Pediatric Thrombectomy: Design and Workflow Lessons from Two Experienced Centers

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Abstract

Endovascular thrombectomy (EVT) has played a major role in advancing adult stroke care and may serve a similar role in pediatric stroke care. However, there is a need to develop better evidence and infrastructure for pediatric stroke care. In this work, we review two experienced pediatric EVT programs and examine key design features in both care environments, including a formalized protocol and workflow, integration with an adult EVT workflow, simplification and automation of workflow steps, pediatric adaptations of stroke imaging, advocacy of pediatric stroke care, and collaboration between providers, among others. These essential features transcend any single hospital environment and may provide an important foundation for other pediatric centers that aim to enhance the care of children with stroke.

Keywords

Acute ischemic stroke; pediatric stroke; stroke workflow; Acute stroke; Pediatrics; Thrombectomy

BACKGROUND

Endovascular thrombectomy (EVT) has proven remarkably effective in treating adults suffering from acute ischemic stroke (AIS) caused by large vessel occlusion (LVO)[1–7]. As a result, considerable effort has been directed toward improving patient triage, facilitating ambulance transport, and optimizing in-hospital clinical workflows to enhance the

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accessibility and efficacy of EVT[8–12]. These process improvements have dramatically increased the number of EVT procedures performed, reducing the overall population burden of disability caused by AIS[13,14].

As many as 70% of children with AIS experience persistent neurologic deficits, with impact felt over decades[15]. Unfortunately, a randomized trial of EVT in childhood AIS is unlikely given the lower incidence of AIS in children compared to adults, relative lack of concentrated pediatric AIS expertise, and perceived loss of equipoise given the strength of adult EVT data. Thus, despite promising outcomes in case reports and case series[16–18] and the development of informal criteria for primary pediatric stroke center designation[19], EVT in children remains an off-label procedure without established guidelines[20,21].

There is a clear need to collect prospective outcome data for EVT in children. In tandem with these efforts, there is a strong operational need to bolster pediatric stroke expertise and pediatric stroke care infrastructure in a variety of settings. While every health system with a pediatric hospital is unique, stroke care can be broadly classified based on the geographical relationship of the pediatric hospital with a partnered adult stroke hospital with EVT experience. Specifically, sites may be considered co-located if they are sufficiently close that vehicular patient transport is not needed between sites, or separated if vehicular transport is needed.

Here, we describe two successful pediatric thrombectomy programs, one co-located and one separated, and review key design features that are likely to be important for other qualified centers that aspire to implement pediatric EVT capability and reduce the long-term harms of pediatric AIS.

THROMBECTOMY PROGRAM ORGANIZATION

Organization of centers reviewed in this work are outlined here and serve as prototypical examples of pediatric EVT programs. Local institutional review board approval was not required for this study.

Co-Located Hospitals

St. Louis Children's Hospital (SLCH) is a free-standing pediatric hospital that is physically connected by enclosed walkways to Barnes-Jewish Hospital, an adult comprehensive stroke center that accepts acute neurovascular referrals from over 40 surrounding hospitals. Both hospitals are part of a large, university-affiliated academic health system centered in the metropolitan area of St. Louis, Missouri. Physicians at both hospitals belong to the same academic physician group and may have privileges at one or both hospitals. Non-physician staff and resources at these two hospitals are administratively separate.

Separated Hospitals

Seattle Children's Hospital (SCH) is a free-standing pediatric hospital located 6 miles from the University of Washington Medicine Stroke Center at Harborview Medical Center, a comprehensive stroke center that accepts acute neurovascular referrals from a multi-state region. Both hospitals are part of a large, university-affiliated academic health system

centered in the metropolitan area of Seattle, Washington. Physicians at both hospitals belong to the same academic physician group and may have privileges at one or both hospitals. Non-physician staff and resources at these two hospitals are administratively separate.

EXAMPLE CLINICAL WORKFLOW

Specific workflow steps inevitably vary based on hospital organization and resource availability. However, key components of any thrombectomy workflow include triage, stroke code, imaging, acute medical intervention, neurointerventional radiology (NIR) consultation, NIR activation, transport, endovascular treatment, and post-EVT care (Figure 1). Here, we describe major workflow steps alongside specific implementation at SLCH, which is similar to SCH.

Triage and Stroke Code

Upon recognition of possible AIS in a child, a pediatric stroke code is activated from anywhere in the hospital or via a centralized hospital operator for a patient en route to the emergency department. The hospital operator then immediately sends a page to the pediatric neurology resident physician and pediatric vascular neurology attending physician with the patient's name, location, and contact phone number.

Simultaneous with stroke code, staff already with the patient obtain pre-specified labs for medical workup, ECG, and non-contrast head CT. The pediatric neurology resident evaluates the patient as soon as possible, focusing on obtaining history, time last seen well, and neurological examination including pediatric NIH Stroke Scale (PedNIHSS). Labs typically include CBC with differential, electrolytes, glucose, prothrombin time, partial thromboplastin time, erythrocyte sedimentation rate, basic toxicology screen, and in females of childbearing age, beta human chorionic gonadotropin. Blood gases and blood coagulation assays such as INR are tested if needed.

Imaging

If initial evaluation suggests the possibility of AIS due to LVO and the patient may be a candidate for EVT, additional neuroimaging is performed using a hyperacute stroke MRI/MRA protocol comprising diffusion-weighted imaging (DWI), time-of-flight magnetic resonance angiography (MRA), fluid-attenuated inversion recovery (FLAIR), along with optional susceptibility-weighted imaging and dynamic susceptibility contrast-enhanced perfusion-weighted imaging (PWI). Required sequences collectively require about 15 minutes to prepare and acquire on a 1.5T system (Siemens Aera, Erlangen, Germany).

A neurologist (resident, fellow, and/or attending) is present in the control room during the scan and a diagnostic neuroradiologist (fellow or attending) is either in the control room or remotely reviewing images in real time. The protocol intentionally prioritizes DWI and MRA sequences that allow identification of infarct and large vessel occlusion, respectively, but excludes T1- or T2-weighted imaging to expedite imaging.

DWI and MRA (and PWI, if performed) sequences are sent for automated processing by RAPID software (iSchemaView, Menlo Park, CA). If a patient cannot safely undergo MRI,

CT angiography can be performed instead. CT perfusion is not performed in children in consideration of radiation dose.

Acute Medical Intervention

In concert with this evaluation, acute medical intervention is undertaken to maintain brain perfusion by initiating blood pressure control, hemodynamic stabilization, and antipyretic measures. Intravenous alteplase is considered based on pre-specified criteria[22] and non-contrast head CT or, ideally, brain MRI. If eligible, consent is obtained and intravenous alteplase is administered.

NIR Consultation

If neuroimaging reveals LVO and other clinical and radiological selection criteria (Table 1) are met, the pediatric neurology resident pages the NIR physician to discuss possible EVT. This discussion follows a pre-specified script (Figure 2) to ensure that necessary information is conveyed with high fidelity. This script is distributed to pediatric neurology residents in the form of an "on-call card" that each resident carries at all times.

NIR Activation

If the neurologist and NIR physician agree that EVT is indicated, the pediatric neurologist will contact the hospital operator to activate the "thrombectomy pager" (Figure 3). Activating the thrombectomy pager leads to immediate recruitment of personnel relevant for pediatric AIS care (Table 2).

Transport

The patient is physically transported from the pediatric hospital to the adult hospital under the supervision of a pediatric ICU physician. Upon arrival to the NIR suite but before the start of EVT, the pediatric ICU attending and anesthesiologist engage in another scripted handoff.

Endovascular Treatment

Pediatric EVT is performed under general anesthesia with close attention to intraoperative blood pressure. Pediatric EVT technique is similar to adult EVT technique and generally involves either aspiration or stent-retriever thrombectomy, typically from a right femoral arterial approach. Intra-arterial thrombolytics are available but rarely used. Hemostasis at the arterial access site is achieved with manual compression, after which the NIR physician discusses the outcome of the case with the neurologist as well as the patient's family.

Post-EVT Care

Following EVT, the patient is transported back to either a general or cardiac ICU at the pediatric hospital for close neurological monitoring and frequent vascular assessment. The duration of post-procedure extremity immobilization is recommended by the neurointerventionalist. Because seizures after AIS are common in children[23,24], electroencephalography (EEG) lead placement is considered to monitor for seizures and

evolving background asymmetry that may prompt acute head imaging. All involved teams evaluate the patient's condition on the day following the thrombectomy procedure.

Alternate Modes of Presentation—The specified clinical workflow is flexible and can accommodate children who present for EVT from settings other than the emergency department. For inpatients, the overall protocol remains similar aside from slight modifications to accommodate the different physical path used to transport patients to the NIR suite. For patients transferred from other centers, the protocol allows bypass of evaluation steps (e.g., neuroimaging) that have been completed elsewhere.

KEY ELEMENTS OF PROGRAMMATIC SUCCESS

While protocol and workflow details differ between our two centers, there are numerous shared design elements that have been key to success. These elements may be foundational design considerations for centers that aim to develop and implement pediatric EVT protocols. A suggested checklist for centers seeking to implement pediatric EVT is provided in Figure 4.

Formalized Protocol and Workflow

A clinical protocol for pediatric EVT was first implemented at SCH in August 2015 and SLCH in May 2018. At both centers, the protocol was developed collaboratively with a pediatric vascular neurologist, neurointerventional radiologist, pediatric anesthesiologist, and diagnostic neuroradiologist, with additional key input from pediatric neurosurgeons, pediatric intensivists, adult anesthesiologists, and pediatric cardiologists. While specific steps and criteria are tailored to account for each hospital's individual strengths, the existence of a formalized protocol that has been developed by a multidisciplinary team of physicians and approved by appropriate hospital leadership is crucial to define and encourage adherence to expected care pathways.

Among the most important elements of a formalized protocol are key inclusion and exclusion criteria for pediatric EVT. While these criteria vary between centers based on the judgment and capability of local experts, and children outside of these criteria can be considered on a case-by-case basis, the process of establishing interdisciplinary consensus is critical for program cohesion and dissemination.

Integration with Adult EVT Workflow

Our protocols take advantage of the close affiliation our pediatric hospitals have with high-volume adult EVT centers. At each site, the pediatric protocol closely mirrors the adult protocol to harness the greater familiarity that stroke physicians have with more commonly used adult workflows. In this manner, potential confusion arising from infrequent activation of the pediatric EVT protocol is mitigated by the large number of adult EVT cases. The parallels between pediatric and adult EVT workflows go beyond superficial similarities. For example, the name and function of the thrombectomy pager are identical in both workflows. This mimicry also allows the pediatric stroke workflow to benefit from improvements in adult stroke workflow[25].

Simplicity and Automation

Our adult EVT protocols are streamlined to achieve better clinical outcomes via reduced door-to-puncture times[8,26,27], and our pediatric EVT protocol is similarly simplified and automated. For example, pre-EVT imaging loads automatically to a mobile viewer. Similarly, the thrombectomy pager notifies key personnel of impending EVT using a single point of contact. The implementation of a consultation script ensures that key information is consistently obtained and that effort is not expended gathering superfluous information.

Pediatric Adaptation of Stroke Imaging

Imaging should be adapted to the particular needs and challenges of imaging young patients. Evaluation of suspected LVO using MRI rather than CT may be particularly beneficial in children. MRI can confirm stroke, which is important due to the high incidence of stroke mimics in childhood[28,29]. It is also much more sensitive than CT to posterior circulation stroke[30], which accounts for up to half of all childhood stroke[31,32].

MRI also avoids the use of ionizing radiation. Because children are more susceptible to long-term carcinogenic effects of ionizing radiation[33], CT imaging should be used judiciously[34,35]. CT perfusion, in particular, delivers high radiation doses and should generally be avoided in pediatric patients[36], which can impede measurement of ischemic volumes that is central to patient evaluation for extended time window EVT.

The principal disadvantages to using MRI over CT are the need for metal implant screening, rapid availability of an MRI technologist, and potentially greater time required for imaging, though the latter is mitigated with dedicated hyperacute stroke MRI protocols[37]. At centers where timely MRI is not available or contraindicated, non-contrast head CT and CT angiography are reasonable when performed with low-dose protocols tailored towards minimizing radiation dose to children.

Pediatric Stroke Care Advocacy

Development of infrastructure to provide high quality care to children with AIS requires time, energy, and resources from physicians and hospital administrators. Centers looking to implement pediatric stroke care infrastructure would do well to identify physicians and nurses who will enthusiastically champion these efforts, actively engage in ongoing program maintenance, and view pediatric AIS as a professional priority.

Though pediatric neurologists and neurointerventionalists are the most visible members of the stroke care team, our programs conspicuously involve pediatric providers in neuroradiology, emergency medicine, intensive care, anesthesiology, and cardiology. Early and robust engagement of physicians across disciplines has reduced barriers to engaging these experts when needed. For example, early participation of the pediatric anesthesiology team in protocol development facilitated routine inclusion of the on-call pediatric anesthesiologist at the time of thrombectomy pager activation in spite of the fact that a different anesthesiologist may ultimately care for the patient.

Comparative Advantage

Centers caring for adults typically see a greater volume of EVT than pediatric-only centers, and this greater experience is known to enhance outcomes[38]. On the other hand, pediatric neurologists provide content expertise pertaining to conditions that increase stroke risk in children, common pediatric stroke mimics, and the pediatric neurological examination. Thus, there is enormous comparative advantage to efficiently incorporating both pools of expertise into the stroke care model.

Both of our centers feature close collaboration between a high-volume adult EVT center and a subspecialized pediatric center. This arrangement allows pediatric and adult providers to bring their respective strengths to the care of children with AIS. Our groups have recognized the comparative advantage created by this arrangement based on the strengths of our centers, but other centers may benefit from alternative arrangements. For example, a minority of pediatric centers do offer pediatric EVT within their own walls, but even these centers often rely on neurointerventionalists that also provide care at nearby adult hospitals.

Trust and Collaboration

Children experiencing AIS are a uniquely challenging population of patients due to complex etiologies, comorbidities, and lack of clinical outcome data. Consequently, optimal management of pediatric AIS is rarely clear-cut and judgment calls are often required. The inherent challenges of making judgment calls in critically ill patients can be mitigated by mutual trust, goodwill, and shared team identity within a multidisciplinary stroke team. Specifically, these considerations can dampen concerns about potential reputational harm arising from decisive calls in high-risk cases.

Routinely including pediatric stroke experts in discussion of adult stroke processes, case review, and stroke education efforts is an effective method of building trust, goodwill, and team identity. This approach allows all team members to witness repeated thoughtful discussion of actual stroke cases, philosophical and technical approaches, and underlying clinical evidence.

ONGOING CHALLENGES

Lack of Pediatric Stroke Outcome Data

The lack of prospective data for EVT in children experiencing AIS pose major challenges[39,40]. Low per-hospital incidence of pediatric AIS was a major factor contributing to the early termination of a prospective trial of tPA in children[28], and similar issues plague the study of pediatric EVT[41]. As a result, EVT efficacy and safety remain largely undefined, which confounds decision-making and warrants discussion of the unproven nature of pediatric EVT prior to intervention. Lack of pediatric data also interferes with pediatric-specific optimizations of workup (e.g., imaging selection thresholds) and EVT itself (e.g., device selection) to account for differences between pediatric and adult stroke. In this context, even perfectly delivered adult EVT may not be tailored to the needs of children. Thus, separate from the need to develop infrastructure to deliver high quality pediatric stroke

care, there is a pressing need for a prospective trial or registry to capture key metrics of EVT safety and efficacy in children.

Lack of Formal Pediatric Stroke Center Accreditation

The development of primary and comprehensive stroke center designations for adult hospitals occurred alongside advances in adult AIS treatment, ultimately producing standardized best practices that result in improved performance and superior outcomes[42–44]. While criteria for pediatric stroke center certification have been suggested[19,45], there is currently no formal accrediting body to manage pediatric stroke certification and facilitate adoption of best practices.

Delays to Presentation

Workflows for pediatric stroke must account for greater delays in stroke recognition and workup[46–48]. Stroke symptoms in children are often underrecognized, impeding what should be rapid progression towards treatment. Aside from diminishing benefit of treatment with longer time delays, such delays also reduce eligibility for intravenous thrombolysis, increase reliance on neurovascular imaging, and may negatively bias outcomes in these patients.

Pediatric Comorbidities

Children experiencing stroke may have very different underlying comorbidities than adults with stroke[39,49,50]. For example, children with congenital heart disease have an elevated risk of AIS and are overrepresented amongst patients being considered for AIS treatment[51]. Similarly, arteriopathies are found in nearly 80% of previously healthy pediatric AIS patients[52]. In children with these or other stroke-related co-morbidities, cardiovascular fragility, altered post-surgical vascular anatomy, and potential thrombotic propensity can alter the safety and efficacy of EVT. Likewise, these co-morbidities may influence choice of treatment, post-treatment prognosis, and the need for long-term antiplatelet or anticoagulation therapy[53]. Indeed, the presence of such comorbidities also complicates efforts to follow evidence-based practice, as the limited pediatric data that is currently available may translate poorly to children with underlying rare conditions. These comorbidities also present practical barriers to follow-up care and rehabilitation.

Economic Considerations

Due to relatively low patient volume for pediatric EVT procedures, recouping fixed costs related to program maintenance, staffing, and equipment may be difficult. For example, the substantial cost of dedicated perfusion imaging software or an overnight MRI technologist in an adult center can be amortized over a large number of patients, but these same costs may present significant barriers for pediatric centers.

The most obvious route to reduce cost is partnership with a high-volume adult center. In the same manner that patient outcomes may be maximized by calling upon the experience of neurointerventionalists at high-volume EVT centers, hospital costs may be minimized by calling upon the specialized stroke care infrastructure that already exists at adult centers. For costs that cannot be reduced, broad involvement of all affected departments in program

development can promote a holistic view of program-related costs and facilitate acceptance as a necessary part of patient care.

CONCLUSION

As in adults, the delivery of high-quality care for children with AIS depends on the presence of well-designed infrastructure. Using two prototypical examples of pediatric EVT programs, we highlight common design features that may provide a foundation to develop such infrastructure in a variety of settings. This guidance may be useful to pediatric centers that aim to bolster their ability to care for children with AIS.

Besides prospective outcome data, the other necessary element for advancing safe, responsible, and high quality AIS care for children is to implement appropriate stroke care infrastructure. We review two successful pediatric EVT programs and identify key design features that may be useful for other centers that aim to bring the advances in adult stroke treatment to children under their care.

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Non-standard abbreviations and acronyms

EVT:	Endovascular thrombectomy
AIS:	Acute ischemic stroke
LVO:	Large vessel occlusion
SLCH:	St. Louis Children's Hospital
SCH:	Seattle Children's Hospital
NIR:	Neurointerventional radiology
PedNIHSS:	Pediatric NIH stroke scale
DWI:	Diffusion weighted imaging
PWI:	Perfusion weighted imaging
PACS:	Picture archiving and communication system

rt-PA:	Recombinant tissue plasminogen activator
MRN:	Medical record number
mRS:	Modified Rankin scale
DOB:	Date of birth
PMH:	Past medical history
NIHSS:	NIH stroke scale
ASPECTS:	Alberta stroke program early CT score
SBP:	Systolic blood pressure
DBP:	Diastolic blood pressure
MRP:	Magnetic resonance perfusion
MRA:	Magnetic resonance angiography

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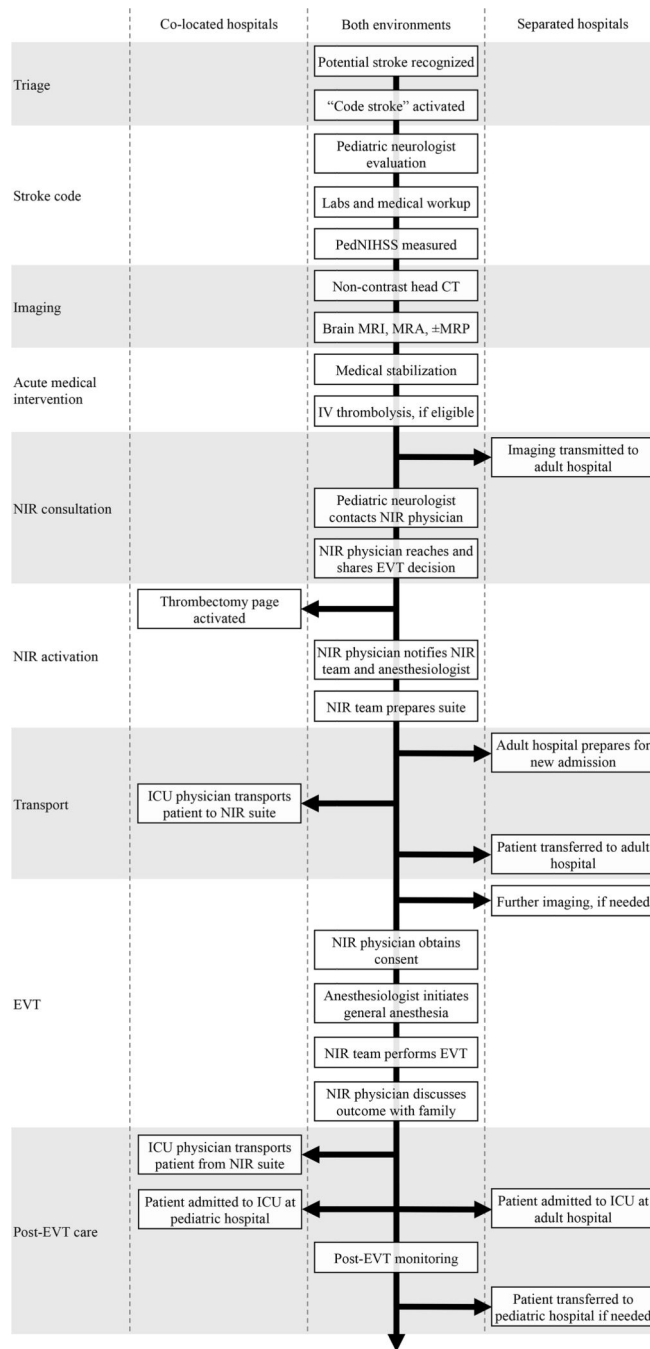
Figure 1:

Pediatric AIS workflows at co-located and separated hospitals. Pediatric neurology physician may refer to a pediatric vascular neurology attending physician or a pediatric neurology resident. NIR physician may refer to an interventional neuroradiology attending physician or an interventional neuroradiology fellow. PedNIHSS = Pediatric NIH stroke scale. MRP = Magnetic resonance perfusion. MRA = Magnetic resonance angiography.

"I am calling about a potential thrombectomy.
This is a [**#**]-year-old male/female; imaging is available on
[**PACS or mobile viewer**] under [**Patient name or MRN**]

Basic stroke details are as follows
    Imaging shows occlusion of [**artery**]
    Last known normal was [**#**] hours ago
    NIH stroke scale is [**#**] due to [**presenting symptoms**]
    rt-PA [**was/was not**] given. [**If not, why?**]

Basic medical history
    Baseline mRS is [**#**]
    Pertinent past medical history includes [**medical problems**]
    Relevant medications include [**medication**]

Basic contact information
    The stroke attending is [**name**]. My name is [**name**] and I can be reached at [**#**]
    Consent can be obtained from [**pt/family/2 physicians**] at [**#**]

Who will be the Neuro IR attending for this case?"

Figure 2:
Scripted communication between pediatric neurologist and neurointerventionalist during pediatric EVT consultation. PACS = Picture Archiving and Communication System; MRN= medical record number; rt-PA = recombinant tissue plasminogen activator; mRS = modified Rankin Scale.
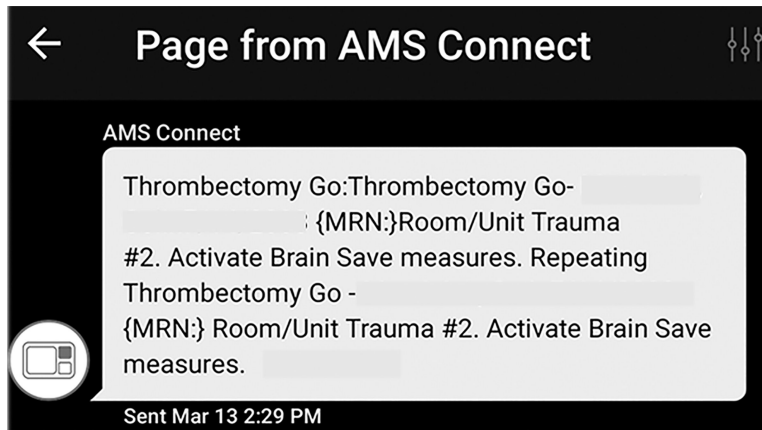
Figure 3:
Sample page following thrombectomy pager activation.

☐ Partnership between pediatric stroke experts and high-volume EVT experts, possibly through partnership with an adult practice.

☐ Written guidelines that are reviewed and agreed upon by all involved parties.

☐ Clear consensus inclusion/exclusion criteria for EVT patients.

☐ Identified champions of pediatric stroke care.

☐ Access to MR imaging 24/7.

☐ Patient volume allows regular activations of stroke workflow to allow maintenance of skills.

☐ Pediatric adaptations of stroke imaging protocols.

☐ Pediatric critical care and subspecialty expertise for children with complex non-stroke comorbidities.

☐ Open and accessible communication channels between members of the stroke team.

Figure 4:
Suggested criteria for offering pediatric EVT.

Table 1.

Sample inclusion and exclusion criteria for pediatric EVT. Treatment decisions in individual patients may deviate from these general criteria based on expert consensus. For instance, patients younger than the specified inclusion criteria may be considered.

	SLCH	SCH
Inclusion criteria	• Age 13 years.	• Age 5 years.
	• Time last seen well <24 hours.	• Time last seen well <24 hours (ages 13–17 years), <6 hours (ages 5–12 years).
	• Radiological evidence of LVO.	• Radiologic evidence of LVO.
	• ASPECTS 6.	• ASPECTS 6.
	• Debilitating symptoms consistent with AIS.	• PedNIHSS >6 with non-improving symptoms.
Exclusion criteria	• Intracranial hemorrhage, mass, or mass effect generating stroke symptoms.	• Intracranial hemorrhage, mass, or mass effect generating stroke symptoms. • ASPECTS <6.
	• Pre-morbid mRS 2 or comorbidities that impact recovery potential.	
	• Severe uncontrolled hypertension (SBP >185 mmHg or DBP >110 mmHg).	
	• Bleeding diathesis (platelet <30,000/microliter, INR >30, or use of direct oral anticoagulants with evident therapeutic effect based on PT, PTT, TT, or anti Factor Xa level).	

ASPECTS = Alberta Stroke Program Early CT Score, which can be assessed using non-contrast CT or diffusion weighted MRI.

Table 2.

Responsibilities of personnel activated by thrombectomy page.

Personnel	Responsibility
NIR physician	Confirm page was received, prepare for procedure.
Pediatric anesthesia attending physician	Go to NIR procedure area, prepare for case.
Pediatric anesthesia resident physician	Assess patient and obtain consent for anesthesia.
Operating room nurse	Schedule case if presenting from off-site.
Adult anesthesia attending physician	Aware of case, assist with anesthesia resource allocation.
Pediatric ICU attending physician	Transport patient to NIR procedure suite.
Medical Transporter	Assist as needed with patient transport to NIR suite.
Pediatric ICU fellow	Be aware of possible admission for stroke.
Pediatric ICU charge nurse	Be aware of possible admission for stroke.
Pediatric neurology resident physician	Notify providers, escort family to appropriate location.
Pediatric neurology attending physician	Notify providers, escort family to appropriate location.
Diagnostic neuroradiology physician	Immediate review of neuroimaging as it is acquired.