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Original Article

Stroke After Cardiac Catheterization in Children

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ABSTRACT

Background: Children with cardiac disease are at high risk for stroke. Approximately one-quarter of strokes in children with cardiac disease occur in the peri-procedural period; yet, the risk factors, clinical presentation, and treatment of post-catheterization stroke in children have not been well defined.
Methods: We conducted a retrospective review of the medical records of patients aged zero to 18 years with a new clinically-apparent arterial ischemic stroke after cardiac catheterization at a tertiary children's hospital from 2006 to 2016. We excluded patients who had cardiac surgery, a cardiac arrest, extracorporeal membrane oxygenation, a ventricular assist device, or an arrhythmia proximate to their stroke.
Results: Twenty children had a new clinically-apparent post-catheterization arterial ischemic stroke. The median age was one year (range, two days to 16 years). The most common procedures were balloon dilation for pulmonary vein stenosis (n = 6) and systemic pulmonary collateral closure (n = 5). The most common presenting symptoms were arm weakness (n = 10) and seizure (n = 8). The median time from catheterization to symptom discovery was 31.5 hours (interquartile range, 16.2 to 47.8 hours; n = 18). The median Pediatric Stroke Outcome Measure score 12 months post-stroke was 0.75 (range, 0 to 2; n = 6).
Conclusions: Although arterial ischemic stroke after cardiac catheterization is rare, better understanding this entity is important as children with cardiac disease and stroke have ongoing morbidity. Ameliorating this morbidity requires efforts aimed at preventing and rapidly detecting stroke, thereby enabling timely institution of neuroprotective measures and treatment with hyperacute therapies.

Introduction

Children with congenital and acquired heart disease are at high risk for stroke. One-quarter of arterial ischemic strokes (AIS) in children with cardiac disease occur in the peri-procedural period.[1] Nevertheless, the risk factors, clinical presentation, and treatment of post-catheterization AIS in children have not been well defined. Eleven children had AIS within 30 days after cardiac catheterization between 1993 and 2010 at a tertiary children's hospital in Australia, representing 15% of AIS in children with cardiac disease during this time period.[2] Thirty-one children had a hemorrhagic or ischemic stroke attributed to cardiac catheterization between 2010 and 2014 at a tertiary children's hospital in the United States, representing 37% of strokes in children with cardiac disease in this cohort.[3] In both of these studies, post-catheterization strokes and other strokes in children with cardiac disease were considered as a whole

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with few details provided specifically about the strokes attributed to cardiac catheterization. Here, we describe 20 patients with a new clinically-apparent AIS occurring within 30 days after cardiac catheterization over the past decade at a tertiary children's hospital in the United States.

Materials and methods

We conducted a retrospective review of the medical records of patients aged zero to 18 years who had a new clinically-apparent AIS within 30 days after cardiac catheterization at a tertiary children's hospital in the United States between December 2006 and December 2016. There were 12,312 cardiac catheterizations performed in patients aged zero to 18 years during this time, 3,538 of which were hemodynamic, 6,957 of which were interventional, and 1,817 of which were for biopsy. The electronic medical record (EMR) was searched using a centralized repository of clinical data for patients discharged from the hospital with the terms "catheterization" and "stroke" in their discharge summary. Patients were included in our cohort if they had a new clinically-apparent AIS confirmed by neuroimaging within 30 days after cardiac catheterization. We excluded patients who also had a cardiac arrest (n = 3), cardiac surgery (n = 5), extracorporeal membrane oxygenation (ECMO) (n = 5), a ventricular assist device (VAD) (n = 2), an arrhythmia (n = 1), a cardiac arrest and ECMO (n = 6), or a cardiac arrest and a VAD (n = 1) during the week before their catheterization or between the time of their catheterization and the time of the neuroimaging study that confirmed AIS. A final diagnosis of AIS was made on the basis of neuroimaging data as reviewed by A.D., a pediatric neuroradiologist with subspecialty expertise in the imaging of stroke and cerebrovascular disorders in children. Pediatric Stroke Outcome Measure (PSOM) scores were calculated retrospectively based on chart review by D.B.H. (stroke and cerebrovascular disorders fellow) and C.L.S. (child neurology fellow); the PSOM is a 10-point validated measure of outcome after pediatric stroke, with zero indicating no deficits and 10 indicating maximal deficits.[4] Study data were collected and managed using Research Electronic Data Capture tools hosted at Boston Children's Hospital.[5] Descriptive statistics were used as needed. This study was approved by the Institutional Review Board of Boston Children's Hospital. Consent was not required.

Results

Patient characteristics

Twenty patients had a new clinically-apparent AIS after cardiac catheterization without a proximate cardiac arrest, cardiac surgery, ECMO, VAD, or arrhythmia. The median age at AIS diagnosis was one year (range, two days to 16 years); 11 (55%) patients were aged less than two years. Nineteen (95%) patients had congenital heart disease, one (5%) had acquired heart disease, and 15 (75%) had previous cardiac surgery (Table 1). Six (30%) patients had single-ventricle physiology with atrial-level mixing due to atrial septal defects (Table 1). One (5%) patient had prior AIS. Four (20%) patients had a pre-existing diagnosis of epilepsy, including the patient with prior AIS. The remaining patients (n = 16, 80%) had no significant neurological history.

Catheterization procedure

Nineteen (95%) catheterizations were interventional and one (5%) was hemodynamic. The most common catheterizations were balloon dilations for pulmonary vein stenosis (n = 6, 30%), three of which were performed with cutting balloons, and systemic pulmonary collateral closure via placement of a coil (n = 5, 25%) (Table 2). Seven (35%) catheterizations involved trans-septal needle puncture (Table 2).

Stroke presentation

Presenting symptoms are detailed in Table 3. The most common presenting symptom was new-onset arm weakness (n = 10, 50%). New-onset leg and facial weakness were seen in seven (35%) and five (25%) patients, respectively, all of whom also had arm weakness. Eight (40%) patients presented with seizure, none of whom had a history of epilepsy. Other presenting symptoms included depressed level of consciousness, aphasia, and bradycardia.

The median time from the end of catheterization to the time that symptoms were first noted by either a parent (n = 8, 44%) or provider (n = 8, 44%) was 31.5 hours (range, 1.75 hours to 19.8 days; interquartile range [IQR], 16.2 to 47.8 hours; n = 18) (Fig A). The time that symptoms were first noted was not documented for two (10%) patients, and for two (11%) patients with a documented time of symptom onset, it was not possible to determine from the EMR who discovered the initial symptoms. Symptoms were discovered within four days of catheterization for all but one patient (Fig A) with hypoplastic left heart syndrome and a fenestrated Fontan who presented almost 20 days after catheterization. Of the 18 patients who had a documented time of symptom discovery, seven (39%) patients had not received a benzodiazepine, narcotic, or paralytic within 24 hours of symptom discovery.

The median time from the end of catheterization to the first documented neurological assessment was 6.1 hours (range, 22 minutes to 3.3 days; IQR, 119 minutes to 20.5 hours; n = 15). Five (20%) patients did not have a documented neurological assessment before discovery of their stroke symptoms. For the majority of patients, the first documented neurological assessment was performed by anesthesiology (n = 3, 20%) or nursing (n = 10, 66%). Twelve (80%) assessments included motor function, five (33%) included pupillary responses, three (20%) included level of consciousness, two (13%) included ability to follow commands, two (13%) included other elements of the mental status examination, and one (7%) included a language assessment. The majority of patients had one (n = 9, 60%) or two (n = 5, 33%) of the above categories assessed. No patient had more than three of the above categories assessed, and no patient had a full screening neurological assessment before discovery of their stroke symptoms.

Stroke diagnosis

The median time from symptoms first being noted to the start of the imaging study that confirmed AIS was 18 hours (range, 0.98 to 68.6 hours; IQR, 4.7 to 29.4 hours; n = 18) (Fig B). AIS was confirmed by computed tomography (CT) in 12 (60%) patients and magnetic resonance imaging (MRI) in eight (40%) patients. The initial imaging obtained was confirmatory of stroke in all but three (15%) patients who had an initial head ultrasound; all head ultrasounds were normal and required follow-up MRI for confirmation of AIS diagnosis.

Infarcts most commonly involved the middle cerebral artery (MCA) territory (n = 18, 90%) (Table 4). The majority of infarcts involved the cortex and subcortical white matter (n = 18, 90%) (Table 4) and were large (n = 17, 85%), defined as partial or full territory of the main cerebral or cerebellar arteries.

Antithrombotic regimen

Fourteen (70%) patients were maintained on an antithrombotic agent (nine aspirin; two aspirin and clopidogrel; one aspirin,

TABLE 1.
Cardiac Diagnosis

Patient	Congenital or Acquired Heart Disease	Cardiac Diagnosis
1	Congenital + arrhythmia	Ebstein's anomaly of tricuspid valve, hypoplastic RV, RVOT s/p staged palliation to extracardiac Fontan; recurrent SVT
2	Congenital	HLHS s/p bilateral BDG
3	Congenital	Heterotaxy, R-dominant CAVC, PA, cor triatriatum, PVS s/p BTS to LPA, BDG to RPA, stenting of pulmonary veins
4	Congenital	Dextrocardia, TAPVR, absent RPA, absent RPVs, bicuspid aortic valve, PVS
5	Congenital	HLHS s/p BDG
6	Acquired + arrhythmia	Dilated cardiomyopathy; ectopic atrial tachycardia
7	Congenital	TAPVR, PVS
8	Congenital	PAPVR, PVS, tricuspid atresia
9	Congenital	Mitral stenosis
10	Congenital	Shone's complex, parachute mitral valve
11	Congenital	Tricuspid regurgitation, PS
12	Congenital + arrhythmia	Heterotaxy, TGA, PA s/p extracardiac Fontan; sinus node dysfunction, intermittent junctional rhythm
13	Congenital + arrhythmia	Dextrocardia, TGA, unbalanced CAVC s/p extracardiac Fontan; AVNRT
14	Congenital	Pentalogy of Cantrell, dextrocardia, TGA, LVOT, subvalvar PS
15	Congenital	HLHS with intact atrial septum
16	Congenital	Heterotaxy, R-dominant CAVC, coarctation of the aorta s/p Fontan with mBTS
17	Congenital	Aortic stenosis
18	Congenital	TAPVR, PVS
19	Congenital	Heterotaxy, DORV, R-dominant CAVC, TAPVR, hypoplastic LV, PA s/p Fontan
20	Congenital	Scimitar syndrome, dextrocardia, absent RPA, cor triatriatum, PAPVR, PVS

Abbreviations:
AVNRT = Atrioventricular nodal reentrant tachycardia
BDG = Bidirectional Glenn
BTS = Blalock-Taussig shunt
CAVC = Complete atrioventricular canal defect
DORV = Double-outlet right ventricle
HLHS = Hypoplastic left heart syndrome
LPA = Left pulmonary artery
LV = Left ventricle
LVOT = Left ventricular outflow tract obstruction
mBTS = Modified Blalock-Taussig shunt
PA = Pulmonary valve atresia
PAPVR = Partial anomalous pulmonary venous return
PS = Pulmonary valve stenosis
PVS = Pulmonary vein stenosis
R = Right
RPA = Right pulmonary artery
RPVs = Right pulmonary veins
RV = Right ventricle
RVOT = Right ventricular outflow tract obstruction
s/p = Status post
SVT = Supraventricular tachycardia
TAPVR = Total anomalous pulmonary venous return
TGA = Transposition of the great arteries

clopidogrel, and warfarin; two therapeutic unfractionated heparin [UFH]) at baseline (24 hours or more before catheterization) (Table 5). Five (25%) patients were not on an antithrombotic agent at baseline, and for one (5%) patient, it was not possible to determine from the EMR whether an antithrombotic agent was used at baseline (Table 5). During the 24 hours before catheterization, four (20%) patients were maintained on an antithrombotic agent (three aspirin; one therapeutic UFH), 11 (55%) were not on an antithrombotic agent, and for five (25%) patients, it was not possible to determine from the EMR whether the patient was on an antithrombotic agent (Table 5). Nineteen (95%) patients were maintained on therapeutic UFH during catheterization (Table 5). In all patients receiving UFH during catheterization, activated clotting time (ACT) was checked every 30 minutes during catheterization with a goal of 200 seconds or greater for hemodynamic cases and 250 seconds or greater for interventional cases as per institutional guidelines. Six (32%) patients had an ACT of less than 200 seconds and an additional seven (37%) had an ACT of less than 250 seconds at least once

TABLE 2.
Type of Catheterization Procedure

Therapeutic Catheterization Procedure(s)	Number of Patients
Trans-septal needle puncture	7 (35%)
Pulmonary vein dilation	6 (30%)
Coil or systemic pulmonary collateral closure	5 (25%)
Dilation of atrial septum	3 (15%)
Balloon dilation of aorta	2 (10%)
Mitral valvotomy	2 (10%)
Atrial pacing	1 (5%)
Electrophysiology with ablation	1 (5%)
Hemodynamic	1 (5%)
Pulmonary valvotomy	1 (5%)
Stenting of atrial septum	1 (5%)
Stenting of left ventricular outflow tract	1 (5%)

TABLE 3.
Presenting Symptoms

Presenting Symptoms	Number of Patients
Arm weakness	10 (50%)
With leg weakness	7 (35%)
With facial weakness	5 (25%)
Seizure	8 (40%)
Depressed level of consciousness	3 (15%)
Aphasia	3 (15%)
Bradycardia	2 (10%)

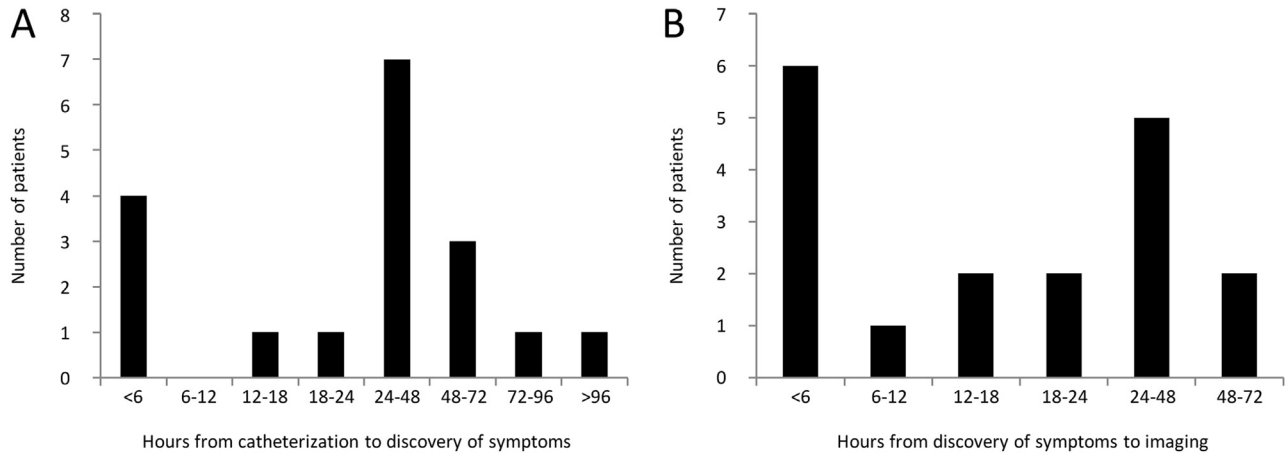

FIGURE. (A) Time (hours) from the end of catheterization to the time that symptoms were discovered. (B) Time (hours) from the discovery of symptoms to the start of the imaging study that confirmed stroke.

during the procedure (Table 5). The remaining patients had an ACT of greater than 250 seconds throughout catheterization. At the time of AIS discovery, 13 (65%) patients were on an antithrombotic agent (three aspirin; one aspirin and clopidogrel; two aspirin and therapeutic UFH; six therapeutic UFH; one low molecular weight heparin), four (20%) were not on an antithrombotic agent, and for three (15%) patients, it was not possible to determine from the EMR whether the patient was on an antithrombotic agent (Table 5).

Risk factor evaluation

The majority of patients had coagulation parameters and a complete blood count measured within 24 hours of stroke discovery (Table 6). Eighteen (90%) patients had a full or partial thrombophilia evaluation (Table 6). Eighteen (90%) patients had an echocardiogram within 48 hours of AIS discovery. One (6%) of these 18 patients had an intracardiac thrombus in the left atrium and one (6%) had a thrombus in the inferior vena cava. Three of 18 (17%) patients, in addition to those with single-ventricle physiology, had a right-to-left shunt. Echocardiography in the remaining patients was not contributory to their AIS diagnosis.

Treatment

After discovery of their AIS, six (30%) patients were started on a new antithrombotic agent relative to their baseline antithrombotic regimen or their antithrombotic regimen at the time of stroke discovery (one aspirin; one aspirin and warfarin; three therapeutic UFH; one LMWH), whereas 10 (50%) patients continued or resumed their baseline antithrombotic regimen or their antithrombotic regimen at the time of stroke discovery (six aspirin; four therapeutic UFH) (Table 5). Two (10%) patients had UFH held in the aftermath of

TABLE 4.
Stroke Characteristics

Patient	Arterial Territory	Sites Affected	Laterality	Number of Strokes
1	MCA	Basal ganglia	R	Single
2	MCA	Cortex, subcortical WM	L	Single
3	MCA	Cortex, subcortical WM, basal ganglia	Bilateral	Multiple
4	MCA	Cortex, subcortical WM	R	Single
5	MCA	Cortex, subcortical WM	R	Single
6	MCA	Cortex, subcortical WM	L	Multiple
7	MCA, PCA	Cortex, subcortical WM	L	Multiple
8	MCA	Cortex, subcortical WM	L	Single
9	MCA (R, L), PCA (R), PICA (L)	Cortex, subcortical WM	Bilateral	Multiple
10	MCA	Cortex, subcortical WM, basal ganglia	L	Single
11	MCA	Cortex, subcortical WM, thalamus	Bilateral	Multiple
12	MCA	Cortex, subcortical WM	L	Single
13	MCA	Cortex, subcortical WM	L	Single
14	MCA	Cortex, subcortical WM	Bilateral	Multiple
15	ACA (L), MCA (R)	Cortex, subcortical WM	Bilateral	Multiple
16	PCA	Cortex, subcortical WM	L	Single
17	ACA, MCA	Subcortical WM	Bilateral	Multiple
18	MCA	Cortex, subcortical WM	R	Single
19	PICA	Cortex, subcortical WM	L	Single
20	MCA	Cortex, subcortical WM	R	Single

Abbreviations:
ACA = Anterior cerebral artery
L = Left
MCA = Middle cerebral artery
PCA = Posterior cerebral artery
PICA = Posterior inferior cerebellar artery
R = Right
WM = White matter

TABLE 5.
Antithrombotic Regimen

Patient	Baseline Antithrombotic Regimen	Antithrombotic Regimen During the 24 hours Before Catheterization	Lowest ACT During Catheterization (Seconds)	Antithrombotic Regimen at Time of Stroke Discovery	Acute Treatment of Stroke
1	Aspirin	None	<250	LMWH	UFH
2	Aspirin	Cannot be determined	<200	None	Aspirin
3	Aspirin/clopidogrel/warfarin	Cannot be determined	<250	UFH	Thrombectomy
4	Aspirin/clopidogrel	None	<250	Aspirin/clopidogrel	UFH
5	Aspirin	Cannot be determined	N/A	Cannot be determined	Cannot be determined
6	Cannot be determined	Cannot be determined	<250	Aspirin/UFH	Aspirin/warfarin
7	Aspirin	Aspirin	<250	Aspirin/UFH	Aspirin; UFH held
8	Aspirin	Aspirin	<250	Aspirin	Aspirin
9	UFH	None	<200	Cannot be determined	LMWH
10	None	None	<250	None	Thrombectomy
11	None	None	N/A	Cannot be determined	Aspirin
12	Aspirin	None	<200	Aspirin	Aspirin
13	None	None	*	UFH	UFH
14	None	None	<200	UFH	UFH
15	None	None	N/A	UFH	UFH
16	Aspirin	Aspirin	N/A	None	UFH
17	UFH	UFH	N/A	UFH	UFH
18	Aspirin	None	<200	None	Aspirin
19	Aspirin	Cannot be determined	<200	Aspirin	Aspirin
20	Aspirin/clopidogrel	None	N/A	UFH	UFH held

Abbreviations:
ACT = Activated clotting time
LMWH = Low molecular weight heparin
N/A = No ACT < 200 seconds
UFH = Unfractionated heparin
* No UFH administered.

their stroke discovery, and for one (5%) patient, it was not possible to determine from the EMR whether changes were made to the antithrombotic regimen (Table 5). Two (10%) patients were treated with mechanical thrombectomy (Table 5). One patient had decreased right-sided movement noted shortly after catheterization with MRI and magnetic resonance angiography notable for multifocal infarcts and bilateral proximal MCA and right posterior cerebral artery (P2/P3 junction) occlusions. The left MCA was recanalized via mechanical thrombectomy performed 8.5 hours after the start of catheterization; the right MCA recanalized spontaneously. At the time of discharge, the patient had severe expressive language and right-sided sensorimotor deficits. The second patient treated with mechanical thrombectomy was noted to have no movement of the right arm approximately five hours after catheterization with MRI and magnetic resonance angiography notable for restricted diffusion in the left MCA territory and abrupt truncation of flow signal at the distal left M1 segment. He underwent mechanical thrombectomy with successful recanalization of the left MCA 11 hours after the start of catheterization. At the time of discharge, he had a moderate right sensorimotor deficit and mild deficits in expressive and receptive language.

Outcome

Nine (45%) patients had seizures as a complication of their AIS, including eight whose initial presentation included seizure and one who had seizure onset shortly after presenting with focal weakness. Seven (78%) of these patients were seen in follow-up three months after discharge, and none had ongoing seizures; two (29%) were taking levetiracetam and three (43%) were taking phenobarbital at follow-up. No patient had hemorrhagic conversion of their infarct, and no patient required an extraventricular drain or hemicraniectomy. No patient died due to AIS.

The median PSOM score at discharge was 0.5 (range, 0 to 4; n = 16), reflecting a mild deficit with no impact on function.[4] Six (38%) patients had a PSOM score of ≥1 at discharge, reflecting at least a moderate deficit with some functional limitations in a single domain or a mild deficit with no impact on function in two

TABLE 6.
Laboratory Evaluation

Test	Number of Patients Tested	Number of Patients With Normal Results	Number of Patients With Abnormal Results
Prothrombin time	16 (80%)	8 (50%)	8 (50%) (1 low; 7 high)
Partial thromboplastin time	15 (75%)	5 (33%)	10 (66%) (3 low; 7 high)
White blood cell count	18 (90%)	8 (44%)	10 (56%) (3 low; 7 high)
Hemoglobin level	19 (95%)	12 (63%)	7 (37%) (1 low; 6 high)
Erythrocyte sedimentation rate	2 (10%)	1 (50%)	1 (50%)
C-reactive protein	4 (20%)	0	4 (100%)
Protein C functional	14 (70%)	7 (50%)	7 (50%) (6 low; 1 high)
Protein S functional	11 (55%)	7 (64%)	4 (36%) (4 low)
Antithrombin III functional	16 (80%)	7 (44%)	9 (56%) (8 low; 1 high)
Homocysteine level	12 (60%)	11 (92%)	1 (8%)
Factor V Leiden functional	13 (65%)	12 (92%)	1 (8%)
Prothrombin gene mutation	13 (65%)	12 (92%)	1 (8%)
Lupus anticoagulant	11 (55%)	10 (91%)	1 (9%)
Anticardiolipin antibodies	12 (60%)	11 (92%)	1 (8%) (indeterminate)

domains.[4] The median PSOM score at the time of neurological follow-up approximately three months later was 1 (range 0 to 3; n = 10). Three patients had interval worsening of their deficits between discharge and three-month follow-up, and six (60%) patients had a PSOM score of ≥1 at three-month follow-up. The median PSOM score on neurological follow-up approximately 12 months after stroke onset was 0.75 (range 0 to 2; n = 6), and three (50%) patients had a PSOM score of ≥1 at 12-month follow-up. Six (30%) patients died due to complications of their underlying cardiac disease by 13 months post-stroke.

Discussion

We describe 20 children who suffered a clinically-apparent AIS following cardiac catheterization between December 2006 and December 2016 at a tertiary children's hospital. Although AIS after cardiac catheterization is rare, it is important to understand this entity better as children with cardiac disease and stroke are at risk of ongoing morbidity. No patient in our cohort died due to AIS; however, six of 10 patients (60%) with a documented follow-up examination at three months and three of six patients (50%) with a documented follow-up examination at 12 months had ongoing functional deficits based on a PSOM ≥1. This is in keeping with prior studies of children with cardiac disease and stroke in which over half to over three-quarters of patients had ongoing deficits attributable to their stroke.[2,3] Of note, the PSOM scores calculated for the patients in our cohort may underestimate the extent of their deficits as the PSOM was scored retrospectively and function across all domains was not always well documented.

Amelioration of this ongoing morbidity requires efforts aimed at preventing AIS in this population. The relatively large number of patients in our cohort with pulmonary vein stenosis who underwent catheterization for pulmonary vein dilation with or without use of a cutting balloon (n = 6, 30%) suggests that this may be an especially high-risk population. This is consistent with previous work that revealed an AIS prevalence rate of 7.6% for patients undergoing pulmonary vein dilation.[6] There was also a relatively large number of patients in our cohort who underwent catheterization for coil or systemic pulmonary collateral closure (n = 5, 25%), suggesting that this may represent another high-risk group. Over half of the patients in our cohort were not maintained on an antithrombotic agent during the 24 hours before catheterization (n = 11, 55%), despite a majority (n = 14, 70%) being maintained on an antithrombotic agent at baseline, and a majority of patients (n = 13, 65%) had an ACT of less than 250 seconds during catheterization. It is possible that a change in practice regarding anticoagulation before and during catheterization might impact the risk of AIS, and this merits further study. Of note, the majority of patients (n = 13, 65%) were maintained on an antithrombotic regimen at the time of AIS discovery. It is possible that their antithrombotic regimen was insufficient to prevent AIS. However, it is also possible that their AIS occurred before resumption of their antithrombotic regimen but, due to a delay in diagnosis, was not detected until after they had resumed treatment with an antithrombotic agent(s).

In addition to efforts aimed at prevention, reducing the morbidity of AIS occurring after cardiac catheterization necessitates decreasing the time to detection of post-procedural AIS, thereby enabling timely institution of neuroprotective measures and treatment with hyperacute therapies. The majority of AIS in our cohort occurred within four days of catheterization. This is consistent with prior studies that show medians of three and 10 days from the time of a cardiac procedure to the onset of clinical symptoms and stroke diagnosis, respectively.[2,3] This suggests that this period represents a key time for heightened awareness of AIS symptoms by both caregivers and clinicians. It remains to be determined whether post-catheterization AIS occurs at the time of catheterization and is not discovered until a few days later when symptoms are noticed or whether, in at least some instances, there is a delay between the time of the procedure and the occurrence of AIS. The time from the end of catheterization to the discovery of symptoms reported here is likely an overestimate of the time to AIS onset given that the patients in our cohort were not undergoing serial neurological examinations and therefore may have had symptoms that went undiscovered for a period of time. In some individuals, this may have been due to the administration of sedating and paralytic medications. The most common presenting symptoms in our cohort were focal weakness and seizures. This is in keeping with prior work showing that 87% of patients with post-procedural AIS present with facial or limb weakness or seizure.[2] Educational interventions aimed at caregivers and clinicians focused on monitoring for new-onset weakness or seizure activity and promptly seeking medical attention should these symptoms appear may enable the more rapid diagnosis of AIS in these children.

In addition to improved caregiver and clinician patient surveillance, treatment of a greater number of children with hyperacute therapies after post-catheterization AIS will require more rapid and timely diagnosis once a child is brought to medical attention. The median time from the discovery of symptoms to the start time of the imaging study that confirmed AIS in our cohort was 18 hours, consistent with prior work demonstrating a median time from symptom onset to diagnosis of AIS of over 20 hours in children.[7-9] Of note, CT was confirmatory of AIS in over half of the patients in our cohort, and no patient who had a CT as their initial imaging modality required an MRI for stroke confirmation. CT is often the only imaging option for confirming AIS in patients with cardiac disease as the presence of critical illness, pacemakers, and pacing wires often precludes MRI. Given that AIS may be missed on CT if imaging occurs within the first six to 12 hours after the ischemic event, CT may have been effective at confirming AIS in our cohort due to the delay between the time that symptoms were first noted and the time that imaging was obtained. It is also possible that patients with post-catheterization AIS were missed as there were patients for whom a neurology consult was called for acute-onset focal neurological deficits who did not have an infarct on CT but who were unable to have an MRI.

Two patients in our cohort were treated with mechanical thrombectomy, and this resulted in re-establishment of blood flow in the occluded arteries. There were no treatment-related complications. This is in keeping with data from case reports and case series that suggest that both intravenous tissue plasminogen activator and endovascular therapy may be safe and effective in the post-catheterization period in adults and children,[10-15] although, notably, there have been no randomized controlled trials in children and the literature on this subject may be subject to a positive publication bias. Of note, both patients were treated outside of the parameters of published adult stroke trials of mechanical thrombectomy for large-vessel occlusions.[16,17]

We identified fewer post-catheterization strokes than Cheng et al.[3] despite querying the same population of children with cardiac disease. This may reflect our strict exclusion criteria; any patient who had a cardiac arrest, cardiac surgery, ECMO, a VAD, or an arrhythmia proximate to the time of their AIS was excluded from our analysis. It is likely that a subset of AIS in the patients excluded from our analysis did indeed result from catheterization; however, given that it was impossible to distinguish between two or more potential causes of AIS, we chose to exclude these patients from further analysis so as to focus on AIS that were highly likely to have been caused by cardiac catheterization.

Our study is limited by the retrospective nature of our study design. It is possible that our search strategy failed to identify a subset of children with post-catheterization AIS given that we used a bioinformatics approach rather than a prospectively acquired database to identify our cohort of patients.[1,3] Moreover, not all data points were available for every patient in our cohort. In addition, all data come from a single center and may not be generalizable to other pediatric centers.

Conclusions

Stroke after cardiac catheterization in children is rare; however, it is accompanied by persistent morbidity. Pulmonary vein dilation and systemic pulmonary collateral closure appear to be especially risky procedures with respect to AIS occurrence. Treatment of children with AIS after cardiac catheterization with mechanical thrombectomy resulted in successful recanalization without complication. Unfortunately, the diagnosis of AIS after cardiac catheterization is often delayed, precluding the use of hyperacute therapies. Development of screening methods to identify AIS more rapidly in this population has the potential to decrease the time to detection of AIS, thereby expanding access to treatment with thrombolysis and mechanical thrombectomy. This, in turn, may attenuate the resulting deficits and improve neurological outcome for this population of children.

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