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## Endovascular Thrombectomy for Pediatric Acute Ischemic Stroke: A Multi-Institutional Experience of Technical and Clinical Outcomes

**BACKGROUND:** Endovascular thrombectomy is a promising treatment for acute ischemic stroke in children, but outcome and technical data in pediatric patients with large-vessel occlusions are lacking.

**OBJECTIVE:** To assess technical and clinical outcomes of thrombectomy in pediatric patients.

**METHODS:** We undertook a retrospective cohort study of pediatric patients who experienced acute ischemic stroke from April 2017 to April 2019 who had immediate, 30-, and 90-d follow-up. Patients were treated with endovascular thrombectomy at 5 US pediatric tertiary care facilities. We recorded initial and postprocedural modified Thrombolysis in Cerebral Infarction (mTICI) grade  $\geq 2b$ , initial and postprocedural Pediatric National Institutes of Health Stroke Scale (PedNIHSS) score, and pediatric modified Rankin scale (mRS) score 0 to 2 at 90 d.

**RESULTS:** There were 23 thrombectomies in 21 patients (mean age  $11.6 \pm 4.9$  yr, median 11.5, range 2.1-19; 52% female). A total of 19 (83%) thrombectomies resulted in mTICI grade  $\geq 2b$  recanalization. The median PedNIHSS score was 13 on presentation (range 4-33) and 2 (range 0-26) at discharge (mean reduction  $11.3 \pm 6.1$ ). A total of 14 (66%) patients had a mRS score of 0 to 2 at 30-d follow-up; 18/21 (86%) achieved that by 90 d. The median mRS was 1 (range 0-4) at 30 d and 1 (range 0-5) at 90 d. One patient required a blood transfusion after thrombectomy.

**CONCLUSION:** In this large series of pediatric patients treated with endovascular thrombectomy, successful recanalization was accomplished via a variety of approaches with excellent clinical outcomes; further prospective longitudinal study is needed.

**KEY WORDS:** Cerebrovascular, Endovascular, Thrombectomy, Anticoagulation, Ischemic stroke, Pediatrics

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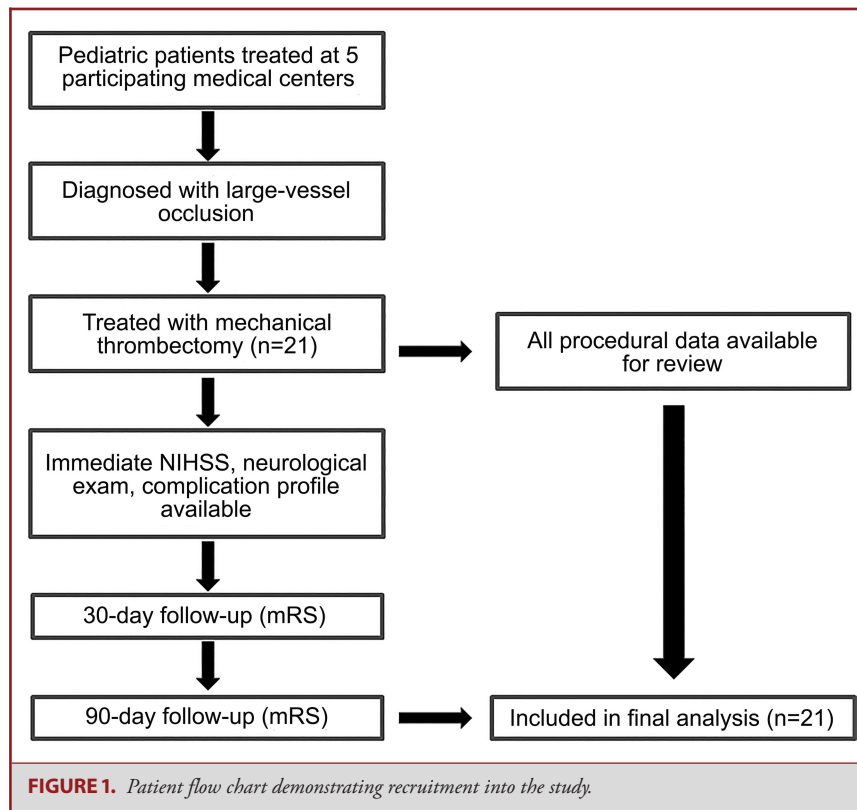
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**A**cute ischemic stroke (AIS) occurs in 2.3 of 100 000 children<sup>1,2</sup> and can carry a mortality rate of 3% to 6% with a 70% morbidity rate.<sup>3,4</sup> Children who experience AIS

tend to have recurrent strokes, lifelong deficits, and decreased quality of life.<sup>3,4</sup>

AIS has not been rigorously studied in pediatric patients because of its rarity, but the phenomenon of AIS in pediatric patients is on the rise, in part as a result of improved survival in children on mechanical circulatory support devices for heart failure.<sup>5-8</sup> Outcomes after AIS in children are often worse than outcomes for adults because of the lack of treatment protocols and delays in diagnosis.<sup>9</sup> Large-vessel occlusions (LVOs), defined as acute blockage of the internal carotid artery (ICA), proximal posterior, middle, and anterior cerebral arteries, intracranial vertebral artery, and/or basilar artery, are clinically important because they have been

**ABBREVIATIONS:** AIS, Acute ischemic stroke; **ASPECT**, Alberta Stroke Program early computed tomography; **CT**, computed tomography; **CTA**, CT angiography; **ICA**, internal carotid artery; **LOVs**, Large-vessel occlusions; **LVAD**, left ventricular assist device; **MCA**, middle cerebral artery; **MRA**, magnetic resonance angiography; **MRI**, magnetic resonance imaging; **mRS**, modified Rankin scale; **mTICI**, modified Thrombolysis in Cerebral Infarction; **PedNIHSS**, Pediatric National Institutes of Health Stroke Scale; **tPA**, tissue plasminogen activator



associated with twice the risk of death in adults when compared with other types AIS.<sup>10,11</sup>

Recent endovascular breakthroughs in therapy for adult AIS have improved the mortality and morbidity rates<sup>12-14</sup> and have led to expanded use of endovascular techniques in the pediatric population.<sup>3,15-17</sup> There is currently no level I evidence for acute revascularization in pediatric patients, but only class IIb recommendations for endovascular therapy in patients with disabling persistent neurological deficits (Pediatric National Institutes of Health Stroke Scale, PedNIHSS,  $\geq 10$  and  $\leq 30$ ) and radiographically confirmed large-vessel cerebral artery occlusion in centers with angiographic experience treating children.<sup>3,18</sup>

By using a multi-institutional cohort, we report the technical and clinical outcomes in a large North American series of pediatric patients presenting with an AIS with a LVO treated

with mechanical thrombectomy for revascularization. We hypothesized that children treated with thrombectomy can have good neurological outcomes, similar to those seen in adults.

## METHODS

This was a retrospective cohort study of patients from 5 tertiary, level-one pediatric trauma centers in the United States with direct affiliation with accredited comprehensive stroke centers. All children who underwent endovascular thrombectomy for the treatment of AIS secondary to LVOs from April 2017 to April 2019 were included in the cohort (Figure 1). Institutional Review and Privacy Board approvals with a waiver of informed consent were obtained at each participating center before data collection. The STROBE checklist was used in preparation of this report.

Medical and radiology records were used for data abstraction. Demographic information collected included treatment center and patient age, sex, and race. Clinical data included etiology for stroke, initial PedNIHSS score,<sup>19</sup> time from last known normal, PedNIHSS score after thrombectomy, 30- and 90-d pediatric modified Rankin scale (mRS) scores, and whether tissue plasminogen activator (tPA) (Alteplase, Genentech, San Francisco, CA) was administered. Radiology records included vessel involvement, laterality, perfusion imaging, magnetic resonance imaging (MRI), and Alberta Stroke Program early computed tomography (ASPECT) score when available.<sup>20</sup>

Procedural details included sheath size, base catheter, aspiration catheter, stent retriever usage, method of retrieval (either contact

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**TABLE 1. Thrombolysis in Cerebral Infarction Scoring<sup>21</sup>**

Grade	Characterization
0	No perfusion. No anterograde flow beyond the point of occlusion.
1	Penetration with minimal perfusion. The contrast material passes beyond the area of obstruction but fails to opacify the entire cerebral bed distal to the obstruction for the duration of the angiographic run.
2a	Only partial filling (<50%) of the entire vascular territory is visualized.
2b	Partial filling $\geq$ 50% territory.
3	Complete perfusion. Anterograde flow into the bed distal to the obstruction occurs as promptly as into the obstruction and clearance of contrast material from the involved bed is as rapid as from an uninvolved other bed of the same vessel or the opposite cerebral artery.

aspiration, stent retriever, or both, which we describe hereafter as “local aspiration”), whether local aspiration was performed, number of passes, time from puncture to recanalization, and modified Thrombolysis in Cerebral Infarction (mTICI) grade<sup>21</sup> (Table 1). Outcome measures included mTICI grade, discharge PedNIHSS and difference from presentation PedNIHSS, and 90-d pediatric mRS. Adverse events surrounding the thrombectomy procedure were also recorded. The primary outcomes of successful revascularization and good clinical outcome were defined a priori as a mTICI grade of  $\geq$ 2b and a pediatric mRS score of 0 to 2 at 90 d, respectively.

### Patient Selection and Management

In this retrospective study, there were no specific selection criteria; thus, the decision to offer mechanical thrombectomy was done on a case-by-case basis at the discretion of the neurologist and neurointerventionalist. General selection criteria for thrombectomy in the setting of LVO were lesions in the intracranial ICA, first segment of the middle cerebral artery (MCA), anterior cerebral artery, posterior cerebral artery, or basilar artery on computed tomography (CT) angiography, magnetic resonance angiography (MRA), or noncontrast head CT in the setting of focal neurological signs or symptoms.

Additional inclusion criteria were age  $\leq$ 19 yr with initial evaluation and diagnosis at a children’s medical center and no evidence of intracranial hemorrhage (ICH) on CT or MRI. Patients received tPA intravenously at the discretion of the treating neurologist and were routinely started on antiplatelet therapy after thrombectomy (at least 24 h after receiving tPA if applicable). If patients were on systemic anticoagulation for cardiac indications, the decision to start an additional antiplatelet therapy was made by the treating pediatric neurology specialist.

### Mechanical Thrombectomy

Femoral access was obtained in standard fashion using a puncture needle. In most cases, a femoral artery sheath was placed, and then a base catheter was advanced into either the ipsilateral ICA or one of the vertebral arteries. Infrequently, a base catheter was used without concomitant placement of a femoral artery sheath. After catheterization and confirmation of an LVO, a microcatheter and microwire were used to cross the occlusion under roadmap guidance. Endovascular mechanical

thrombectomy was then performed using a stent retriever alone, contact aspiration alone, or a combination of both (ie, local aspiration with stent retriever). In some cases, a balloon guide catheter was used as the base catheter and was inflated during mechanical thrombectomy for circulatory flow arrest.

### Statistical Analysis

Data from all centers were collected and managed by the first author. The data were descriptively reported as mean (SD) or median, with relative proportions as percentages. Descriptive statistics were calculated. Frequencies were calculated for categorical and ordinal variables and means and standard deviations for continuous variables.

## RESULTS

### Patient Characteristics

A total of 23 thrombectomies were performed in 21 children at the 5 institutions. The mean age at thrombectomy was  $11.6 \pm 4.9$  yr of age (median 11.5, range 2.1-19 yr); 52% of patients were female. The median PedNIHSS score on presentation was 13 (range 4-33). The main presentation symptoms were hemiparesis/hemiplegia (10 patients), cranial nerve deficit (3), agitation/unresponsiveness (4), syncope (2), seizure (1), headache (1), and aphasia (2); however, patients experienced multiple symptoms in 13 cases. The median time from last known normal was 363 min (range 70-1440, mean  $514 \pm 436.4$  min). Solitary occlusions were located in the basilar artery (6), ICA (7), and MCA (7), and multiple occlusions occurred in 2 cases: 1 of the left M1 and left A1 segments (patient #11) and 1 tandem occlusion of the right ICA and M1 (patient #21). A total of 9 of the lesions were left sided, 8 were right sided; 6 lacked laterality.

A cardiogenic cause was identified in 14 cases (61%): 2 in the setting of septic emboli (in a single patient who had 2 procedures), 2 left ventricular assist device (LVAD), 1 atrial fibrillation, 1 heart block, 5 congenital defects (2 atrial septal defect (in a single patient who had 2 procedures), 1 patent foramen ovale, 1 ventricular septal defect, and 1 paradoxical embolization), 1 Wolf-Parkinson-White syndrome and hypertrophic cardiomyopathy, and 2 after cardiac catheterization. Dissection was the cause in 6 (29%), and cryptogenic causes in 3 (14%).

CT angiography (CTA) was used to diagnose the occlusion in 14 patients, MRA in 4, 2 patients underwent both CTA and MRA, and 3 patients only underwent head CT showing hyperdensity along the vessel and were presumed to have LVO. Only 4 patients had perfusion imaging before intervention, and 10 patients had MRI before thrombectomy. The median ASPECT score on CT scan was 9 (range 4-10).

Two patients underwent 2 separate thrombectomies (Table 2). For patient #1, the repeat thrombectomy was performed in the same setting in a different vascular distribution. Patient #11 experienced reocclusion in a similar distribution (left M2 initially followed by left M1/A1 48 h later).

**TABLE 2. Thrombectomy Device Use for Pediatric Cases**

Patient #/age (years)	Location of occlusion	Baseline MRI or CT perfusion imaging	ASPECTS score	Femoral sheath used (Y/N)/Size	Base catheter	Aspiration catheter	Stent retriever	Contact aspiration or stent retriever thrombectomy (device used if available)	Local aspiration <sup>a</sup>	Number of passes	TICI score
1/4	Basilar, ICA <sup>b</sup>	MRI	NA	Yes/5F	UCSF II	None	Yes	Stent retriever (Solitaire 4 × 20) <sup>c</sup>	No	2 in 1st; 4 in 2nd	2b
2/17	Basilar	MRI	NA	Yes/9F	Neuron Max 088	ACE 64	No	Contact aspiration	No	6	2a
3/17	Basilar	None	NA	Yes/8F	7F Concentric BGC	None	Yes	Stent retriever (Solitaire 4 × 20) <sup>c</sup>	No	3	2a
4/16	Basilar	MRI	NA	Yes/9F	8F Concentric BGC	None	Yes	Stent retriever (Solitaire 4 × 20) <sup>c</sup>	No	2	3
5/10	MCA	None	7	Yes/6F	6F Envoy MPD	3 MAX	Yes	Stent retriever (Solitaire 4 × 20) <sup>c</sup>	Yes	3	3
6/14	ICA	CT perfusion	9	Yes/7F	7F Concentric BGC	4.3F DAC	Yes	Stent retriever (Solitaire 4 × 20) <sup>c</sup>	Yes	1	3
7/17	Basilar	None	NA	Yes/7F	7F Concentric BGC	None	Yes	Stent retriever (Solitaire 4 × 20) <sup>c</sup>	No	1	2b
8/12	MCA	CT perfusion	9	Yes/7F	Benchmark 071	None	Yes	Stent retriever (Solitaire 4 × 40) <sup>c</sup>	No	1	3
9/9	MCA	None	NA	Yes/6F	6F shuttle	None	Yes	Stent retriever (Trepo 4 × 20, 6 × 25) <sup>d</sup>	No	5	2b
10/11	ICA	None	NA	Yes/8F	8F Flowgate BGC	None	Yes	Stent retriever (Trepo 4 × 30) <sup>d</sup>	No	1	3
11/19	M2, M1/A1 <sup>p</sup>	MRI	NA	Yes/8F	8F Flowgate BGC	CAT6 in 1st, ACE68 in 2nd	Yes	Stent retriever (Trepo 4 × 30, 6 × 25) <sup>d</sup>	Yes	1 in 1st, 4 in 2nd	3 in 1st, 3 in 2nd
12/17	ICA	None	NA	Yes/8F	8F Flowgate BGC	ACE 68	Yes	Stent retriever (Trepo 4 × 30, 6 × 25) <sup>d</sup>	Yes	4	2c
13/8	MCA	None	NA	Yes/8F	8F Flowgate BGC	CAT6	Yes	Stent retriever (Trepo 4 × 20, 6 × 25) <sup>d</sup>	Yes	4	2b
14/11	MCA	MRI	NA	No	Infiniti 088	ACE68	Yes	Stent retriever (Solitaire 4 × 20) <sup>c</sup>	Yes	1	3
15/8	ICA	MRI	NA	No	Infiniti 088	CAT5	No	Contact aspiration	No	3	2b
16/15	MCA	MRI	9	Yes/6F	Neuron Max	5 Max	No	Contact aspiration	No	3	3
17/6	ICA	MRI	9	Yes/6F	Neuron Max	5 Max	No	Contact aspiration	No	2	2b
18/2	MCA	None	4	Yes/5F	Envoy 5F	044 Revive	Yes	Stent retriever (Solitaire 4 × 40) <sup>c</sup>	Yes	3	2a
19/4	Basilar	MRI	NA	Yes/5F	Envoy 5F	None	Yes	Stent retriever (Solitaire 4 × 40) <sup>c</sup>	No	3	2b
20/17	ICA	CT perfusion	10	Yes/6F	Neuron Max	JET 7	Yes	Stent retriever (Solitaire 4 × 40) <sup>c</sup>	Yes	2	3
21/10	ICA/M1	CT perfusion	8	Yes/8F	Neuron Max	4 Max	Yes	Stent retriever (Solitaire 4 × 40) <sup>c</sup>	Yes	2	3

ICA, internal carotid artery; MCA, middle cerebral artery; MRI, magnetic resonance imaging; CT, computed tomography; NA, not available; BGC, balloon guide catheter.

<sup>a</sup>Contact aspiration and stent retriever both used.

<sup>b</sup>Two separate thrombectomy procedures in the same patient.

<sup>c</sup>Medtronic, Irvine, California, USA.

<sup>d</sup>Stryker, Fremont, California, USA.

## Procedural Characteristics and Interventions

Two patients received intravenous tPA before endovascular therapy (patients #14 and #15), 1 child received intra-arterial tPA (patient #1) prior to mechanical thrombectomy, and 1 patient was given half-dose eptifibatid (Integrilin, Baxter International Inc, Deerfield, Illinois) for persistent re-occlusion and placed on a continuous drip for 24 h (patient #3).

General anesthesia was used in all but 2 cases (patients #16 and #20). All cases were performed using a transfemoral approach; right femoral groin access was used in all cases, with groin sheaths ranging in size: 9F (2 cases), 8F (7 cases), 7F (3 cases), 6F (5 cases), and 5F (4 cases). Two cases involved no sheath. The procedural details are similar to those published previously for adult thrombectomy.<sup>12-14</sup> The types of base catheters and aspiration catheters used varied across institutions; a detailed assessment of technical details is reported in Table 2. The median number of passes was 3 (range 1-6). Stent retrievers were used in 19/23 (83%) cases; contact aspiration only was employed in 4/20 (20%) cases. Concomitant local aspiration was performed in 10 cases when a stent retriever was used (53%). The median time from puncture to recanalization was 56 min (range 18-158, mean 73.3  $\pm$  46.8 min).

## Outcomes

A total of 19 (83%) of the thrombectomy procedures resulted in mTICI  $\geq$  2b recanalization (Tables 1 and 2, Figures 2 and 3). The median PedNIHSS score at discharge was 2 (range 0-26), yielding a mean reduction of 11.3  $\pm$  6.1. A total of 14 (66%) patients had a pediatric mRS of 0 to 2 at 30-d follow-up; 18/21 (86%) achieved this by 90 d. The median pediatric mRS was 1 (range 0-4) at 30 d and 1 (range 0-5) at 90 d. There was 1 adverse event in which a patient required a blood transfusion after thrombectomy—secondary to chronic cardiac illness and not from a groin hematoma. A mTICI score of  $\geq$  2b was achieved in 3 of 4 (75%) instances when contact aspiration alone was used. No additional stenting procedures were performed in any children. There were no immediate neurological complications. No children required decompressive hemicraniectomy. Additionally, no patients experienced delayed ICH. There was 1 death > 90 d after thrombectomy from cardiac complications.

For the 6 children who had a pediatric mRS score of  $\geq$  3 at 30 d, the median age was 11 yr (mean 16 yr). Similarly, in the 3 children with pediatric mRS  $\geq$  3 at 90 d, the median age was 8 yr (mean 9 yr).

## Anterior Circulation vs Posterior Circulation

A total of 6 thrombectomy procedures were performed for basilar artery occlusions in patients with a mean age of 12.5 yr (median 16.5, range 4-17 yr). About 66% had a pediatric mRS < 3 at 30-d follow-up and 100% at 90-d follow-up. The median preprocedure PedNIHSS was 10 (range 5-25), and after thrombectomy the median was 1 (range 0-5).

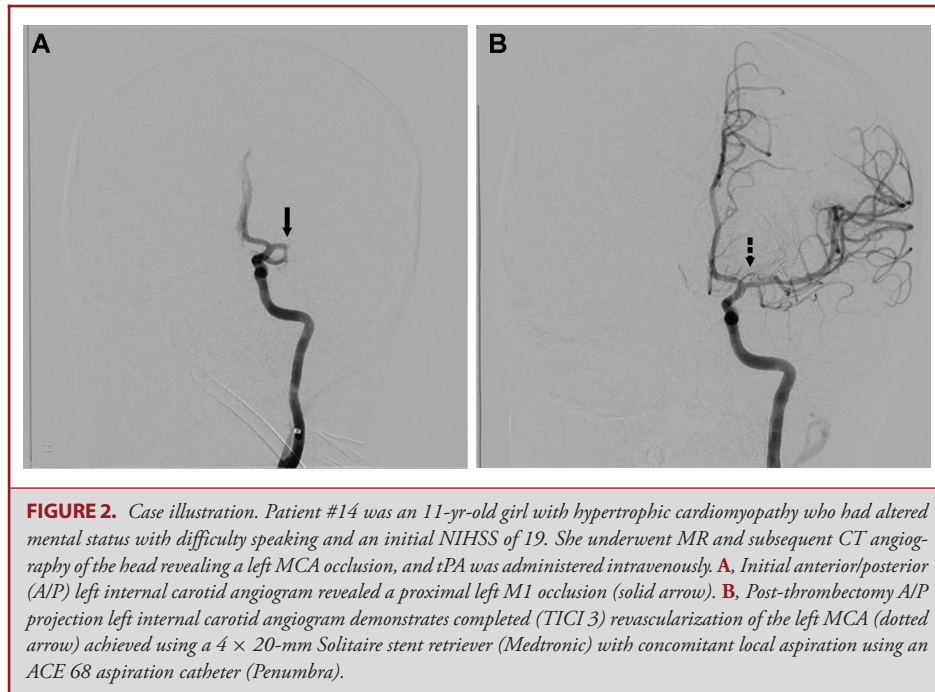
A total of 17 thrombectomy procedures were performed for anterior circulation pathology (Table 2) in patients with a mean age of 11.6 yr (median 11, range 4-19 yr). The median 30-d pediatric mRS was 2 (0-4). The median 90-d pediatric mRS was 1 (0-4), with 86% with a pediatric mRS < 3. The median preprocedure PedNIHSS was 14 (range 4-25), and after thrombectomy the median was 2 (range 0-6).

## DISCUSSION

We present a contemporary series of pediatric patients undergoing mechanical thrombectomy for LVO in which a recanalization of at least mTICI 2b was achieved in 83% of cases and 86% of children had a pediatric mRS of 0 to 2 at 90 d. Thrombectomy was done at median time from last known normal of 363 min and a mean of 514 min. Our findings supported the hypothesis that children treated with thrombectomy can have good neurological outcomes with successful technical revascularization.

In 2017, Cobb et al<sup>15</sup> performed a comprehensive review of 68 cases of endovascular treatment of stroke in pediatric patients ranging from 1.8 to 18 yr of age. The average time to treatment was 13.7 h with a maximum of 72 h, representing a significantly later time to treatment compared with the patients in our series. A total of 24 (35%) patients in that study underwent endovascular treatment with use of intra-arterial fibrinolytics alone, with the remaining 44 (65%) patients undergoing mechanical thrombectomy (29 underwent mechanical thrombectomy alone, 5 had mechanical thrombectomy after intravenous tPA administration, and 10 had concomitant intra-arterial tPA administration). TICI 2b/3 recanalizations were achieved in 67.2%, and 65.7% of patients experienced a good clinical outcome, with a 5.3-mo average follow-up time.<sup>15</sup> Patients who underwent mechanical thrombectomy experienced better TICI 2b/3 recanalization rates (79.1% vs 38.9%;  $P = .0020$ ), more good clinical outcomes (79.5% vs 20.5%;  $P = .001$ ), and fewer complications (13.6% vs 37.5%;  $P = .006$ ) than those treated with intra-arterial fibrinolysis alone.<sup>15</sup> In contrast, our operators used a stent retriever in a higher proportion of patients and achieved a higher rate of mTICI 2b/3 recanalization. The clinical outcomes reported herein were also better, likely owing to the superior revascularization rate. Of note, however, our clinical and radiographic outcomes were very similar to the subgroup of 44 patients reported by Cobb et al who underwent mechanical thrombectomy, reflecting the apparent superiority of endovascular mechanical thrombectomy over intra-arterial fibrinolysis alone.

Shoirah et al<sup>22</sup> reported 19 cases of thrombectomy with similar rates of successful revascularization (89.5%), good neurological outcomes at 90 d (89.5%), but a smaller reduction in NIHSS from admission to discharge (10.2, vs 11.5 in the current series). Like the patients included in our series, no children were treated with primarily intra-arterial tPA, and only a minority of patients



**FIGURE 2.** Case illustration. Patient #14 was an 11-yr-old girl with hypertrophic cardiomyopathy who had altered mental status with difficulty speaking and an initial NIHSS of 19. She underwent MR and subsequent CT angiography of the head revealing a left MCA occlusion, and tPA was administered intravenously. **A.** Initial anterior/posterior (A/P) left internal carotid angiogram revealed a proximal left M1 occlusion (solid arrow). **B.** Post-thrombectomy A/P projection left internal carotid angiogram demonstrates completed (TICI 3) revascularization of the left MCA (dotted arrow) achieved using a 4 × 20-mm Solitaire stent retriever (Medtronic) with concomitant local aspiration using an ACE 68 aspiration catheter (Penumbra).

who underwent mechanical thrombectomy had intravenous tPA administered. The median last known well to groin puncture time was 323 min, which was also very similar to our series. Interestingly, there were a higher proportion of patients who underwent endovascular mechanical thrombectomy with contact aspiration with a shorter time from groin puncture to recanalization in the study by Shoirah et al.<sup>22</sup>

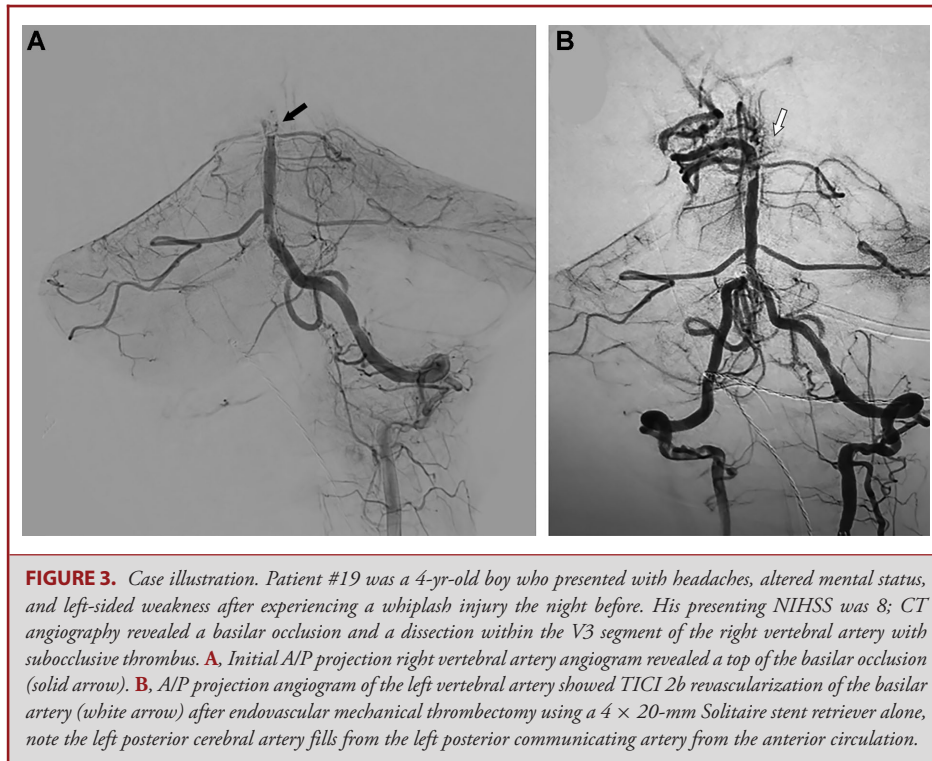
Historically, AIS in children is an area of ongoing research interest. An open-label multicenter NIH-sponsored trial (Thrombolysis in Pediatric Stroke) of the use of intravenous tPA and intra-arterial thrombolysis was terminated early because of an inability to recruit patients.<sup>23,24</sup> In a meta-analysis of 113 cases of mechanical thrombectomy performed in 110 patients,<sup>25</sup> ~91% had good long-term neurological outcomes defined as mRS 0 to 2 and 88% had successful angiographic recanalization (mTICI score 2b/3) offering Level C evidence that thrombectomy for LVO should be considered in patients aged 1 to 18 yr (Class IIb recommendation). This is in parallel with the 83% successful revascularization and 86% with good long-term neurological outcomes achieved in our study. Although there were 2 deaths as a result of ICH among the 113 cases reported in the meta-analysis, there were no cases of ICH in the current series.

More recent findings in 73 children treated at 27 centers across the US and Europe demonstrated the safety profile for thrombectomy in children does not differ from that of adult patients in randomized clinical trials.<sup>26</sup> The median age of 11.3 yr was very similar to the current cohort, and their reported median mRS score of 1 at 6 mo and 24 mo with longer-term follow-up

was also similar to ours. They also reported a lower proportion of symptomatic ICH events in their retrospective cohort vs adults (1.37 vs 2.79). The authors also performed a subanalysis with respect to age and demonstrated worse NIHSS, mRS, and ASPECT scores on follow-up in younger patients (ages 0–6 yr). Our investigation did not find similar conclusions; the 6 children with a pediatric mRS  $\geq 3$  at 30 d had a median age of 11 yr (mean 16 yr) and the 3 children with pediatric mRS  $\geq 3$  at 90 d had median age of 8 yr (mean 9 yr). These contradictory data may be secondary to nonuniform selection criteria and indicate further study is needed and careful consideration should be given to young children with LVO.

One of the pediatric patients included in this series was previously published as a case of mechanical thrombectomy in the setting of a LVAD.<sup>5,22</sup> Two of our patients underwent 2 separate thrombectomies. Ikenberg et al<sup>27</sup> reported that 40% of recurrent LVOs requiring repeat thrombectomy occur in the same location as the prior occlusion. We speculate this may occur secondary to intrinsic vessel injury at the initial site of occlusion and/or global hypercoagulability; maintaining patients on systemic antiplatelet agents or anticoagulation may help prevent this, but this hypothetical at this point.

There were no access-related complications in this series in the 90-d period; however, long-term complications including leg length discrepancies and arterial occlusions may develop in a delayed fashion. The larger French catheters used in this series are a reflection of a large number of teenage patients. It is imperative to consider access-related morbidity when treating children because it is thought to be more prominent among younger



children. Heran et al<sup>28</sup> reported that more access-related complications are observed in children <15 kg.

### Challenges in Pediatric Ischemic Stroke

Management of AIS can be challenging in the pediatric population because of delayed recognition; although children are commonly brought in early after symptom onset (1.7 h after onset), there is a 12.7-h median time to diagnosis, with >50% of diagnoses made >24 h after arrival.<sup>29-32</sup> The differential diagnoses that often deter the primary evaluation of children with stroke include epilepsy, complex migraine headaches, varying presentation of inflammatory disease, intracranial infection, and brain tumors.<sup>15</sup> This delay in diagnosis and, in turn, treatment represents a crucial factor and potential improvement in the care of pediatric patients with AIS.

There is, as yet, no level I evidence for the use of intravenous tPA within 4.5 h of symptom onset and mechanical thrombectomy for LVO within 6 h of symptom onset in pediatric patients as in adults.<sup>13,14,33</sup> The most recent recommendations by the American Heart Association include only conservative measures (eg, maintaining normal temperature, good oxygenation, and blood pressure control and avoiding hyper- and hypoglycemia) because there are no additional level I recommendations. The guidelines provide information on dosing, but not indications, for antiplatelet and anticoagulant medications.<sup>34</sup> The recent trials demonstrating successful broadening of the time window for mechanical thrombectomy in adult

AIS continue to push the field forward.<sup>35,36</sup> The findings of our study, with median time from last normal of 380 min, reflecting a large proportion of “late-window” patients, and a good clinical outcome rate of 80%, adds to the evidence supporting thrombectomy for LVO in pediatric patients, particularly in those presenting >6 h from onset. Strict selection criteria need to be developed for delayed thrombectomy; in our investigation, 13 thrombectomies occurred after >360 min (6 h), and 8 of those had imaging to support the presence of penumbra that could benefit from revascularization (5 MRI, 3 CT perfusion).<sup>37</sup>

We did discover an improvement of pediatric mRS from 30 d to 90 d, which may be a reflection of broader pediatric brain plasticity relative to adults, and this may imply that the natural history of untreated AIS in children is likely quite different than in adults.

### Limitations

There are several limitations of this study. The retrospective design of the study is inherently limited by the information available in the electronic medical record. Although this represents the experience of 5 stroke centers, treatment and practice patterns were not standardized. Treatment decisions were made on a case-by-case basis often by multidisciplinary teams, so treatment bias and techniques used by each center make generalization difficult. The small sample size makes comparison of thrombectomy techniques difficult; further study of each technique is necessary.

Because this study was retrospective and only included children who underwent thrombectomy, there is no comparison with those not treated with endovascular therapy and, in applicable cases, with intravenous thrombolysis. An additional significant limitation includes the lack of uniform tPA treatment protocol at each of the centers, which is a reflection of limited experience at pediatric centers with LVO. Although this is a multicenter study, larger numbers of sites and patients are needed to analyze efficacy for different treatment modalities and provide conclusions and recommendations based on these data.

## CONCLUSION

Endovascular thrombectomy can be efficacious in pediatric patients. The technical and clinical success in >80% of patients in our study support the concept of revascularization for LVO in pediatric patients.

## Disclosures

Dr Taussky is a consultant for Medtronic, Stryker Neurovascular, and Cerenovus. Dr Hassan is a consultant for Medtronic, Stryker, Microvention, Penumbra, Balt, GE Healthcare, Genentech, and Viz. Dr Zaidi is a consultant for Microvention. Dr Kan is a consultant for Stryker Cerebrovascular. Dr Grandhi is a consultant for Medtronic Neurovascular, Cerenovus, and BALT Neurovascular. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article. The views expressed herein are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the US Government.

## REFERENCES

- Fullerton HJ, Wu YW, Zhao S, Johnston SC. Risk of stroke in children: ethnic and gender disparities. *Neurology*. 2003;61(2):189-194.
- Engle R, Ellis C. Pediatric stroke in the U.S.: estimates from the kids' inpatient database. *J Allied Health*. 2012;41(3):e63-e67.
- Ellis MJ, Amlie-Lefond C, Orbach DB. Endovascular therapy in children with acute ischemic stroke: review and recommendations. *Neurology*. 2012;79(13 Suppl 1):S158-S164.
- deVeber GA, MacGregor D, Curtis R, Mayank S. Neurologic outcome in survivors of childhood arterial ischemic stroke and sinovenous thrombosis. *J Child Neurol*. 2000;15(5):316-324.
- Stowe RC, Kan P, Breen DB, Agarwal S. Mechanical thrombectomy for pediatric acute stroke and ventricular assist device. *Brain Dev*. 2018;40(1):81-84.
- Alnaami I, Buchholz H, Ashforth R, et al. Successful use of solitaire FR for stroke in a pediatric ventricular assist device patient. *Ann Thorac Surg*. 2013;96(3):e65-e67.
- Rhee E, Hurst R, Pukenas B, et al. Mechanical embolectomy for ischemic stroke in a pediatric ventricular assist device patient. *Pediatr Transplant*. 2014;18(3):E88-E92.
- Byrnes JW, Williams B, Prophan P, et al. Successful intra-arterial thrombolytic therapy for a right middle cerebral artery stroke in a 2-year-old supported by a ventricular assist device. *Transpl Int*. 2012;25(3):e31-e33.
- Abma R. Diagnosing and treating childhood stroke. *Neurol Rev*. 2010;18(9):7.
- Malhotra K, Gornbein J, Saver JL. Ischemic strokes due to large-vessel occlusions contribute disproportionately to stroke-related dependence and death: a review. *Front Neurol*. 2017;8:651.
- Smith WS, Lev MH, English JD, et al. Significance of large vessel intracranial occlusion causing acute ischemic stroke and TIA. *Stroke*. 2009;40(12):3834-3840.
- Arnold M, Schroth G, Gralla J. Endovascular treatment for acute ischemic stroke. *N Engl J Med*. 2013;368(25):2431.
- Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372(24):2296-2306.
- Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372(11):1019-1030.
- Cobb MIH, Laarakker AS, Gonzalez LF, Smith TP, Hauck EF, Zomorodi AR. Endovascular therapies for acute ischemic stroke in children. *Stroke*. 2017;48(7):2026-2030.
- Gervelis WL, Golomb MR. Mechanical thrombectomy in pediatric stroke: report of three new cases. *J Stroke Cerebrovasc Dis*. 2020;29(2):104551.
- Satti S, Chen J, Sivapatham T, Jayaraman M, Orbach D. Mechanical thrombectomy for pediatric acute ischemic stroke: review of the literature. *J Neurointerv Surg*. 2017;9(8):732-737.
- Burger IM, Murphy KJ, Jordan LC, Tamargo RJ, Gailloud P. Safety of cerebral digital subtraction angiography in children: complication rate analysis in 241 consecutive diagnostic angiograms. *Stroke*. 2006;37(10):2535-2539.
- Ichord RN, Bastian R, Abraham L, et al. Interrater reliability of the pediatric national institutes of health stroke scale (PedNIHSS) in a multicenter study. *Stroke*. 2011;42(3):613-617.
- Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS study group. Alberta stroke programme early CT score. *Lancet*. 2000;355(9216):1670-1674.
- Zaidat OO, Yoo AJ, Khatri P, et al. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. *Stroke*. 2013;44(9):2650-2663.
- Shoimah H, Shallwani H, Siddiqui AH, et al. Endovascular thrombectomy in pediatric patients with large vessel occlusion. *J Neurointerv Surg*. 2019;11(7):729-732.
- Amlie-Lefond C, Chan AK, Kirton A, et al. Thrombolysis in acute childhood stroke: design and challenges of the thrombolysis in pediatric stroke clinical trial. *Neuroepidemiology*. 2009;32(4):279-286.
- Amlie-Lefond C, deVeber G, Chan AK, et al. Use of alteplase in childhood arterial ischaemic stroke: a multicentre, observational, cohort study. *Lancet Neurol*. 2009;8(6):530-536.
- Bhatia K, Kortman H, Blair C, et al. Mechanical thrombectomy in pediatric stroke: systematic review, individual patient data meta-analysis, and case series. *J Neurosurg Pediatr*. published online: August 9, 2019 (doi:10.3171/2019.5.PEDS19126).
- Sporns PB, Strater R, Minnerup J, et al. Feasibility, safety, and outcome of endovascular recanalization in childhood stroke: the save child's study. *JAMA Neurol*. 2019;77(1):25-34.
- Ikenberg B, Rosler J, Seifert CL, et al. Etiology of recurrent large vessel occlusions treated with repeated thrombectomy. *Interv Neuroradiol*. 2020;26(2):195-204.
- Heran MK, Abruzzo TA. Diagnostic cerebral angiography and the Wada test in pediatric patients. *Tech Vasc Interv Radiol*. 2011;14(1):42-49.
- McGlennan C, Ganesan V. Delays in investigation and management of acute arterial ischaemic stroke in children. *Dev Med Child Neurol*. 2008;50(7):537-540.
- Gabis LV, Yangala R, Lenn NJ. Time lag to diagnosis of stroke in children. *Pediatrics*. 2002;110(5):924-928.
- Mallick AA, Ganesan V, Kirkham FJ, et al. Diagnostic delays in paediatric stroke. *J Neurol Neurosurg Psychiatry*. 2015;86(8):917-921.
- Goldenberg NA, Bernard TJ, Fullerton HJ, Gordon A, deVeber G, International Pediatric Stroke Study Group. Antithrombotic treatments, outcomes, and prognostic factors in acute childhood-onset arterial ischaemic stroke: a multicentre, observational, cohort study. *Lancet Neurol*. 2009;8(12):1120-1127.
- Saver JL, Goyal M, Bonafe A, et al. Solitaire with the intention for thrombectomy as primary endovascular treatment for acute ischemic stroke (SWIFT PRIME) trial: protocol for a randomized, controlled, multicenter study comparing the solitaire revascularization device with IV tPA with IV tPA alone in acute ischemic stroke. *Int J Stroke*. 2015;10(3):439-448.
- Roach ES, Golomb MR, Adams R, et al. Management of stroke in infants and children: a scientific statement from a special writing group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the Young. *Stroke*. 2008;39(9):2644-2691.
- Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378(1):11-21.
- Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378(8):708-718.



37. Lee S, Heit JJ, Albers GW, et al. Neuroimaging selection for thrombectomy in pediatric stroke: a single-center experience. *J Neurointerv Surg.* 2019;11(9):940-946.

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### COMMENT

**T**he authors present a retrospective study of twenty-one cases of pediatric thrombectomy at 5 US centers. The authors are to be commended on their study involving a rare, though growing condition.

There are a few notable takeaways from this paper. First, the long time between last known normal and treatment and accordingly low use of tPA. This demonstrates that there is both a difficulty in diagnosis as well as a need for increased education among pediatric specialists. The other interesting aspect of this paper is the table demonstrating the various devices used in children of different ages, which is an important refresher for endovascular neurosurgeons who may not perform routine pediatric interventions.

This paper along represents a useful addition to the pediatric thrombectomy literature along with the SAVE CHILDS STUDY published last year.

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