The Turkish Journal of Pediatrics 2023; 65: 309-320
https://doi.org/10.24953/turkjped.2022.350

Original Article

Evaluation of risk factors, functionalities, and quality of life in patients with pediatric acute arterial ischemic stroke

Fatih Mehmet Akif Özdemir[1], Ülkühan Öztoprak[1], Ali Fettah[2], Utku Arman Örün[3], Mustafa Kılıç[4], Fatma Gül Sarıkaya[5], Betül Derinkuyu[6], Deniz Yüksel[1]

[1]Department of Pediatric Neurology, University of Health Sciences, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara; [2]Department of Pediatric Hematology-Oncology, University of Health Sciences, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara; [3]Department of Pediatric Cardiology, University of Health Sciences, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara, [4]Department of Pediatric Metabolism, University of Health Sciences, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara, [5]Department of Physical Medicine and Rehabilitation, University of Health Sciences, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara, [6]Department of Pediatric Radiology, University of Health Sciences, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara, Türkiye.

ABSTRACT

Background. This study aimed to evaluate the etiology and prognosis of patients followed up for pediatric acute arterial ischemic stroke.

Methods. The clinical characteristics and etiology of patients aged 1 month-18 years who had acute arterial ischemic stroke between January 2010 and December 2020 were retrospectively evaluated. At last follow-up, the patients' functionality (Barthel Index, Functional Independence Measure), quality of life (SF-36 questionnaire), and motor outcomes (Gross Motor Function Classification System) were recorded prospectively/cross-sectionally.

Results. Forty children (25 boys) with a median current age of 112.5 months (range: 3.6-294) were included in the study. The most frequent etiology was prothrombotic disorders, and the most important factor associated with long-term mortality was valvular heart disease. Of the 27 (67.5%) surviving patients, 29.6% had positive motor outcomes and 29.6% were independent according to the Barthel Index. In terms of quality of life, SF-36 scores were highest in the pain scale and lowest in emotional role difficulty.

Conclusions. Determining the etiology and evaluating prognosis are important to plan effective treatment and rehabilitation for pediatric acute arterial ischemic stroke.

Key words: pediatrics, acute arterial ischemic stroke, etiology, risk factors, prognosis.

Arterial ischemic stroke (AIS) accounts for almost half of all strokes in children.[1] Recent epidemiological data show that the annual incidence of pediatric stroke has increased to 1.2-8/100 000 children.[2] The mortality rate of pediatric stroke is 10-40%, with more than half of survivors developing a major neurologic deficit and 15-50% developing epilepsy.[3-5] Cardiac disorders, arteriopathies, and rheumatologic, metabolic, infectious, and genetic diseases are the common risk factors for pediatric stroke.[1,2,4,6-12] In this study, we aimed to evaluate the etiological profiles, functionality, and quality of life, and motor function of pediatric patients followed for acute AIS in a single center.

✉ Fatih Mehmet Akif Özdemir
fatihmehmetakif@hotmail.com

Received 19th April 2022, revised 18th July 2022, 14th September 2022, accepted 7th December 2022.

This study was presented as a poster at the 17th International Child Neurology Congress in Antalya, Türkiye in 3-7 October 2022.

Material and Methods

Pediatric patients between the ages of 1 month and 18 years diagnosed with acute AIS were identified by retrospective review of pediatric neurology consultation notes taken between January 2010 and December 2020 at the University of Health Sciences Dr. Sami Ulus Maternity and Children's Training and Research Hospital which is a tertiary care hospital in Ankara, Türkiye. Arterial ischemic stroke was identified as an acute neurological deficit (or isolated seizures in the infants <6 months) with acute infarct(s) corresponding to the arterial regions determined by magnetic resonance imaging (MRI).[2] Excluded from the study were patients whose records could not be accessed, patients with metabolic stroke in the absence of primary cerebrovascular involvement (e.g., organic academia), and patients with transient ischemic attack without infarct, hypotensive watershed injury, reversible hypertensive leukoencephalopathy, or diffuse hypoxic encephalopathy. The patients were evaluated retrospectively in terms of current age, age at the time of diagnosis, sex, parental consanguinity, family history of stroke, initial clinical presentation, laboratory findings, imaging findings (MRI, computed tomography), vascular involvement pattern/trace, electroencephalogram (EEG), comorbidities, treatments, follow-up period, and prognosis.

In treatment, the use of heparin is preferred in patients with high risk of recurrence and patients without bleeding risk. The use of heparin in AIS is indicated in patients with arterial dissection, prothrombotic risk, and embolism risk associated with congenital or acquired heart diseases. The use of warfarin in children is recommended in the presence of congenital or acquired heart disease, arterial dissection, and recurrence despite aspirin therapy.[13]

The patients were divided into three groups according to age at AIS (1 month to <2 years, 2 to <5 years, and ≥5 years) to enable statistical analysis. The following patient data at initial presentation to the hospital were evaluated: complete blood count, serum glucose, serum electrolytes, blood urea nitrogen, creatinine, liver function tests, erythrocyte sedimentation rate, C-reactive protein (CRP), lipid profile, coagulation parameters, metabolic screening, tests related to infectious and vasculitis etiology, electrocardiography, and echocardiography. Additional data included in the analysis were lipoprotein (a), protein C, protein S, fibrinogen, antithrombin III, homocysteine, and factor VII, VIII, IX, XI, XII, XIII levels, active protein C resistance, anti-cardiolipin antibodies, antiphospholipid antibodies, genetic analyses for factor V Leiden, prothrombin G20210A, and methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C mutations, and any other genetic examinations, if performed.

Of these parameters, protein C, protein S, and antithrombin III levels were considered significant if still low at 3 months after AIS. Lipoprotein (a) level higher than 30 mg/dL, homocysteine level higher than 27.9 mmol/L[14], and factor VIII level higher than 150% were accepted as risk factors. Homozygous MTHFR C677T mutation was accepted as a risk factor on its own, while heterozygous MTHFR C677T, and homozygous or heterozygous MTHFR A1298C mutations were considered a risk factor if accompanied by elevated homocysteine. Among the prothrombotic risk factors, we also evaluated dyslipidemia because of its prothrombotic mechanism of action.[1,15-18] Lipid profile risk factors were defined as total cholesterol above 200 mg/dL, low-density lipoprotein (LDL) cholesterol above 130 mg/dL, triglycerides above 100 mg/dL for children aged 0-9 years and above, 130 mg/dL for those aged 10-18 years, and high-density lipoprotein (HDL) cholesterol below 40 mg/dL.[19] Apart

from prothrombotic risk factors, sickle-cell anemia, hemolytic anemia, polycythemia and thrombocytosis were accepted as hematologic risk factors.[11,20] Polycythemia was defined as a hemoglobin level above the 97th percentile for the patient's age.[21]

Mortality status was ascertained from medical records or phone calls. Deaths occurring during the patient's first hospitalization were classified as acute mortality, and all deaths including those that occurred after discharge were defined as long-term mortality.

At last follow-up, surviving patients (n=27) underwent a prospective, cross-sectional prognostic evaluation including functional assessment using the Barthel Index and WeeFIM (Pediatric Functional Independence Measure) and quality of life evaluation using the Short Form 36 (SF-36) quality of life questionnaire.[22-25] Full independence according to the Barthel Index was evaluated as a positive prognosis. Moreover, motor disability was measured using the Gross Motor Function Classification System (GMFCS). A GMFCS score of 1 was accepted as a positive motor outcome. The WeeFIM is an 18-item ordinal instrument that measures functional performance in the motor and cognitive domains. Items are rated from level 1 to 7, where level 1 represents complete dependence, and at level 7 the child completes the task independently without the need for any assistance or device and with no concern regarding safety or taking a prolonged amount of time. Due to the COVID-19 pandemic, assessments of functional ability and quality of life were done by telephone interview. In addition, the presence of aphasia, hemiplegia, recurrence, and epilepsy were recorded at last follow-up.

Statistical methods

Data were analyzed using IBM SPSS version 23. Data distributions were examined with Shapiro-Wilk test. Comparisons of categorical data between groups were made using chi-square and Fisher's exact tests. In comparisons of quantitative data between dichotomous groups, independent two sample t-test was used for normally distributed data and Mann-Whitney U test for non-normally distributed data. Risk factors associated with mortality were examined using binary logistic regression analysis. Backward: Wald model was used to include independent risk factors in the multivariate model. Results were presented as mean, standard deviation, median, and range for quantitative data and as frequency and percentage for categorical data. Statistical significance was accepted at the $p<0.05$ level.

Ethical approval

Ethics committee approval was obtained for the study (date: 07 April 2021, protocol number: E-21/04-143, decision number: 2020-KAEK-141/147, University of Health Sciences, Dr. Sami Ulus Training and Research Hospital). All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the parents or guardians of the patients in the prospective part of the study and assent was obtained from the patients themselves when appropriate.

Results

A total of 40 children were included in the study, 25 of whom were male. The most common presenting symptom was seizure. Selected demographic and clinical characteristics of the patients are summarized in Table I.

Multiple risk factors were present in 85% of the patients, and the most frequent etiologic risk factor was prothrombic factors, seen in 67.5% patients. The most common prothrombotic factor in our patients was low HDL cholesterol

(n=14, 35%), followed by high triglycerides (n=11, 27.5%), presence of lupus anticoagulant (n=7, 17.5%), homozygous MTHFR C677T mutation (n=4, 10%), heterozygous factor V Leiden mutation (n=3, 7.5%), high total cholesterol (n=3, 7.5%), high lipoprotein (a) (n=2, 5%), high factor VIII level (n=2, 5%), high LDL cholesterol (n=2, 5%), protein C deficiency (n=1, 2.5%), protein S deficiency (n=1, 2.5%), anti-cardiolipin IgG/IgM positivity (n=1, 2.5% for each), anti-phospholipid IgG positivity (n=1, 2.5%), heterozygous prothrombin G20210A mutation (n=1, 2.5%), and presence of activated protein C resistance (n=1, 2.5%).

Table I. Patient demographics and clinical characteristics (n=40).

Current age (months), mean±SD, median (range)	116.4 ± 72.8, 112.5 (3.6-294)
Age at initial presentation (months), mean±SD, median (range)	69.4 ± 62.1, 45 (1.2-204.7)
Sex (male), n (%)	25 (62.5)
Parental consanguinity, n (%)	18 (45)
Family history of stroke, n (%)	6 (15)
Risk factors, n (%)	
Prothrombotic disorders	27 (67.5)
Cardiac disorders	26 (65)
Infections	13 (32.5)
Hematologic disorders	12 (30)
Arteriopathy/rheumatologic diseases	5 (12.5)
Genetic diseases	3 (7.5)
Metabolic diseases	1 (2.5)
Multiple risk factors	34 (85)
Presenting symptoms, n (%)	
Seizure	17 (42.5)
Motor deficit/weakness	10 (25)
Sensory abnormalities*	1 (2.5)
Change in consciousness	3 (7.5)
Headache	1 (2.5)
Ataxia	2 (5)
Chorea	2 (5)
Ocular motility disorder**	2 (5)
Diplopia	2 (5)
Treatment, n (%)	
Heparin	Initial: 5 (12.5)
Low molecular weight heparin	Initial: 20 (50), Ongoing: 21 (52.5)
Aspirin	Initial: 8 (20), Ongoing: 12 (30)
Warfarin	Initial: 1 (2.5)
Others	Initial: 6 (15), Ongoing: 7 (17.5)
Outcomes, n (%)	
Aphasia	1 (2.5)
Hemiplegia	16 (40)
Development of epilepsy	24 (60)
Recurrence	3 (7.5)
Acute/Long-term (overall) mortality	6 (15) / 13 (32.5)

*Numbness in the right leg and tongue, **Outward deviation of the left eye in one patient and strabismus in another patient

Initial treatment consisted of heparin in five patients (12.5%), low molecular weight heparin (LMWH) in 20 patients (50%), aspirin in eight patients (20%), and warfarin in one patient (2.5%) (Table I). Heparin was used in five patients, most of whom had multiple risk factors (predominantly cardiac; metabolic in one patient), due to suspicion of high recurrence risk. Warfarin was used as the initial treatment in one patient who was followed for cardiac disorder and continued with LMWH during follow-up.

MTHFR polymorphisms without hyperhomocysteinemia are not associated with cerebral stroke. Homocysteine data were available for 16 of the 17 patients with MTHFR polymorphisms. In these 16 patients, the mean homocysteine level was 8.7±2.8 mmol/L (median: 8.7, range: 4-14.6). Homozygous MTHFR C677T mutation was a risk factor in only four patients (10%). The MTHFR polymorphisms detected in the other patients were not considered significant risk factors because their homocysteine values were within normal limits.

The patients' mean hemoglobin level was 12.3±2.5 g/dL (median: 12, range: 7.9-18.2) and 17.5% of the children had polycythemia.

Anterior circulation AIS was present in 45% of the patients, posterior circulation AIS in 32.5% of the patients, and both anterior and posterior circulation AIS were present in 22.5% of the patients. There was basal ganglion infarct in 32.5% of the children, thalamic infarct in 20%, cerebellar infarct in 17.5%, and brain stem infarct in 15% of the children. Ischemic involvement of multiple lobes was present in 16 of the 21 patients with cortical involvement. Five percent of the patients also had hydrocephaly.

Stroke recurred in three patients, all of whom had multiple risk factors. One of these patients had phenylketonuria, homozygous MTHFR C677T mutation, high total and LDL cholesterol, and lupus anticoagulant positivity as risk factors, and recurrence was observed despite receiving heparin and LMWH after the first stroke. The second patient's risk factors included moyamoya disease, chronic hepatitis B virus infection, left ventricular hypertrophy, high total and LDL cholesterol, low HDL cholesterol, and recurrence occurred despite receiving aspirin therapy. In the third patient, risk factors included cardiac disorder, anti-rubella IgM and IgG positivity, anti-hepatitis A virus IgM and IgG positivity, and recurrence was observed despite receiving heparin and LMWH therapy.

Seizure was the initial symptom in 15 (62.5%) of the 24 patients who developed epilepsy.

The mean follow-up period of the patients was 13 months (range: 0.1-108.0). The results of the prognostic assessment of functionality (Barthel Index, WeeFIM), quality of life (SF-36), and motor outcomes (GMFCS) in the 27 surviving patients are shown in Table II. It was determined that eight patients (29.6%) were fully independent (positive prognosis) according to the Barthel Index and eight patients (29.6%) had a GMFCS score of 1 (positive motor outcome).

When quality of life was evaluated according to risk factors, scores for physical role difficulty and emotional role difficulty were higher in patients with arteriopathy/rheumatologic disease compared to those without, and lower in patients with hematologic risk factors compared to those without. In addition, quality of life scores in the psychological well-being domain were lower in patients with hematologic risk factors and higher in patients with genetic risk factors ($p<0.05$).

During follow-up, six patients (15%) died in the acute period and another seven died after the acute period, for a long-term mortality rate of 32.5%. Table III includes a summary of the factors associated with long-term mortality/survival among our patients.

Factors associated with long-term mortality were further analyzed by binary logistic regression analysis using univariate and multivariate models (Table IV). The multivariate model was created with the risk factors of valvular heart disease, follow-up period, and white blood count. When the multivariate model results were examined, the most important finding was that the mortality risk was 268 times higher in patients with valvular heart disease.

Table II. Prognostic assessment of functionality, quality of life, and motor outcomes (n=27).

Functionality – Barthel Index		
	n (%)	
Fully independent	8 (29.6)	Positive prognosis
Lowly dependent	1 (3.7)	Prognosis not positive
Moderately dependent	9 (33.3)	
Highly dependent	7 (25.9)	
Fully dependent	2 (7.4)	
	Mean ± standard deviation	
Barthel Index	68.0 ± 28.9	
Functionality – WeeFIM		
	Mean ± standard deviation	
Motor	66.0±23.3	
Cognitive	28.6±8.4	
Total	94.5±29.8	
Self-care	28.2±11.5	
Sphincter control	11.2±3.6	
Transfers	16.0±5.8	
Locomotion	10.6±4.0	
Communication	11.7±3.4	
Social interaction	16.9±5.1	
Quality of Life – SF-36		
	Mean ± standard deviation	
Physical functioning	49.1±39.1	
Physical role difficulty	37.5±48.6	
Pain	83.6±27.5	
General health perception	38.6±19.7	
Energy/vitality	43.6±17.6	
Social functioning	63.1±31.5	
Emotional role difficulty	36.4±49.2	
Psychological well-being	53.3±10.9	
Motor Outcomes – GMFCS		
	n (%)	
1	8 (29.6)	Positive
2	12 (44.4)	Not positive
3	2 (7.4)	
4	3 (11.1)	
5	2 (7.4)	

GMFCS: gross motor function classification system, SF-36: short form 36, WeeFIM: pediatric functional independence measure

Table III. Statistically significant factors associated with long-term mortality.

		Mortality (n=13)	Survival (n=27)	P
Age range of 2-<5 years	%	46.2	3.7	<0.001
Consanguineous marriage		76.9	29.6	0.005
Presence of ventricular septal defect		38.5	7.4	0.027
Presence of cardiomyopathy		23.1	0	0.029
Valvular heart disease		69.2	29.6	0.018
Presence of lupus anticoagulant		30.8	11.1	0.019
Elevated aspartate aminotransferase		53.8	22.2	0.043
Elevated alanine aminotransferase		30.8	0	0.010
Sodium abnormality		53.8	11.1	0.011
Hypocalcemia		23.1	0	0.029
Elevated C-reactive protein		76.9	33.3	0.034
Follow-up period <6 months		69.2	3.7	0.001
White cell count		15313±6289	10075±2916	0.012
Absolute neutrophil count	/mm^3, mean±SD	10006±5716	5865±3125	0.022
Platelet count		269153±231469	337666±128101	0.039
Pyruvate	mg/L, mean±SD	3.7±0.2	1.0±0.6	0.031
D-dimer	ng/mL, mean±SD	5835.1±8575.5	870.4±1103.0	0.004

Presented as percentages unless indicated otherwise. SD: standard deviation

Table IV. Logistic regression analysis of factors associated with long-term mortality.

	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Age range (1 month-<2 years)				
2-<5 years	2 (0.09–44.35)	0.661		
>5 years	0.053 (0.004–0.648)	0.021		
Consanguinity (no)	7.917 (1.711–36.633)	0.008		
Absence of VSD	7.812 (1.262–48.356)	0.027		
Absence of valvular heart disease	5.344 (1.268–22.523)	0.022	268.204 (1.21–59441.503)	0.042
Normal sodium	8 (1.537–41.637)	0.013		
Normal CRP	6.296 (1.374–28.855)	0.018		
AST	1.025 (0.999–1.053)	0.059		
ALT	1.05 (0.994–1.111)	0.083		
Sodium level	1.037 (0.888–1.21)	0.648		
CRP level	1.091 (0.993–1.198)	0.07		
Follow-up period	0.929 (0.876–0.986)	0.016	0.906 (0.824–0.997)	0.043
Calcium	0.104 (0.021–0.513)	0.005		
White cell count	1.0003 (1.00007–1.0005)	0.007	1.001 (1–1.001)	0.034

ALT: alanine aminotransferase, AST: aspartate aminotransferase, CRP: C-reactive protein, VSD: ventricular septal defect

Discussion

Pediatric AIS is a life-threatening condition that also causes persistent motor deficits in most survivors and is often accompanied by epileptic, cognitive, or behavioral abnormalities.[3,12,26] In this study, 40 patients with pediatric AIS followed in a major tertiary referral children's hospital were retrospectively evaluated in terms of etiology and clinical characteristics

and prospectively/cross-sectionally evaluated in terms of prognosis (functionality, quality of life, motor outcomes, recurrence, epilepsy development, and mortality). Most (85%) of the patients had more than one risk factor, with the most common etiologic risk factor being prothrombic factors (67.5%). At last examination, 40% of the patients had hemiplegia, 60% had epilepsy, and 7.5% had a recurrence. Acute and long-term mortality rates were 15% and 32.5%, respectively.

Etiological risk factors for stroke vary between studies. Similar to our findings, prothrombotic risk factors were present in 63% of pediatric cases in another study.[27] Prothrombotic disorders, infections, and arteriopathy have been reported as the most frequent risk factors for pediatric stroke in various studies.[6,10,12,28,29] deVeber et al.[2] determined that arteriopathy unrelated to infection was the most important risk factor for pediatric stroke (49%), followed by cardiac disorders (28%). Central nervous system infection was a risk factor in only 3% of the AIS cases in their series.[2] In another study examining pediatric AIS cases, the most common risk factor was heart disease (17%), followed by head trauma (13%), rheumatologic disorders (7.5%), meningitis, and encephalitis (4%).[30] Developments in etiological studies have made it possible to better define risk factors. In our study, we determined that prothrombic risk factors were most common, followed by cardiac disorders, infections, hematologic causes, arteriopathy/rheumatologic, genetic, and metabolic diseases. Prothrombotic risk factors were more common in the etiology of stroke in our study than that described in the literature. However, our results are consistent with the literature in identifying prothrombotic risk factors and congenital heart diseases as common risk factors for AIS.[6,10,12,28-30] In addition, considering the negative impact of cardiac risk factors on mortality, we suggest that more studies are needed on the prevention and treatment of AIS in patients with prothrombotic and/or cardiac risk factors.

Our study provides important data on the etiology and prognosis of pediatric AIS. Defining lipid profile changes as a definite prothrombotic risk factor in our study may have contributed to prothrombotic risk factors emerging as the most common etiology. In our patients, high cholesterol level in three patients (7.5%), high triglycerides in 11 (27.5%), high LDL cholesterol in two (5%), and low HDL cholesterol in 14 patients (35%) were identified as risk factors. Lipid profile abnormality was detected in 17 (43%) of our patients. Our results support recent studies emphasizing that dyslipidemia and hypertriglyceridemia are more common in pediatric AIS patients.[31]

More than two-thirds of the patients in our study had multiple risk factors, which was previously reported to be a predictor of stroke recurrence.[5] In the literature, a 7-14% risk of recurrence has been reported for childhood stroke, with rates of recurrence related to a number of causes, the most common of which are heart disease, moyamoya disease and genetic thrombophilia.[5,28,32] All three of our patients with stroke recurrence were found to have more than one risk factor.

It was reported that children who have an acute seizure during stroke or within 24 hours after hospitalization have a higher likelihood of developing epilepsy than children without seizure at the time of stroke.[33,34] Similarly, most (88.2%) of the 17 patients who presented with seizure later developed epilepsy according to the 2014 practical clinical definition of epilepsy of the International League Against Epilepsy.[35] In our study, of the 29 patients with EEG data obtained at initial presentation, five (12.5%) had focal epileptic activity and nine (22.5%) had abnormal background activity. Of the nine patients with background abnormality, slowing of background activity was noted in six (67%), background asymmetry in two (22%), and voltage suppression in one patient (11%). However, long-term video EEG monitoring was not technically possible for every patient, which is a limitation of our study in terms of

the diagnosis of non-convulsive seizures/status epilepticus.

Stroke-related mortality rates between 1-32% have been reported in previous series.[2-4,10,36] In our study, the mortality rate was 15% in the acute period and 32.5% in the long term. The AIS-related acute mortality rate in our study is consistent with the studies in the literature, which have reported pediatric AIS-related in-hospital mortality rates of 14-16.5%.[37-39] Important factors associated with long-term mortality in our patients were parental consanguinity, cardiac disorders, liver function test abnormalities, electrolyte imbalance, high CRP, pyruvate, and D-dimer levels, and young age. In multivariate analysis, valvular heart disease was found to be associated with a 268 times higher risk of death. These data support the literature data pointing to congenital heart disease as the most important risk factor affecting the long-term mortality of pediatric AIS.[38,40-42] In follow-up studies of Canadian stroke patients with an average follow-up period of three years, deVeber et al.[2,3] reported 5% stroke-related mortality and neurologic deficits in 72% of patients (>50% mild). In our study, the rate of stroke-related mortality was 15% in the acute period and 32.5% in the long term, and at last follow-up it was determined that 40% of the patients had hemiplegia, 60% had epilepsy, and 7.5% had stroke recurrence.

Most studies on childhood stroke have shown that neurological deficits occur in 50-85% of survivors.[3,43] In our study, a positive motor outcome according to the GMFCS and full independence according to Barthel Index was achieved in approximately 30% of surviving patients over long-term follow-up (median of 48 months). According to functional assessment using the modified Rankin scale, 56% of children and 55% of young adults were reported to have acceptable functional outcomes after a median follow-up period of 6.9 years.[44] The long-term outcomes of acquired brain disease are known to be better in children than adults because of the plasticity of the brain. However, Simonetti et al.[44] compared the long-term clinical outcomes of stroke in patients younger than 16 years of age and young adult patients (aged 16-44 years) but detected no significant difference in long-term functional outcomes in terms of disability, mortality, or recurrence rates. We observed that 46.2% of the patients who died after the acute period had AIS between the ages of two and five years, while 92.6% of surviving patients had AIS after the age of five years ($p<0.001$). In our study, this supports the view that having a stroke after the age of five is a good prognostic indicator. Another study shows that having a stroke between the ages of 15 and 19 years is associated with higher mortality risk.[45]

It was reported in a prospective observational study on pediatric AIS that according to assessment with the Pediatric Stroke Outcome Measure (PSOM), 61% of children in the study group had an emotional-motor deficiency, 24% had a cognitive and behavioral deficit, 15% had a language production disorder, and 6% had a difficulty understanding language.[10] Felling et al.[46] evaluated data from the International Pediatric Stroke Study and determined that 24.7% of 413 children had moderate to severe deficits according to PSOM scores at 2-year follow-up.The mean WeeFIM total score of our patients was 94.5, the mean motor component score was 66.0, and the mean cognitive component score was 28.6. In a study of 18 patients with childhood stroke (13 of which were ischemic) admitted to a pediatric rehabilitation unit on mean post-stroke day 688, the mean total WeeFIM score was 74.9 at discharge from the unit (mean 55 days after admission).[47] When compared with the literature, functional outcomes of our patients were better according to their follow-up WeeFIM scores. The difference in the etiologic and demographic profiles of the patients, and different clinicians conducting the evaluation at follow up may be possible factors accounting for the outcomes. When we evaluated our patient group within itself according to risk factors, median

WeeFIM scores in the communication domain differed significantly based on the presence of arteriopathy/rheumatologic disease. No other differences in WeeFIM scores were detected in association with the other risk factors.

When quality of life was assessed using the SF-36, we observed that the patients' highest mean score was in the pain scale and the lowest score was in emotional role difficulty. In our review of the literature, we found no previous study using the SF-36 to assess quality of life in pediatric stroke. However, we conducted this evaluation because there is a study on adults in our country which defined the normative SF-36 scores of the regional population.[48] Our results suggest that childhood stroke has important negative effects on emotional development and that children should be supported emotionally after AIS.

The strength of our study is that we evaluated patients with pediatric AIS followed using a detailed multidisciplinary approach in a major tertiary referral children's hospital over a period of 11 years. However, a limitation of our study is that it included a relatively small sample because it was based on data from a single center.

In summary, the most frequent etiology of pediatric AIS in our study was prothrombotic risk factors. Mortality rates were 15% in the acute period and 32.5% in the long term. The most important factor associated with long-term mortality was the presence of valvular heart disease. When the survivors were evaluated, nearly 30% were independent or had positive motor outcomes and 60% had epilepsy. We conclude that determining the etiology and evaluating prognosis are important to plan effective treatment and rehabilitation for pediatric AIS.

Acknowledgements

We would like to thank all children, their parents, and all health professionals who took part in the care of our patients.

Ethical approval

The ethics committee of University of Health Sciences, Dr. Sami Ulus Training and Research Hospital approved this study (date: 07.04.2021, protocol number: E-21/04-143, decision number:2020-KAEK-141/147).

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: FMAÖ, ÜÖ, AF, UAÖ, MK, FGS, BD, DY; data collection: FMAÖ, ÜÖ, AF, UAÖ, MK, FGS, BD, DY; analysis and interpretation of results: FMAÖ, ÜÖ, AF, UAÖ, MK, FGS, BD, DY; draft manuscript preparation: FMAÖ, ÜÖ, AF, UAÖ, MK, FGS, BD, DY. All authors reviewed the results and approved the final version of the manuscript.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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