Outcome in Childhood Stroke

Mardee Greenham, PGDipPsych; Anne Gordon, PhD; Vicki Anderson, PhD; Mark T. Mackay, MBBS

Contrary to commonly held views, children do not recover better than adults after a stroke. The lifelong individual, family, and societal burden of stroke is likely to be greater than in adults because infants and children surviving stroke face many more years living with disability. The key difference between children and adults is that childhood stroke (occurring during the perinatal period and beyond) results primarily in a changed ability to achieve, rather than lose, functional independence. The extent and severity of deficits across motor, sensory, cognitive, social, and behavioral domains may not be apparent in the short-term after stroke, particularly in newborns and preschool children, who typically grow into their deficits.

The World Health Organization’s International Classification of Functioning (ICF), Disability, and Health can be applied to childhood stroke to describe its impact across health domains, including impairment in body structures and functions, activity limitations and participation restrictions at individual, institutional and social levels. This review will focus on childhood stroke, defined as stroke from 1 month to 18 years of age, and where possible use the ICF framework to describe outcome after arterial ischemic stroke (AIS) and hemorrhagic stroke (HS).

Body Structures and Functions

Mortality After Childhood Stroke

Stroke is among the top 10 causes of death in the pediatric population. The reported mortality for AIS ranges from 7% to 28% and from 6% to 54% for HS. In the US study reporting stroke mortality during a 10-year period from 1979 to 1998, 4881 deaths could be attributed to childhood stroke, giving average annual mortality rates of 0.09 per 100,000 person-years for AIS 0.14 for intracerebral hemorrhage and 0.11 for subarachnoid hemorrhage. Risk of death was higher in infants, males, blacks, and children living in the South-Eastern Stroke belt States. Declining mortality rates have been observed in childhood HS, possibly related to improvements in critical care, but there have been much smaller decreases in AIS mortality rates. This may be partially because of the underlying risk factors associated with AIS, such as heart disorders, which has an increased risk of mortality. It may also be because modifiable risk factors such as hypertension, smoking, and hyperlipidemia do not play important roles in pathogenesis in childhood stroke.

Risk Factors and Causes

A diverse range of risk factors have been identified in association with childhood stroke. In AIS, there is increasing evidence for factors, such as vasculopathy, infection, trauma, cardiac and hematologic disorders from case-control and cohort-based studies. Contrasting with adults, atherosclerosis is a rare cause for childhood AIS. Chronic diseases of childhood frequently underlie childhood AIS; however, approximately half of the children are previously healthy. Multiple risk factors converge in >50% of children with AIS but at least 10% remain idiopathic.

The common causes of nontraumatic HS are arteriovenous malformation, hematologic abnormalities, and brain tumor, with other pathogeneses, including cavernous hemangioma, vasculopathy, vasculitis, and infections.

Stroke Recurrence

Rates of recurrent AIS ranges from 6% to 35%. Population-based data suggest 5-year recurrence rates approach 50%. Presence of arteriopathy is the most important predictor of recurrent AIS with rates of >65% reported. Other factors associated with increased risk of recurrence or reinfarction include genetic thrombophilia, previous TIA, bilateral infarction, immunodeficiency, and leukocytosis.

The relative efficacy of various secondary stroke prevention interventions is unknown because of a lack of randomized controlled trials. There are however, some data to support specific interventions in conditions associated with high recurrence risk. In addition to primary prevention of stroke in children with an abnormal transcranial doppler, regular transfusions to reduce hemoglobin S to <20% to 30% protect against cerebrovascular events in children sickle cell disease and radiological evidence of silent cerebral infarction. Surgical revascularization procedures are successful at improving perfusion and reducing recurrent stroke or transient
ischemic attacks in children with Moyamoya disease. In contrast, a randomized controlled secondary prevention trial in children with complex congenital heart disease undergoing the Fontan procedure found no difference in the frequency of thrombotic events between those treated with antiplatelet or anticoagulant therapy. The study however, was not designed to identify asymptomatic cerebrovascular events.

There are less data on risk factors for recurrent HS in children. In a population-based cohort study of 2.3 million children, 116 cases of nontraumatic HS were identified during 11 years with a 5-year cumulative recurrence rate of 10%.

Almost two thirds of bleeds occurred within the first 6 months of diagnosis. No child with idiopathic HS had a recurrent event, whereas 13% of children with structural abnormalities such as AVMs or tumors and medical pathogeneses such as thrombocytopenia or hypertension had recurrent events.

**Post Stroke Epilepsy**

Post stroke epilepsy occurs in ≈15% to 20% of children with childhood AIS and ≤17% of HS. Larger cortical lesions are associated with higher risk of developing seizures.

Emerging data from the International Pediatric Stroke study suggest that the incidence of a first remote seizure is 1% per month, with a cumulative 13% incidence of active epilepsy by 1 year after childhood AIS. Younger age, multifocal or cortical infarction, involvement of the middle cerebral artery territory, presence of focal cerebral arteriopathy, presence and duration of symptomatic seizures at the time of diagnosis are associated with increased risk of epilepsy. Children with epilepsy complicating AIS have poorer cognitive outcomes and quality of life than those who do not.

**Neurological, Motor, and Speech Impairments After Childhood Ischemic Stroke**

A recent Swiss population-based study comparing long-term neurological outcomes in children and young adults with AIS found almost half of the children had long-term neurological impairments. Mortality, disability, psychosocial impairments, and quality of life outcomes did not differ for children and young adults with the exceptions of behavioral problems (more common in children) and impaired daily living skills (more common in adults). Long-term outcome in children was predicted by initial stroke severity. Another recent study investigating recovery across multiple domains of health, reported significant motor impairments in children at both 1- and 6-month post-AIS, in addition to deficits in adaptive behavior at 6 months. A large multinational observational study of 612 children with AIS found that almost 3 quarters of children had neurological deficits at the time of discharge. Poorer neurological outcomes were more common in children with altered consciousness at presentation, bilateral infarction, and presence of arteriopathies on brain imaging. Moderate or severe neurological deficits were observed in >40% of children and mild deficits in 20% of children in another Canadian study. Independent predictors of poor neurological outcome include AIS subtype, associated neurological disorders, and need for rehabilitation. Few studies reporting neurological impairments after childhood stroke have stratified outcome by pathogenic subgroup. Arteriopathy was associated with increased odds of adverse early outcome, defined as death or neurological deficit at discharge, in a large international multicentre study. Cardiac disease, and Moyamoya were associated with higher rates of neurological impairment in another French study. In contrast, other studies from the United Kingdom, Canada, and Switzerland found no association between specific risk factors or pathogeneses and poorer outcomes.

Physical and motor impairment are common after childhood AIS. Cross-sectional follow-up studies reporting motor impairments ranging from mild clumsiness to significant hemiparesis in 50% to 80% of children. Hemiplegia is reported in 3 quarters of children. Infarcts involving >10% of the supratentorial intracranial volume are typically associated with poor outcome. Different patterns of motor recovery in neonates compared with older children suggest age-dependent vulnerability of brain structures or varying capacity for corticomotor reorganization. However, trajectories of motor recovery from acute phase through to long-term remain unknown. Speech and language impairments have not been widely reported, but 1 study described language deficits in 30% of children 12 months after AIS. Language impairment is most common in left hemisphere strokes, but this may depend on age at onset. A study investigating long-term language outcomes in children with left subcortical AIS reported deficits in 6 of 9 patients, including naming difficulties, reduced fluency, repetition difficulties, and written language difficulties. They found posteriorly located lesions and younger age at stroke were associated with poorer language outcomes. Another study comparing children with left and right basal ganglia infarcts found no difference between the groups, but did note greater variation in performance of the patients with left hemispheric stroke. Further examination showed language deficits were associated with abnormalities in left hemisphere cortical language areas remote from the lesion site.

**Cognitive Function After Childhood AIS**

Studies investigating intellectual function after childhood AIS have found intelligence quotient scores are skewed toward the lower end of average and significantly lower than control groups and standardized test norms. Some studies report weaknesses in complex cognitive skills, including attention, executive function, visuconstructive skills, processing speed, and working memory. Rates of cognitive impairment are not frequently reported, but 1 study found attention and executive function deficits in 30% to 67%.

Larger lesion volume and infarcts affecting cortical and subcortical regions are associated with poorer cognitive outcomes. The effect of lesion laterality is unclear, with some studies reporting better neuropsychological outcomes after right hemisphere AIS and other studies demonstrating no laterality effects. Age at AIS also affects cognitive outcome, with possible periods of vulnerability and plasticity related to growth spurts within the brain. Earlier age at onset (before 1 year of age) has been found to be associated with poorer cognition in some studies, whereas others report poorer outcomes in later-onset AIS, when brain maturity is more
advanced. Cognitive outcomes vary widely between studies, possibly because of large cross-sectional design and differing methodology, such as varying age range of cohorts and wide range in time since diagnosis.

The majority of studies reporting cognitive and functional outcomes after childhood stroke have not assessed the influence of risk factors or pathogenesis on outcome. A recent Swiss multicentre study, however, found no association between risk factors and cognition.

**Neurological and Cognitive Impairments After HS**

HS has received less attention despite accounting for almost half of childhood strokes. Poor outcomes were reported in 25% to 52% of children after HS in a retrospective case series, Specific outcomes are usually not defined, but a recent US study of 19 children described mild to moderate neurological impairments and significantly lower quality of life than normative means in the majority of survivors. Predictors of poorer neurological outcomes include younger age, depressed conscious state at presentation in some, but not other studies, intracerebral hemorrhage volume and presence of vascular anomaly.

A recent review of functioning and disability after childhood stroke found that over half had physical impairments with paresis or cerebellar ataxia with a similar proportion, showing cognitive deficits when compared with premorbid academic functioning. These findings are consistent with an earlier US study of 26 patients, which reported motor and cognitive deficits in 38% and 50% of survivors, respectively.

**Activity Limitations and Participation Restrictions**

Most activity limitations and participation restrictions after childhood stroke occur in motor function, self-care skills, communication, educational problems, and social isolation. Reductions in family and school participation have been reported in 25% to 52% of children after HS in a retrospective case series. Specific outcomes are usually not defined, but a recent US study of 19 children described mild to moderate neurological impairments and significantly lower quality of life than normative means in the majority of survivors. Predictors of poorer neurological outcomes include younger age, depressed conscious state at presentation in some, but not other studies, intracerebral hemorrhage volume and presence of vascular anomaly.

A Dutch study describing long-term outcome in 31 survivors of childhood HS found that over half had physical impairments with paresis or cerebellar ataxia with a similar proportion, showing cognitive deficits when compared with premorbid academic functioning. These findings are consistent with an earlier US study of 26 patients, which reported motor and cognitive deficits in 38% and 50% of survivors, respectively.

A recent review of functioning and disability after childhood stroke found that over half had physical impairments with paresis or cerebellar ataxia with a similar proportion, showing cognitive deficits when compared with premorbid academic functioning. The severity of motor deficits varies, but most children gain or regain independent mobility. However, even mild motor impairment may limit a child’s ability to participate in activities and affect self-confidence. Task-based hand use has received limited attention, but 1 study reported bimanual tasks, such as eating and dressing, were a significant concern for parents. Findings from studies exploring adaptive behavior vary widely, with some reporting that most children attain age-appropriate independence, whereas others document poor outcomes in 60% of children.

Attention deficit/hyperactivity disorder symptoms (learning difficulties, attention problems, anxiety, and impulsivity) have been reported in 50% of children, externalizing behaviors in 44% and emotional problems in 25%. One study found 59% of children with stroke developed psychiatric disorders compared with only 14% of controls. Few studies have explored specific components of social function, but there is a trend toward reduced overall social function, lower levels of participation, and reduced peer acceptance. Associations have been reported between poorer psychosocial outcome and lesions in the ventral putamen and attention deficit/hyperactivity disorder symptoms and between lesions in the medial and orbital prefrontal correct and inattentive symptoms. Others, using less specific measures, report no link between psychological problems and lesion characteristics.

**Impact of Childhood Stroke on Quality of Life**

Quality of life has been investigated in several studies, all reporting reduced levels of well-being across a variety of domains. Severity of neurological impairment, sex (girls rate their quality of life lower than boys), younger age at stroke onset, cognitive function, self-esteem, and family factors, including parent well-being and family functioning have all (separately) been associated with poorer quality of life.

**Environmental Factors**

The ICF includes consideration of the impact of environmental factors (physical, social, and attitudinal) that may act as barriers or facilitators for effective daily living, but this area remains largely unexplored in childhood stroke outcome studies. The economic burden of childhood stroke on families and health services has, however, been reported. Higher stroke costs correlate with more impairment and poorer quality of life. A recent retrospective study estimated the 5-year direct medical cost of neonatal and childhood stroke to be $110,921, representing a 15-fold cost increase compared with controls. Costs were higher for childhood stroke ($135,611) than for neonatal stroke ($51,719) and higher for HS than AIS. Families experience substantial out of pocket expenses, related to lost wages, transportation and nonreimbursed health care.

**Outcome Measures for Childhood Stroke**

The childhood stroke literature uses measures and describes outcomes that focus predominantly on the domain of impairments in body structures and functions. There is currently no gold standard outcome measure for childhood stroke, and recent reviews have shown a wide variety of measures that have been used across studies. Many of the measures are author derived, and the majority of the standardized measures used are validated for use in children with other medical conditions, such as cerebral palsy and head trauma, and not appropriately sensitive to detect the focal and often mild deficits of childhood stroke. Many standardized, stroke-specific measures, such as the modified Rankin Scale and Barthel Index, have been developed for adults and rely on self-report and independence of daily living, making them inappropriate for young children. The Pediatric Stroke Outcome Measure is the only...
validated disease-specific measure for the childhood stroke population. The Pediatric Stroke Outcome Measure evaluates neurological impairment across sensorimotor, language, cognitive, and behavioral domains. High inter-rater reliability and construct validity of the Pediatric Stroke Outcome Measure has been found with excellent agreement for prospective and retrospective scoring. The Stroke Recovery and Recurrence questionnaire, derived from the Pediatric Stroke Outcome Measure for use as a telephone questionnaire, also demonstrates good agreement between total scores across both measures in a recent validation study.

Limitations of the Current Literature and Priorities for Future Research

The infrequent occurrence of childhood stroke means that most studies reporting outcomes consist of single-center cross-sectional or retrospective cohorts with variable duration of follow-up, thus limiting the strength of evidence. There is also limited reporting of the clinical, radiological, and environmental factors that may influence outcome (Table). As highlighted in a recent review, relatively few studies have explored outcome beyond body structure and function (as classified using the ICF-CY). Therefore, our knowledge of outcomes and contributing factors remains limited. Few studies provide details of which specific domains are affected, and use of terminology including impairments, outcome, and function vary widely. Standardized outcome measures are not always used, making it difficult to compare results, and only a small proportion of studies address daily life abilities of those affected by childhood stroke, instead focusing on specific domains of impaired body functions. These substantial gaps in knowledge mean there is little consensus to assist in guiding rehabilitation. Larger, prospective multicentre studies are required, using consistent diagnostic definitions and adequate outcome measures, to generate better outcome data. Future research should compare neurological and functional outcomes in children with cryptogenic stroke, to those with preexisting conditions such as congenital heart disease or sickle cell disease, to guide the development of targeted interventions to improve outcomes. Further investigation of other variables that potentially influence outcomes such as age and lesion characteristics may also assist in identifying children most at risk. In addition, longitudinal studies are essential, particularly in infants and younger children where it is more difficult to predict outcome and neurological deficits are not immediately apparent at the time of diagnosis.

Conclusions

Stroke is among the top 10 causes of death in children and is a significant cause of childhood disability. Most children will experience long-term neurological, motor, and cognitive impairments. Using the ICF classification, research to date has largely focused on body structures and functions, with little attention given to activity limitations and participation restrictions. Studies focusing on quality of life, psychosocial functioning, and daily living have begun to emerge in recent years but further research is required in these areas. It is therefore difficult to provide clear recommendations to clinicians about the optimal rehabilitation and long-term care of children affected by stroke. A recent Delphi Consensus Process surveyed parents of children with AIS to identify the most important and acceptable research outcomes from a community perspective. The consensus from parents was that studies focusing on assessment of motor, cognitive, and communication outcomes were of most interest. It is important that outcome research is informed by the expressed needs of the children, young people, and families, with an anticipation of the change in needs over time as a young person grows and matures. This needs to be undertaken alongside the

| Table. Factors Influencing Outcome in Childhood Arterial Ischemic Stroke |
|-----------------------------|---------------------|---------------------|---------------------|
| Outcomes | Death | Recurrent Stroke | Neuro Impairment |
| Reported rates | 7%–28% | 6%–35% | 50%–80% |
| Association | Yes | No | Yes | No | Yes | No |
| Demographics | | | |
| Age | ✓ | ✓ | ✓ | ✓ | ✓ |
| Sex | ✓ | ✓ | ✓ | ✓ | ✓ |
| SES | ✓ | ✓ | ✓ | ✓ |
| Ethnicity | ✓ | ✓ | ✓ | ✓ |
| Pathogenesis | | | |
| Risk factors | ✓ | ✓ | ✓ | ✓ |
| Associated neurological disorder | ✓ | ✓ | ✓ | ✓ |
| All arteriopathy | ✓ | ✓ | ✓ | ✓ |
| Moyamoya | ✓ | ✓ | ✓ | ✓ |
| SSD | ✓ | ✓ | ✓ | ✓ |
| Cardiac disease | ✓ | ✓ | ✓ | ✓ |
| Infection | ✓ | ✓ | ✓ | ✓ |
| Prothrombotic disorder | ✓ | ✓ | ✓ | ✓ |
| Type of antithrombotic Rx | ✓ | ✓ | ✓ | ✓ |
| Infarct characteristics | | | |
| Bilateral infarcts | ✓ | ✓ | ✓ | ✓ |
| Circulation | ✓ | ✓ | ✓ | ✓ |
| Location | ✓ | ✓ | ✓ | ✓ |
| Hemorrhagic change | ✓ | ✓ | ✓ | ✓ |
| Size | ✓ | ✓ | ✓ | ✓ |

This table summarizes the findings in the literature to date. Cross-study comparison is limited by large variation in study methodology, cohort characteristics, and time to assessment after stroke. SES indicates socioeconomic status; and SSD, sickle cell disease.
development of service delivery models that can provide flexible, targeted, and effective intervention and support.

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**Disclosures**

None.

**References**


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