ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF THREE DIMENTIONAL DIGITAL SUBSTRACTION ANGIOGRAPHY (3D DSA) IN CORRELATION WITH COMPUTED TOMOGRAPHIC ANGIOGRAPHY (CTA) AND MAGNETIC RESONANCE ANGIOGRAPHY (MRA) IN EVALUATION OF ANEURYSMAL SUBARACHNOID HAEMORRHAGE : A COMPARATIVE STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

OBJECTIVES: Subarachnoid hemorrhage from ruptured intracranial aneurysm is a serious condition, which can only be prevented by early diagnosis and treatment before rupture. In this study, we have assessed the performance of CTA and MRA in detecting, localizing and sizing intracranial aneurysms in patients of aneurysmal subarachnoid haemorrhage compared to 3D DSA and effects of above parameters on the sensitivity of these imaging modalities, taking DSA as gold standard. **METHODS:** We investigated 25 consecutive patients of subarachnoid haemorrhage referred to our department between November 2017 and April 2018 after they met the inclusion criteria. Each patients underwent CTA, MRA and conventional rotational digital substraction angiography from which three dimentional reconstructed images were obtained and the findings were recorded and analysed. **RESULTS:** We found that the sensitivity of each of CTA and MRA for identification of intracranial aneurysms is 57.1 % in small, 88.8 % in medium and 100% in large sized aneurysms. Overall, both CTA and MRA were 20% less sensitive than 3D DSA in detection of intracranial aneurysms, specially for small and medium sized ones. **CONCLUSION:** Hence, 3D DSA is more sensitive and accurate for evaluation of aneurysmal subarachnoid hemorrhage than CTA and MRA.

Keywords: Subarachnoid hemorrhage (SAH), Digital Substraction Angiography (DSA), Digital Rotational Angiography (DRA), Computed Tomographic Angiography (CTA), Magnetic Resonance Angiography (MRA), Time of Flight (TOF)

List of abbreviations: (SAH) Subarachnoid hemorrhage, (3D) Three Dimentional, (DSA) Digital Substraction Angiography, (DRA) Digital Rotational Angiography, (MRS) Modified Rankin Scale, (CTA) Computed Tomographic Angiography, (CE) Contrast Enhanced, (MRA) Magnetic Resonance Angiography, (TOF) Time of Flight;

Introduction

Subarachnoid hemorrhage (SAH) caused by ruptured cerebral aneurysm is frequently associated with poor outcome. The only approach that could prevent this outcome is to diagnose and treat cerebral aneurysms before rupture. Though Non-contrast CT Brain is the imaging modality of choice for initial screening of subarachnoid hemorrhage, 2D Digital Substraction Angiography is considered as gold standard in detec-

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tion of intracranial aneurysms. Recently, rotational Digital Substraction Angiography with 3D reconstructed images (3D-DSA) have emerged as a useful technique to visualize intracranial vascular lesions. Compared to the conventional DSA, 3D-DSA can detect intracranial aneurysms with greater levels of sensitivity and accuracy. Among other alternative diagnostic tests, CT Angiography (CTA) and MR Angiography (MRA) have attracted much attention as a substitute due to their high accuracy, non invasive nature, availability and favourable technical aspects as three dimensional, multiplanar imaging, short acquisition time, intravenous rather than intra-arterial contrast. Non contrast enhanced MRA methods do not even require contrast and in general, MRA has advantage of not using any ionising radiation. In the present study, we have assessed the performance of CTA and MRA in detecting, localizing and sizing intracranial aneurysms in patients of aneurysmal subarachnoid haemorrhage compared to 3D DSA and effects of above parameters on the sensitivity of these imaging modalities, taking DSA as gold standard.

Materials and Methods

A prospective study was done at our institute between November 2017 and April 2018. 25 consecutive patients of subarachnoid haemorrhage referred to our department between were included in the study after they met the inclusion criteria.

Institutional Ethics Committee:
Approval from institutional ethics committee obtained.

Inclusion criteria:
1. Patients of spontaneous subarachnoid haemorrhage detected clinically and by CT scan, therefore of high clinical suspicion for aneurysmal SAH
2. Patients who gave consent to take part in the study

Exclusion criteria:
1. Traumatic subarachnoid haemorrhage
2. Intra cerebral haemorrhage

Pre-procedure work-up:
Before the The following informations were collected from each patient:

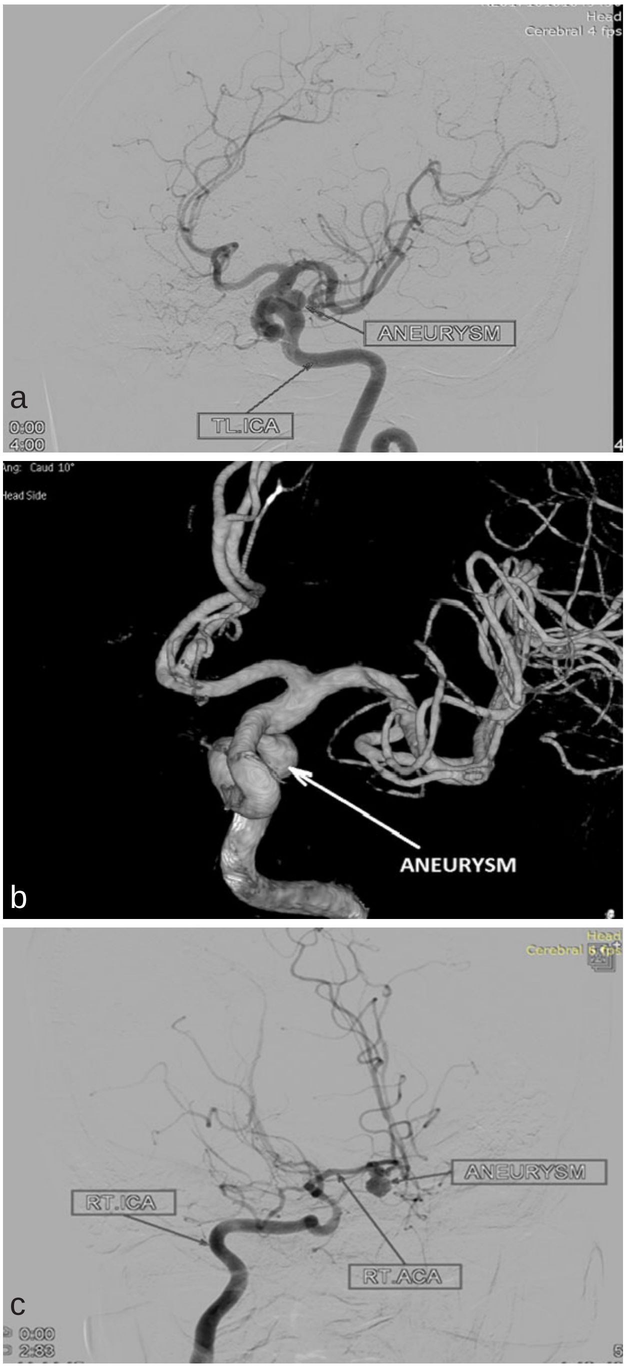
• Age, Sex
• H/O hypertension, diabetes mellitus, hypercholesterolemia, current or previous smoking, previous incidence of SAH,
• Family history of subarachnoid haemorrhage and family history of kidney disease.
• Detailed drug history.
• Clinical features and examination findings were noted
• Investigations like CBC, serum lipid profile, blood sugar, serum creatinine, ECG, Chest X-ray were also done.

Each patients underwent CTA, MRA and conventional rotational digital substraction angiography from which three dimentional reconstructed images were obtained. Findings were recorded in predesigned and pretested case record sheet.

Results

The mean age of the patients having features of subarachnoid haemorrhage was 46.5 years. Male female ratio was almost 1.5:1. All the study patients (100%) had headache and vomiting and 11 patients (44%) presented with unconsciousness. Signs of meningeal irritation were found in 16 (64%) and 4 patients (16%) complained of weakness of extremities. Regarding the presence of risk factors, 48% patients were smoker and 56% were hypertensive. A total of 20 aneurysms in 16 patients among the 25 patients (Male-8, Female-8, Male female ratio = 1:1) were identified on DSA. Mean age of patients whose aneurysms were identified on DSA was 49.1 years. Among them mean age of male patients were 48.6 years and mean age of female patients were 49.7 years.
Aneurysms of </= 4 mm were categorized as small sized and of 5-12 mm size were categorized as medium sized aneurysms, whereas aneurysms of >/= 13 mm were categorized as Large sized aneurysms. Among 20 aneurysms identified on 3D DSA, 7 were of small size, 9 were of medium size and 4 were identified as large sized aneurysms. Among 7 small sized aneurysms identified on 3D DSA, CTA and MRA both missed 3 aneurysms,and among 9 medium sized aneurysms, CTA and MRA failed to detect 1 aneurysm

each, in different patients. However, all 4 large aneurysms were diagnosed correctly on 3D DSA, CTA and MRA. The sensitivity of each of CTA and MRA for identification of intracranial aneurysms turned out to be 57.1 % in small, 88.8 % in medium and 100% in large sized aneurysms. Overall, both CTA and MRA were 20% less sensitive than 3D DSA in detection of intracranial aneurysms, specially for small and medium sized ones.



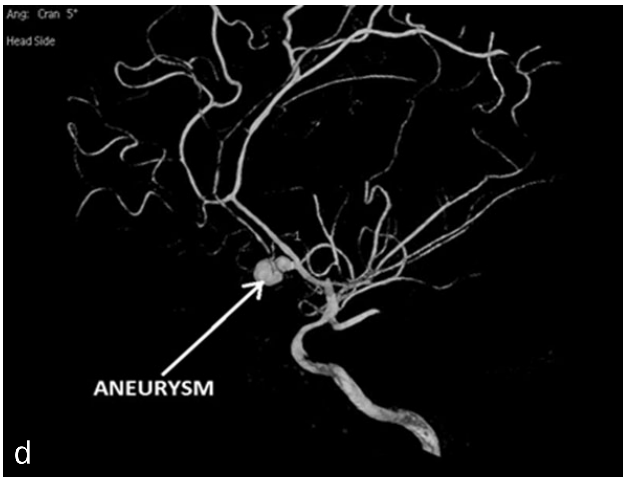
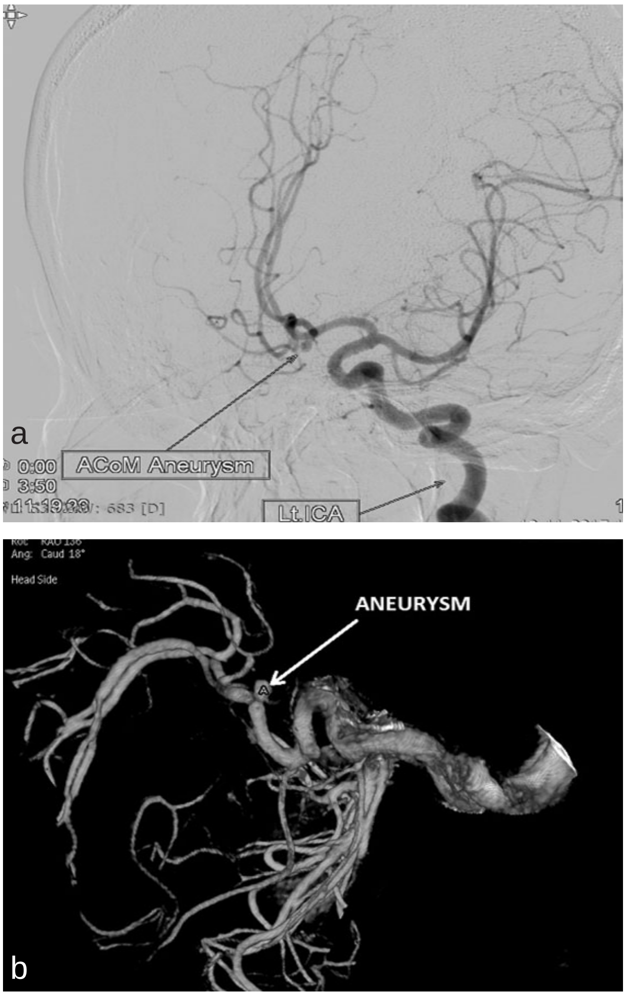


Figure 1: Delineation of Aneurysms in two patients by 2D Digital Substraction Angiography and rotational Digital Substraction Angiography with 3D reconstructed images (3D-DSA)-
2D DSA **(a)** and 3D DSA **(b)** show an aneurysm in Cavernous segment of Left Internal Carotid Artery in a patient, and
2D DSA **(c)** and 3D DSA **(d)** show a pedunculated aneurysm in the A1 segment of Right Anterior Cerebral Artery in another patient.



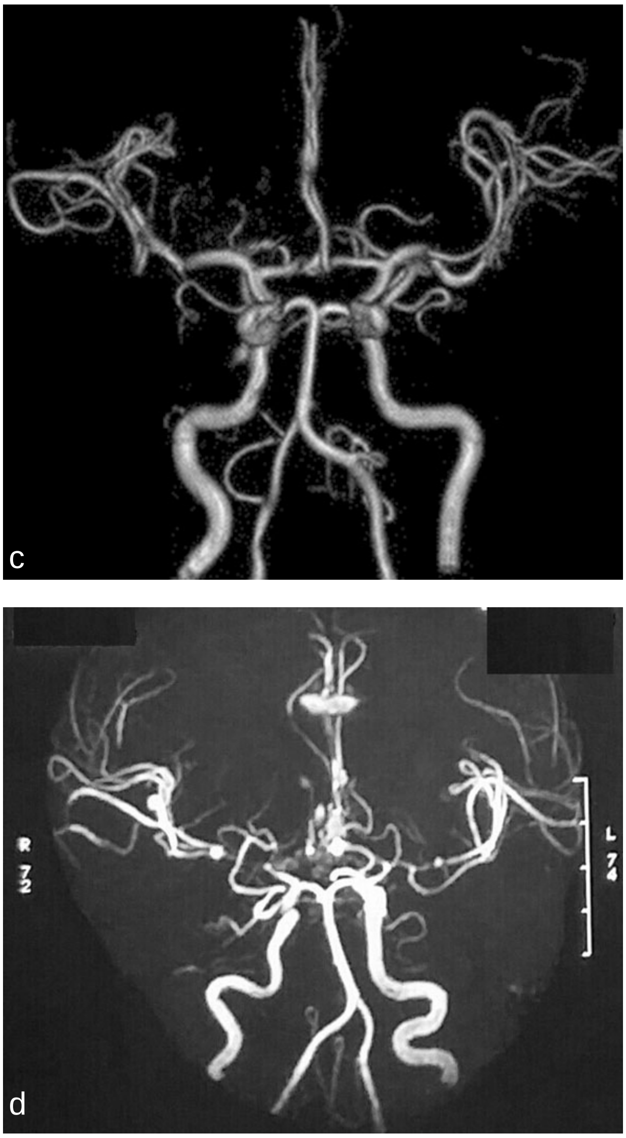


Figure 2: A case where a small aneurysm in the Anterior communicating artery was identified on 2D DSA **(a)** and 3D DSA **(b)** but CTA **(c)** and MRA **(d)** failed to demonstrate it.

S.#	Age (Yrs.)	Sex	No. of Aneu-rysms	Location	Cate-gory	DSA	CTA	MRA
1	54	M	1	Right MCA	Large	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
2	45	M	2	Bilateral MCA	Small Small	Correctly diagnosed	Missed	Missed
3	50	F	1	Right AICA	Medium	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
4	55	F	1	Left ACA	Medium	Correctly diagnosed	Correctly diagnosed	Missed
5	30	F	1	Right ACA	Medium	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
6	48	F	1	Right ICA	Small	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
7	60	M	2	Left ICA, Right ACA	Large Small	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
8	48	F	1	Acom	Medium	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
9	81	M	1	Left ICA	Large	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
10	35	M	1	Acom	Small	Correctly diagnosed	Missed	Missed
11	52	F	2	Basilar, Right ICA	Medium Small	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
12	50	F	1	Right ACA	Medium	Correctly diagnosed	Missed	Correctly diagnosed
13	42	M	1	Basilar	Large	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
14	65	F	1	Left MCA	Small	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
15	38	M	2	Bilateral MCA	Medium Medium	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed
16	34	M	1	Left PCA	Medium	Correctly diagnosed	Correctly diagnosed	Correctly diagnosed

Table 1: Abbreviations: M= Male; F= Female; MCA= Middle Cerebral Artery; AICA= Anterior Inferior Cerebellar Artery; Acom= Anterior Communicating Artery; ACA= Anterior Cerebral Artery; ICA= Internal Carotid Artery; PCA= Posterior Cerebral Artery.

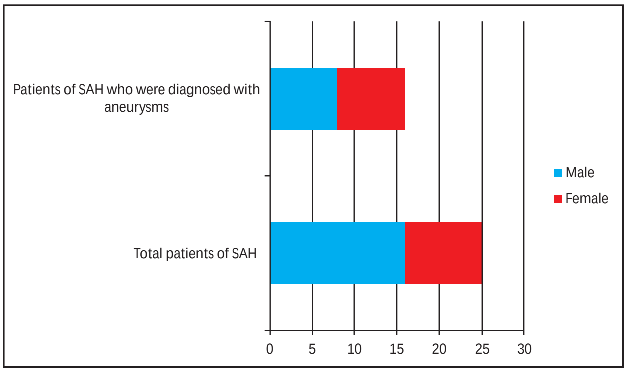


Figure 3: Comparison of sex distribution of the total patients of SAH and patients of SAH who were diagnosed with aneurysms

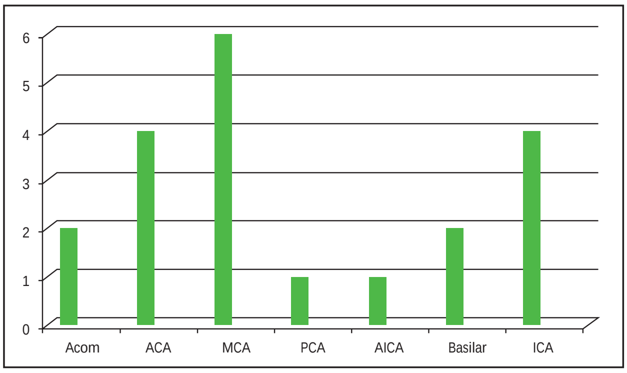


Figure 4: Spatial distribution of Aneurysms of patients of this study

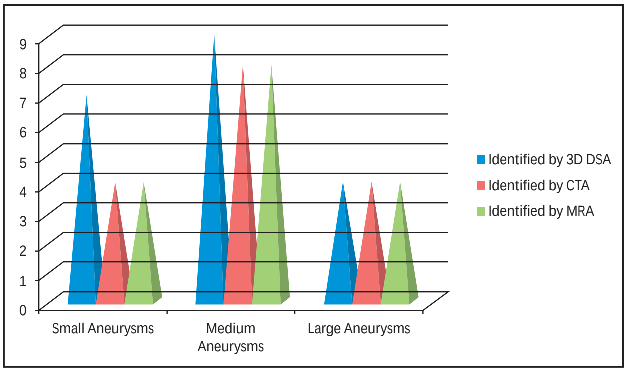


Figure 5: Comparison of ability of 3D DSA, CTA and MRA in identification of aneurysms of different sizes.

Discussion

Subarachnoid hemorrhage from rupture of an intracranial aneurysm is a serious condition. Death before reaching the hospital is 15%. Average mortality rate of patients who reach hospital is 44%. Significant lifestyle modifications among survivors is 12%. Dependents (MRS 4 and 5) is about 6.5%.[1] The location, size and angiomorphology (e.g low wall shear stress, irregular domes, daughter sacs etc) of incidentally diagnosed unruptured cerebral aneurysms predicts the risk of future rupture, whereas aneurysms that have already ruptured carry a much higher risk of rehemorrhage.[2,3,4] So, accurate assessment of aneurysms is essential to guide the timely and appropriate management and neuroimaging plays a critical role in it.

A non-contrast-enhanced CT scan is usually used as the first-line imaging modality for evaluating subarachnoid hemorrhage as it is rapid, inexpensive, and widely available. If performed within the first six hours, it can identify the distribution of SAH with 100% sensitivity and gives an idea of the location of the aneurysm, presence of Intra ventricular hemorrhage and degree of hydrocephalus which guides about treatment and prognosis. Although, from six hours to one week after hemorrhage, in the subacute setting, brain's normal degradation of hemorrhagic blood products significantly drops the predictivity of CT to detect SAH.[5,6] In these situations, a negative non-contrast CT is commonly supplemented with a lumbar puncture to evaluate for xanthochromia.

In instances of high index of clinical suspicion and a negative non-contrast CT, CT angiography (CTA) is used to increase the detection rate of ruptured cerebral aneurysms. McCormack et al. showed that a negative non-contrast CT followed by a negative CT angiogram carries a post-test probability of 99.43% of being negative for aneurysmal subarachnoid hemorrhage.[7] CTA is performed on multi-detector helical CT scanners that allow multi-planar reformats, sub-millimeter slice thickness, and 3D reconstructions. Several studies has shown that current multi-detector scanners have a spatial resolution that can reliably diagnose aneurysms greater than 4 mm with nearly 100 % sensitivity.[8] For aneurysms 3 mm and smaller, however, early CT technology has been shown to be of inadequate sensitivity. The higher the numbers of detectors, scans can be performed more quickly with thinner collimation, higher resolution, and better contrast bolus timing. Further increases in spatial resolution will likely allow greater sensitivity in detecting smaller aneurysms and small associated branch vessels. Time-resolved CTA, or 4D-CTA can evaluate the flow dynamics of aneurysms by obtaining multiple acquisitions of a region of interest for a period of time. It has the ability to separate different blood flow phases and can identify aneurysms previously difficult to distinguish from surrounding vessels, such as in the case of intranidal aneurysms associated with arteriovenous malformations. Electrocardiogram-gated 4D-CTA are currently being investigated for its ability to detect aneurysm pulsations with the cardiac cycle and higher risk of growth and rupture.[9] Computational fluid dynamics study is example of another recent development which seeks to simulate blood flow within the aneurysm to calculate variables that would presumably correlate with rupture risk such as aneurysmal wall shear stress and peak wall tension. It shows significant promise to assist with the management of cerebral aneurysms.[10]

MRI is usually reserved for patients with a high pre-test probability of aneurysmal subarachnoid hemorrhage and a negative initial work-up with CT scans and/or cerebral angiography due to higher cost and longer acquisition times. MRI has advantages over CTA in that it does not use ionizing radiation and offers the ability to obtain images without the need for administration of intravenous contrast agents. It has the added advantage of screening for other pathologies that may present with similar symptoms such as meningitis, meningeal carcinomatosis, leptomeningeal metastasis, adjacent neoplasms, subdural hematoma and dural venous thrombosis. Fluid-attenuated inversion recovery (FLAIR) sequences produce strong T2 weighting while suppressing the cerebrospinal fluid (CSF) signal and can be particularly useful for detecting subacute SAH. Gradient echo T2*-weighted imaging was found to be better than FLAIR to detect even older SAH. Da Rocha et al. demonstrated a 100 % sensitivity for detection of subarachnoid hemorrhage with FLAIR compared with a 66 % sensitivity on CT n a study of patients with acute and subacute SAH.[11]

The use of time-of-flight (TOF) sequences on MRA do not require contrast agents, which may be contraindicated in patients with renal failure or contrast allergy and is found to have similar sensitivity as Contrast enhanced MRA (CE-MRA) for the detection of aneurysms.[12,13] CE-MRA is better than TOF-MRA to eliminate flow related artifacts and spin saturation but had lower spatial resolution than CTA.[14] Despite lower spatial resolution small branch vessels were reportedly better visualized on 3T MRA over CTA due to lack of venous contrast contamination.[15] Researchers have recently developed black-blood T1-weighted MRI sequences that help identify rupture site in patients with aneurysmal SAH by demonstrating the inflamed, enhancing wall of the recently ruptured aneurysm. These techniques can identify the causative rupture site in patients with multiple intracranial aneurysms, allowing for more accurate and timely treatment.[16] Aneurysm wall permeability can also be quantified using dynamic contrast-enhanced (DCE)-MRI and the perfusion parameter K trans, which is a size independent predictor of rupture risk.[17] High-field-strength 7 T MRI scanners have an extremely high signal-to-noise ratio, allowing the spatial resolution needed to detect variations in aneurysm wall thickness, which may be a marker of rupture risk.[18] Another advanced imaging technique combines MRA with post-processing algorithms from computational fluid dynamics to show 4D flow and aneurismal wall motion abnormalities.[19] Time-resolved MRA, or 4D MRA, directly measures flow velocities and shear stresses within an aneurysm and allow for the identification of the inflow zone of aneurysms and may guide endovascular treatment.[20]

Digital subtraction angiography (DSA) is an operator expertise dependent invasive procedure that requires use of ionizing radiation and iodinated contrast. Despite being invasive and operator expertise dependent procedure, complication rate is significantly low, about 0.3 %.[21] It has the temporal resolution to separately visualise the arterial, capillary, and venous phases of the injection and has high spatial resolution to identify aneurysms that may be missed on CTA or MRA. DSA is considered as the gold standard for evaluating intracranial aneurysms. In addition to conventional DSA, 3-dimensional rotational angiography (3DRA) further increases the sensitivity of small aneurysms less than 3 mm in size. Delayed repeat DSA is indicated when DSA fails to demonstrate an aneurysm in the setting of spontaneous SAH. One literature review revealed that delayed repeat DSA from one to six weeks after the initial study identified 37 aneurysms out of 368 angiography-negative SAH patients.[22] Another advantage of DSA is that endovascular therapy can be done in the same diagnostic setting, if required.

Conclusion

Imaging helps to determine the size, location, morphology, rupture status and potential for rupture of cerebral aneurysms and guides towards appropriate timely management, sometimes in the same setting. In this study, 3D DSA correlated perfectly with CTA and MRA in detection of Large aneurysms. However, 3D DSA is more sensitive in identification of aneurysmal site and in detecting small and medium sized aneurysms than CTA, MRA and conventional rotational DSA. The performance of DSA in identification of aneurysmal site is also better than CTA and MRA. Hence, 3D DSA is more sensitive and accurate for evaluation of aneurysmal SAH than CTA and MRA.

Conflict of interest: There are no conflicts of interest.

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