ARTICLE

Clinical features, course, and outcomes of a UK cohort of pediatric moyamoya

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Abstract

Objective

To describe characteristics and course of a large UK cohort of children with moyamoya from multiple centers and examine prognostic predictors.

Methods

Retrospective review of case notes/radiology, with use of logistic regression to explore predictors of outcome.

Results

Eighty-eight children (median presentation age 5.1 years) were included. Thirty-six presented with arterial ischemic stroke (AIS) and 29 with TIA. Eighty had bilateral and 8 unilateral carotid circulation disease; 29 patients had posterior circulation involvement. Acute infarction was present in 36/176 hemispheres and chronic infarction in 86/176 hemispheres at the index presentation. Sixty-two of 82 with symptomatic presentation had at least one clinical recurrence. Fifty-five patients were treated surgically, with 37 experiencing fewer recurrences after surgery. Outcome was categorized as good using the Recovery and Recurrence Questionnaire in 39/85 patients. On multivariable analysis, presentation with TIA (odds ratio [OR] 0.09, 95% confidence interval [CI] 0.02–0.35), headache (OR 0.10, 95% CI 0.02–0.58), or no symptoms (OR 0.08, 95% CI 0.01–0.68) was less likely to predict poor outcome than AIS presentation. Posterior circulation involvement predicted poor outcome (OR 4.22, 95% CI 1.23–15.53). Surgical revascularization was not a significant predictor of outcome.

Conclusions

Moyamoya is associated with multiple recurrences, progressive arteriopathy, and poor outcome in half of patients, especially with AIS presentation and posterior circulation involvement. Recurrent AIS is rare after surgery. Surgery was not a determinant of overall outcome, likely reflecting surgical case selection and presentation clinical status.

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Glossary

ACA = anterior cerebral artery; **AIS** = arterial ischemic stroke; **CA** = catheter angiography; **CASCADE** = Childhood Arterial Ischemic Stroke Standardized Classification and Diagnostic Evaluation; **GOSH** = Great Ormond Street Hospital for Children; **LI** = local investigator; **MCA** = middle cerebral artery; **MRA** = magnetic resonance angiography; **mRS** = modified Rankin Scale; **OR** = odds ratio; **PSOM** = Paediatric Stroke Outcome Measure.

Moyamoya is a cerebrovascular condition characterized angiographically by occlusive disease of the terminal internal carotid artery, anterior cerebral artery (ACA), or middle cerebral artery (MCA) and a network of basal collaterals.[1] In Japan and East Asia, where moyamoya is most prevalent,[2] reported natural history has been of high rates of progressive disease, recurrent events, and cognitive decline, with major functional effects.[3–5] However, a recent population screening study in Japan identified many asymptomatic cases, suggesting that natural history may be more variable.[6] As moyamoya is rare outside East Asia,[7,8] the disease phenotype has not been well-characterized elsewhere. Available data suggest a more benign disease course and a lower rate of cerebral hemorrhage.[9,10] Most non-Eastern series are subject to substantial ascertainment bias, with potential overreporting of severe presentations. The diagnostic label of moyamoya is applied variably to cases of bilateral cerebral occlusive arteriopathy but specific radiologic features are likely to be important in defining clinically important subgroups.[11]

Surgical revascularization is widely offered in moyamoya to prevent ischemic symptoms. Although symptom reduction and good functional outcomes are reported in Eastern patients[12,13] and others,[14–16] uncertainty regarding natural history and prognostic predictors makes it difficult to identify optimal surgical candidates and to objectively evaluate the efficacy of surgery.

We describe the clinical and radiologic features, course, outcomes, and their predictors in an 11-year cohort of UK pediatric moyamoya patients.

Methods

Children (aged up to 18 years) with a new diagnosis of moyamoya (whether symptomatic or incidentally identified, and whether idiopathic [moyamoya disease] or secondary to a recognized association [moyamoya syndrome]) between January 1, 2004, and December 31, 2014, were eligible for inclusion. All cases were considered as a single group, with separate consideration of the influence of a recognized risk factor for moyamoya. Moyamoya was defined as stenosis or occlusion of the terminal internal carotid artery or MCA or ACA with basal collaterals (Childhood Arterial Ischemic Stroke Standardized Classification and Diagnostic Evaluation [CASCADE] category 3A [bilateral] or 2A [unilateral][17]). Intracranial occlusive arteriopathy without basal collaterals (unilateral [CASCADE 2B, C, D] or bilateral [CASCADE 3B, C]) were excluded to enable comparison with published series. Angiographic features were confirmed by review of imaging (V.G. and D.S.) in all cases.

Patients were identified from 2 sources:

1. The multidisciplinary moyamoya clinic at Great Ormond Street Hospital for Children (GOSH) that accepts United Kingdom–wide referrals for diagnostic opinions or evaluation for revascularization surgery. Patients were evaluated uniformly with clinical assessment, brain MRI and magnetic resonance angiography (MRA), and catheter angiography (CA). Surgery was considered in patients with a demonstrable tendency to recurrence—i.e., more than one clinical or radiologic event—although ultimately surgical decisions were made on a case-by-case basis. The hospital audit department confirmed that ethical approval was not required for review of existing clinical and radiologic material that was obtained as part of standard clinical care in these patients.
2. The British Paediatric Moyamoya Study Group: A local investigator (LI) was identified at each pediatric regional neuroscience center in the United Kingdom. Cases were notified by them and additional cases sought via the British Paediatric Neurology Surveillance group, a national collaboration of UK pediatric neurologists who receive a monthly email requesting notification of rare conditions under study. The study was reviewed and approved by the London and Bloomsbury research ethics committee (ref 14/LO/0323) and opened in 17 sites, with local governance approval at each site. Two regional centers did not open as study sites as it was anticipated (and confirmed at study closure) that cases were unlikely to be seen. The LIs sought assent from patients; the GOSH team obtained informed consent. Clinical data were obtained from parental interview by telephone. Relevant imaging studies were electronically transferred (with consent) to GOSH and centrally reviewed.

Data on patient demographics, comorbidities, family history, clinical presentation, recurrent events, treatment, and outcomes were obtained from clinic letters, case notes, or parent interview.

Demographic data included age, sex, family history, comorbidities, and other diagnoses. Presentation was categorized as TIA, arterial ischemic stroke (AIS), cerebral hemorrhage, seizures, headache, chorea, or other (including silent infarcts).

All medical and surgical interventions were noted. Recurrent events were categorized as for presenting symptoms and also in terms of temporal relationship to any surgical intervention.

Scans were reviewed to confirm study eligibility. Brain MRI findings were summarized according to infarct distribution (unilateral/bilateral) and infarct timing (acute/established). For serial imaging studies, the first and most recent scans were compared to ascertain new changes. Cerebrovascular findings were summarized from MRA or CA. Initial findings were categorized according to whether the disease was unilateral or bilateral, and for posterior circulation involvement. First and most recent cerebrovascular imaging was compared to ascertain progression of arteriopathy (defined as more extensive abnormality of previously abnormal artery or involvement of a new artery).

Clinical outcome was evaluated from case notes or parent interview using a combination of the modified Rankin Scale (mRS) and the type of school attended (mainstream or needing educational support). This has been previously validated for evaluation of outcome after childhood AIS[18] and confirmed to have good concordance with the Paediatric Stroke Outcome Measure (PSOM), a commonly used childhood stroke outcome scale. Good outcome was defined as mRS ≤2 and attendance at mainstream school without additional support; poor outcome was defined as mRS ≥3 or attendance at a special school or mainstream school with additional support.[18]

Statistical analysis was undertaken using SPSS Statistics v22 (SPSS Inc., Chicago, IL). Univariable logistic regression was used to explore the relationship between clinical/radiologic variables and outcome. Significant and clinically important variables were then entered into a multivariable model. Predictors that did not significantly alter the odds ratios (ORs) were removed to create the final model.

Results

Patient demographics

Figure 1 summarizes the identification pathway for the patients whose data are reported here. Eighty-eight children were included (56 girls). Ethnicity was white (57%), black (19%), or South Asian (15%); no patients were East Asian. Thirty-one (35%) had a risk factor known to be associated with moyamoya (moyamoya syndrome, table 1). Eight had a family history of moyamoya, including sibling pairs from 2 families, without an identified genetic or syndromic diagnosis.

Initial clinical and radiologic findings

Median age at initial presentation was 5.1 years (range 0.3–16.4 years), with most children presenting during primary school years. Patients presented predominantly with ischemic symptoms, 36 (40.9%) with AIS and 29 (33.0%) with TIA. Other presentations included cerebral haemorrhage in 1 case, seizures in 4 cases, headache in 10 cases, and hemichorea in 2 cases. Six children were asymptomatic at diagnosis and had MRI scans for other indications such as sickle cell disease and microcephalic osteodysplastic primordial dwarfism type II.

Initial radiologic findings

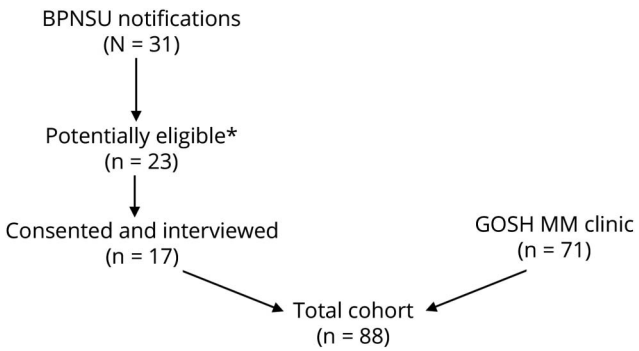
All patients had brain MRI at presentation that showed acute focal infarction in 36/176 hemispheres in the 88 children. Eighty-six hemispheres additionally had evidence of chronic ischemic injury on the index MRI, indicating previous, clinically silent, ischemic damage. MRA of the circle of Willis showed bilateral arteriopathy in 80 cases (CASCADE 3A) and unilateral disease in the remaining 8 (CASCADE 2A). The findings from the initial brain MRI and MRA are schematically summarized in figure 2.

Subsequent course

The patients' clinicoradiologic course is summarized in table 2, divided into those who had had surgical revascularization and those who did not. Surgical revascularization was undertaken in 55 children (unilateral surgery = 19, bilateral surgery = 36), 44 with recurrent clinical symptoms and a further 7 who had had further cerebral infarction on reimaging. The specific surgical indication was not available in the remaining 4 as this was not apparent from parental interview. The median age at first surgery was 6.3 years (range 1.3–17.6 years), a median of 1.1 years (range 0.1–7.4 years) from initial presentation. The 45 patients surgically treated at GOSH had pial synangiosis; procedural details in the others could not be obtained from parental interview. One patient with bilateral disease treated surgically with pial synangiosis went on to have multiple burr holes due to refractory ischemic symptoms, with some clinical improvement.

Ten patients (18%) had a neurologic event within 1 week of surgery; 7 had a TIA (5 of which related to the surgical hemisphere), 1 had a cerebral hemorrhage (while anticoagulated),

Figure 1 Patient identification



Source of patient identification; *8 patients were ineligible as they did not meet age/study time period criteria. BPNSU = British Paediatric Neurology Surveillance group; GOSH = Great Ormond Street Hospital for Children; MM = moyamoya.

Table 1 Risk factors and comorbidities of the patient cohort

Comorbidity	Patients, n
Down syndrome	14
Sickle cell disease	11
Neurofibromatosis type 1	3
Congenital heart disease	17
Renal/renovascular disease	5
Cranial radiotherapy/proton beam therapy	3

and 2 had AIS. The latter 3 patients experienced new neurologic deficits related to these events.

Seventy-three (83.0%) patients were on antiplatelet therapy (73 on aspirin; 1 also on clopidogrel and 1 also on dipyridamole). Six (6.8%) patients were on anticoagulants.

Median duration of follow-up was 43 months (0.3–135 months): 47 months in the surgical group (2–145 months) and 36 months in the nonsurgical group (0.3–109 months). In total, 62 of the 82 patients with symptomatic presentation had at least 1 recurrent event (40 TIA, 28 AIS [not mutually exclusive]). Of the 6 who had been asymptomatic at the time of initial diagnosis, 2 went on to have TIAs. Of the 36 patients with initial AIS, 17 went on to have recurrent AIS (3 of whom also had recurrent TIA) and 7 had subsequent TIA; 12 children in this group did not have further recurrences after the index AIS. Fifty-two patients had more than one recurrent event.

Thirty-three patients of the 55 in the surgical group had clinical recurrence of cerebral ischemia (29 TIA, 4 AIS) after surgical revascularization (including the postoperative events described above). However, 37/55 of the surgical group had an absolute reduction in the frequency or severity of recurrences compared with preoperative levels.

Fifty-seven patients (18 nonsurgical and 39 surgical group) had repeat brain imaging, undertaken 0.2–10.2 years from initial diagnosis. Comparing initial and final MRI and MRA, 18 patients had evidence of new ischemic damage on MRI, a median of 3.6 years from presentation, including new brain injury identified after surgical revascularization in 7 cases. This was usually in deep gray structures or white matter—i.e., relatively deep in the brain. Five of the 7 who developed new infarcts after surgery had had a corresponding clinical event. Twenty-one patients had further transient clinical events without new infarcts on reimaging.

Twenty-seven patients had evidence of progressive arteriopathy (including 23 who had had surgery); however, the timing of arteriopathy progression could not be precisely evaluated in relation to surgery due to variable imaging time points. It is of note that surgery patients were significantly more likely to have progressive arteriopathy (23/39 compared with 4/18, $p = 0.01$), suggesting patients with potentially more aggressive disease are being selected for surgery. It is difficult to meaningfully comment on the rates of new infarcts in the patients imaged serially, either preoperatively or postoperatively, as these represent a subset without any systematic imaging schedule.

Outcomes

One child died secondary to cerebral hemorrhage. Outcome data were available for 85 survivors; the remaining 3 were preschoolers who could not be assigned a mRS score. Outcome was categorized as good in 39 (44.3%) patients. Interestingly, of patients who had been managed in centers other than GOSH, outcome was classed as good in 2 patients and poor in 14 patients (compared with 37 good and 32 poor in the GOSH cohort; Fisher exact text $p < 0.01$); as will be discussed, the reasons for this are likely to be complex. A breakdown of the mRS, type of school attended, and overall outcomes in the surgical and nonsurgical patients is shown in table e-1 (links.lww.com/WNL/A194).

Prognostic predictors

Predictors of poor outcome are shown in table e-2 (links.lww.com/WNL/A194) (univariable) and table 3 (multivariable). In univariable analysis, children with non-AIS presentation were significantly less likely to have a poor outcome; presence of a risk factor associated with moyamoya was also a predictor of poor outcome (OR 6.00, 95% confidence interval 2.11–17.06).

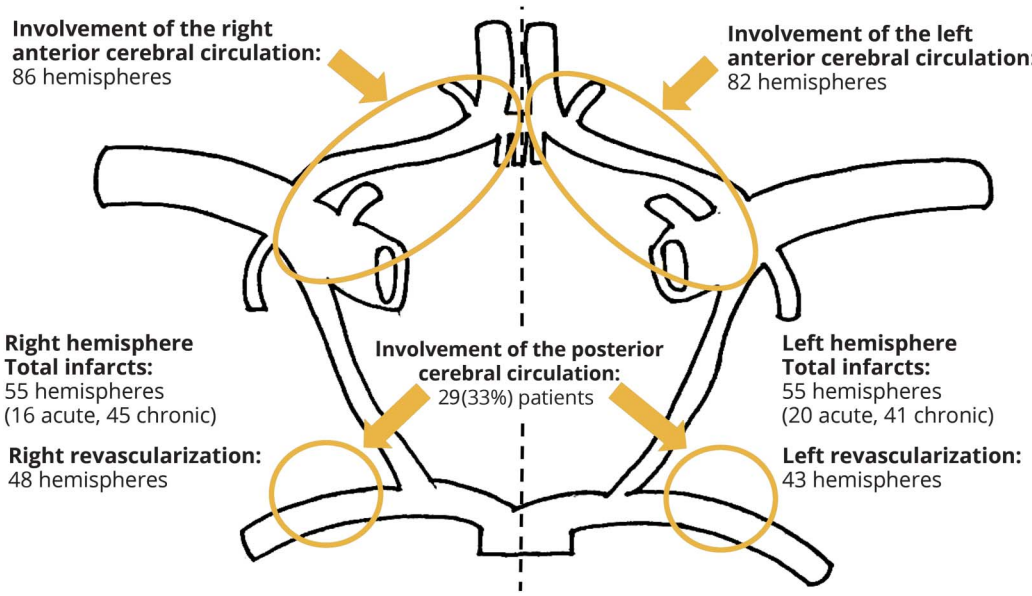
Multivariable analysis confirmed that presentation with TIA, headache, or no symptoms was significantly associated with a lower chance of poor outcome than AIS presentation. Having controlled for other variables, posterior cerebral circulation involvement was also a predictor of poor outcome; however, having a moyamoya risk factor (moyamoya syndrome) was no longer significant.

Discussion

We present data from a recent multicenter UK cohort of childhood moyamoya confirming frequent ischemic presentations. Approximately half of patients had a good neurologic outcome, although it is difficult to dissect the contribution of surgical revascularization as surgical cases were selected on the basis of their presumed higher risk for progression. Adverse prognostic features were AIS presentation and posterior circulation involvement.

In order to enable comparison to other, particularly East Asian, series, our cohort was selected according to strict radiologic criteria. We may have inadvertently excluded early cases of bilateral moyamoya (prior to collateral development, CASCADE 3B), but we believed radiologic homogeneity was important as, in a previous study of young children with

Figure 2 Distribution of arterial disease and brain infarcts



A schematic of the Circle of Willis showing the major cerebral arteries, summarizing the distribution of arterial disease and brain infarcts. The number of hemispheres that went on to be treated by surgical revascularization is also indicated.

bilateral cerebral arteriopathies, disease trajectory was different in those with and without collaterals.[11] There may also be cases of unilateral cerebral arteriopathy without collaterals (CASCADE 2B) that represent early cases of unilateral moyamoya. Without a robust disease biomarker for moyamoya, there is risk of both underascertainment and overascertainment but, by applying consistent and transparent radiologic criteria, we aimed to identify a relatively uniform group.

The lack of serial imaging in a proportion of patients reflects the long ascertainment period (with variations in practice), differences in approach between centers, and short follow-up in a small number of cases. We may have underascertained clinically silent progression of brain injury and arteriopathy as this was apparent in some reimaged patients. However, the clinical significance of asymptomatic disease progression is unclear, especially since arteriopathy progression appeared to continue even after surgery. We have not used progressive radiologic change as an outcome measure and therefore this issue should not alter our conclusions.

While it would be incorrect to present this as an epidemiologic study, we have attempted to reduce ascertainment bias by involving a national network of pediatric neurologists. Pediatric neuroscience centers in the United Kingdom generally work in a multidisciplinary model and it would be extremely unusual for patients to present to other professionals (e.g., neurosurgeons) without pediatric neurology involvement. Thus, it is likely that the vast majority of UK pediatric cases between 2004 and 2014 were identified. We had a high rate of enrollment but recognize that ascertainment was likely incomplete. For example, many children with sickle cell disease and cerebrovascular disease are managed by pediatric hematologists, not neurologists. There appear to be differences in clinical outcomes between children seen in GOSH, with a higher proportion of these with good outcomes. The reasons for this are likely to be diverse and

Table 2 Clinicoradiologic features of the cohort

	Surgical patients (n = 55)		
Clinicoradiologic feature	**Preoperative**	**Postoperative**	**Nonsurgical patients (n = 33)**
Recurrent events	44	33	18
Headache	21	15	14
Vascular disease progression	23/39 Reimaged patients		4/18 Reimaged patients
New infarcts	8/39 Reimaged patients	7/39 Reimaged patients	3/18 Reimaged patients

Table 3 Multivariable analysis of clinical and radiologic predictors of poor outcome

Predictor	OR (95% CI)	*p* Value
Initial presentation		
AIS (reference category)		
TIA	0.09 (0.02–0.35)	0.001
Headache	0.10 (0.02–0.58)	0.010
Chorea	Undefined (n = 2)	NA
Cerebral hemorrhage	Undefined (n = 1)	NA
Seizure	0.50 (0.04–6.56)	0.593
Asymptomatic	0.08 (0.01–0.68)	0.021
Posterior cerebral circulation involvement	4.22 (1.23–15.53)	0.022
Moyamoya risk factor[a]	2.45 (0.64–9.36)	0.189

Abbreviations: AIS = arterial ischemic stroke; CI = confidence interval; NA = not applicable; OR = odds ratio.
[a] Risk factors include Down syndrome, neurofibromatosis type 1, sickle cell disease, and cranial radiotherapy/proton beam therapy.

impossible to tease out—but this observation suggests that the potential referral center bias for more severe presentations did not hold true in this cohort. Comparing the groups, this difference seems more likely to be due to clinical state at diagnosis, rather than any difference in management approach. Thus, with the reservations discussed, we believe this study presents useful data on a large non-Eastern pediatric cohort.

The majority of patients in our study presented with ischemic events, consistent with findings from both East Asian and Western studies.[16,19–21] Posterior cerebral circulation involvement is common in moyamoya[22,23] and, unsurprisingly, an adverse prognostic feature, presumably due to impairment of an alternate source of collateral circulation. Also unsurprising is the relationship between AIS and poor outcome as these children have irreversible brain injury at presentation. While the apparent adverse effect of comorbidities on outcome appeared to be accounted for by presentation and posterior circulation involvement, the high rate of these in moyamoya pose an additional challenge to dissecting out the relative effects of the disease, its treatment, and additional factors.

While the mRS/school type assessment has been shown to relate well to the PSOM,[24] we acknowledge that it is only a crude assessment of function, with a major motor bias. Young age and comorbidities also expose the limitation of this outcome assessment. These limitations mean that there is a likely underestimate of good outcomes. Naturally prospective studies should aim to be more comprehensive and to use standardized measures, ideally within the International Classification of Functioning, Disability and Health framework.

The main aim of surgical revascularization in moyamoya is to prevent AIS, and only 4 of the 55 surgical patients experienced postsurgery AIS, and three-quarters of patients with recurrent events prior to surgery experienced a reduction in the frequency or severity of these, consistent with previous United Kingdom, United States, and Japanese studies.[12,14,15] It is difficult to compare studies as many only report reductions in TIA symptoms, while our study reports reductions in all types of recurrences. In addition, MRI identified new infarcts in 7 patients after surgery, suggesting that, while surgery appears successful in preventing clinical recurrence, it may not prevent radiologic disease progression, as was also evident by the rates of arteriopathy progression observed.

We were interested to observe that outcome was categorized as poor in over half of patients who underwent surgical revascularization, in contrast to the higher proportions of favorable outcomes (using different measures) reported in previous studies.[16,25] The possible reasons behind this are complex and we emphasize that the surgery and nonsurgery groups are not inherently comparable, nor randomly allocated. Potential explanations are that surgery does not influence the natural history of moyamoya, thus its effects on outcome are limited. Alternatively, patients who underwent surgery might have had poor preoperative functional and cognitive abilities due to established brain injury, such that postoperative outcome would continue to be categorized as poor. Given that many patients presented with AIS, this is an important consideration, but in our retrospective study we were not able to ascertain preoperative functional status and naturally accept this as a limitation. A further reason might be that all nonsurgical patients were accurately predicted to have a good outcome, which was why they were not offered surgery. It is difficult to draw any wider conclusions from these

data but they challenge the concept that surgery is mandatory in all moyamoya patients. From an ethical and logistic perspective, it seems unlikely that there will ever be a trial of surgical revascularization in moyamoya, and unclear on what basis one would randomize patients. However, data such as those presented here could form the basis of expert consensus, to standardize management and enable prospective critical appraisal of practice.

Author contributions

Sara Tho-Calvi collected and analyzed the data and wrote the manuscript. Dominic Thompson reviewed surgical data and critically appraised the manuscript. Dawn Saunders reviewed anonymized imaging and critically appraised the manuscript. Shakti Agrawal ran the study at his center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Anna Basu ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Manali Chitre ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Gabriel Chow ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Frances Gibbon ran the study at her center (including governance permissions, patient identification and data collection) and critically reviewed and provided feedback on the manuscript. Anthony Hart ran the study at his center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Krishnaraya Kamath Tallur ran the study at his center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Fenella Kirkham ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Rachel Kneen ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Helen McCullagh ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Leena Mewasingh ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Grace Vassallo ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Kayal Vijayakumar ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Elizabeth Wraige ran the study at her center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Tong Hong Yeo ran the study at his center (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript. Vijeya Ganesan had oversight of the study (including obtaining ethical approval, patient identification at GOSH, and reviewing brain imaging) and wrote the manuscript. The members of the British Paediatric Neurology Association Moyamoya Study group listed above individually ran the study at their centers (including governance permissions, patient identification, and data collection) and critically reviewed and provided feedback on the manuscript.

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Disclosure

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Clinical features, course, and outcomes of a UK cohort of pediatric moyamoya

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Study question

What factors can predict outcomes in children with moyamoya?

Summary answer

Arterial ischemic stroke (AIS) presentation and posterior circulation involvement predict poor outcomes in children with moyamoya.

What is known and what this paper adds

Moyamoya is rare outside of East Asia, so the disease phenotype in non-Eastern populations is poorly characterized. This study clarifies the clinical features and outcome predictors of moyamoya in a UK pediatric population.

Participants and setting

The study examined 88 UK children who were diagnosed with moyamoya between 2004 and 2014. The median age at initial presentation was 5.1 years (range 0.3–16.4 years).

Design, size, and duration

The study retrospectively reviewed case notes and parent interviews to determine the children's demographic and clinical characteristics. The study used multivariable logistic regression to determine whether various factors predicted clinical outcomes; good = modified Rankin Scale (mRS) score ≤2 and mainstream school without additional support; poor = mRS score ≥3 and special school or mainstream school with additional support.

Main results and the role of chance

Three preschool-aged children could not be assessed for outcomes. Among the remaining 85 children, 39 (45.9%) had good outcomes, and 46 (54.1%) had poor outcomes. Of the various initial presentations, AIS was a better predictor of poor outcome than transient ischemic attack (p = 0.001), headache (p = 0.010), or asymptomaticity (p = 0.021). Posterior cerebral circulation involvement also predicted poor outcomes (p = 0.022). No predictive power was detected for seizures at initial presentation (p = 0.593) or the presence of moyamoya risk factors (p = 0.189). Surgical revascularization, which was undertaken in patients with progressive or recurrent symptoms, did not predict outcome, probably related to neurologic status at presentation, or patient selection for surgery.

Table

Predictor	Odds ratio (95% CI)
Initial presentation	
Transient ischemic attack	0.09 (0.02–0.35)[a]
Headache	0.10 (0.02–0.58)[a]
Asymptomatic	0.08 (0.01–0.68)[a]
Posterior circulation involvement	4.22 (1.23–15.53)

[a] Relative to AIS.

Bias, confounding, and other reasons for caution

The strict radiologic criteria of this study might have caused early moyamoya cases to be excluded. Outcomes were assessed with a crude procedure that might have mischaracterized some good outcomes as poor.

Generalizability to other populations

The study probably included the vast majority of pediatric moyamoya cases occurring in the UK between 2004 and 2014, so it should be strongly representative of a large non-Eastern population and therefore generalizable to other such populations.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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