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## Inter-Rater Reliability of the CASCADE Criteria:

### Challenges in Classifying Arteriopathies

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### Abstract

**Background and Purpose**—There are limited data about the reliability of subtype classification in childhood arterial ischemic stroke, an issue that prompted the IPSS (International Pediatric Stroke Study) to develop the CASCADE criteria (Childhood AIS Standardized Classification and Diagnostic Evaluation). Our purpose was to determine the CASCADE criteria's reliability in a population of children with stroke.

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### Disclosures

R.I is a member of clinical event committee for Berlin EXCOR pediatric ventricular assist device trial. S.R. is a journal editor for Elsevier. W.L. is a consultant for Creativ-Ceuticals on costs of pediatric stroke. The other authors report no conflicts.

**Methods**—Eight raters from the IPSS reviewed neuroimaging and clinical records of 64 cases (16 cases each) randomly selected from a prospectively collected cohort of 113 children with arterial ischemic stroke and classified them using the CASCADE criteria. Clinical data abstracted included history of present illness, risk factors, and acute imaging. Agreement among raters was measured by unweighted  $\kappa$  statistic.

**Results**—The CASCADE criteria demonstrated a moderate inter-rater reliability, with an overall  $\kappa$  statistic of 0.53 (95% confidence interval [CI]=0.39–0.67). Cardioembolic and bilateral cerebral arteriopathy subtypes had much higher agreement ( $\kappa=0.84$ ; 95% CI=0.70–0.99; and  $\kappa=0.90$ ; 95% CI=0.71–1.00, respectively) than cases of aortic/cervical arteriopathy ( $\kappa=0.36$ ; 95% CI=0.01–0.71), unilateral focal cerebral arteriopathy of childhood (FCA;  $\kappa=0.49$ ; 95% CI=0.23–0.76), and small vessel arteriopathy of childhood ( $\kappa=-0.012$ ; 95% CI=-0.04 to 0.01).

**Conclusions**—The CASCADE criteria have moderate reliability when used by trained and experienced raters, which suggests that it can be used for classification in multicenter pediatric stroke studies. However, the moderate reliability of the arteriopathic subtypes suggests that further refinement is needed for defining subtypes. Such revisions may reduce the variability in the literature describing risk factors, recurrence, and outcomes associated with childhood arteriopathy.

## Keywords

attention; classification; cohort studies; consensus; incidence; pediatrics; risk factors

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Childhood arterial ischemic stroke (AIS) has received increasing attention as a cause of morbidity and mortality in the pediatric population. Several population-based studies in the United States demonstrate an incidence of childhood AIS at 2 cases per 100 000 children per year,<sup>1</sup> with an incidence in other studies from Asia and Europe ranging from 0.2 to 7.9 per 100 000 children per year.<sup>2</sup> Of the estimated children in the United States,<sup>3</sup> >1000 will suffer an AIS this year. The pathogenesis, risk factors, recurrence rates, outcomes, and optimal treatment strategies for childhood AIS have only recently been explored. International networks, such as the IPSS (International Pediatric Stroke Study), have initiated large multicenter cohort studies demonstrating the basic natural history of this disease.<sup>4</sup> Even with these early studies, much remains unknown about childhood AIS.

One of the greatest barriers to childhood AIS research has been the lack of a validated and reliable classification system.<sup>5</sup> As in adult stroke,<sup>6–8</sup> multicenter efforts to determine cause, risk factors, treatment, and outcomes in childhood AIS will depend on a reliable and validated classification system. Adult classification systems are not applicable to children, in whom AIS causes are vastly different. Previous efforts to create classification systems have not been widely adopted,<sup>9,10</sup> leading the IPSS to create a consensus-based classification system, the CASCADE criteria (Childhood AIS Standardized Classification and Diagnostic Evaluation).<sup>11</sup> Briefly, the primary CASCADE classification is based on anatomic site of disease including the heart, the great vessels of the neck, or the intracranial vessels (Table 1). Secondary subtypes include additional information like genetic causes of arteriopathy, hemoglobinopathy, or infections (Table 1). Acute classification is based on clinical history and imaging within the first month after the incident stroke, and the chronic classification allows incorporation of findings after 1 month.

Although the initially reported  $\kappa$  statistic for inter-rater reliability of the CASCADE system was encouraging ( $\kappa=0.61-0.78$ ), it was based on a limited number of raters in an unpowered analysis of 7 cases.<sup>11</sup> In addition, the reliability of each individual primary subcategory and the secondary criteria were not tested. The objective of this study was to describe the reliability of the CASCADE criteria using a large number of prospectively collected cases using raters trained in a standardized format. In addition, data were analyzed to preliminarily test the CASCADE criteria's secondary subtypes.

## Methods

Cases were randomly selected for the current cross-sectional study from an existing multicenter cohort of 113 prospectively enrolled children with AIS with IRB approval at each participating center. This prospectively collected cohort of childhood AIS cases was originally designed to test the reliability of the Pediatric National Institutes of Health Stroke Scale (PedNIHSS).<sup>12</sup>

Eight raters from high-enrolling IPSS centers were randomly paired, and each of the 4 pairs was randomly assigned 16 cases to review (Figure) and compared with each other. With a sample size of 64, an a priori power analysis predicted that if results reveal a  $\kappa$  of 0.75, it could be concluded with 95% confidence that the true value of  $\kappa$  is between 0.70 and 0.80. Cases previously known to the raters were excluded from randomization. Deidentified case files were created for each case and included the acute magnetic resonance imaging on Compact Disc Read-Only Memory (CD-ROM), the radiology report of the magnetic resonance imaging, the initial history of present illness from the attending neurologist at the time of stroke, and the 3-month follow-up note from the neurology clinic (when available). The PedNIHSS study's case report form also included information about demographics, family history, medical evaluation, and treatment for each case. In addition, acute vascular imaging (at least one of the following: computed tomography angiography [CTA], magnetic resonance angiography, or conventional angiogram) was included for all 64 cases. When available, chronic imaging (>30 days) was included in case files as well (6/64).

To reduce potential bias, case files were systematically redacted by trained personnel (R.B. and A.H.) and then rechecked by a pediatric stroke neurologist (J.A.-W.) before dissemination. Eliminated data included (1) any notation of working diagnosis or classification of stroke subtype, (2) all assessments and plans, and (3) any official diagnosis on radiographic reports.

Each case was rated by 2 randomly paired experts in childhood stroke (7 neurologists and 1 hematologist: N.A.G., W.L., M.M.D., H.J.F., C.A.L., L.C.J., A.K., and L.A.B.). All 8 raters were provided a manual detailing the study procedures and the CASCADE rating system. Each rater also participated in a standardized 30-minute phone and Power Point training session on the implementation of the CASCADE criteria. Each rater was permitted to use local expertise at his or her center; specifically, the examiner could consult with an institutional pediatric neuroradiologist or cardiologist to assist in the classification of cerebrovascular and cardiac findings, respectively (as would be performed in actual clinical settings).

Initial review included only acute information available at presentation and within 30 days after stroke onset and was termed the acute classification. The raters then classified each case using: (1) the primary CASCADE criteria basic 7 subtypes, (2) the primary CASCADE criteria expanded 19 subtypes, (3) the CASCADE criteria secondary subtypes, and (4) their current (ad hoc) classification system (Table 1).<sup>11</sup> A second review—termed the chronic classification—was then undertaken with all data beyond 30 days post stroke (n=62/64) available. The raters then reclassified each case using: (1) the primary CASCADE criteria basic 7 subtypes, (2) the primary CASCADE criteria expanded 19 subtypes, (3) the CASCADE criteria secondary subtypes, and (4) their current (ad hoc) classification system (Table 1). Raters were also asked to rate the usability of the system and their confidence in their classification throughout their case review.

Inter-rater reliability for the CASCADE criteria was then evaluated by chance-adjusted agreement by calculating a  $\kappa$  statistic, along with 95% confidence intervals (95% CI) using the (Wald/other) method. An overall  $\kappa$  was determined for the cases in the acute and chronic setting for the primary 7 subtypes, primary expanded 19 subtypes, and secondary subtypes. As proposed by Landis and Koch,<sup>13</sup> we used the following interpretations of  $\kappa$  values: >0.8, near-perfect agreement; 0.61 to 0.80, substantial agreement; 0.41 to 0.60, moderate agreement; 0.21 to 0.40, fair agreement; and <0.20, slight agreement.

## Results

Raters obtained an overall agreement in 40 out of 64 cases using the basic 7-subtype CASCADE criteria with a  $\kappa$  of 0.53 (95% CI=0.39–0.67), demonstrating a moderate agreement (Table 2) that was similar among the 4 pairs. When using the expanded 19-subtype criteria, inter-rater reliability demonstrated fair agreement, with a  $\kappa$  of 0.39 (95% CI=0.25–0.52). Follow-up rating for chronic classification using the basic 7-subtype system was also moderate ( $\kappa$ =0.49; 95% CI=0.35–0.64) for the 62 cases with data beyond 30 days and was similar to agreement in the acute classification ( $P$ =0.97). Inter-rater agreement, as measured by unweighted  $\kappa$ , varied greatly among each of the basic 7 subcategories in the acute setting (Table 3). Acutely, near-perfect agreement occurred in cases of cardioembolic stroke (n=32/36;  $\kappa$ =0.84; 95% CI=0.70–0.99) and bilateral cerebral arteriopathy of childhood (n=10/11;  $\kappa$ =0.90; 95% CI=0.71–1.00). Moderate agreement was attained in cases of unilateral FCA (n=14/25;  $\kappa$ =0.49; 95% CI=0.23–0.76), whereas fair agreement was observed in aortic/cervical arteriopathy (8/15;  $\kappa$ =0.36; 95% CI=0.01–0.7) and the other subcategory (n=16/33;  $\kappa$ =0.33; 95% CI=0.09–0.56). Small vessel arteriopathy of childhood (n=0/2;  $\kappa$ =–0.02; 95% CI=–0.04 to 0.01) and multifactorial disease (n=0/6;  $\kappa$ =–0.04; 95% CI=–0.09 to 0.00) had no agreement.

Raters reported that they were confident or very confident in their acute primary classification in 70 out of 128 cases when using the CASCADE criteria, while reporting a similar confidence when using their own system (71/128). Chronic classification had similar distributions. Although all 64 cases had magnetic resonance angiography imaging available of the head, 5 cases had additional CTA imaging provided by their center. In cases with additional CTA imaging, there was agreement in 4 out of 5 cases classified as FCA (1), cardioembolic (1), and other (2). When asked about imaging, raters reported that imaging

quality had little, very little, or no impact on their ability to rate the vignettes in 110 out of 128 (86%) of cases. In 14 cases (11%), the raters reported that the quality of the image impaired the ability of the raters to classify “somewhat” and in 4 cases “very much” or “a great deal.”

In the secondary classification, the inter-rater reliability was measured independently for each category, as these selections are not mutually exclusive (Table 4). Acutely, the genetic vasculopathy subtype demonstrated substantial agreement ( $\kappa=0.78$ ; 95% CI=0.56–1.00), whereas the inflammatory subcategory had moderate agreement ( $\kappa=0.55$ ; 95% CI=0.09–1.00). Toxin, hematologic, and infectious subcategories all had slight to fair agreement.

## Discussion

In 2012, the child CASCADE criteria was established as a consensus-based classification in childhood AIS via a modified Delphi method by 12 pediatric stroke experts.<sup>11</sup> This is the first powered reliability analysis of the primary 7-subtype criteria, using 64 prospectively collected cases. In addition, this is the first study examining the inter-rater reliability of the expanded 19-subtype CASCADE criteria and the secondary CASCADE criteria. A previous report, using a small number of cases (7) and the 7-subtype CASCADE criteria, had demonstrated a  $\kappa$  statistic of 0.61 to 0.78, suggesting substantial agreement among raters.<sup>11</sup> The current powered analysis suggests that the CASCADE is a useful tool for classification of childhood AIS. The primary 7-subtype criteria demonstrate moderate inter-rater agreement, with a  $\kappa$  of 0.53, and a CI spanning moderate to substantial agreement. This  $\kappa$  statistic compares favorably with the initial inter-rater reliability of the first adult stroke classification (the Trial of Org 10172 in Acute Stroke Treatment criteria), which had a  $\kappa$  of 0.54 when originally evaluated by trained raters.<sup>14,15</sup> When using the expanded 19-subtype criteria, agreement in the CASCADE criteria decreases into the fair category, with a  $\kappa$  of 0.39. The fair agreement within the 19-subtype criteria suggests that in future applications of the CASCADE criteria—with adjustments from these data—the 19-subtype system may provide a more granular, yet reliable system for classification. The first-ever testing of the secondary classification suggests that the genetic and inflammatory categories have adequate definitions for use with moderate to substantial reliability, whereas the infectious and hematologic categories need further refinement.

Most interestingly, inter-rater reliability within subcategories varied greatly with near-perfect agreement in the cardioembolic and bilateral cerebral arteriopathy categories and only fair to moderate agreement in the aortic/cervical arteriopathy and FCA categories. Although the raters for this study are all experienced pediatric stroke specialists and had participated in formal training sessions, a lack of substantial agreement in the aortic/cervical arteriopathy and FCA categories remained, highlighting the difficulty in categorizing stenotic focal arteriopathies in children. These findings suggest that even specialists in this area, who are guided by standardized definitions, have different interpretations of the clinical and radiographic data in children with stroke and arteriopathic abnormalities.

Furthermore, the lack of substantial agreement in these categories may explain some of the variable reports about arteriopathy subtypes in the literature. As an example, reported

recurrence risk of childhood stroke because of arteriopathy is highly variable, with a cohort of 50 children from the United Kingdom with stroke and intracranial arteriopathy only having 5 recurrent events (10%) at a median interval follow-up of 38 months,<sup>16</sup> whereas a US cohort of 22 children with stroke and arteriopathy had a recurrence risk of 66% at 5 years.<sup>17</sup> Although methods and treatment strategies likely differed in these cohorts, the large discrepancy between their findings suggests that a lack of standardized definitions may play a role in these vastly different conclusions. The majority of disagreement in the current study came from cases that were identified as arteriopathy by one rater and other by another rater, emphasizing the uncertainty of this category. Indeed, our results suggest that even when using standardized definitions from the CASCADE criteria, inter-rater reliability of aortic/cervical arteriopathy and FCA are only fair to moderate.

The inter-rater reliability of small vessel arteriopathy in the CASCADE criteria is the most unreliable of any subtype within the study, although this conclusion is limited by small numbers in this category. This result may also be influenced by a wide spectrum of preexisting definitions of vasculitis used among the raters. Indeed, previous reports in the literature suggest a vastly different incidence of vasculitis in childhood stroke, depending on study location. Although an international multicenter cohort of 525 patients identified only 6% (33/525) of their subjects as having vasculitis, a single Canadian cohort identified 24 patients with small vessel primary central nervous system vasculitis at a single tertiary care center from 2002 to 2009.<sup>18</sup> These findings are likely the result of variable definitions for vasculitis in the pediatric stroke field, as well as variability in work-up including lumbar puncture and brain biopsy.

This study has several limitations. The primary limitation is the small number of cases identified with small vessel arteriopathy and several of the secondary subtypes. Given the small numbers in these subcategories, generalization about the reliability of classification is difficult. A second limitation was the lack of a standardized evaluation for children with acute stroke. Although this is likely a real-world scenario, variability of work-up, especially vascular imaging, may have led to challenges in classification. In addition, the quality of vascular imaging may have played a role in misclassification, as raters considered poor imaging quality as somewhat to greatly influential in 14% of cases they rated. Interestingly, when raters were provided CTA imaging they agreed in 4 out of 5 cases, suggesting that future studies should explore the possibility that precise imaging may increase inter-rater reliability. Numbers are too few, however, to make meaningful conclusions about imaging modality in this article. In addition, missing data, especially for the chronic cases, may have caused an inability to determine a precise classification. Finally, these cases were selected from a cohort of patients identified in North America with exclusion criteria that included acute traumatic brain injury; meningitis or encephalitis; and status epilepticus.<sup>12</sup> Therefore, generalizability to cases from international and less circumscribed populations needs to be explored.

## Conclusions

Although the CASCADE criteria is a reliable and standardized system currently available for classification of childhood AIS, future efforts are needed to improve classification. These



efforts should focus on FCA, aortic/cervical arteriopathy, and small vessel arteriopathy primary categories, as well as on more precise definitions for hematologic and infectious disease secondary subtypes. One possible next step could be combining many of the techniques for classifying arteriopathies from the VIPS study (Vascular Effects of Infection in Pediatric Stroke),<sup>19</sup> within an all-inclusive classification system such as the CASCADE criteria. This approach could lead to an improved system available for general use. Improvements in vascular imaging, such as imaging of the arterial wall itself, are also needed to better differentiate arteriopathies with distinct pathophysiologies. In addition, the use of computer-assisted classification and evidence-based criteria as they become available, will also likely enhance the reliability of the CASCADE criteria as has occurred in adult stroke.<sup>20,21</sup> Finally, the challenge of uniformly agreeing on classification of focal intracranial arteriopathic remains—even among experts in the field—suggesting that continued efforts to refine classification tools are urgently needed in this field.

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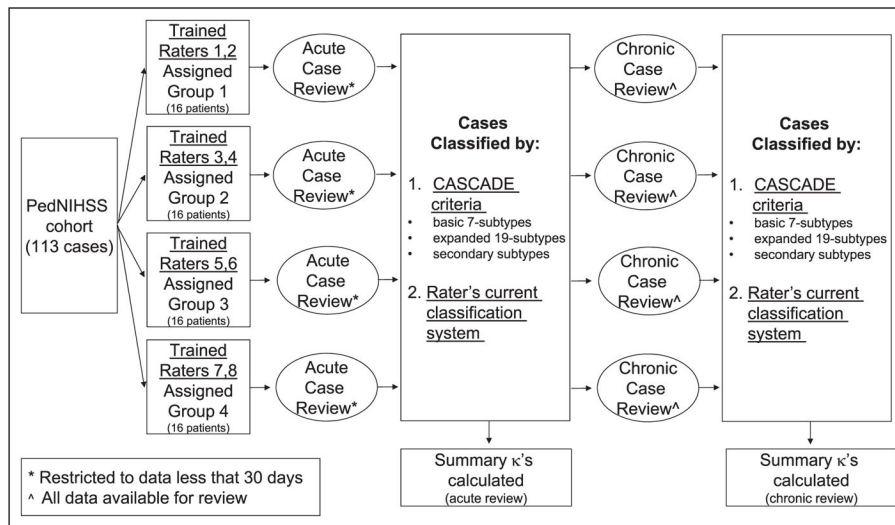
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**Figure.** Case assignment and rater classification flow chart. AIS indicates arterial ischemic stroke; CASCADE, Childhood AIS Standardized Classification and Diagnostic Evaluation.

**Table 1**

## CASCADE Criteria Primary Subtypes

Basic 7-Subtype CASCADE Criteria (Only One Selected)	Expanded 19-Subtype CASCADE Criteria (Only One Selected)
<input type="checkbox"/> SVA	SVA
	<input type="checkbox"/> Definitive
	<input type="checkbox"/> Radiographic confirmation
	<input type="checkbox"/> Biopsy confirmation
	<input type="checkbox"/> Probable
<input type="checkbox"/> Unilateral FCA	FCA
	<input type="checkbox"/> Anterior circulation with collaterals
	<input type="checkbox"/> Anterior circulation without collaterals
	<input type="checkbox"/> Posterior circulation
	<input type="checkbox"/> Other
<input type="checkbox"/> Bilateral cerebral arteriopathy of childhood	Bilateral cerebral arteriopathy of childhood
	<input type="checkbox"/> With collaterals
	<input type="checkbox"/> Without collaterals
	<input type="checkbox"/> Other
<input type="checkbox"/> Aortic/cervical arteriopathy	Aortic/cervical arteriopathy
	<input type="checkbox"/> Dissection
	<input type="checkbox"/> Takayasu arteritis
	<input type="checkbox"/> Other
<input type="checkbox"/> Cardioembolic	Cardioembolic
	<input type="checkbox"/> Definite
	<input type="checkbox"/> Probable
<input type="checkbox"/> Other	Other
	<input type="checkbox"/> Undetermined cause
	<input type="checkbox"/> Other
<input type="checkbox"/> Multifactorial	Multifactorial
	<input type="checkbox"/> Multifactorial
CASCADE criteria secondary subtypes	
Secondary subtypes (select as many as apply)	Examples
<input type="checkbox"/> Genetic: vasculopathy	PHACES syndrome, Williams syndrome, trisomy 21, neurofibromatosis, Alagille syndrome, and sickle cell disease
<input type="checkbox"/> Infectious	Postvaricella arteriopathy, meningitis, and HIV vasculopathy
<input type="checkbox"/> Hematologic/thrombotic	Hemoglobinopathy, antiphospholipid antibody syndrome, inherited coagulation regulatory protein deficiency (protein S, protein C, antithrombin III), factor V Leiden or prothrombin mutation, elevated homocysteine, protein-losing states (enteropathy, hepatopathy, and nephropathy), and anemia
<input type="checkbox"/> Inflammatory	Idiopathic (primary central nervous system vasculitis), systemic inflammatory, or autoimmune disease (eg, lupus)
<input type="checkbox"/> Genetic: metabolic	Mitochondrial cytopathy

<b>Basic 7-Subtype CASCADE Criteria (Only One Selected)</b>	<b>Expanded 19-Subtype CASCADE Criteria (Only One Selected)</b>
<input type="checkbox"/> Drug/toxin exposure	Intravenous immunoglobulin, l-asparaginase, drugs of abuse, and postcranial irradiation
<input type="checkbox"/> Vasospasm	Reversible vasospastic syndromes

Definitions provided in Bernard et al.<sup>11</sup> AIS indicates arterial ischemic stroke; CASCADE, Childhood AIS Standardized Classification and Diagnostic Evaluation; FCA, focal cerebral arteriopathy; PHACES, posterior fossa brain malformations, hemangiomas of the face, arterial abnormalities, cardiac anomalies, eye anomalies, sternal cleft/supraumbilical raphe; and SVA, small vessel arteriopathy.

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**Table 2**

Pairwise Agreement Between Raters by Basic 7-Subtype CASCADE Criteria

Subtype	Timeframe	SVA	FCA	Bilateral Cerebral Arteriopathy of Childhood	Aortic/Cervical Arteriopathy	Cardioembolic	Other	Multifactorial	Total
SVA	Acute	0*	0	0	0	0	0	1	1
	Chronic	0*	0	0	0	0	0	1	1
FCA	Acute	0	7*	0	1	0	1	1	10
	Chronic	0	7*	0	0	0	1	1	9
Bilateral cerebral arteriopathy of childhood	Acute	0	0	5*	0	0	0	0	5
	Chronic	0	0	3*	0	1	0	1	5
Aortic/cervical arteriopathy	Acute	0	2	0	4*	0	0	1	7
	Chronic	0	3	0	3*	0	0	1	7
Cardioembolic	Acute	0	0	0	0	16*	2	0	18
	Chronic	0	0	0	0	15*	1	1	17
Other	Acute	1	6	1	3	1	8*	2	22
	Chronic	1	7	1	2	2	9*	1	23
Multifactorial	Acute	0	0	0	0	1	0	0*	1
	Chronic	0	0	0	0	0	0	0*	0
Total	Acute	1	15	6	8	18	11	5	64
	Chronic	1	17	4	5	18	11	6	62

Each cell represents the number of times one reviewer gave the response in the column label while the other gave the response in the row label. AIS indicates arterial ischemic stroke; CASCADE, Childhood AIS Standardized Classification and Diagnostic Evaluation; FCA, focal cerebral arteriopathy; and SVA, small vessel arteriopathy.

\* Entries represent agreement.

**Table 3**

Inter-Rater Reliability of CASCADE Criteria by Primary Stroke Subtype

Subtype	Acute Inter-Rater Reliability ( $\kappa$ )	Chronic Inter-Rater Reliability ( $\kappa$ )
SVA of childhood	-0.01 (95% CI=-0.04 to 0.01)	na <sup>*</sup> (95% CI=na)
Unilateral FCA of childhood	0.49 (95% CI=0.23 to 0.76)	0.47 (95% CI=0.22 to 0.72)
Bilateral cerebral arteriopathy of childhood	0.90 (95% CI=0.71 to 1.00)	0.64 (95% CI=0.27 to 1.00)
Aortic/cervical arteriopathy	0.36 (95% CI=0.01 to 0.71)	0.30 (95% CI=-0.08 to 0.69)
Cardioembolic	0.84 (95% CI=0.70 to 0.99)	0.80 (95% CI=0.64 to 0.97)
Other	0.33 (95% CI=0.09 to 0.56)	0.38 (95% CI=0.16 to 0.61)
Multifactorial	-0.04 (95% CI=-0.09 to 0.00)	0.45 (95% CI=0.09 to 0.81)
Combined	0.53 (95% CI=0.39 to 0.67)	0.49 (95% CI=0.35 to 0.64)

AIS indicates arterial ischemic stroke; CASCADE, Childhood AIS Standardized Classification and Diagnostic Evaluation; CI, confidence interval; FCA, focal cerebral arteriopathy; na, not applicable; and SVA, small vessel arteriopathy.

\* All rated negative.

**Table 4**

Inter-Rater Reliability of CASCADE Criteria by Secondary Stroke Subtype

Subtype	Agreement Subtype Present	Agreement Subtype Absent	Disagreement	Inter-Rater Reliability ( $\kappa$ )
Genetic: vasculopathy	7/64 (10.9%)	54/64 (84.4%)	3/64 (4.7%)	0.80 (95% CI=0.56 to 1.00)
Infectious	1/64 (1.6%)	50/64 (78.1%)	13/64 (21.5%)	0.03 (95% CI=-0.22 to 0.28)
Hematologic	6/64 (9.4%)	37/64 (57.8%)	21/64 (32.8%)	0.16 (95% CI=0.08 to 0.41)
Inflammatory	2/64 (3.1%)	59/64 (92.2%)	3/64 (4.7%)	0.55 (95% CI=0.09 to 1.00)
Genetic: metabolic	0/64 (0.0%)	63/64 (98.4%)	1/64 (1.6%)	na <sup>*</sup>
Toxin	1/64 (1.6%)	60/64 (93.8%)	3/64 (4.7%)	0.38 (95% CI=0.18 to 0.93)
Vasospasm	0/64 (0.0%)	62/64 (96.9%)	2/64 (3.1%)	na <sup>*</sup>

AIS indicates arterial ischemic stroke; CASCADE, Childhood AIS Standardized Classification and Diagnostic Evaluation; CI, confidence interval; and na, not applicable.

<sup>\*</sup> All rated negative.