerebral angiograms obtained as the initial diagnostic component of a therapeutic procedure performed during the investigated period were not included in the analyzed dataset. The studied population included 115 boys and 90 girls, with age ranging from 1 week to 18 years (mean±SD, 12±5 years). The angiographic diagnoses for the studied population are listed in Table 2.

Angiographic Protocol

Arterial access was obtained in every patient via femoral puncture. A micropuncture set was used in most cases, with the exception of some teenagers of adult size. Sonographic assistance was required for a few small children with no or barely palpable pulses. 4F systems (arterial sheaths and diagnostic catheters) were used in almost all cases, whereas 5F systems were occasionally used in teenagers of adult size. Continuous flushing of the sheath with heparinized saline was maintained throughout the procedure (30 mL/h, 4000 heparin U/L of normal saline solution). A bolus dose of heparin (100 U/kg, to a maximum of 2000 U) was administered intravenously after femoral arterial access was obtained, with the exception of children investigated for acute intracranial hemorrhage. At the end of the study, hemostasis was obtained by manual compression. In the vast majority of cases, contrast agent injections were performed by hand. The maximum dose of contrast agent used in children under 16 years of age was 2 mL/kg. For children >16 years of age, the adult maximum dose of 175 mL was applied (though never reached in this series). Iodixanol (Visipaque 320, Amersham Health), an iso-osmolar (290 mOsmol/kg water), non-ionic, water-soluble, iodinated (320 mg I/mL) radiographic contrast agent, was used in most cases. A standard nonionic contrast agent (iohexol, Omnipaque 300, Amersham Health) was used only in children >16 years of age.

All angiography was performed in dedicated biplane neuroangiography suites. Most children were investigated under general anesthesia. Exceptions were represented by a few older children (16 years of age or above), who were investigated under conscious sedation and local anesthesia, and by children undergoing a WADA test, in whom either local anesthesia only (n=34) or spinal anesthesia (n=1) was performed. Outpatients were observed for a 5- to 6-hour period in the neuroangiography recovery area. Discharge evaluation in outpatients always included puncture site status and femoral and distal pulses, whereas inpatients were checked during evening rounds. In small children or in children unable to cooperate, the lower extremity used for arterial access was secured to a cushioned board to prevent, as much as possible, hip flexion.

Data Acquisition

The outcomes of interest in this study were the rates of complication of cerebral DSA occurring during the intraprocedural and immediate postprocedural periods. This information was acquired prospectively and recorded into an IRB-approved pediatric neuroangiography database. In addition, in consideration of the potential risk of delayed lower-extremity complications in the pediatric population, the parents or guardians of children <11 years old were personally contacted by phone (3 months to 4 years after the procedure) to inquire about signs and symptoms of such complications (eg, leg pain, walking difficulties, limping, or leg length discrepancy). These interviews were the object of a separate approval from the IRB.

The information was stored and analyzed by commercially available database and statistical software (FileMaker Pro 7, FileMaker, Santa Clara, Calif; Stata 9, Stata Corp LP, College Station, Tex).

Results

Intraprocedural Complications

All of the angiograms were technically successful. No intraprocedural complication was noted; in particular, there was no occurrence of iatrogenic vessel injury (arterial dissection) and no transient or permanent neurological deficit secondary to a thromboembolic event. There was no instance of contrast agent allergy and no evidence of contrast nephrotoxicity. The rate of intraprocedural complications was therefore 0.0% (95% CI, 0.0% to 1.4%).

Postprocedural Complications

One immediate postprocedural complication occurring 3 hours after the angiographic procedure was observed (0.4%; 95% CI, 0.01% to 2.29%). A comatose 6-year-old girl transferred for investigation of a large temporal hemorrhage was diagnosed with a type IV dural arteriovenous fistula of the right transverse sinus, with extensive cortical venous drainage. Subtotal embolization of the lesion was performed uneventfully, with excellent recovery and return to baseline neurological examination (including cognitive slowing present before the acute event) at discharge. A follow-up angiogram was obtained 6 months later because of recurrent

TABLE 2. Angiographic Diagnoses for the Studied Children (n=205)

<table>
<thead>
<tr>
<th>Angiographic Diagnosis</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>80</td>
</tr>
<tr>
<td>Arterial stenosis/occlusion</td>
<td>18</td>
</tr>
<tr>
<td>Dural/cortical venous thrombosis</td>
<td>5</td>
</tr>
<tr>
<td>Cerebral aneurysm</td>
<td>13</td>
</tr>
<tr>
<td>Vascular malformation</td>
<td>93</td>
</tr>
<tr>
<td>Vascular tumor</td>
<td>4</td>
</tr>
<tr>
<td>Vascular trauma</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
</tr>
</tbody>
</table>

The total number of angiographic lesions for the 205 patients was 225 because some children had >1 vascular lesion. The normal angiograms (n=80) included patients undergoing a WADA test as part of their presurgical workup (n=35) as well as follow-up angiograms after successful treatment of a vascular lesion.
peri-orbital venous engorgement and acute headache. The angiography was performed uneventfully and showed new arteriovenous shunts in a nontreated segment of the transverse sinus, with drainage through a large posterior fossa varix. The patient awoke from anesthesia without deficit but with slight nausea. Approximately 3 hours after angiography, she reported worsening of the nausea and had an episode of vomiting, after which she complained of a sudden, severe headache and became comatose. Emergent CT showed a posterior fossa hemorrhage at the site of the varix. She was immediately brought to the operating room but died of uncontrollable hemorrhage.

Minor Postprocedural Events
Although no groin hematomas were observed, 2 minor events are worth mentioning here. In 1 child investigated under general anesthesia and who was slightly hypothermic at the end of the procedure, hemostasis of the femoral puncture site necessitated 1 hour of continuous groin compression. One 6-month-old baby had a minor leak from the femoral puncture site 1 hour after the end of the procedure, necessitating an additional 20-minute period of groin compression. In both cases, the follow-up was simple, without groin hematoma or other complications.

Delayed Lower-Extremity Complications in Smaller Children (Age 11 and Younger)
The parents of 47 of the 71 patients aged 11 and younger could be contacted by phone (66.2%). The median follow-up time was 28 months (range, 5 to 85 months). No evidence of lower-extremity complication was reported (including leg pain, difficulty walking, limping, and leg length discrepancy).

Discussion
Despite the significant advances recently made in the field of noninvasive neurovascular imaging, cerebral DSA remains the most accurate technique for the diagnosis of vascular disorders of the central nervous system. Although the number of diagnostic angiograms performed for evaluation of carotid atheromatous disease has sharply decreased, this decline has been in part compensated by an increase in angiographic studies aimed at clarifying anomalies or suspicious findings revealed by MRA and CTA. In our practice, this applies to the pediatric population as well, with a steady increase in the number of requested studies documented during the past few years. The growing attention given to cerebrovascular disorders in children, a population in which this type of diseases was, until recently, either ignored or considered with undue fatalistic attitude, is certainly playing a role in this trend. This is clearly the case, in particular for the field of pediatric stroke. However, if recent studies have established the safety of diagnostic cerebral angiography in the adult population, no recent study has specifically investigated the complication rates observed in children. In adult patients, risk factors known to significantly influence the rate of neurological complication during cerebral angiography have been identified, notably advanced age and the preexistence of symptomatic atheromatous disease. In 1994, Heiserman et al reported a significant rate of permanent deficit (0.5%) but noted that all of the complications occurred in patients presenting with a history of stroke, transient ischemic accident, or carotid bruit. Dion and coauthors similarly observed that, in their series, all permanent ischemia was the worsening of a preexisting phenomenon. These findings are consistent with the study of Cloft and colleagues, who documented a 0.07% risk of complication in patients investigated for aneurysms or vascular malformations. Most of the risk factors known to have an influence on the rate of neurological complication during cerebral angiography, such as long procedures (>60 minutes), use of a large volume of contrast agent, increased serum creatinine levels, symptomatic atheromatous disease, and studies necessitating the use of 3 or more catheters, are not usually, if at all, encountered in the pediatric population. Pediatric cerebral angiography is typically characterized by short procedures performed in patients without atheromatous changes, with a low volume of contrast agent, and rarely necessitating 1 catheter. In small children, for example, 4-vessel cerebral angiography is routinely performed with 15 to 20 mL of contrast agent and 2 to 3 minutes of total fluoroscopy time. The risk of a transient or permanent neurological deficit from an intraprocedural adverse event, resulting from either a thromboembolic phenomenon or a traumatic mechanism, such as an arterial dissection, remains nonetheless the main factor contributing to the reluctance of referring physicians to consider catheter angiography in children. In a study focusing solely on iatrogenic embolization during pediatric cerebral angiography published 25 years ago by Pettersson and colleagues, thromboembolic events occurred in 14 of 1581 children (0.9%; 95% CI, 0.5% to 1.5%), or 0.4% of the studied vessels (14 of 3731). The authors emphasized the milder aspect of periangiographic thromboembolic events in the pediatric population when compared with similar events occurring in adult patients: only 1 child had transient neurological symptoms (0.06%), whereas there was no incidence of permanent deficit. They also noted that the relative incidence of inadvertent embolization was slightly higher, yet not significantly so, for the less-experienced angiographies and during longer procedures. Our report shows that these rates may nowadays be even lower, because no transient or permanent neurologic deficit was observed in our patients, and no thromboembolic event or arterial dissection was documented radiologically or clinically in our series.

The reduction in the risk of intraprocedural complication during the last 2 decades is certainly multifactorial. A major role has to be attributed to improvements in the quality of angiographic devices, including the development of smaller and softer catheters, the introduction of hydrophilic biomaterials, and micropuncture access systems. The routine use of biplane angiographic equipment, by offering 2 simultaneous projections for each contrast agent injection, provides a double gain in study duration and contrast load. The introduction of nonionic and, more recently, iso-osmolar contrast agents may help decrease the risk of nephrologic complications. Intraprocedural antiocoagulation, both systemic and through flushing of the arterial sheath and catheters, represents a major factor in the prevention of thromboembolic complication. Systemic antiocoagulation is routinely used, with the exception of patients investigated for an acute hemorrhage. A
very low incidence of arterial thrombosis at the access site can be achieved in the pediatric population with systemic heparinization.\textsuperscript{15} It should be noted that although heparinized saline (at a concentration of 4000 U/L of normal saline solution) is used liberally to flush the sheath and catheters throughout the procedure, this heparin flush alone does not provide adequate anticoagulation in the pediatric population.\textsuperscript{16} We routinely use an initial bolus of 100 U/kg, with a maximal dose of 2000 U for diagnostic angiography, administered intravenously immediately after arterial access has been gained.

One major complication potentially related to cerebral angiography was documented in our series. A 7-year-old girl died of a ruptured posterior fossa varix 3 hours after completion of an uneventful cerebral angiogram. This patient had initially presented a few months earlier in a comatose state resulting from a similar hemorrhagic episode. The second, fatal bleeding occurred shortly after the patient complained of nausea and vomited several times. We think it possible that the rupture of the varicose vein may have been coincidental or precipitated by the straining induced by the vomiting. It is indeed unlikely that intra-arterial contrast agent administration (in this case, gentle injections performed by hand) might have provoked the rupture of a remote venous structure 3 hours after completion of the study. Although it happened in the immediate postprocedural period, this complication therefore may be technically unrelated to the angiogram itself.

An interesting and, to some extent, unexpected finding in our series was the absence of groin complications. No hematomas were documented in our patients, despite the difficulty represented by immobilizing the leg of small children for a 5- to 6-hour period. It is possible that manual hemostasis is more efficient in children owing to the superficial position of the femoral artery. In our practice, femoral hemostasis in children is performed only by senior fellows or attending physicians, a factor that may play a role as well. One child required prolonged groin compression before hemostasis was achieved, without subsequent hematoma, despite the absence of a documented coagulation anomaly. This child, however, was slightly hypothermic at the end of the procedure, a condition known to alter the coagulation pathways.\textsuperscript{17} Another child had a mild femoral leak shortly after the procedure that required additional groin compression, again without hematoma. Follow-up interviews of the parents of 47 of the 67 children aged 10 or younger did not document signs or symptoms of delayed limb complication, such as pain, limping, or leg length discrepancy. It should be noted, however, that iliac or femoral artery occlusion may remain asymptomatic in children, thanks to their capacity at establishing a collateral blood supply.

Although the present study was mainly aimed at evaluating the rate of periprocedural complications, the potential long-term risk related to radiation exposure needs to be mentioned. Children are particularly sensitive to radiation exposure, a factor that obviously plays a role when posing the indication for any radiological investigation based on ionizing radiation.\textsuperscript{18,19} The relative radiation exposure from conventional angiography compared with CTA is still unclear. A recent study comparing radiation doses from multislice CT coronary angiography and conventional diagnostic angiography has shown the dose to be significantly higher for CTA.\textsuperscript{20} The same was found for CT urography versus conventional urography,\textsuperscript{21} whereas a similar study investigating pulmonary angiography showed a slightly lower dose for CT.\textsuperscript{22} The fluoroscopy times required for pediatric DSA are typically low, a factor that may tilt the balance in favor of DSA in children, although dedicated investigations in this field are required.

In 1974, Gypes\textsuperscript{23} ended the preface to the first textbook dedicated to pediatric angiography by remarking that “... high-quality angiograms, performed by interested and competent radiologists on sound clinical indications are the best means to educate ... about the usefulness of angiography in children.” This must remain true today, as cerebral angiography continues to be the “gold standard” in neurovascular imaging, playing a decisive role when clinical questions are not resolved by non-invasive techniques such as CTA and MRA.

In summary, our report shows that diagnostic cerebral angiography can be performed in children with extremely low periprocedural complication rates. Potential complications of pediatric cerebral angiography that were not long ago regarded as significant,\textsuperscript{24} eg, spasm induced by large catheters, bleeding at puncture sites, and emboli from catheter tips, have nowadays been reduced to very low levels (none of these complications occurred in our study). It is obviously an important ethical responsibility for referring physicians and angiographers to carefully determine the appropriateness of an invasive procedure in a child; it is, however, equally important not to deny pediatric patients the potentially crucial assistance of an invasive technique based on unwarranted assumptions of danger.

Disclosures

None.

References


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