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Comparative study of posterior and anterior circulation stroke in childhood

Results from the International Pediatric Stroke Study

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Abstract

Objective

To compare risk factors, clinical presentation, and outcomes after posterior circulation arterial ischemic stroke (PCAIS) and anterior circulation arterial ischemic stroke (ACAIS) in neonates and children.

Methods

In this international multicenter observational study including neonates and children up to 18 years of age with arterial ischemic stroke (AIS), we compared clinical and radiologic features according to stroke location.

Results

Of 2,768 AIS cases, 507 (18%) were located in the posterior circulation, 1,931 (70%) in the anterior circulation, and 330 (12%) involved both. PCAIS was less frequent in neonates compared to children (8.8% vs 22%, $p < 0.001$). Children with PCAIS were older than children with ACAIS (median age 7.8 [interquartile range (IQR) 3.1–14] vs 5.1 [IQR 1.5–12] years, $p < 0.001$), and more often presented with headache (54% vs 32%, $p < 0.001$) and a lower Pediatric NIH Stroke Scale score (4 [IQR 2–8] vs 8 [IQR 3–13], $p = 0.001$). Cervicocephalic artery dissections (CCAD) were more frequent (20% vs 8.5%, $p < 0.001$), while cardioembolic strokes were less frequent (19% vs 32%, $p < 0.001$) in PCAIS. Case fatality rates were equal in both groups (2.9%). PCAIS survivors had a better outcome (normal neurologic examination at hospital discharge in 29% vs 21%, $p = 0.002$) than ACAIS survivors, although this trend was only observed in children and not in neonates.

Conclusion

PCAIS is less common than ACAIS in both neonates and children. Children with PCAIS are older and have a higher rate of CCAD, lower clinical stroke severity, and better outcome than children with ACAIS.

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Coinvestigators are listed at [links.lww.com/WNL/B34](https://www.links.lww.com/WNL/B34).

Glossary

ACAIS = anterior circulation arterial ischemic stroke; **AIS** = arterial ischemic stroke; **BCAIS** = arterial ischemic stroke of both the anterior and posterior circulation; **CCAD** = cervicocephalic artery dissection; **CI** = confidence interval; **IPSS** = International Pediatric Stroke Study; **IQR** = interquartile range; **OR** = odds ratio; **PCAIS** = posterior circulation arterial ischemic stroke; **PedNIHSS** = Pediatric NIH Stroke Scale; **TCA** = transient cerebral arteriopathy.

Current knowledge about pediatric posterior circulation arterial ischemic stroke (PCAIS) is largely based on a few, mostly single-center retrospective studies that report PCAIS in 10%–43% of cases of childhood arterial ischemic stroke (AIS), and rarely in neonates.^{1–7} Cerebral vasculopathies are the most commonly identified etiologies of childhood PCAIS, and recurrence rates are reportedly higher when compared to anterior circulation arterial ischemic stroke (ACAIS).^{1,2,4,8} Clinical outcomes for children with PCAIS are available through a limited number of studies and range from a good outcome in 55% of children with no case fatalities to fatality rates as high as 26% and poor outcome in 45% of survivors.^{1–4,8}

These discrepant reports in the literature and the fact that PCAIS has not been directly compared to ACAIS except for stroke recurrence led us to review data from a large prospective multicenter study, the International Pediatric Stroke Study (IPSS), over a 10-year period to provide comparative information on risk factors, clinical presenting features, and outcomes following ACAIS and PCAIS in neonates and children. We hypothesized that children with PCAIS frequently have nonspecific symptoms such as headache or altered level of consciousness, have different risk factors, and differ in terms of stroke outcomes and recurrence compared to children with ACAIS.

Methods

The methods of the IPSS have been described in detail.^{9,10} In brief, the IPSS is an international multicenter observational study prospectively including children and neonates with arterial ischemic stroke or cerebral sinovenous thrombosis since 2003. All participating centers are listed in appendix 1. Figure e-1 (doi.org/10.5061/dryad.1250k52) illustrates the IPSS enrollment.

For this analysis, we included all patients (neonates aged 0 to 28 days of life and children aged 29 to <19 years at onset) with AIS registered between 2003 and 2014 for whom stroke location was known. Children with a stroke involving both the anterior and the posterior circulation were excluded.

Variable definitions

AIS was defined as an acute event with clinical and radiologic evidence of cerebral ischemia, including (1) a focal neurologic deficit of acute onset and (2) CT or MRI showing infarct in location consistent with neurologic signs and symptoms.

Patients with diffuse or bilateral infarction related to hypoxic ischemic events were included only if a definite focal, single arterial infarct in a specified vascular territory was also present. Stroke locations were reported by local site investigators as isolated involvement of the posterior circulation (PCAIS), isolated involvement of the anterior circulation (ACAIS), or involvement of both the anterior and posterior circulation (BCAIS). The anterior circulation was defined as the territory of the internal carotid, middle, or anterior cerebral artery; the posterior circulation as the territory of the vertebral, basilar, cerebellar, or posterior cerebral arteries. Clinical stroke severity at diagnosis was assessed with the Pediatric NIH Stroke Scale (PedNIHSS).¹¹ Outcome was assessed with an examination by a pediatric neurologist and the Pediatric Stroke Outcome Measure, a standardized neurologic outcome measure validated for pediatric ischemic stroke.¹² In addition, parents or guardians answered 2 outcome questions at follow-up: (1) “Has your child recovered completely from the stroke?” (2) “Does your child need extra help with day-to-day activities compared with other children of the same age?” Hemorrhagic transformation of AIS was defined according to the European–Australasian Cooperative Acute Stroke Study (ECASS II).¹³ Recurrent ischemic events were defined as any clinical or subclinical ischemic event after the index stroke.

Statistical analyses

Statistical analyses were performed using Stata version 15 (StataCorp LP, College Station, TX). Data are reported descriptively as numbers and frequencies. For variables with missing data, the term valid n indicates the number of patients for whom information was available. Continuous data are expressed as median and interquartile ranges (IQR). Groups were compared according to stroke location (ACAIS vs PCAIS) using the Mann-Whitney *U* test for continuous variables, and Fisher exact or Pearson χ^2 test for categorical variables, as appropriate. A 2-sided *p* value ≤ 0.05 was considered statistically significant. Multivariable logistic regression analysis was performed to identify predictors of recurrent ischemic events and neurologic deficits at hospital discharge, including variables with a *p* value ≤ 0.1 in the univariable logistic regression analysis.

Standard protocol approvals, registrations, and patient consents

The study protocol was approved by relevant local authorities in all participating centers and conducted according to national rules concerning ethics committee approval and informed consents. The IPSS is registered at ClinicalTrials.gov (NCT00084292).

Data availability

All data used for analysis are presented in the tables and figure in this article. Data will be shared after ethics approval if requested by other investigators for purposes of replicating the results.

Results

Stroke location was recorded in 2,768 (87%) patients with AIS (88% of neonates, 86% of children), with the majority being ACAIS ($n = 1,931$, 70%), followed by PCAIS ($n = 507$, 18%) and BCAIS ($n = 330$, 12%). After excluding the 330 patients with BCAIS, 2,438 participants were included in this study (703 neonates and 1,735 children). PCAIS was less frequent in neonates than children (8.8% vs 22%, $p < 0.001$).

Childhood stroke

Children with PCAIS were older (median age 7.8 years, IQR 3.1–14 years) than children with ACAIS (median age 5.1 years, IQR 1.5–12 years, $p < 0.001$). Age distribution according to stroke territory is displayed in the figure.

The male preponderance was more marked in PCAIS (64%) than ACAIS (56%) ($p = 0.002$). This difference persisted after adjusting for preceding head trauma ($p = 0.014$), but was no longer present when adjusting for cervicocephalic artery dissection (CCAD, $p = 0.3$).

The most common presenting signs and symptoms in PCAIS were limb paresis (65%), headache (54%), speech disturbance (48%), and ataxia (47%). Apart from obvious differences due to stroke location, displayed in detail in table 1, children with PCAIS more often had headache at stroke onset ($p < 0.001$), while seizures were less frequent than in ACAIS ($p < 0.001$). Altered level of consciousness ($p = 0.27$) and visual field defects ($p = 0.15$) did not differ.

Stroke severity at presentation was reported in 273 patients (16% of ACAIS, 15% of PCAIS) and was lower in PCAIS with a median PedNIHSS of 4 (IQR 2–8) compared to ACAIS (median PedNIHSS 8 [IQR 3–13], $p = 0.001$).

Time from symptom onset to radiologic confirmation of diagnosis was available in 449 children (25% of ACAIS, 28% of PCAIS), and was similar in both groups, with a median of 19.8 (IQR 6.8–48) hours in PCAIS compared to 13 (IQR 5–28) hours in ACAIS ($p = 0.25$). MRI was the imaging modality most frequently required to diagnose PCAIS (MRI 68%, CT 32%), while a CT scan was sufficient for diagnosis in nearly half of ACAIS cases (MRI 56%, CT 44%, $p < 0.001$).

Vasculopathy and chronic illness were the 2 most common risk factors for both PCAIS and ACAIS. However, the distribution of subtypes within these groups differed, with CCAD being more common in PCAIS (20%) than in ACAIS (8.5%, $p < 0.001$), while moyamoya and transient cerebral arteriopathy (TCA) were more frequent in ACAIS than in PCAIS (moyamoya 14% vs 2.8%, $p < 0.001$, TCA 5% vs 2%, $p = 0.033$). Hematologic disease, including iron deficiency anemia, sickle cell disease, or any kind of prothrombotic state, were less frequent in PCAIS (2%) than ACAIS (7%, $p = 0.001$). Cardioembolic conditions and acute systemic illness were less common in PCAIS than in ACAIS, while acute and chronic diseases affecting the head or neck including migraine were more frequent in PCAIS (table 2).

Children with PCAIS more often received an antithrombotic agent during the acute phase than did children with ACAIS (84% in PCAIS, 77.1% in ACAIS, $p < 0.003$). Thrombolysis was rarely performed for stroke in any location (5.1% in ACAIS, 2% in PCAIS, $p = 0.07$); 5 thrombectomies were performed, all in ACAIS. Hemorrhagic transformation of

Figure Age distribution according to stroke territory

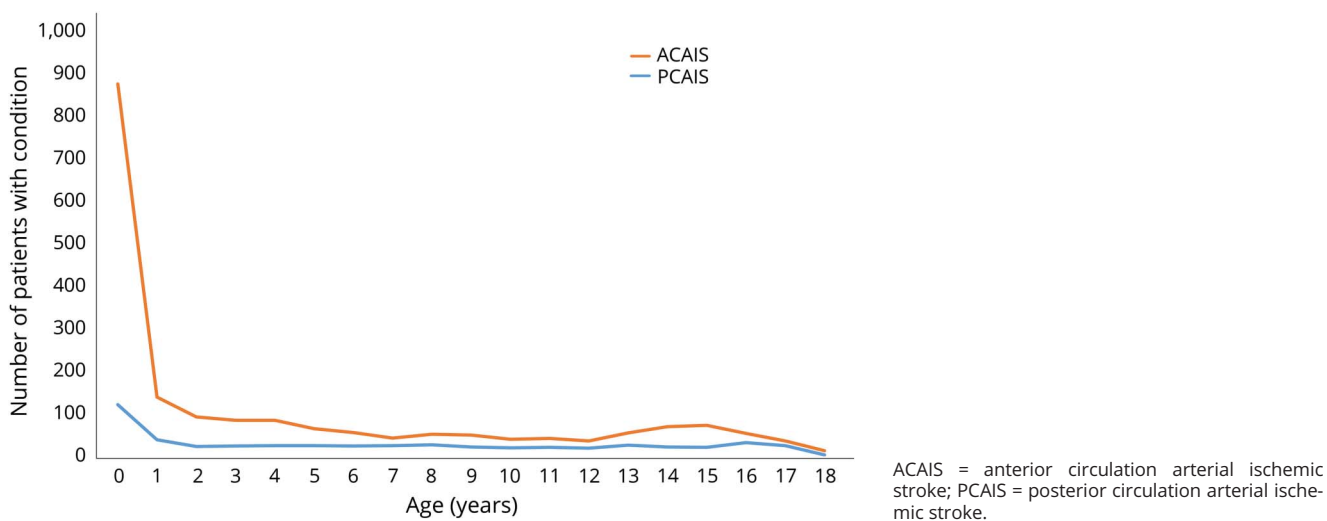


Table 1 Clinical presentation stratified by stroke territory in 1,735 children with acute arterial ischemic stroke

Characteristics	Posterior stroke (n = 436)	Anterior stroke (n = 1,299)	Posterior vs anterior stroke, 2-tailed p Value
Paresis of extremities, any	268/410 (65)	1,093/1,265 (86)	<0.001
Quadriparesis	22/410 (5.4)	25/1,265 (2)	0.001
Hemiparesis	246/410 (60)	1,068/1,265 (84)	<0.001
Headache	194/357 (54)	306/969 (32)	<0.001
Speech disturbance, any	189/391 (48)	722/1,183 (61)	<0.001
Ataxia, any	22/47 (47)	30/126 (24)	0.005
Visual field defect, any	159/384 (41)	428/1,153 (37)	0.15
Nausea/vomiting	25/61 (41)	40/160 (25)	0.03
Altered consciousness	144/372 (39)	465/1,105 (42)	0.27
Vertigo	15/51 (29)	10/126 (7.9)	0.01
Seizure	76/408 (19)	396/1,222 (32)	<0.001

Values are n with condition/valid n (%).

stroke, occurring in 5.5% of PCAIS and 6.6% of ACAIS cases ($p = 0.53$), and neurosurgical procedures, such as decompressive craniotomy or CSF drainage, performed in 14% of ACAIS and 9.1% of PCAIS cases ($p = 0.1$), were similar.

The fatality rate was identical for PCAIS and ACAIS (both 2.9%). In survivors, outcome data were obtained in 92% of patients with PCAIS and 97% of patients with ACAIS at discharge and in 52% of patients with PCAIS and 46% of patients with ACAIS after a median follow-up duration of 1.5

(IQR 0.5–3.1) years, which did not differ between the groups ($p = 0.5$).

Survivors of PCAIS were more frequently reported to have a normal neurologic examination at hospital discharge than survivors of ACAIS (table 3). In the multivariable logistic regression analysis, the risk for a neurologic deficit at discharge was decreased in children with PCAIS (odds ratio [OR] 0.61, 95% confidence interval [CI] 0.45–0.84; $p = 0.002$) and cardioembolic stroke (OR 0.67; 95%

Table 2 Risk factors stratified by stroke territory in 1,735 children with acute arterial ischemic stroke

Characteristics	Posterior stroke (n = 436)	Anterior stroke (n = 1,299)	Posterior vs anterior stroke, 2-tailed p Value
Vasculopathy^a	129/407 (32)	413/1,206 (34)	0.36
Cardioembolic conditions	79/417 (19)	403/1,263 (32)	<0.001
Acute systemic illness	83/417 (20)	338/1,244 (27)	0.003
Underlying chronic illness	131/431 (30)	415/1,287 (32)	0.51
Hematologic disease	10/431 (2.3)	95/1,287 (7.4)	<0.001
Acute head and neck conditions	106/421 (25)	250/1,244 (20)	0.03
Head trauma	61/376 (16)	92/1,086 (8.5)	<0.001
Meningitis	4/319 (1.3)	46/1,040 (4.4)	0.006
Chronic head and neck conditions	51/420 (12)	96/1,255 (7.6)	0.007
Migraine	22/391 (5.6)	28/1,187 (2.4)	0.002
Family history positive for stroke	67/257 (26)	163/768 (21)	0.12

Values are n with condition/valid n (%).

^a Vasculopathy subtypes include cervicocephalic artery dissection, moyamoya disease/syndrome, transient cerebral arteriopathy, postvaricella arteriopathy, vasculitis, and arteriopathy not otherwise specified.

Table 3 Recurrent ischemic events and outcome stratified by stroke territory in 1,735 children with acute arterial ischemic stroke

Characteristics	Posterior stroke (n = 436)	Anterior stroke (n = 1,299)	Posterior vs anterior stroke, 2-tailed <i>p</i> Value
Recurrent ischemic event	66/217 (30)	115/522 (22)	0.02
Any antithrombotic medication before recurrence	16/17 (94)	31/36 (86)	0.65
Outcome			
Death	12/410 (2.9)	35/1,196 (2.9)	1.0
Normal neurologic examination at discharge	111/389 (29)	235/1,142 (21)	0.002
Discharge destination	Valid 376	Valid 1,113	<0.001
Home	325 (86)	861 (77)	
Rehabilitation hospital	46 (12)	205 (18)	
Other hospital	5 (1.3)	47 (4.2)	
Increased need of help 1 year after stroke	13/65 (20)	52/135 (39)	0.67
Increased need of help at last follow-up visit	51/153 (33)	161/369 (44)	0.03
“Child has recovered completely from the stroke” (as reported by parents at last follow-up visit)	87/220 (40)	176/543 (32)	0.07
PSOM score at last follow-up visit, median (IQR)	0.5 (0–1) Valid 204	1 (0.5–2) Valid 524	<0.001

Abbreviations: IQR = interquartile range; PSOM = Pediatric Stroke Outcome Measure. Values are n with condition/valid n (%).

CI 0.49–0.91; *p* = 0.01), and increased with CCAD (OR 1.88, 95% CI 1.11–3.17; *p* = 0.02) (table 4).

Full recovery was reported by parents of roughly a third of children after PCAIS and ACAIS at the last follow-up visit (table 3).

Recurrent ischemic events were more frequent in PCAIS than ACAIS despite similar rates of secondary preventive antithrombotic treatment. The multivariable logistic regression

analysis revealed PCAIS (OR 1.69, 95% CI 1.08–2.65; *p* = 0.02) and CCAD (OR 2.39, 95% CI 1.36–4.22; *p* = 0.003) as risk factors for recurrent ischemic events (table 5).

Neonatal stroke

Neonates with PCAIS did not differ from neonates with ACAIS in terms of clinical presentation, sex distribution, risk factors, diagnostic imaging modality, complications such as hemorrhagic transformation, recurrence, and outcome (table 6). Cardiac disease was present in the only patient with recurrent

Table 4 Predictors of neurologic deficit at discharge in children

Variable	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	<i>p</i> Value	OR (95% CI)	<i>p</i> Value
PCAIS (vs ACAIS)	0.65 (0.50–0.85)	0.001	0.61 (0.45–0.84)	0.002
CCAD	1.94 (1.17–3.24)	0.011	1.88 (1.11–3.17)	0.02
Cardioembolic stroke	0.78 (0.60–1.01)	0.063	0.67 (0.49–0.91)	0.01
Male sex	0.92 (0.48–0.72)	0.48	—	—
Age, y	0.99 (0.97–1.01)	0.52	—	—
Recurrent ischemic event	1.02 (0.68–1.54)	0.91	—	—
Underlying chronic illness	0.99 (0.77–1.28)	0.95	—	—

Abbreviations: ACAIS = anterior circulation arterial ischemic stroke; CCAD = cervicocephalic artery dissection; CI = confidence interval; OR = odds ratio; PCAIS = posterior circulation arterial ischemic stroke.

Table 5 Predictors of recurrent ischemic events in children

Variable	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	<i>p</i> Value	OR (95% CI)	<i>p</i> Value
PCAIS (vs ACAIS)	1.55 (1.08–2.21)	0.016	1.69 (1.08–2.65)	0.02
Age, y	1.03 (1.00–1.06)	0.042	1.01 (0.98–1.05)	0.5
CCAD	2.64 (1.52–4.58)	0.001	2.39 (1.36–4.22)	0.003
Male sex	0.93 (0.66–1.30)	0.66	—	—
Cardioembolic stroke	0.83 (0.56–1.22)	0.34	—	—

Abbreviations: ACAIS = anterior circulation arterial ischemic stroke; CCAD = cervicocephalic artery dissection; CI = confidence interval; OR = odds ratio; PCAIS = posterior circulation arterial ischemic stroke.

ischemic event after PCAIS, and more frequent in recurrences after ACAIS (13% vs 2% in noncardiac patients, $p = 0.001$). Complete recovery from stroke at last follow-up visit (median follow-up 2 years) was reported in more than one third of neonates with PCAIS.

Discussion

This large international observational study comprehensively compares PCAIS with ACAIS throughout the pediatric age groups, demonstrating that pediatric PCAIS is less frequent than ACAIS in both neonates and children, and confirming our hypothesis of a distinct clinical presentation, risk factor profile, and outcome in children, but not in neonates with PCAIS compared with ACAIS.

PCAIS presenting beyond the newborn period is associated with older age at stroke onset and different risk factor profiles, with higher rates of CCAD, acute/chronic head and neck conditions, and migraine, and lower rates of cardioembolic conditions, transient cerebral arteriopathy, moyamoya arteriopathy, acute systemic illnesses, and hematologic disease, when compared to ACAIS. In a systematic review of CCAD and stroke in childhood, patients with CCAD leading to PCAIS were younger than those with ACAIS,¹⁴ while CCAD occurred at any age throughout childhood in a more recent prospective study.¹⁵ Lower rates of cardioembolic events in PCAIS are not unexpected as the anterior circulation carries the majority of the cerebral blood supply, and as a consequence emboli from the heart are more likely to travel to the middle or anterior cerebral artery.¹⁶ In children, cardioembolic events often occur in the perioperative period in younger children with complex congenital heart disease.¹⁷ Similarly, involvement of the posterior circulation occurs later in children with moyamoya syndrome.¹⁸

A marked male preponderance has been reported in PCAIS.^{1–4,8} These previous studies did not correct for potential confounding factors such as preceding trauma and CCAD. In the current study, the association between PCAIS

and male sex persisted even when correcting for trauma, but not for CCAD. The reason for this finding remains to be determined. Higher testosterone levels have been reported in some pediatric stroke patients compared to healthy controls, but these findings were not analyzed further according to stroke location or etiology.¹⁹ A male preponderance has also been noted in adult patients with CCAD,^{20,21} but was more marked in the anterior than in the posterior circulation,²² and sex differences in putative risk factors, such as hypertension, hypercholesterolemia, or past smoking, may explain the higher frequency of CCAD in men.

Clinical presentation did differ, as hypothesized, with non-specific symptoms such as headache, vertigo, nausea, and vomiting being more common in PCAIS. However, seizures that may also mislead and delay the diagnosis were less common in PCAIS than in ACAIS, while altered consciousness was reported equally in both groups. In contrast to a previous report, these differences in clinical presentation did not seem to lead to a longer time to diagnosis.²³

MRI remains the imaging modality of choice to radiologically confirm diagnosis in PCAIS, as our data and previous studies show. CT has lower sensitivity for detection of acute infarction, particularly for smaller brainstem or cerebellar lesions, due to bony artifacts from the base of the skull.^{23–25} This study also highlights the importance of vascular imaging, including sequences for vessel wall pathologies, such as CCAD, which are highly prevalent in PCAIS.^{26,27}

Fatality rates were identical for PCAIS and ACAIS. In survivors, outcome was better and the need for inpatient rehabilitation was lower in PCAIS compared with ACAIS at discharge. Similar differences were observed at a median of 1.5 years after the stroke, even though children with PCAIS more often had recurrent ischemic events. Cervicocephalic artery dissections were associated with increased odds of neurologic deficits but outcomes differed for children with PCAIS vs ACAIS. While neurologic deficits occurred more often in CCAD compared with non-CCAD (93% vs 76%, $p < 0.001$) in ACAIS, this was not the case in PCAIS. This difference is no

Table 6 Characteristics, treatment, and outcome stratified by stroke territory among 703 neonates with acute arterial ischemic stroke

Characteristics	Posterior stroke (n = 71)	Anterior stroke (n = 632)	Posterior vs anterior stroke, 2-tailed p Value
Male	42 (59)	371 (59)	1.0
Clinical presentation			
Seizures	49/65 (75)	476/606 (79)	0.53
Altered consciousness	23/58 (40)	218/548 (40)	1.0
Time from onset of symptoms to diagnosis, h, median (IQR)	24 (1–68) Valid 7	32 (12–72) Valid 75	0.47
Maternal risk factors			
Arterial hypertension	5/52 (9.6)	43/503 (8.5)	0.15
Fever	2/52 (3.8)	54/495 (11)	0.80
Age, y	28 (23–34) Valid 40	29 (25–33) Valid 451	0.4
Neonatal risk factors			
Meningitis	3/63 (4.8)	12/560 (1.2)	0.19
Cardiac disease	13/65 (20)	173/565 (31)	0.09
Vasculopathy	2/66 (3)	11/564 (2)	0.64
Apgar score at 1 minute, % with score <4, median (IQR)	7 (4–9), 14% Valid 48	8 (6–9), 10% Valid 466	0.13
Apgar score at 5 minutes, % with score <4, median (IQR)	9 (8–9), 1.4% Valid 50	9 (8–9), 2.3% Valid 481	0.39
Any antithrombotic therapy	8/64 (12.5)	95/585 (16)	0.59
Hemorrhagic transformation	7/55 (12.7)	49/467 (11)	0.64
Recurrent ischemic event	1/27 (3.7)	14/261 (5.4)	1.00
Outcome			
Death	0	7/604 (1.2)	1.0
Normal neurologic examination at discharge	37/60 (62)	343/572 (60)	0.89
“Child has recovered completely from the stroke” (as reported by parents at last follow-up visit)	11/30 (37)	124/285 (44)	0.56

Abbreviation: IQR = interquartile range.
Values are n with condition/valid n (%).

longer present in the multivariable analysis because ACAIS cases outnumber PCAIS cases and because only a minority of strokes occurred as a consequence of CCAD (20% in PCAIS and 9% in ACAIS).

Relatively good outcome in children compared with adults has already been described after basilar artery stroke.²⁸ However, recent reports comparing ACAIS and PCAIS in adults show more similarities than differences, not only in initial stroke severity,²⁹ but also in terms of clinical outcome, which was favorable (modified Rankin Scale score 0–2) in a majority of patients with ACAIS and patients with PCAIS.³⁰

Previously reported as a rare occurrence in neonates,^{5,6} this study shows that PCAIS accounts for almost 10% of AIS in this age group. No significant differences between neonates with PCAIS and ACAIS were identified. A prior case series described 18 neonates with posterior cerebral artery stroke, 5 of whom did not have concomitant hypoxic-ischemic encephalopathy or hypoglycemia.⁷ We did not have serum glucose measurements available for cases recruited to the current study but Apgar scores were similar in all stroke territories; 14% of patients with PCAIS and 10% of patients with ACAIS had an Apgar score <4 at 1 minute and 1.4% of patients with PCAIS and 2.3% of patients with ACAIS had an Apgar score <4 at 5 minutes.

The main strengths of this study were the prospective international multicenter design, allowing enrollment of a large number of children, data collection according to a predefined standardized protocol, and comparison of neonates and children with PCAIS and ACAIS. However, information on some variables of interest, such as the PedNIHSS, which indicates stroke severity, recurrent ischemic events, and outcome data after discharge from hospital were missing in a substantial part of the study participants. Furthermore, selection bias towards more severe cases is a possibility because most enrolling sites were tertiary pediatric care centers. This may also explain the higher recurrence rates after neonatal stroke observed in the current study, compared to the previous literature. The IPSS does not provide detailed information on imaging modalities such as the rate of cervical angiographies performed or the MRI sequences used; thus diagnosis of certain conditions such as vasculopathies may be underrecognized or overestimated.

PCAIS is less common than ACAIS in the pediatric population. Children with PCAIS are older, have higher rates of CCAD and other head and neck conditions, lower stroke symptom severity at presentation, increased stroke recurrence risk, and better outcome than children with ACAIS.

Author contributions

B.G.S. designed/conceptualized the study, analyzed/interpreted the data, drafted the manuscript, and collected data. M.F.R. designed/conceptualized the study, interpreted the data, collected data, and reviewed and edited the manuscript for content. M.C., W.D.L., L.A.B., L.L.B., C.K.F.: data collection, critical review of the manuscript, editing manuscript for content. A.P. analyzed/interpreted the data and reviewed the manuscript, editing manuscript for content. M.T.M., M.S.: initiated, designed, conceptualized, and supervised the study, analyzed/interpreted the data, revised the manuscript, and collected data. All authors agreed on submission of the present version of the manuscript.

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