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Screening for cerebrovascular disorder on the basis of family history in asymptomatic children.

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Previous presentation of work:

Portions of this work were presented in poster form at the Society of British Neurological Surgeons Autumn Meeting, London, 2018, and the associated abstract was published in the British Journal of Neurosurgery.

Abstract:

Background - Cerebrovascular disorders represent a group of uncommon, heterogeneous, and complex conditions in children. We reviewed the screening practice for the detection of cerebrovascular disorder in asymptomatic children referred to our neurovascular service on the basis of a positive family history and parental and/or treating physician concern.

Methods - Retrospective case-note review of referrals to our neurovascular service (July 2008 - April 2018). Patients were included if the referral was made for screening, on the basis of a positive family history of cerebrovascular disorder. Symptomatic children, those with previous cranial imaging, or children under the care of a clinical geneticist (i.e. due to the child or their relative having HHT or mutations in KRIT1) were not eligible for inclusion.

Results - Forty-one children were reviewed, 22 males (Median age 10.7 years, range 0.6-15.6 years). This represented 22% of the total number of referrals over a 10-year period. Twenty-nine children had an MRI/MRA brain. Twenty-eight children were referred due to a family history of intracranial aneurysm and/or subarachnoid haemorrhage, but only two had two first-degree relatives affected. Ten children were referred due to a family history of arteriovenous malformation. Three children were referred due to a family history of stroke. No cerebrovascular disease was detected during the study period (n=29).

Conclusions - Parental and/or physician concern generated a substantial number of referrals but no pathology was detected after screening. Whilst general screening guidance exists for the detection of intracranial aneurysms, consensus guidelines for the screening of children with a positive family history do not, but are required both to guide clinical practice and to assuage parental and/or physician concerns.

Key words:

Screening, cerebrovascular, aneurysm, arteriovenous malformation, family history

Introduction:

Cerebrovascular disorders in children constitute a broad group of relatively rare and distinct pathologies, and represent one of the top ten causes of mortality in patients aged 5 to 24 years (Heron, 2013). Although uncommon, stroke in children (from all causes) over one month of age has an estimated incidence of 13 per 100,000 children (Giroud et al., 1997). Due to the heterogeneity of cerebrovascular conditions, the risk of having a cerebrovascular condition based on genetic inheritance with a positive family history, is difficult to determine. Congenital paediatric cerebrovascular diseases are very rare, with estimates of only 3 cases per 100,000 per year (Goyal et al., 2019). The rarity and heterogenous nature of cerebrovascular disease in children therefore requires expertise and experience to guide their management. Some guidelines do exist to inform aspects of paediatric cerebrovascular disease management, but are essentially restricted to stroke in children (Singhal et al., 2013), and screening in families with Hereditary haemorrhagic telangiectasia (HHT) (Faughnan et al., 2011). The majority of care decisions are therefore based on expert opinion, and extrapolation of evidence from literature pertaining to adult cohorts, for instance regarding the screening for intracranial aneurysms (IC) in asymptomatic members of families with two or more affected first-degree relatives (Schievink, 1997). There are no general guidelines to inform screening practice in asymptomatic children with similarly affected first-degree family members, for either IC or non-HHT AVM.

In 2008, a monthly neurovascular multidisciplinary team (MDT) clinic was established at Alder Hey Children's Hospital (Liverpool, United Kingdom) with representation from paediatric neurosurgery, neurology, neuroradiology, and neuroscience specialist nurses, all with an interest in paediatric cerebrovascular disease. The purpose of this multidisciplinary clinic was to coordinate and streamline the paediatric neurovascular patient journey, whilst building and concentrating specialist expertise within the trust, to improve patient care. A proportion of the referrals to the MDT are for the purpose of requesting radiological screening of asymptomatic children from families with a positive family history of cerebrovascular disease. Whilst merit could be argued for screening children with two or more first-degree relatives with IC, many children are referred not meeting this criterion, but are reviewed due to parental or treating physician concern, and subsequently screened.

We present this cohort of asymptomatic children referred to the MDT, and subsequently reviewed for consideration of radiological screening on the basis of their positive family history. We describe the nature of the family history, degree of relatedness, screening investigations undertaken, and the outcome following review. We discuss the utility of radiological screening in this cohort over the past 10-years, and make suggestions to assist clinicians faced with this scenario, in the absence of child specific guidelines.

Methods:

Study design

The cohort for this service evaluation was generated following retrospective review of a prospectively maintained database of children referred to the paediatric neurovascular MDT clinic at Alder Hey Children's Hospital between July 2008 and April 2018. Referrals to the MDT for clinical review and a discussion regarding screening were accepted from any treating physician with a concern which included general practitioners, paediatricians, neurologists, and other colleagues both locally and from within the wider catchment area. Local audit committee approval was acquired. Parental consent was not required as the data collected was extracted from routine clinical records.

Patient selection

We included any asymptomatic child who was reviewed in the MDT for the purpose of discussing radiological screening, due to concerns from family or a treating physician of a positive family history of cerebrovascular disease. Symptomatic children, those with previous cranial imaging, or children under the care of a clinical geneticist (i.e. due to the child or their relative having HHT or mutations in KRIT1) were not eligible for inclusion. We therefore infer that the study cohort represents referrals made to the neurovascular MDT due to parental or treating physician concern regarding a degree of positive family history of cerebrovascular disease only. Patients were less than 18 years at the time of clinic review.

Data Collection

Cases were compiled, extracted, and stored in Microsoft Excel® (Microsoft Inc., Seattle, WA) in a predesigned template. All data were securely stored on a hospital server. We recorded patient demographics including age in months, sex, along with clinical details including the patients' medical history, the reason for referral, family member(s) affected, degree of relatedness to the patient, family member cerebrovascular disease, details of investigations performed (imaging and genetic testing), the management plan, and referral outcome.

Patient categorization

To analyze our included cases, we categorized patients according to the primary family pathology generating the referral from review of case note history only. To subdivide referrals further, we recorded the relation of each first-degree relative with positive family history. For second-degree relatives, we recorded only the number of individuals with positive history and their primary pathology. This was also the case for 'other' relatives, that were neither first- or second-degree relatives to the patient.

Results:

Demographics

Forty-one children were referred due to a positive family history of cerebrovascular disease and concern regarding elevated risk to the child from family or a treating physician. This represented 22% of the total number of referrals during the study period (screening referrals n=41, total referrals n=190). Twenty-two children were male, and nineteen females. The median age at the time of referral was 10.7 years (range 0.6-15.6 years).

Screening practice by pathology

All forty-one referrals could be broadly categorized as having family history encompassing one of three pathologies; namely aneurysmal subarachnoid haemorrhage (aSAH), arteriovenous malformation (AVM), or stroke. Each of these categories is discussed in turn and summarized, with reference to screening practice, management plan, and neurovascular MDT clinic outcome (Figure 1). Surprisingly, there were no referrals for screening children with a positive family history of sporadic cavernoma.

Aneurysmal subarachnoid haemorrhage (aSAH)

The most common reason for referral was due to concern regarding the potential risk of aneurysmal subarachnoid haemorrhage in the child (n=28); due to a documented positive family history of aSAH (n=21), SAH but without a specific cause (n=5), or the coincidental presence of an IC in a relative (n=2). Three children had dual positive family histories for cerebrovascular disease, however these are summarised with the AVM cohort as IC was not the primary pathology of concern (Patients 31 & 32, twins with a sister who had an AVM from which she had bled, but also demonstrated an aneurysm, and patient 37, who had a second-degree relative with an AVM but also two more distant relatives with a history of aneurysm).

Patients were grouped according to degree of relatedness into one of three categories 1) 2x first-degree relatives (n=2), 2) 1x first-degree relative (n=17), and 3) at least one second-degree relative (n=9). Only two children had 2 first-degree relatives with a history of aSAH and were siblings (Patients 1 & 2). The children's father had a history of aSAH, and the children's older adult brother was receiving treatment for an unruptured intracranial aneurysm. Both children underwent Magnetic Resonance Angiography (MRA), both of which were negative. Both were reassured that no further screening should take place until they are in their twenties, and a referral letter was sent to the local adult neurovascular service.

In total, twenty-one children underwent MRI/MRA all of which were negative. As would be expected, the proportion of children screened was greater in those with a single first-degree relative with positive family history (14 out of 17) compared to those with only a second-degree relative with positive family history (5 out of 9). Sixteen children were recommended to have a scan in adulthood (Figure 2).

Arteriovenous malformation (AVM)

The second most common reason for referral was due to concern regarding a positive family history of intracranial AVM, in the absence of known HHT (n=10). Six patients were screened with MRA and no cerebrovascular pathology was identified. Three children were recommended to have a future scan in adulthood. The majority of patients within this category had one or more first-degree relatives with a history of AVM (8 out of 10). A summary of the screening practice and subsequent management plans for this category are summarised (Figure 3).

Stroke

Three patients were referred due to concern regarding a family history of stroke and haemorrhage. There were insufficient clinical details to understand the exact nature of the pathology. One patient whose brother had suffered a brain haemorrhage was referred but not subsequently screened (Patient 39). The outcome from this referral was actually a referral to a counselling service for the child's mother. One patient with two second-degree relatives who had suffered 'brain haemorrhages' underwent an MRI scan which was negative, at the insistence of the family (Patient 40). This patient was discharged from the clinic. Finally, one patients' mother had suffered a stroke and had two second-degree relatives with a history of stroke also (Patient 41). This patient underwent an MRA, again due to insistence from the family, which was negative and so this child was also discharged.

Discussion:

Our cohort

Referrals for screening asymptomatic children represented (22%) of the clinic caseload (screening referrals n=41, total referrals n=188), which is not comparable to what has been observed in other reports of dedicated neurovascular multidisciplinary clinic caseloads (Ladner et al., 2015, Mattila et al., 2015). Imaging was undertaken prior to referral in these two series, but decision to image, and choice of imaging modality was made after referral in our cohort. The approach taken through our MDT was to provide face-to-face clinical review for any family where concern exists, but we are unable to compare or estimate differences in levels of concern experienced in other geographical regions.

Two-thirds of referrals pertain to parental concern regarding a family history of aneurysmal SAH, SAH, or the presence of aneurysm. For the purpose of our analysis, we considered these together, assuming that they collectively represent the same concern for the child. The remainder, with the exception of three cases of non-specific stroke/intracranial haemorrhage, were for concern regarding intracranial AVM in families without a history of HHT.

Twenty-nine children underwent MRI/MRA screening, but not a single child had demonstrable cerebrovascular disease. However, it could be argued that only two children passed a reasonable threshold to justify screening (Patients 1 & 2) if we extrapolate from adult guidance (Schievink, 1997). Decisions to screen were not reliably extractable from analyzing retrospective records. However, a general theme of a mutual decision between the clinical team and the parent/s was evident. Twelve patients were not screened and were therefore successfully reassured after clinical review. The threshold to screen may have been lower for seven children who reported a past medical history of headache/migraine on clinical review and a higher level of anxiety was therefore associated with not performing radiological screening.

All children that were referred were discharged from our paediatric hospital after negative imaging or after clinical review/counselling if they did not have a scan. One patient (Patient 33), who was only 13 months old with a family history of AVM (Father) at the time of review, was deferred until 5 years old. Where a future management plan was recommended, families were reassured that this should not be undertaken until adulthood. Timings of future scans were variable but all consisted of a first future scan in early adulthood, to be arranged by the local adult neurovascular team at an appropriate time.

Demography and Epidemiology of Intracranial aneurysms in children

Whilst much is known about the clinical and radiological features, and treatment outcomes for IA in adults, the same cannot be said for that in the paediatric population, with an evidence base consisting of mainly small case-series. Despite this, there are clear and consistent differences between the demographics, pathology, and treatment outcomes between paediatric and adult IA, including a

male predominance, a higher proportion of posterior circulation and internal carotid bifurcation aneurysms, and a greater number of giant aneurysms (Aeron et al., 2012).

IA in children constitute between 0.5%-4.6% of the total number observed in all ages (Krishna et al., 2005). However, estimating the true prevalence of paediatric IA in general is much more difficult, but estimates of 1 to 3 per million population have been postulated (Levy et al., 2020). Paediatric autopsy series have consistently failed to demonstrate intracranial aneurysm in children, suggesting that IA are not congenital (although there has been observation of an early peak in presentation of aSAH in the first 6-months of life). Kapoor and Kak demonstrated only one aneurysm in a patient under the age of 20 while examining 1000 human cadaveric brains (Kapoor and Kak, 2003). In a similar study, Chason and Hindman failed to locate any aneurysm in patients under the age of 20 (Chason and Hindman, 1958).

Adult risk factors for aneurysm development are generally absent in children (for instance, smoking and hypertension), and this, along with a differing demography, and distinct aetiologies (Aeron et al., 2012), allows one to confidently conclude that paediatric IA are, on the whole, a different entity. The probability of aneurysmogenesis is determined by the balance between intrinsic vessel integrity (of which there are a variety of mutations which have been implicated), extrinsic vessel insults (such as trauma, infection, sickle cell disease, an immunocompromised state, and cardiac anomalies) , and underlying vasculopathies (Ghali et al., 2018), which may be present in up to one-tenth of cases (Beez et al., 2016).

A well-known study published in 1966 describing the natural history of SAH and IA reported 6368 cases of ruptured aneurysms, consisting of only 44 cases in patients younger than 19 years (Locksley, 1966). Patel and Richardson reported 58 cases of ruptured intracranial aneurysms in patients under 19 years of age out of a study population of 3000 (Patel and Richardson, 1971). There is a high-burden of events associated with intracranial aneurysm in the paediatric population, with 10%-15% of spontaneous intracranial haemorrhage being observed in those under 20 years of age (Jordan et al., 2009), suggesting a higher rate of aSAH in the paediatric population, but with the true prevalence of intracranial aneurysm in children unknown, there may be an overestimate of the likelihood of aneurysm rupture.

Should we screen for IA in asymptomatic children with affected family members?

In this cohort, the question of whether to screen or not assumes that there is an increased risk of IA due to familial aggregation. Familial intracranial aneurysm genes (FIA) are inherited as susceptibility traits (Broderick et al., 2005), in that they require extrinsic environmental factors, such as hypertension and smoking, to reveal the aneurysm phenotype (Brown et al., 2008). Whilst 10%-20% of aneurysmal subarachnoid haemorrhage is associated with a family history of intracranial aneurysm, FIAs account for only 5% of intracranial aneurysm in patients presenting in the first two decades of life (Aeron et al., 2012). Furthermore, a study of more than 440 FIA families has shown that the FIA genes rarely (less than 2%) express aneurysm phenotype during the first two decades of

life (Aeron et al., 2012). There are no general guidelines to inform screening practice in asymptomatic children with affected family members. Extrapolation from adult data currently provides the best guidance, but even this is questionable. One study that employed this approach found evidence of IA in 37 out of 400 (9%) of asymptomatic individuals in 68 families with a history of aSAH (Ronkainen et al., 1995). Despite this, the benefit of screening in the adult population has not been conclusively proven. The American Stroke Association guidelines conclude that whilst there may be an increased incidence of IA, the cost-effectiveness of this practice has not been evaluated, and suggest that screening decisions should be made on an individual basis (Bederson et al., 2000, Bederson et al., 2009, Connolly et al., 2012). Therefore, a single negative MRA in children with two or more affected first-degree relatives should be sufficient to provide reassurance that IA is absent, and to then subsequently offer future screening in early adulthood, but again, this decision should be made on an individual basis. As previously described, children that do harbour IC are likely to be very young and are more likely to present with SAH, and there is no evidence to suggest that these children are subject to familial aggregation.

Should a child require intracranial imaging, a general anaesthetic is likely be required. Whilst modern anaesthesia is very safe and unlikely to result in serious complications, it is not without risk. For a child in good health; headache, nausea & vomiting, a sore throat, or dizziness are not uncommon side-effects. Mild allergic reactions to an anaesthetic drug are in the order of 1%, whilst cardiac arrest attributable to anaesthesia is in the order of 0.65 per 10,000 anaesthetics, but this risk is higher in neonates (Flick et al., 2007).

There is no evidence to suggest that a well child, without convincing evidence of increased familial risk, and without the passage of time to allow extrinsic factors to reveal an aneurysm phenotype would seem to be at no demonstratable greater risk of intracranial aneurysm, above that of the general population. Whilst we cannot accurately estimate the prevalence of intracranial aneurysm in children, with estimates in the order of 1 to 3 per million children, parental concern should be balanced against the small but not insignificant risk of harm from screening, which carry an order of risk, if only minor, far greater than the general prevalence of intracranial aneurysm. Conversely, considering a child who is not screened, and subsequently presents with SAH; it is slightly more reassuring that in children, overall survival, and good functional outcomes are much more likely (Beez et al., 2016, Hetts et al., 2009, Mehrotra et al., 2012, Yasin et al., 2019). We appreciate that parental anxiety could be very high, and therefore, there is an important role for parent (and patient) education and counselling, along with signposting to patient support groups and psychological services, through a specialist neurovascular multidisciplinary clinic such as this one.

Demography and Epidemiology of arteriovenous malformations in children

Intracranial AVMs in children account for up to 55% of paediatric haemorrhagic strokes, and produce a large burden of persistent neurological deficit (Ravindra et al., 2019). They are generally considered as sporadic and congenital, developing due to either the persistence of a primitive AV connection or due to the development of a new connection after a normal closure process (El-Ghanem

et al., 2016). *De novo* occurrence has been described in case-reports (Yeo et al., 2015, Santos et al., 2018). The general prevalence of intracranial AVM is between 0.5%-1% with approximately 20% being diagnosed in children, usually due to rupture (Di Rocco et al., 2000), with an estimated rate between 2%-4% per year, leading to a greater cumulative lifetime rupture risk for children (Darsaut et al., 2011). Of note, AVMs which rupture have a higher rate of re-rupture, tend to be larger, and associated with greater morbidity and mortality (Di Rocco et al., 2000).

Which children should be screened for intracranial arteriovenous malformation?

The main distinction to make is whether there is a family history of HHT or not. This study is not concerned with children who have a family history of HHT. If there is a family history of HHT, one should follow the international guidelines for the diagnosis and management of HHT (Faughnan et al., 2011). Genetic screening is recommended for asymptomatic children of a parent with HHT, which can then be extended further to at risk relatives, which should be initiated prior to vascular imaging (Faughnan et al., 2011). The prevalence of cerebral AVM in HHT is between 10% to 23% dependent on the population being studied (Shovlin, 2010, Faughnan et al., 2011, Brinjikji et al., 2016), compared to 650 per 100,000 in the general population (Gross and Du, 2013).

Instances of familial AVM in the absence of HHT are reported, whereby two or more relatives are affected. A systematic review of familial intracranial AVM was performed and subsequently identified 22 families with 47 affected individuals, who were mostly first-degree relatives (van Beijnum et al., 2007). In families with at least two successive generations with intracranial AVM, children were younger at the time of their diagnosis, with the difference not explained by screening, suggesting a possible anticipation mechanism (van Beijnum et al., 2007). Only 3 patients with familial AVM were identified after screening, and therefore the authors did not recommend screening of asymptomatic relatives of patients with an intracranial AVM (van Beijnum et al., 2007). It is important to note that familial AVM (given the very small numbers of patients identified) may actually represent accidental aggregation of the general prevalence of sporadic AVM.

Limitations

Whilst the number of cases within this cohort is small at forty-one, it does represent a decade of real-life clinical practice in a single specialist paediatric hospital with a dedicated neurovascular clinic. We would be interested to see pooled international data, or data from adult screening practice initiated during childhood. This study would benefit from long-term follow up in order to identify cases which may eventually become positive on screening, but we recognize the difficulty of this, as the ability to trace these patients in the future may not be possible, especially when children transition from paediatric to adult services. There is merit in having a national and even a global registry of patients with neurovascular disease to ensure volume and consistency of data recording. We look forward to reporting on both our own long-term outcomes, and the wider global practice in the future.

Conclusions:

Forty-one asymptomatic children were referred to the neurovascular multidisciplinary clinic at Alder Hey Children's Hospital over a 10-year period for the purpose of screening, due to a positive family history of cerebrovascular disorder and parental and/or treating physician concern. Despite 29 children undergoing radiological screening, including two children with two first-degree relatives with IC, no cerebrovascular pathology was detected. No paediatric specific screening guidelines exist for detecting IA, but adult guidelines are extrapolated to children. We recommend that in those families with a strong history of cerebrovascular disease (two or more first-degree relatives), a single MRA may be appropriate in childhood to alleviate concern, prior to future screening in adulthood, but appropriate counselling should be offered to all, including those that seek referral without a strong family history of cerebrovascular disorder. There are no guidelines to recommend screening children with an affected relative with intracranial AVM without HHT. In the absence of availability of robust data supporting screening, we do not see merit in routine screening (with MRI) of children with a family history of AVM. A consensus screening policy for children should be developed. Attendance at this clinic can be used as an opportunity to highlight known risk factors, such as smoking, a lack of exercise, and poor diet; which could be avoided to lower any potential risk for the development of IC in the future.

Disclosure:

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Conflict of interest:

The authors report no conflict of interest concerning the materials or methods used in this study or findings specified in this paper.

Ethical approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Medical University of Vienna and the Ethics Committee of the Medical University of Vienna and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Formal consent:

Formal consent was not required for this study.

Figure legends:

Figure 1 – Table summarising all patients included in the study (n=41). Patient study number, age (years), and sex are given. Associated patient history is described and treatment received prior to neurovascular clinic review. Patients are grouped by primary family pathology, and further grouped by degree of relatedness and volume of family burden. Note that aSAH and SAH are separated where it was not explicit that the primary pathology was aneurysmal in nature. Relationship of 1st degree relative is given, for 2nd degree and other relatives the number of affected individuals is given and the breakdown of pathology. Finally, the screening tests performed, and the outcome and management plan are given for each patient.

Figure 2 – Summary of degree of relatedness, screening practice, and future scan recommendations for children with a family history of aSAH, SAH, & Aneurysm. Only those children with a primary family history of aSAH, SAH, & Aneurysm are included in this analysis (n=28). Patients were initially grouped on the degree of relatedness of the positive family history. Each group is further subdivided, where applicable, into those that undergo screening and those which do not. The number of future scan recommendations is given for each subsequent group. The total number of children screened, and the total number of children recommended to have a future scan are given.

Figure 3 – Summary of degree of relatedness, screening practice, and future scan recommendations for children with a family history of AVM (without history of HHT) (n=11). Patients were initially grouped on the degree of relatedness of the positive family history. Each group is further subdivided, where applicable, into those that undergo screening and those which do not. The number of future scan recommendations is given for each subsequent group. The total number of children screened, and the total number of children recommended to have a future scan are given.

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Pt No.	Age (Years)	Sex	Patient history	Primary family pathology	1st degree relative	2nd degree relative	Other relatives	Screening tests	Outcome & Management Plan
1	15.6	M		aSAH	Father & Brother			MRA	D/C, scan after 20 & 40 years
2	14.1	M		aSAH	Father & Brother			MRA	D/C, scan after 20 & 40 years
3	10.4	F		aSAH	Father	3x (SAH)		MRA	D/C, scan after 20 & 30 years
4	10.2	F		aSAH	Father	1x (SAH)			D/C
5	9.6	F		aSAH	Father	1x (aSAH)			D/C, scan at 18 years
6	11.8	F		aSAH	Father	1x (aSAH)		MRA	D/C
7	8.3	M		aSAH	Father	1x (aSAH)		MRA	D/C, scan at 18 & after 30 years
8	15	M		aSAH	Mother	1x (SAH)		MRA	D/C, scan at 30 years
9	11.8	M	Migraine – Px Pizotifen	aSAH	Father	1x (aSAH)		MRA	D/C, scan at 18 & after 30 years
10	12.1	M		aSAH	Mother		4x (Aneurysm)	MRA	D/C
11	6.3	M		aSAH	Mother		4x (Aneurysm)	MRA	D/C
12	13.1	F		aSAH	Father		2x (SAH)	MRA	D/C, scan at 18 & 30 years
13	8.6	F		aSAH	Mother		1x (SAH)	MRA	D/C
14	14.9	F		aSAH	Mother		1x (SAH)	MRA	D/C, scan at 30 years
15	14.8	F		aSAH	Mother		1x (SAH)	MRA	D/C, scan at 30 years
16	4.6	F		aSAH	Sister			MRA	D/C, scan at 16 years
17	13.6	M	Migraines	aSAH	Father			MRA	D/C
18	14	M	Intermittent headaches	aSAH		1x (aSAH)	1x (aSAH)		D/C
19	13.3	F	Migraine – Px Pizotifen	aSAH		1x (aSAH)			D/C
20	8	F		aSAH		4x (1x aSAH, 3x Aneurysm)		MRA	D/C, scan after 18 years
21	13.5	M		aSAH		2x (aSAH)		MRA	D/C
22	13	F		SAH	Father	1x (SAH)			D/C
23	8.9	M	Intermittent headaches	SAH		2x (SAH)	1x (SAH)	MRI	D/C, scan after 20 years
24	8	M		SAH		3x (1x SAH)		MRA	D/C, scan at 18 years
25	6.2	M		SAH		2x (SAH)		MRA	D/C, scan at 18 years
26	10	F		SAH		1x (SAH)			D/C
27	14.8	F		Aneurysm	Mother	1x (SAH)		MRA	D/C
28	5.1	F		Aneurysm		1x (Aneurysm)	1x (Aneurysm)		D/C
29	8.1	M		AVM	Mother & Sister			MRA, HHT - ve	D/C
30	11	F		AVM	Mother	3x (AVM)		MRA	D/C
31	10.7	M		AVM & Aneurysm	Sister		3x (SAH)	MRA, HHT - ve	D/C
32	10.7	M		AVM & Aneurysm	Sister		3x (SAH)	MRA, HHT - ve	D/C, scan at 25 & 40 years
33	1.1	F		AVM	Father		3x (ICH)		Scan at 5 years (Parental fear)
34	14.3	M		AVM	Sister			MRA	D/C
35	7.2	M		AVM	Mother				D/C
36	5.2	M		AVM	Mother				D/C
37	14.8	F		AVM & Aneurysm		1x (AVM)	4x (2x aSAH, 2x Stroke)	MRA	D/C, scan after 18 years
38	0.6	M		AVM			3x (1x AVM, 2x Haem)		D/C
39	14	M		Haemorrhage	Brother				D/C, mother ref to counselling
40	9.8	F	Migraine – Px Pizotifen	Haemorrhage		2x (Haem)		MRI	D/C
41	12.5	M	Migraines	Stroke	Mother	2x (Stroke)		MRA	D/C

Fig. 1

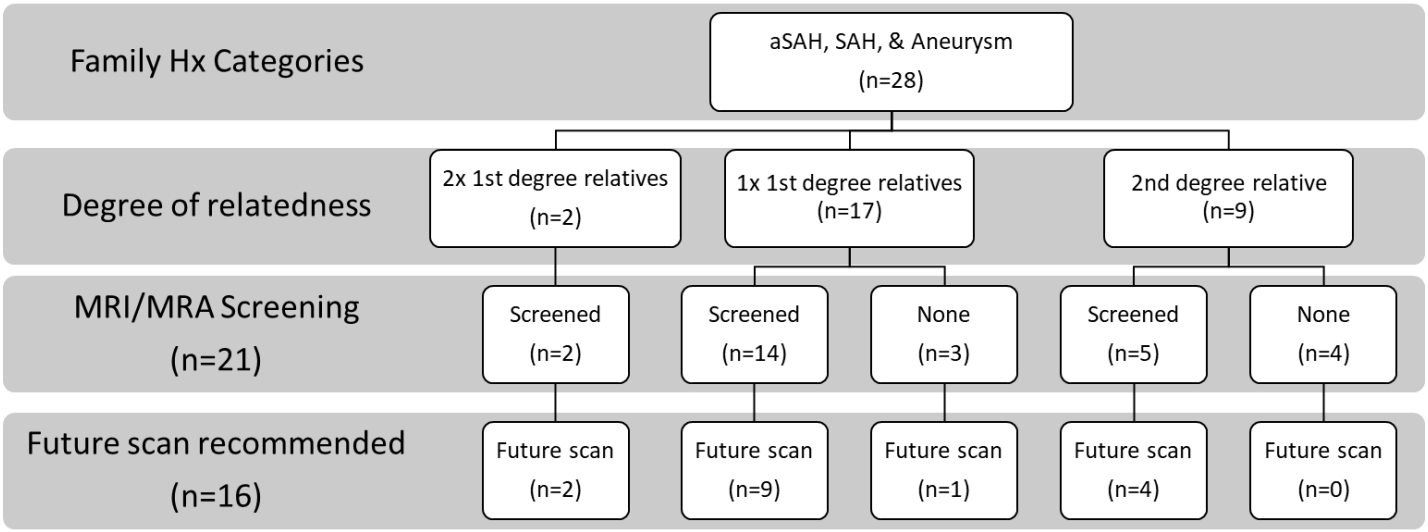
Family Hx Categories
aSAH, SAH, & Aneurysm
(n=28)
Degree of relatedness
2x 1st degree relatives
(n=2)
1x 1st degree relatives
(n=17)
2nd degree relative
(n=9)
MRI/MRA Screening
(n=21)
Screened
(n=2)
Screened
(n=14)
None
(n=3)
Screened
(n=5)
None
(n=4)
Future scan recommended
(n=16)
Future scan
(n=2)
Future scan
(n=9)
Future scan
(n=1)
Future scan
(n=4)
Future scan
(n=0)

Fig. 2

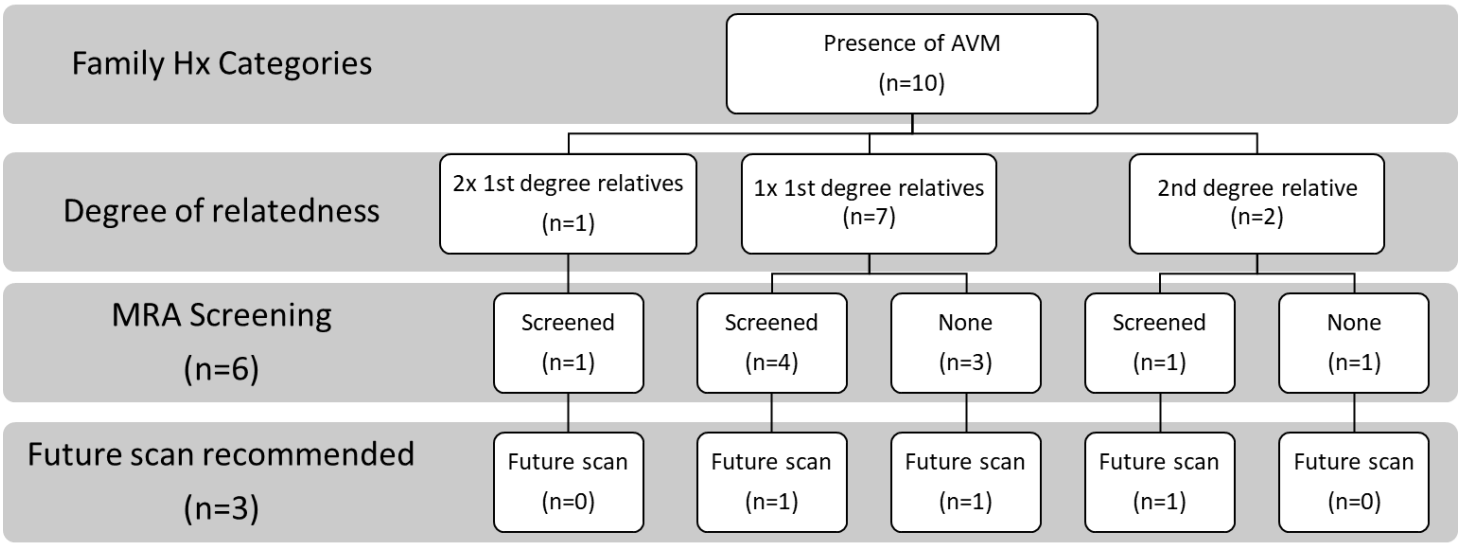
Family Hx Categories
Presence of AVM
(n=10)
Degree of relatedness
2x 1st degree relatives
(n=1)
1x 1st degree relatives
(n=7)
2nd degree relative
(n=2)
MRA Screening
(n=6)
Screened
(n=1)
Screened
(n=4)
None
(n=3)
Screened
(n=1)
None
(n=1)
Future scan recommended
(n=3)
Future scan
(n=0)
Future scan
(n=1)
Future scan
(n=1)
Future scan
(n=1)
Future scan
(n=0)

Fig. 3