

## Stroke Diagnosis in the Pediatric Emergency Department An Ongoing Challenge

Lauren A. Beslow, MD, MSCE

See related article, p XXX

Diagnosis of pediatric stroke is often delayed, which has ramifications for the eligibility of children for hyperacute treatments such as thrombolysis and endovascular recanalization. Delayed pediatric stroke diagnosis occurs across developed countries, and delays occur at multiple stages of the prehospital, emergency room, and hospital course. In a Canadian cohort, median interval from symptom onset to diagnosis of arterial ischemic stroke (AIS) was 22.7 hours.<sup>1</sup> Median delay in diagnosis was 29 hours in those with out-of-hospital strokes and 11.6 hours in those with in-hospital strokes. Interestingly, among those with out-of-hospital strokes, median time from symptom onset to hospital arrival was 1.7 hours, which indicates that most of the delay in diagnosis is on the part of medical staff. In fact, the median time from symptom onset to neuroimaging was 8.5 hours in the out-of-hospital group and 10.5 hours in the hospitalized group even though initial assessment was performed almost immediately in the hospitalized children. Lower Pediatric National Institutes of Health (NIH) Stroke Scale score, lack of seizure, and nonabrupt symptom onset were among predictors of prehospital delays. Lower Pediatric NIH Stroke Scale score also predicted delayed diagnosis in the hospitalized children. Merely 10% were diagnosed within 3 hours and 20% within 6 hours, precluding most from consideration for hyperacute therapies. In a population-based cohort from the United Kingdom, median time from symptom onset to diagnostic neuroimaging among children with AIS was 24.3 hours.<sup>2</sup> A risk factor for delayed diagnosis for ischemic stroke was a normal head computed tomography scan, in which case median time to diagnosis was 44 hours. The Canadian study included children presenting from the early 1990s to the mid 2000s,<sup>1</sup> but among children presenting between 2009 and 2013 in the United States, the median time from emergency department (ED) arrival to magnetic resonance imaging (MRI) was 17 hours,<sup>3</sup> indicating that delayed diagnosis continues to be a major problem and barrier to timely therapy initiation.

Just like physicians, parents often do not consider that a child might be having a stroke. Among 25 parents of children with confirmed AIS, despite abrupt symptom onset in 23 children, fewer than half of parents considered the possibility of

stroke.<sup>4</sup> Although nearly 85% of parents thought that presenting symptoms indicated a serious problem, only 36% called an ambulance.

When examining elements that influence time to pediatric stroke diagnosis, understanding factors in the ED that may lead to delays is important. In this issue of *Stroke*, Mackay et al<sup>5</sup> report on the accuracy and reliability of pediatric emergency physicians' diagnosis of stroke among children presenting with focal neurological deficits that persisted at ED presentation. Of 287 children with 301 presentations that were evaluated in a tertiary care hospital ED, 21 had strokes (7% of presentations). Of 20 children in whom stroke was suspected, 13 (65%) had a stroke. Eight children who were ultimately diagnosed with stroke were thought to have other causes for their presentations. The sensitivity of stroke diagnosis by the ED physician was 62% with a specificity of 98%. The initial physician impression–final diagnosis  $\kappa$  for stroke was 0.61, which indicates substantial agreement. The physician impression–final diagnosis agreement ranged greatly for other causes of focal neurological deficits from  $-0.01$  and  $0.0$  (poor agreement) for demyelination and cerebellitis to 0.96 (almost perfect agreement) for Bell's Palsy. Although the physician impression may have been recorded before neuroimaging was performed, physician decisions about whether to obtain neuroimaging as well as type and timing of neuroimaging are likely informed by initial diagnostic considerations. The authors note that future studies should investigate the diagnostic impressions at various time points in the child's course, that is, on presentation and then again after various investigations. The authors also compare the sensitivity of emergency physician stroke diagnosis at their center (62%) to that reported in adult studies, which can be as high as 90%.<sup>6</sup> Younger adult patients are more likely to be misdiagnosed, especially if the strokes are located in the posterior circulation.<sup>7</sup> In children, over 30% of strokes involve the posterior circulation,<sup>8</sup> and this may contribute to the frequency of stroke misdiagnosis. Furthermore, stroke mimics are more common in the young. In 1 adult study, 21% of those younger than 50 years admitted to a stroke unit had other diagnoses.<sup>9</sup> By comparison, only 3% of those older than 50 years admitted to the unit had stroke mimics. In another study of final diagnoses among 124 stroke alerts in a pediatric ED, 76% had stroke mimics.<sup>10</sup> However, in a different tertiary care hospital cohort, only 21% of children evaluated by the stroke team for acute presentations concerning for stroke had mimics.<sup>11</sup> Neuroimaging was required to differentiate strokes from mimics.<sup>10,11</sup>

The present study underscores the high frequency of stroke mimics in children, which makes the job of emergency physician evaluators even more difficult. Although the overall specificity of ED physician suspicion of stroke was high, the sensitivity was only moderate to good. Thus, clinical screening

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia and Division of Neurology, Children's Hospital of Philadelphia, PA.

Correspondence to Lauren A. Beslow, MD, MSCE, 3501 Civic Center Blvd, 10th Floor, Philadelphia, PA 19104. E-mail beslow@email.chop.edu (*Stroke*. 2017;48:00-00).

DOI: 10.1161/STROKEAHA.117.016868.)

© 2017 American Heart Association, Inc.

*Stroke* is available at <http://stroke.ahajournals.org>

DOI: 10.1161/STROKEAHA.117.016868

tools with improved sensitivity are essential. Mackay et al<sup>12</sup> have previously identified wellness in the week before presentation, inability to walk, and face and arm weakness as factors associated with a stroke diagnosis versus stroke mimic in children presenting to the ED. Although these factors may be helpful when triaging children presenting with focal neurological symptoms to the ED, the factors may not be generalizable to the hospitalized population in which strokes often occur in critically ill children. The Face Arm Speech Test and Recognition of Stroke in the Emergency Room score have also been retrospectively applied to determine whether these screens can successfully identify AIS in children.<sup>13</sup> Of 47 children with acute AIS, 78% had 1 positive variable on Face Arm Speech Test, and 81% had a score of  $\geq 1$  on the Recognition of Stroke in the Emergency Room scale. Although emergency room and hospital screening tools for stroke will likely aid early diagnosis and delivery of prompt therapies, it would also be ideal to screen for possible stroke accurately in the pre-hospital setting. Prehospital and emergency room screens that accurately identify childhood stroke are critical for improved care and outcomes and should be evaluated prospectively.

The current study was performed before the implementation of an in-hospital stroke code alert system. As the authors state, pediatric acute stroke response teams are becoming more prevalent. The TIPS trial (Thrombolysis in Pediatric Stroke) was a catalyst for the formation of pediatric stroke centers with improved stroke readiness.<sup>14</sup> Although the trial closed early because of poor enrollment, of 17 TIPS centers surveyed, <25% had acute stroke teams, stroke-specific order sets, and around-the-clock MRI capability before the trial's initiation. After the trial, >80% of surveyed sites had these in place. Among 124 stroke alerts at 1 site that participated in the TIPS trial, the median time from arrival in the ED to head computed tomography was 59 minutes and to MRI was 94 minutes. Furthermore, MRI was the first study in over 75% of children.<sup>10</sup> At a non-TIPS center, after implementation of a pediatric stroke clinical pathway, the median time from ED arrival to MRI decreased from 17 hours to 4 hours.<sup>3</sup> The triggers for this pediatric stroke clinical pathway were detailed and included presenting neurological symptoms and pertinent medical history, such as congenital heart disease or sickle cell disease. The results of the studies by DeLaroche et al<sup>3</sup> and Ladner et al<sup>10</sup> are encouraging because they demonstrate that with implementation of systems and pathways, children can be diagnosed with stroke in a time frame in which they can be evaluated for hyperacute therapies. Although intravenous alteplase remains untested in the pediatric population, the results of endovascular trials that demonstrated efficacy in adult stroke<sup>15–19</sup> offer additional hyperacute therapies for which selected children may be eligible.

The work in the current issue highlights that the differential diagnosis for stroke-like symptoms in children is broad, which makes stroke diagnosis more difficult. Even the reliability of diagnosing conditions that mimic stroke in children is highly variable. Although the sensitivity of stroke diagnosis by ED physicians moderate to good, when time is brain, diagnostic screening tools to increase sensitivity further and pathways that permit urgent multidisciplinary action and rapid neuroimaging are requisite for excellence.

## Disclosures

None.

## References

- Rafay MF, Pontigon AM, Chiang J, Adams M, Jarvis DA, Silver F, et al. Delay to diagnosis in acute pediatric arterial ischemic stroke. *Stroke*. 2009;40:58–64. doi: 10.1161/STROKEAHA.108.519066.
- Mallick AA, Ganesan V, Kirkham FJ, Fallon P, Hedderly T, McShane T, et al. Diagnostic delays in paediatric stroke. *J Neurol Neurosurg Psychiatry*. 2015;86:917–921. doi: 10.1136/jnnp-2014-309188.
- DeLaroche AM, Sivaswamy L, Farooqi A, Kannikeswaran N. Pediatric stroke clinical pathway improves the time to diagnosis in an emergency department. *Pediatr Neurol*. 2016;65:39–44. doi: 10.1016/j.pediatrneurol.2016.09.005.
- Mackay MT, Stojanovski B, Mosley I, Churilov L, Donnan GA, Monagle P. Parental care-seeking behavior and prehospital timelines of care in childhood arterial ischemic stroke. *Stroke*. 2016;47:2638–2640. doi: 10.1161/STROKEAHA.116.014728.
- Mackay MT, Yock-Corrales A, Churilov L, Monagle P, Donnan GA, Babl E. Accuracy and reliability of stroke diagnosis in the pediatric emergency department. *Stroke*. 2017;48:xxx–xxx. doi: 10.1161/STROKEAHA.116.015571.
- Morgenstern LB, Lisabeth LD, Moccozzi AC, Smith MA, Longwell PJ, McFarling DA, et al. A population-based study of acute stroke and TIA diagnosis. *Neurology*. 2004;62:895–900.
- Kuruvilla A, Bhattacharya P, Rajamani K, Chaturvedi S. Factors associated with misdiagnosis of acute stroke in young adults. *J Stroke Cerebrovasc Dis*. 2011;20:523–527. doi: 10.1016/j.jstrokecerebrovasdis.2010.03.005.
- Beslow LA, Smith SE, Vossough A, Licht DJ, Kasner SE, Favilla CG, et al. Hemorrhagic transformation of childhood arterial ischemic stroke. *Stroke*. 2011;42:941–946. doi: 10.1161/STROKEAHA.110.604199.
- Vroomen PC, Buddingh MK, Luijckx GJ, De Keyser J. The incidence of stroke mimics among stroke department admissions in relation to age group. *J Stroke Cerebrovasc Dis*. 2008;17:418–422. doi: 10.1016/j.jstrokecerebrovasdis.2008.06.007.
- Ladner TR, Mahdi J, Gindville MC, Gordon A, Harris ZL, Crossman K, et al. Pediatric acute stroke protocol activation in a children's hospital emergency department. *Stroke*. 2015;46:2328–2331. doi: 10.1161/STROKEAHA.115.009961.
- Shellhaas RA, Smith SE, O'Tool E, Licht DJ, Ichord RN. Mimics of childhood stroke: characteristics of a prospective cohort. *Pediatrics*. 2006;118:704–709. doi: 10.1542/peds.2005-2676.
- Mackay MT, Yock-Corrales A, Churilov L, Monagle P, Donnan GA, Babl FE. Differentiating childhood stroke from mimics in the emergency department. *Stroke*. 2016;47:2476–2481. doi: 10.1161/STROKEAHA.116.014179.
- Yock-Corrales A, Babl FE, Mosley IT, Mackay MT. Can the FAST and ROSIER adult stroke recognition tools be applied to confirmed childhood arterial ischemic stroke? *BMC Pediatr*. 2011;11:93. doi: 10.1186/1471-2431-11-93.
- Bernard TJ, Rivkin MJ, Scholz K, deVeber G, Kirton A, Gill JC, et al; Thrombolysis in Pediatric Stroke Study. Emergence of the primary pediatric stroke center: impact of the thrombolysis in pediatric stroke trial. *Stroke*. 2014;45:2018–2023. doi: 10.1161/STROKEAHA.114.004919.
- Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, et al; SWIFT PRIME Investigators. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015;372:2285–2295. doi: 10.1056/NEJMoa1415061.
- Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al; MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11–20. doi: 10.1056/NEJMoa1411587.
- Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al; EXTEND-IA Investigators. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009–1018. doi: 10.1056/NEJMoa1414792.
- Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al; ESCAPE Trial Investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372:1019–1030. doi: 10.1056/NEJMoa1414905.
- Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al; REVASCAT Trial Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296–2306. doi: 10.1056/NEJMoa1503780.

KEY WORDS: Editorials ■ childhood ■ delayed diagnosis ■ diagnosis ■ neuroimaging ■ pediatric ■ stroke

# Stroke

JOURNAL OF THE AMERICAN HEART ASSOCIATION



## Stroke Diagnosis in the Pediatric Emergency Department: An Ongoing Challenge

Lauren A. Beslow

*Stroke*. published online March 23, 2017;

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2017 American Heart Association, Inc. All rights reserved.

Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://stroke.ahajournals.org/content/early/2017/03/23/STROKEAHA.117.016868.citation>

**Permissions:** Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the [Permissions and Rights Question and Answer](#) document.

**Reprints:** Information about reprints can be found online at:  
<http://www.lww.com/reprints>

**Subscriptions:** Information about subscribing to *Stroke* is online at:  
<http://stroke.ahajournals.org/subscriptions/>