Complications of cerebral angiography in children younger than 3 years of age

Clinical article

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Object. The therapeutic potential for cerebral angiography (CA) in young children is expanding. However, its use in this patient population is limited by presumed higher complication rates among children. Therefore, to improve the accuracy of counseling of the parents/guardians of these patients and to identify modifiable risk factors, the authors evaluated complications after CA in young children.

Methods. The authors reviewed data for 309 consecutive cerebral angiograms obtained in 87 children younger than 36 months of age from 2004 to 2010 at a single institution. They analyzed demographics, diagnosis, angiographic findings, and complications.

Results. The patient population comprised 40 boys and 47 girls; mean age was 14.36 months (range 1–36 months) and mean weight was 10.8 kg (range 3.7–21.0 kg). For 292 of the 309 procedures, intraarterial chemotherapy was administered; the remaining 17 procedures were for vascular malformations, stroke, tumor embolization, and intracranial hemorrhage. The rate of neurological complications was 0.0%. The rate of nonneurological complications was 2.9%: 7 cases of contrast allergy or bronchospasm, 1 groin hematoma (body weight 7 kg), and 1 transient femoral artery occlusion (body weight 10.8 kg). The rate of radiographic complications was 1.3%; 1 case of transient asymptomatic intraarterial dissection and 3 cases of asymptomatic vasospasm. Postprocedural MRI was performed for 33.3% of patients with no evidence of ischemia. There were no delayed complications. Mean follow-up time was 16.6 months. No association was found between complications and age, duration of anesthesia, number of vessels catheterized, size of the sheath, or diagnostic versus interventional procedures. Despite a trend toward a higher rate of complications for patients who weighed less than 15 kg, this finding was not significant (p = 0.35).

Conclusions. The rate of complications for CA in young children is comparable to rates reported for older children and lower than rates reported for adults. When appropriately indicated, CA should not be omitted from the therapeutic strategy of children younger than 36 months of age.

Key Words • morbidity • cerebral angiography • infant • vascular disorders

Although cerebral angiography (CA) is becoming less necessary as a diagnostic tool, as the accuracy of noninvasive imaging modalities such as CT angiography and MR angiography increases, the therapeutic applications of CA for young children are increasing. These increases are the result of continued technical advances, the advent of intraarterial chemotherapy for retinoblastoma, and increasing awareness of the significance of cerebrovascular disorders and stroke in the pediatric population.1,2,6,18,22,27,33 Despite this increase in therapeutic potential, hesitation to perform CA in young children remains. This hesitation stems from a persistent assumption that the rate of complications resulting from femoral access and intracranial catheter navigation are higher for this population because of the smaller vessel-to-catheter ratio and resultant higher risk for vasospasm, dissection, and peripheral vascular injury. Although the historical and current literature indicates that complications from CA in children are minimal, the procedure is often withheld from or delayed for younger children because of reports of increased complications among patients of younger age and lower body weight.3,4,10,12,25,26,31,35 Although older studies included infants in analyses of angiographic complications, they reported on methods that are no longer used, such as direct carotid artery or retrograde brachial access. In addition, the more current reports of low complication rates among pediatric patients is difficult to extrapolate.
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to young children because the mean ages in these studies ranged from 7 to 12 years. None of the studies in the literature about pediatric patients identify risk factors for angiography in this population (Table 1). Current reports of risk factors for angiography in small children also largely draw on cardiac catheterization data; no corresponding literature specifically addresses cerebral procedures. We therefore aimed to assess the complications and associated risk factors for CA specifically among young children. We used current technology, methods, and therapeutic indications to provide guidelines for accurate counseling of the parents/guardians of these patients and appropriate use of the procedure.

Methods

With institutional review board approval, we reviewed all diagnostic and interventional cerebral digital subtraction angiography studies performed from 2004 to 2010 at a single institution (NewYork-Presbyterian Hospital). We identified 309 procedures performed in 87 children younger than 36 months of age. All procedures were performed by 3 interventional neuroradiologists. We reviewed details regarding diagnostic and therapeutic indications, duration of anesthesia, vascular access, and number of vessels catheterized. All procedure-related complications were reported, even if they resulted in no clinical sequelae. Complications were categorized as neurological (stroke, transient ischemic attack, or intracranial hemorrhage), nonneurological (groin hematoma, femoral artery occlusion/limb ischemia, retroperitoneal hematoma, pseudoaneurysm, contrast allergy, or contrast-induced nephropathy), or radiographic (asymptomatic vasospasm or dissection, or subclinical ischemia).

Angiographic Protocol

After informed consent was obtained, each patient was positioned supine on the fluoroscopic table in a dedicated biplane angiography suite. General anesthesia was administered. A micropuncture set was used to gain femoral access; ultrasonography was not routinely used to identify the femoral artery. Vascular access sheath and catheter selection was determined on a case-by-case basis; 4-F sheaths were used for intraarterial chemotherapy and diagnostic angiography, and 5-F sheaths were used for complex interventional cases. For the more recent cases, 3-F sheaths were used for intraarterial chemotherapy. Heparin (70 U/kg) was administered to all patients after femoral artery puncture unless contraindicated by a pre-existing condition such as intracranial hemorrhage or coagulopathy. Omnipaque 300 (GE Healthcare) (2–3 ml/kg) was used as the contrast agent of choice. Regarding radiation dose, pediatric settings as low as reasonably achievable (ALARA principle) were used on a GE Healthcare angiography machine. Anticoagulation was not routinely reversed at the conclusion of the procedure. Manual pressure was used to obtain local hemostasis.

Clinical and Angiographic Follow-Up

Intraprocedural complications were determined at the time of the angiogram. Immediate postprocedural complications were determined by postoperative examination and observation in the recovery room. All outpatients who had undergone uncomplicated procedures were discharged on the same day, after the appropriate leg had been immobilized for 5 hours. Long-term follow-up was necessary for most patients who were undergoing continued treatment and observation for retinoblastoma. As a result, long-term complications were determined by review of follow-up clinic assessments. Subclinical post-procedural thromboembolic events were evaluated by clinically indicated MRI performed primarily to follow disease status in retinoblastoma patients. Diffusion-weighted sequences were performed for all patients reviewed, and all studies were specifically evaluated for the presence of infarcts. To assess clinical outcome, we used the modified Rankin Scale (mRS) as follows: no symptoms (mRS score of 0), no significant disability (mRS score of 1), slight disability (mRS score of 2), moderate disability (mRS score of 3), moderately severe disability (mRS score of 4), severe disability (mRS score of 5), and death (mRS score of 6).

Statistical Analyses

Wilcoxon rank-sum analyses were performed to identify any association between complications and length of procedure, number of vessels catheterized, number of angiograms performed, interventional versus diagnostic procedure, patient age, and size of sheath used. A p value of 0.05 was used to determine significance.

Results

Patients

In this study, records were reviewed for 87 patients (40 boys and 47 girls) who had undergone cerebral digital subtraction angiography; mean age was 14.36 months (range 1–36 months), and mean body weight was 10.8 kg (range 3.7–21.0 kg). The indications for this procedure found in this study are summarized in Table 2. Of the 309 procedures, 12 were diagnostic and 297 were interventional. The mean duration of anesthesia was 151.9 minutes, and an average of 3.6 angiograms were obtained per patient. From the 309 consecutive angiograms, a total of 770 vessels were catheterized; 708 (91.9%) were cerebral arteries and 62 (8.1%) were external carotid arteries and branches. The mean numbers of vessels catheterized per patient were 2.29 for cerebral arteries and 0.2 for external carotid arteries. Cerebral vessels included the internal carotid artery, ophthalmic artery, M1 segment of the middle cerebral artery, and the vertebrobasilar system. External carotid vessels included the external carotid artery trunk, the internal maxillary artery, and the middle meningeal artery. Vascular access was through the right common femoral artery for 177 procedures (57.3%) and the left common femoral artery for 132 procedures (42.7%).

Procedural Complications and Follow-Up Times

For the 309 procedures, the overall rate of complications was 4.2% (13 complications). The rate of neurologi-
cal complications was 0.0%, and the rate of nonneurological complications was 2.9% (9 complications). Of these 9 complications, 7 (77.7%) consisted of contrast allergy (defined as hemodynamic changes at the time of administration) or bronchospasm (defined as increased airway pressures and reduced tidal volumes), and the remaining 2 (22.2%) were related to access (1 groin hematoma and 1 transient femoral artery occlusion). The mean weight of these patients was 8.9 kg. The groin hematoma measured 5 cm and resolved with manual compression and 1 dose of protamine. The patient experienced no clinical sequelae and was discharged home the next day. Femoral artery occlusion was noted incidentally the day after the procedure, when the left limb was felt to be cooler than the contralateral limb, but there were no signs of ischemia. The patient was given aspirin, and repeat ultrasonography 1 week later demonstrated vessel patency. There were no clinical sequelae. Radiographic complications were seen for 4 (1.3%) patients. Three cases of asymptomatic vasospasm resolved during the procedure after administration of verapamil. One transient dissection of the supraclinoid internal carotid artery occurred during catheterization with a balloon microcatheter. For selective introduction of chemotherapy into the ophthalmic artery, a HyperForm 4 × 7 eV3 balloon catheter (Codivien) was used to occlude the internal carotid artery distal to the ophthalmic artery. The dissection did not limit flow, and angiography performed 30 minutes after the balloon was removed indicated no vessel injury. The patient awoke intact from anesthesia. Aspirin was given and no symptoms developed. There were no immediate or delayed neurological sequelae in any of these cases. Mean body weight did not differ significantly between patients with and without complications (p = 0.49). There was a trend toward a higher complications rate among patients who weighed less than 15 kg, but this trend was not significant (p = 0.35). Postprocedural MRI was available for 33.3% of patients with no evidence of subclinical ischemia associated with angiography (Table 3).

No contrast-induced nephropathy developed in any patient. The median numbers of internal and external vessels catheterized were not associated with complications (p = 0.36 and 0.26, respectively). Median duration of anesthesia was similar for patients with and without complications (p = 0.42). A 3-F or 4-F sheath was used for 284 patients, and a 5-F or 6-F sheath was used for the remaining 25. There was no association between catheter size and complications (p = 0.58). Mean follow-up time was 16.6 months (range 0.3–41.1 months). There was a trend toward complications in younger patients (mean age 14.36 months among patients without complications vs mean age 10.92 months among patients with complications), but this trend was not significant (p = 0.25) (Table 4).

### Discussion

Diagnostic and therapeutic CA has become an indispensable tool for the multimodal assessment and treatment of vascular malformations and tumors. It has increased the accuracy of diagnosis, limited surgical intervention, and decreased operative time for patients with these disorders. As advancements in endovascular technology have been made by way of new catheter design, novel embolization materials, new contrast media, and in-
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TABLE 4: Associated risk factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Complications</th>
<th>No Complications</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>patient age (mos)</td>
<td>10.92</td>
<td>14.36</td>
<td>0.25</td>
</tr>
<tr>
<td>vessels catheterized (mean)</td>
<td>2.0</td>
<td>2.0</td>
<td>0.36</td>
</tr>
<tr>
<td>anesthesia duration (mins)</td>
<td>133.5</td>
<td>150.0</td>
<td>0.42</td>
</tr>
<tr>
<td>catheter size</td>
<td></td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td>4-F</td>
<td>3.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4-F</td>
<td>4.0</td>
<td></td>
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In comparison, there are few corresponding studies regarding the complications and risk factors of CA in the pediatric population, and there is no current literature regarding the safety and risk factors for angiography in young children. Earlier reports analyzing the complications of CA included younger children. In 1975, Goto et al. reported on 59 children younger than 7 years of age and described 3 cases of femoral thrombus formation requiring balloon catheter thrombectomy; they did not report any neurological complications. In 1968, Newton and Gooding included infants in their analysis and reported no neurological or nonneurological complications. In 1969, Cerullo et al. included 288 infants in their analysis and found no neurological complications, a 1.8% rate of nonneurological complications, and a 1.1% rate of radiographic complications. Although these studies indicate low complication rates for cerebral angiography in children, these rates reflect complications associated with the initial use of the Seldinger femoral access technique and use of older catheters and materials; these studies did not consistently focus on complication rates in infant patients. More recent reports, from 2005 through 2009, also indicate low complication rates (0% neurological, 0%–1.2% radiographic, and 0%–4.5% nonneurological), potentially reflecting increased experience with femoral access and updated catheter materials. However, the mean age of children in these studies (7–12 years) makes it difficult to extrapolate these findings to young children. Regarding identification of risk factors, Heran et al. examined factors associated with complications in young children during cardiac catheterization and reported a greater risk for vasospasm as well as femoral artery thrombosis and long-term limb-length discrepancy among children who weighed less than 15 kg. No corresponding literature describes similar study of risk factors for CA in young children. As a result, although previous and current literature on CA in children points to a low rate of complications, lower than that reported for adults, current clinical practice for this population is guided by assumptions among interventional neuroradiologists and vascular neurosurgeons regarding sources of complications in small children.

In our study of 309 CA procedures among 87 infants, the mean patient age was 14.36 months. Most patients (94.4%) underwent CA for the treatment of retinoblastoma with intraarterial chemotherapy. As a result, most patients did not undergo 4-vessel angiography. Therefore, in our study, the rate of intracranial vasospasm and dissection might be lower than that for a population in which standard 4-vessel angiography is performed for most patients. In addition, angiography was performed by interventional neuroradiologists and dual-trained neurosurgeons, which might not represent the ability and experience of most angiographers. The number of interventional procedures was high, however, which might therefore reflect greater overall procedural risk. All prior series that assessed angiographic complications in children referenced diagnostic studies. It is therefore assumed that the reported risks are lower than the expected risks for patients undergoing interventional procedures. The fact that our complication rate was comparable to that currently reported in the literature, even in the setting of a primarily interventional cohort, therefore indicates a lower than expected complication rate. Regarding the increased use of intraarterial chemotherapy administration for retinoblastoma, multi-
ple recent publications address the feasibility and success rates for this procedure. Discussion of the complications in these series, however, does not include complications of angiography. As this procedure becomes increasingly integrated into the treatment strategy for infants, therefore, assessment of risk becomes essential. In the remaining patients (without retinoblastoma), 8 procedures were performed for the assessment of vascular malformations, 2 for possible tumor embolization, 4 for assessment of stroke, and 3 for assessment of the etiology of intracranial hemorrhage. In these cases in which 4-vessel angiography was used, there was no increase in complications to indicate that the risk for vasospasm, dissection, or access-related events were higher.

The mean follow-up time of 16.6 months (range 0.33–41.13 months) is significant with regard to our ability to detect delayed subclinical ischemic events with MRI. This follow-up time was possible because most of the patients were followed for long-term management of retinoblastoma, enabling continued clinical follow-up and imaging studies after angiography.

In keeping with the current literature on pediatric and adult patients, the low rate of complications and absence of neurological complications among the 87 patients reported here confirms that angiography is not more likely to result in symptomatic dissection or vasospasm in young children. The fact that children do not possess the primary angiographic risk factors identified for adults (that is, atherosclerosis, hypertension, hypercholesterolemia, and advanced age) decreases children's risk for neurological complications. Of the nonneurological complications that occurred among these patients, 2.9% were clinical and 1.3% were radiographic. Of these clinical complications, most (77.7%) were associated with bronchospasm and contrast allergy. This finding is contrary to the assumption that access-related injury would predominate among younger children. Heran et al. defined 15 kg as a cutoff weight for higher access-related rates of complications. Despite a trend toward higher rates of complications among patients who weighed less than 15 kg, the number of patients is too small to determine significance. The 2 patients with access-related injuries weighed 7 kg and 10.8 kg; the overall mean weight was 10.8 kg. However, no significant association was found between mean weight of patients with and without complications. However, because very few patients reported here weighed more than 15 kg, comparison with the current literature is difficult.

Contrast allergy was defined as significant change in hemodynamics after administration of contrast medium. Bronchospasm was defined as increased airway pressure and decreased tidal volume. This bronchospastic reaction has been reported by Gobin et al. for children receiving intraarterial chemotherapy. In these patients, the reaction typically occurs during the second or subsequent catheterization when the cavernous or ophthalmic artery is stimulated and is easily reversed with a small dose of epinephrine. Because in our study the incidence of systemic reactions was slightly higher than expected for isolated contrast allergy and lower than expected for isolated bronchospasm, an overlap in these 2 reactions is possible. For example, some bronchospastic events might have been masked by prophylactic administration of steroids or epinephrine and therefore might have gone unrecognized. Similarly, it is possible that reactions after administration of contrast medium were truly the result of bronchospastic reactions to catheter manipulation, falsely elevating our reported rate of contrast allergy. Our observed rate of systemic reactions might result from contrast sensitivity, indicating that this type of reaction is elicited more often in small children because of differences in immune function and response. In all cases, these systemic reactions were mild, did not significantly affect outcome or length of hospital stay, and were not associated with age (they occurred in patients 3–24 months of age, and occurrence was not higher among the younger children).

Regarding our 2 access-related injuries, the patient who sustained the groin hematoma was one of the younger patients in our study (6 months of age). The patient with the transient femoral artery occlusion was 12 months of age. Because there were only 2 cases of access-related complications, we cannot determine whether the rate of access-related injury is higher among younger children, but we can note it as a possible association in this series.

As indicated previously, among the variables that we assessed (age, number of vessels catheterized, catheter size, and duration of anesthesia), no associated risk factors were identified. Despite a trend toward younger age, this finding was not significant, contrary to current assumptions.

Conclusions

At our institution, the short- and long-term rates of complications from CA in infants are comparable to rates reported for older children and lower than rates reported for adults. We found no significant association between complications and the current assumed risk factors of age, catheter size, and procedure duration. As a result, when indications are appropriate, angiography should not be withheld from the diagnostic or treatment plan of young children.

Disclosure

Dr. Souweidane reports being a consultant for Aesculap.

Author contributions to the study and manuscript preparation include the following. Conception and design: Hoffman, Gobin, Souweidane. Acquisition of data: Hoffman, Santillan, Rotman. Analysis and interpretation of data: Hoffman, Souweidane. Drafting the article: Hoffman, Santillan. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Hoffman. Administrative/technical/material support: Souweidane. Study supervision: Gobin, Souweidane.

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