



Radiological investigations in non-aneurysmal subarachnoid haemorrhage: A 5-year review



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1. Introduction

Spontaneous subarachnoid haemorrhage (SAH) remains an important clinical entity with considerable morbidity and mortality globally. Historically, approximately 85% of non-traumatic SAH can be attributed to ruptured intracranial aneurysms with an estimated all-cause mortality rate of up to 40% (Mohan et al., 2019a). Rupture of other vascular malformations such as arteriovenous malformations (AVMs) account for approximately 5% whilst no overt cause can be found in the remainder despite thorough radiological investigation (Macdonald and Schweizer, 2017). While the origin of non-aneurysmal bleeding remains uncertain and often remains diagnosed, studies have shown this sub-type of SAH to have favourable outcomes compared with SAH secondary to aneurysmal rupture (Van der Schaaf et al., 2004; Bashir et al., 2018).

As both conditions present in a clinically similar manner, it is essential that sensitive and specific imaging is utilised to avoid the devastating consequences of an undiagnosed ruptured intracranial aneurysm. The re-bleeding rate from an untreated, ruptured aneurysm has been estimated at approximately 50% in the month after initial ictus (Fujii et al., 1996; Naidech et al., 2005).

Consequently, digital subtraction angiography (DSA) has been the mainstay of investigation in SAH and considered the 'gold standard' with reported sensitivity rates of up to 99% in detecting intracranial aneurysms (Iuo et al., 2012; Yeung et al., 2009). However, the development of non-invasive neurovascular imaging techniques in recent years has meant that CT angiography (CTA) has rivalled DSA and even replaced it in some centres as the primary imaging modality in this setting (Agid et al., 2010).

However, the role of CTA as a primary mode of investigation remains controversial due to the significant consequences of missing an intracranial aneurysm and its lower reported sensitivity and specificity in this setting compared with DSA (Fox et al., 2008; Prestigiacomo et al., 2010). Some studies have shown a detection rate for vascular abnormalities of up to 14% with DSA in patients who have had a negative CTA (Heit et al., 2016).

In spite of this, more recent studies have shown that DSA may not add further diagnostic value to CTA in some SAH patients depending on the distribution and extent of subarachnoid blood on initial CT scan (Mohan et al., 2019b). Most existing studies have focused on the perimesencephalic SAH pattern which is radiologically characterised by blood confined to the perimesencephalic or prepontine cisterns (Rinkel et al., 1991). In this group, some have proposed that initial CTA alone is sufficient in excluding intracranial aneurysms (Yeole et al., 2020). However, patients with non-aneurysmal SAH may also present with CT brain showing widespread distribution of subarachnoid blood with extension to the ambient cisterns or Sylvian fissures which provides diagnostic difficulty as an aneurysmal SAH mimic.

No established consensus therefore exists with regards to initial and follow-up imaging in patients presenting with SAH with local centres employing their own individual and varying protocols (Mohan et al., 2019a).

The aim of this study is to evaluate a non-aneurysmal SAH patient cohort and whether invasive DSA is required in all of these patients.

2. Materials and methods

2.1. Patient characteristics

This retrospective, observational study conducted at a single tertiary care centre evaluated patients admitted to Northern Ireland's regional neurosurgical department (Royal Victoria Hospital, Belfast) over a 5-year period from January 1, 2015 to December 31, 2019 with spontaneous subarachnoid haemorrhage. Records of patients presenting to the department were maintained in local prospective databases of aneurysmal and non-aneurysmal SAH cases.

Patients were included in the study if the diagnosis of SAH was confirmed on CT brain, they had a CTA negative for any abnormality and proceeded to catheter angiography. Those with negative CT brain but positive lumbar puncture were excluded from analysis. Patients with a relevant history of trauma and those with convexity SAH alone were also

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excluded. Patients with parenchymal or intraventricular haemorrhages were excluded. Information on patient demographics, clinical parameters and radiological investigations were extracted from these databases and medical records where required.

Of those admitted for investigation of SAH, a total of 872 cases were reviewed to screen for those who had CT brain positive for SAH, a negative CTA and who then went on to have catheter angiography positive for a causative abnormality.

2.2. Classification of SAH on CT scans

All CT scans of SAH patients were reviewed by the same consultant neurosurgeon who assigned each a Fisher grading according to established criteria (Fisher et al., 1980). The location of subarachnoid blood was also classified into two distinct patterns: 1) ‘Localised’ – confined to the interpeduncular, prepontine and perimedullary cisterns and 2) ‘Diffuse’ – extending to the Sylvian and/or interhemispheric fissures.

2.3. Local imaging protocol

Local protocol states that patients presenting with spontaneous, non-traumatic SAH will undergo CTA and proceed to catheter angiography with follow-up MRI as an outpatient if this is negative. Repeat catheter angiography may be performed if clinically or radiologically indicated at the discretion of the clinical team.

2.4. Data analysis

Data analyses were performed using IBM Statistics for Mac OS (IBM Corp., Armonk, New York, USA) and Microsoft Excel (Microsoft, Redmond, Washington, USA).

3. Results

3.1. Patient and radiological characteristics

A total of 124 patients met the inclusion criteria of CT brain positive for SAH, negative CTA and having undergone catheter angiography. Patient and radiological characteristics for the catheter angiogram negative group are contained in Table 1.

It is best to look at those with no identified bleeding source and those with a potential bleeding source identified on catheter angiography separately.

1. No identified bleeding source on catheter angiography

This group comprised 105 patients. It consisted of 62 (59%) males and 43 (41%) females. The mean age of patients at the time of presentation was 52 (SD 12) years. The mean length of stay was 9 (SD 5) days and 16 (15%) had early hydrocephalus on their initial CT brain. Eighty-three (79%) patients attended follow-up at a neurosurgical outpatients' clinic and forty-four (42%) of these remained symptomatic at the time of review. Mean time to follow-up was 5.6 months. Patients who were ‘symptomatic’ at follow-up reported one or more of headache, fatigue, memory loss, tinnitus, photosensitivity or mild motor weakness. Individual practice varied as to whether patients who did not attend follow-up were re-appointed. Given that Northern Ireland has only one neurosurgical centre, any instances of re-bleeding would have been referred and therefore captured in our dataset.

Twenty-six patients (25%) presented with Fisher grade 2 bleed on CT scan while 68 (65%) had a Fisher grade 3 bleed and 11 (11%) were Fisher grades 4. Forty-six (44%) patients had subarachnoid blood limited to the basal cisterns while 59 (56%) had blood diffusely distributed into the interhemispheric or Sylvian fissures. Ninety-two (88%) patients underwent follow-up MRI scan with only one (1%) of these patients having a scan result showing a potential source of bleeding (vasculopathy).

Table 1

Patient demographic and clinical parameters of the true non-aneurysmal group ($n = 105$).

Characteristic	Catheter Angiogram Negative Group
Total (%)	105
Age, mean (SD), years	52 (12)
Sex (%)	
Male	62 (59)
Female	43 (41)
Length of stay, mean (SD), days	9 (5)
Hydrocephalus on CT (%)	
Yes	16 (15)
No	89 (85)
Fisher Grading (%)	
2	26 (25)
3	68 (65)
4	11 (11)
Location of Blood (%)	
Localised to basal cisterns	46 (44)
Diffuse into sylvian or interhemispheric fissures	59 (56)
Symptomatic at follow-up (%)	
Yes	44 (42)
No	39 (37)
N/A	22 (21)
Mean time to follow-up, months	5.6
Follow-up MRI (%)	
Yes	92 (88)
No	11 (11)
MRI Positive for Source of Bleed (%)	
Yes	1 (1)
No	91 (87)

Abbreviations: SD, standard deviation; CT, computed tomography; MRI, magnetic resonance imaging.

2. Potential bleeding source identified on catheter angiography

Nineteen patients with positive catheter angiography after negative CTA were included in analysis and are shown in Table 2. This group included 18 aneurysms and one dural arteriovenous fistula. The mean age at presentation was 57 (SD 14) years with 5 (26%) males and 14 (74%) females. The mean length of stay was 22 (SD 14) days. Nine (47%) patients in this group had an initial CT with hydrocephalus. One (5%) patient died during admission due to the massive SAH. There were no (0%) patients in this group with Fisher grade 2 bleed. However, the group contained seven (37%) patients with Fisher grade 3 and 12 (63%) with Fisher grade 4 bleeds. No patients (0%) in this positive catheter angiography group had a blood distribution limited to the basal cisterns, all having a Diffuse pattern of bleeding.

Table 2

Patient demographic and clinical parameters of the catheter angiogram positive group ($n = 19$).

Characteristic	Catheter Angiogram Positive Group
Total (%)	19
Age, mean (SD), years	57 (14)
Sex (%)	
Male	5 (26)
Female	14 (74)
Length of stay, mean (SD), days	22 (14)
Hydrocephalus on CT (%)	
Yes	9 (47)
No	10 (53)
Fisher Grading (%)	
2	0 (0)
3	7 (37)
4	12 (63)
Location of Blood (%)	
Localised to basal cisterns	0 (0)
Diffuse into sylvian or interhemispheric fissures	19 (100)

Abbreviations: SD, standard deviation; CTA, computed tomography.

3.2. Unreported abnormalities on CTA

CTA provided a false negative result (as confirmed with catheter angiography) in a total of 19 patients. The radiological features of these abnormalities are listed in Table 3. Of the abnormalities missed on CTA, four (21%) were blister-like aneurysms and two (11%) were dissecting aneurysms. A lobulated aneurysm and a dural arteriovenous fistula were the missed abnormality on one (5%) occasion each. The remaining eleven (58%) were berry aneurysms. Abnormalities were not identified in multiple vessels with the internal carotid artery being the most common site with six (32%) missed abnormalities. The basilar, posterior communicating, anterior communicating and superior cerebellar arteries followed this with two (11%) abnormalities missed in each of these locations. The majority (13, 68%) of missed abnormalities were between 1 and 5 mm in size with three (16%) measuring <1 mm and two (11%) measuring 5 mm or more. Two (11%) aneurysms failed to be reported in district general hospitals (DGH) but were noted upon retrospective review by a neuroradiologist.

3.3. Repeat catheter angiography

A total of forty-four (35%) of the patients included within this study underwent at least one repeat catheter angiogram. Data for these patients are presented in Table 4. Three of the nineteen missed abnormalities (16%) were detected only on a repeat catheter angiogram. Initial DSA imaging was retrospectively reviewed at the relevant neurovascular multidisciplinary meetings attended by other neuroradiologists. All patients who underwent repeat catheter angiography had their repeat DSA carried out within approximately two weeks of the initial angiogram. Of those having more than one catheter angiogram, thirty-eight (86%) patients underwent one repeat DSA, five (11%) had two repeat DSAs while one (2%) patient underwent three repeat catheter angiograms. The most common indication for repeat angiogram was due to the distribution or extent of subarachnoid haemorrhage (19, 43%). Nine (20%) patients had a repeat catheter angiogram due to concerns about a possible abnormality on the initial DSA or MRA – none (0%) of this subgroup of patients was found to have an abnormality on follow-up. The three (7%) repeat

Table 3
Radiological characteristics of abnormalities missed on CTA.

Characteristic	Number of patients
Total	19
Type (%)	
Blister-like aneurysm	4 (21)
Lobulated aneurysm	1 (5)
Dissecting aneurysm	2 (11)
Dural AV fistula	1 (5)
Berry aneurysms	11 (58)
Location	
Internal carotid artery	6 (32)
Basilar artery	2 (11)
Posterior communicating artery	2 (11)
Anterior communicating artery	2 (11)
Superior cerebellar artery	2 (11)
Anterior inferior cerebellar artery	1 (5)
Posterior cerebral artery	1 (5)
Middle cerebral artery	1 (5)
Vertebral artery	1 (5)
Aneurysm ^a size (mm)	
≤1 mm	3 (16)
1-5 mm	13 (68)
≥5 mm	2 (11)
N/A ^b	1 (5)
Other	
Aneurysms not detected by DGH on CTA	2 (11)

Abbreviations: CTA, computed tomography angiogram; DGH, district general hospital.

^a Includes pseudo-aneurysms from dissection.

^b Not applicable as dural AV fistula.

Table 4

Evaluation of patients undergoing repeat catheter angiography.

Characteristic	Number of patients
Total (%)	44
Repeat DSAs positive for abnormality	3 (7)
Number of repeat DSAs	
1	38 (86)
2	5 (11)
3	1 (2)
Indication for repeat DSA	
Diffuse SAH	19 (43)
Vasospasm	1 (2)
Queried abnormality	9 (20)
Other	2 (5)
Unspecified	13 (30)

Abbreviations: DSA, digital subtraction angiography; SAH, subarachnoid haemorrhage.

angiographies which detected an abnormality were all performed due to extensive SAH blood load.

4. Discussion

The clinical outcomes of non-aneurysmal SAH are well established as being significantly superior to aneurysmal SAH which has substantial risk of vasospasm, hydrocephalus and rebleeding (Yeole et al., 2020). As both entities have a similar clinical presentation, it is essential to safely identify patients with ruptured intracranial aneurysms. It is also important, however, to consider whether invasive DSA is essential in all of these patients and no consensus has been reached on this to date.

DSA has therefore had an historically important role as the ‘gold standard’ in the investigation of SAH (Maher et al., 2020). This is reflected in our own local protocol with all SAH patients proceeding to at least one DSA. However, DSA is an invasive imaging technique with risks including stroke and vascular injury. Neurological complications have been estimated by some to be as high as 1.8% with persisting deficits in as many as 0.5% (Willinsky et al., 2003). Non-neurological complications may also occur in less than 1% of patients (Bakker et al., 2014). Some have suggested that the risk of DSA-complications is under-reported (Mohan et al., 2019b) and balance this versus the relatively benign course of non-aneurysmal SAH. Considerable attention has therefore been focused on CTA as a non-invasive and less resource-intensive alternative to DSA.

Numerous studies have demonstrated that CTA has a detection rate for intracranial aneurysms that rivals DSA (Howard et al., 2019). Our study revealed a CTA sensitivity rate of 96.35% for aneurysm detection when the entire cohort of non-aneurysmal and emergency SAH patients was considered. These findings are similar to the existing literature (Chappell et al., 2003; Germans et al., 2015; White et al., 2000). Some recent studies have found that improved CTA techniques increase the sensitivity to as high as 98% (Menke et al., 2011; Westerlaan et al., 2011). The utility of CTA is also likely to increase in future when the notable recent results of dual-energy CTA in detecting intracranial aneurysms are considered with its substantial reduction in radiation exposure (Zhang et al., 2010). This is reinforced by the advantages of CTA over DSA including its increased availability, relatively quick time of completion and its ability to image surrounding tissues as well as its lower risk profile (Hoh et al., 2004).

CTA has therefore become the primary imaging modality and has replaced DSA as the first line, and in some cases only, imaging modality in patients presenting with SAH (McDonald et al., 2013; Catapano et al., 2020). However, despite these optimistic findings, a number have studies have expressed uncertainty as to the diagnostic validity of CTA alone (Philipp et al., 2017). Some older studies have postulated that up to 30% of culprit vascular lesions are not identified by initial CTA (Duong et al., 1996; Bradac et al., 1997). In this study, 19 abnormalities were missed on CTA and subsequently detected on catheter angiography. Some of the

features of these abnormalities that CTA was unable to detect were also ascertained and included blister-like aneurysms, a dissection and a dural AV fistula. The missed abnormalities were identified on multiple vessels with the internal carotid artery being the most common site which differs from other research (Willinsky et al., 2003). The majority of missed aneurysms for which size could be determined were 1–5 mm in size. Our findings are therefore in agreement with studies which have found relatively low sensitivity rates for CTA in detecting aneurysms smaller than 5 mm in size (Pradilla et al., 2013). It is therefore essential to acknowledge the potential limitations of CTA in the presence of such vascular abnormalities when applied to patients presenting with SAH as a general cohort.

Previously, numerous studies have suggested a narrower focus and evaluated CTA in perimesencephalic SAH as a pattern of limited haemorrhage which has been associated with negative findings on DSA (Agid et al., 2010; Catapano et al., 2020). While some studies have advised a more cautious approach, recent research has found false negative CTA results as low as 0% in patients with perimesencephalic SAH and some have concluded that DSA adds no diagnostic value in such patients (Huttner et al., 2006; Catapano et al., 2020). Our study adds to this discussion in finding that all patients with a Fisher 2 bleed identified on initial CT scan and negative CTA also had a negative catheter angiography. Similar findings were reported for patients with a 'Limited' pattern of SAH where blood was localised to the basal cisterns and in a truly perimesencephalic distribution. All patients with missed abnormalities on CTA had CT scans showing blood extending into the Sylvian and/or interhemispheric fissures.

It is also important to note that our study highlighted 2 cases where aneurysms were not detected on radiological reports issued by district general hospitals (DGH) but were subsequently detected by neuroradiologists prior to the patient undergoing catheter angiography. Similar cases have been reported previously with one study revealing that 19 aneurysms overlooked on initial review were detected retrospectively (White et al., 2003). Such omissions may negatively impact the reported sensitivity rates for CTA detection of intracranial aneurysms and be a contributory factor to false-negative reports (Wong et al., 2018). Similarly, other studies have demonstrated that specialist neuroradiologists perform superiorly to other reviewers in detecting intracranial aneurysms and that performance increases with observer experience (Pedersen et al., 2001; Jayaraman et al., 2004). Therefore, we would recommend that patients who do not proceed to catheter angiography have their CTA reviewed by at least one specialist neuroradiologist to minimise the chance of false negative reports.

Our study also reports data on repeat catheter angiograms which were performed in a total of 44 (35%) patients. An aneurysm missed on CTA was detected in 3 (7%) of these patients. Comparable yields for repeat DSAs have been reported elsewhere (Catapano et al., 2020). The commonest reason for repeat DSA was high subarachnoid blood load on CT brain. While this study offers little to the debate surrounding optimal timing for repeat DSA (all initial DSAs were performed within 2 weeks of ictus), it does reinforce the fact that a vascular lesion may still be the culprit in patients with both negative CTA and DSA, especially in cases where there is a large volume of SAH. Various reasons have been proposed to explain this including small aneurysmal size or high blood load compressing the lesion (Van Gijn and haemorrhage, 2001). In the context of evidence which shows that delayed diagnosis is significantly more common in diffuse SAH compared with more limited haemorrhage patterns, and in Fisher grades 3 and 4, it is reasonable to conclude that such patients are investigated thoroughly with DSA to exclude missed aneurysms and optimise clinical outcomes (Almandoz et al., 2012). However, further consideration should be given to whether repeat CTA in the first instance might be appropriate for these patients. If initial imaging was negative due to aneurysm thrombosis with later recanalization, repeat CTA may provide a less invasive investigation with high sensitivity for diagnosing vascular abnormalities in this group.

The inclusion of outpatient MRI in our local protocol also enabled evaluation of the utility of this imaging modality in the follow-up of DSA-negative patients. In this study, MRI identified a potentially causative bleeding source (vasculopathy) in 1% of patients. In the detection of intracranial aneurysms, magnetic resonance imaging has yielded inferior results in sensitivity and specificity when compared with DSA and CTA in the acute setting (Connolly et al., 2012; Topcuoglu et al., 2003; Andaluz and Zuccarello, 2008). Its relatively absent role in this context is compounded by its susceptibility to motion artefact and increased time requirements. However, the utility of later magnetic resonance imaging has been supported by at least one other study which showed a relatively high rate of delayed diagnosis of greater than 5% in patients who previously underwent DSA with some further yield for spinal imaging (Mohan et al., 2019a; Germans et al., 2015; Sadigh et al., 2018). Therefore, we would suggest that MRI can diagnose other causes of haemorrhage, such as vasculopathy and cavernoma, and should be considered a useful adjunct in these patients.

There were several limitations inherent to our study including its design as retrospective analysis. Insufficient information was available from patients' online records to consistently identify the period of time between onset of ictus and initial CT scan used for classification.

We are therefore unable to propose a time period after the initial ictus for which the findings of this study may be applicable. Substantial heterogeneity also exists across studies in describing patterns of SAH which may also limit comparisons with the literature. Future prospective studies addressing these limitations may contribute further to the development of standardised guidelines for the initial and subsequent investigation of patients with SAH.

5. Conclusions

There exists considerable debate within scientific literature surrounding the most appropriate initial and follow-up imaging in patients presenting with spontaneous SAH. This retrospective study sought to present data on a local cohort of true non-aneurysmal SAH patients and evaluate whether CTA alone is sufficient to exclude ruptured intracranial aneurysms in selected cases.

Our study presents interesting findings regarding the clinical burden of non-aneurysmal SAH including surprisingly high rates of hydrocephalus on imaging (15%) and a significant minority with persisting symptomatology at outpatient follow up (42%). As an important clinical entity in itself, its significance is likely to continue to grow with proportionally fewer cases of aneurysmal SAH per year and several case reports have also suggested links with Covid-19 (Harrogate et al., 2021; Cezar-Junior et al., 2020).

The results of our study support the evidence that CTA alone may be sufficient to exclude ruptured intracranial aneurysms in carefully selected patients. Significantly, we found that all patients with a Fisher 2 bleed identified on initial CT scan and negative CTA also had a negative catheter angiography. In light of our findings, in the context of the existing literature, we should consider whether invasive catheter angiography is necessary in patients presenting with Fisher 2 bleed and negative CTA. Patients not proceeding to DSA should have their imaging reviewed by a specialist neuroradiologist. Given that Fisher grade 3 and 4 bleeds, as well as the Diffuse pattern of SAH, were associated with undetected abnormalities on CTA in some cases, we advise that these patients should still proceed to catheter angiography. However, consideration should also be given to the value of repeat CTA initially in this patient group.

Our previous policy of all CT positive SAH patients requiring catheter angiogram is perhaps cautious when reviewing the information found here and that in the literature. This approach is weighed against the risk of missing an aneurysm which will often rebleed with significant consequences.

Declaration of competing interest

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