

Childhood AIS Standardized Classification and Diagnostic Evaluation (CASCADE)
classification for pediatric stroke etiology, according to Bernard et al.⁷

CASCADE Criteria Primary Subtypes	
Basic-Subtype CASCADE Criteria (Only One Selected)	Expanded-Subtype CASCADE Criteria (Only One Selected)
☐ Small Vessel Arteriopathy (SVA)	SVA
	☐ Definitive
	☐ Radiographic confirmation
	☐ Biopsy confirmation
	☐ Probable
☐ Unilateral Focal Cerebral Arteriopathy (FCA)	FCA
	☐ Anterior circulation with collaterals
	☐ Anterior circulation without collaterals
	☐ Posterior circulation
	☐ Other
☐ Bilateral cerebral arteriopathy of childhood	Bilateral cerebral arteriopathy of childhood
	☐ With collaterals
	☐ Without collaterals
	☐ Other
☐ Aortic/cervical arteriopathy	Aortic/cervical arteriopathy
	☐ Dissection
	☐ Takayasu arteritis
	☐ Other
☐ Cardioembolic	Cardioembolic
	☐ Definite
	☐ Probable
☐ Other	Other
	☐ Undetermined cause ☐ Other
☐ Multifactorial	Multifactorial
	☐ Multifactorial

CASCADE criteria secondary subtypes	
Secondary subtypes (select as many as apply)	Examples
Genetic: vasculopathy	PHACES syndrome, Williams syndrome, trisomy 21, neurofibromatosis, Alagille syndrome, and sickle cell disease
Infectious	Postvaricella arteriopathy, meningitis, and HIV vasculopathy
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
Inflammatory	Idiopathic (primary central nervous system vasculitis), systemic inflammatory, or autoimmune disease (eg, lupus)
Genetic: metabolic	Mitochondrial cytopathy
Drug/toxin exposure	Intravenous immunoglobulin, l-asparaginase, drugs of abuse, and postcranial irradiation
Vasospasm	Reversible vasospastic syndromes

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.

Sex, Age at stroke onset (years)	Occluded MCA (side, segment) Other affected homolateral arteries	Arterial involvement	Recanalisation treatment Patency at 48hrs	Collaterals: presence, delay after stroke (mths), type	Stroke recurrence / Arterial worsening after 12 months	Stroke etiology (Cascade Subtype)
M, 13.6	L, pM2 C1, A1	Unilateral	IV r-tPA Residual stenosis	-	- / -	Aortic/cervical arteriopathy dissection
M, 11.9	L, pM2 C1	Unilateral	IV r-tPA Occlusion	-	- / -	Aortic/cervical arteriopathy dissection
M, 9.2	R, pM1 C1, A1	Unilateral	- nd	-	+ / -	Aortic/cervical arteriopathy other (systemic disease, FARSA deficiency)
F, 8.6	L+R, dM1 C1, A1	Bilateral	IV r-tPA nd	+, 0, perforating	- / -	Bilateral cerebral arteriopathy of childhood with collaterals, moyamoya angiopathy
F, 4.1	L, pM2 none	Bilateral	- Occlusion	+, 16.6, U-PSAB + perforating	+ / +	Bilateral cerebral arteriopathy of childhood with collaterals, moyamoya angiopathy (sickle cell disease)
F, 4.3	R, pM1 C1, A1	Bilateral	- nd	+, 0, perforating	- / +	Bilateral cerebral arteriopathy of childhood with collaterals, moyamoya angiopathy
M, 0.3	L, pM1 C1, A1	Unilateral	- nd	-	- / -	Cardioembolic definite
M, 6.5	R, pM2 None	Unilateral	IV r-tPA Patent	-	+ / -	Cardioembolic definite
M, 5.5	L, dM1 None	Unilateral	IV r-tPA, MT Occlusion	-	+ / -	Cardioembolic definite
F, 1.2	R, dM1 None	Unilateral	- nd	-	- / -	Cardioembolic definite
F, 0.1	L, pM1 A1	Unilateral	- nd	-	- / -	Cardioembolic definite
F, 11.9	L, pM2 None	Unilateral	IV r-tPA Patent	-	+ / -	Cardio-embolic probable
F, 14.2	R, pM1 None	Unilateral	IA r-tPA Occlusion	-	- / -	Hematologic/Thrombotic

M, 6.1	R, pM2 None	Unilateral	- Occlusion	-	+ / -	Hematologic/Thrombotic
M, 0.6	L, dM1	md	- nd	+, 23.8 U-PSAB	- / -	Unilateral FCA Anterior circulation with collaterals
M, 6.3	L, pM1 C1, A1	Unilateral	- nd	+, 11.7 U-PSAB	- / -	Unilateral FCA Anterior circulation with collaterals
F, 3.6	L, pM1	md	- nd	+, 3.1 U-PSAB	- / -	Unilateral FCA Anterior circulation with collaterals
M, 0.5	R, pM2 C1, A1	Unilateral	- nd	+, 7.2 U-PSAB	- / -	Unilateral FCA Anterior circulation with collaterals
F, 1.6	R, pM2 none	Unilateral	IV r-tPA, MT Occlusion	+, 5.3 U-PSAB	- / -	Unilateral FCA Anterior circulation with collaterals
M, 0.2	L, pM1 A1	Unilateral	- nd	+, 17.5 U-PSAB	- / -	Unilateral FCA Anterior circulation with collaterals
F, 2.3	L, pM1 C1	Unilateral	- Occlusion	+, 4.2 U-PSAB	- / -	Unilateral FCA Anterior circulation with collaterals
F, 9.1	L, pM1 A1	Unilateral	IV r-tPA Residual stenosis	+, 11.3 U-PSAB	- / -	Unilateral FCA Anterior circulation with collaterals
F, 10.2	L, pM1 C1 + A1	Unilateral	IV r-tPA, MT Residual stenosis	none	- / -	Unilateral FCA Anterior circulation without collaterals
M, 0.6	R, pM2 none	Unilateral	- nd	none	- / -	Unilateral FCA Anterior circulation without collaterals
M, 0.6	L, pM1 C1, A1	Unilateral	- Occlusion	none	- / -	Unilateral FCA Anterior circulation without collaterals
M, 3.7	L, pM1 none	Unilateral	- Residual stenosis	none	- / -	Unilateral FCA Anterior circulation without collaterals

Supplemental Table 1: Characteristics of patients with anterior circulation AIS and LVO

Legends: +: present, -: absent, L: left, R: right, p: proximal, d: distal, MT: mechanical thrombectomy, U-PSAB: unilateral post-stroke anastomotic bridge, FCA: focal cerebral arteriopathy

	Unilateral FCA - Anterior circulation with collaterals (n=8)	Unilateral FCA - Anterior circulation without collaterals (n=4)	Bilateral cerebral arteriopathy of childhood with collaterals - moyamoya angiopathy (n=3)	Cardioembolic (definite or probable) (n=6)	Aortic/cervical arteriopathy - dissection (n=3)	Hematologic / Thrombotic (n=2)
Median age at stroke onset (years old)	1.9	2.2	4.3	3.4	12	10.2
Presence of a stroke risk factor (% , n)	0%, 0/8	25%, 1/4 Recent benign TBI	33%, 1/3 Sickle cell anemia	67%, 4/6 Malformative cardiopathy n=3, Cardiac arrhythmia & ECMO n=1	33%, 1/3 Multivisceral disease with FARSA deficiency	50%, 1/2 Leukemia
Stroke location						
Deep MCA (D-MCA) territory (n)	88%, 7/8	100%, 4/4	33%, 1/3	67%, 4/6	100%, 3/3	50%, 1/2
Superficial MCA (S-MCA) territory (n)	88%, 7/8	100%, 4/4	100%, 3/3	83%, 5/6	33%, 1/3	50%, 1/2
ACA territory (n)	0%, 0/8	25%, 1/4	0%, 0/3	17%, 1/6	33%, 1/3	0%, 0/2
Stroke severity						
Large stroke (D-MCA + S- MCA or D- or S-MCA + ACA) (n)	75%, 6/8	100%, 4/4	33%, 1/3	67%, 4/6	33%, 1/3	0%, 0/2
Recanalization treatment (n)	25%, 2/8 IV r-tPA n=1, IV r-tPA + MT n=1	25%, 1/4 IV r-tPA + MT	33%, 1/3 IV r-tPA	50%, 3/6 IV r-tPA n=2, IV r-tPA + MT n=1	67%, 2/3 IV t-tPA	50%, 1/2 IA r-tPA
Recurrent stroke during follow-up (n)	0%, 0/8	0%, 0/4	33%, 1/3	50%, 3/6	33%, 1/3	50%, 1/2

Supplemental Table 2: Comparison of characteristics and outcomes in stroke patients according to stroke etiology (CASCADE classification).

FCA: Focal Cerebral Arteriopathy, ECMO: extra-corporeal membrane oxygenation, MT: mechanical thrombectomy