

Detection and characterization of intracranial aneurysms: 3T magnetic resonance angiography versus digital subtraction angiography with 3D and reconstruction

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Abstract: Cerebral aneurysms with a prevalence of 0.5-5% are common vascular anomalies of intracranial arteries. Rupture of an intracranial aneurysm is the commonest cause of non-traumatic subarachnoid haemorrhage. The principle aim of this study is to compare MRA at 3T with 3D-DSA, the reference standard, in detection and characterization of intracranial aneurysms and help determine the accurate therapy.

Materials and methods: In our study, 85 patients with clinical suspicion of cerebral aneurysm underwent MRA at 3T. Three sequences of MRA i.e. 3D-TOF, PC-MRA and CEMRA were taken. MRA findings were interpreted combining findings of all 3 sequences in source images, MIP and processed images. After MRA, each patient underwent DSA with 3D and its reconstruction. Results of MRA were compared with those of DSA taking DSA as gold standard invasive modality. Sensitivity, specificity, positive and negative predictive values were calculated for MRA in detection and characterization of intracranial aneurysms and tested by statistical software. To test the reliability, inter test agreement was measured between the two test results

Results: Intracranial aneurysms are more common in females and in 5th decade of life. MRA when performed at 3T with above mentioned three sequences resulted in sensitivity of 98.1% and specificity of 100% in detecting cerebral aneurysms.

Conclusion: MRA (3T) with 3D-TOF, PC-MRA and CEMRA can be reliably used as screening test to diagnose and characterize intracranial aneurysms, though it has some limitations.

Keywords: MRA: Magnetic Resonance Angiography, TOF: Time Of Flight, PC: Phase contrast, DSA: Digital subtraction angiography

Date of Submission: 08-06-2019

Date of acceptance: 25-06-2019

I. Introduction

The word "aneurysm" has been taken from the combination of two Greek words "ana" meaning 'across' and "eurys" meaning 'broad'. An aneurysm is an abnormal bulging in the walls of arteries. Aneurysms of intracranial vessels are relatively common with a prevalence of 3-6% in the general population, predominantly in women.¹ Risk factors associated with the formation of intracranial aneurysms are age over 50 years, female gender, current cigarette smoking and cocaine use. Patients with polycystic kidney disease, Marfan syndrome, coarctation of the aorta, fibromuscular dysplasia, family history of saccular aneurysm, and Ehlers-Danlossyndrome have increased risk for intracranial aneurysm. Cerebral aneurysms typically become symptomatic in people aged 40-60 years and are uncommon in children accounting for fewer than 2% of all cases.² Rupture of an intracranial aneurysm is the most common cause of non-traumatic subarachnoid hemorrhage (SAH), which constitutes 77% cases of spontaneous SAH. An approximate occurrence rate for aneurysmal rupture is 12/100,000 populations per year.³ One of the most important objectives in the management of aneurysmal SAH is to prevent aneurysmal re-bleeding and delayed cerebral ischemia caused by arterial vasospasm. Therefore, early detection and prompt localization of the aneurysm is critical for determining the appropriate neurosurgical or endovascular intervention. CT scan is the first diagnostic study performed to evaluate the possibility of SAH. Cranial CT scan can also demonstrate intraparenchymal hematomas, hydrocephalus, and cerebral edema and can help to predict the site of aneurysm rupture.⁴ Intra-arterial digital subtraction angiography (IA-DSA) is the gold standard investigation for intracranial aneurysmal disease.⁵ However, it is an invasive test with risk of 1% potentially severe complications like cerebral embolism,

dissection, rupture of cerebral arteries and haemorrhage, arterial vasospasmand 0.5% rate of persistent neurological deficit.⁶Concerns over the small but potentially significant risk of permanent neurological complications associated with IA-DSA have generated growing interest in the use of alternative non-invasive techniques.⁷ Magnetic resonance angiography (MRA) has evolved as an attractive non-invasive and non-ionizing alternative for imaging intracranial vasculature. With the development of MRA, absolute reliance on DSA for aneurysm detection and surgical planning is changing. For the purpose of determining therapy accurate assessment of the presence of an aneurysm and comprehensive visualization of the aneurysm location, orientation, size, morphology, neck and relationship to the parent vessel are crucial.⁸The principle aim of this study was to evaluate the accuracy of MRA in the diagnosis of intracranial aneurysms and to compare MRA with IA-DSA, the reference standard, in detection and characterization of intracranial aneurysms.

II. Material And Methods

This prospective comparative study was carried out on patients of department of neurology and neurosurgery at IPGMER, SSKM and Bangur Institute Of Neurosciences, Kolkata from 1st feb2015 to 31st July 2016. In this study eighty five (85) patients were studied over a period of one and half year. Patients presented in outpatient and emergency department of neurology and neurosurgery with history of severe headache and few of them had some focal neurological deficits. Complete history and neurological examinations were done by the concerned neurologist/neurosurgeon. On preliminary non-contrast CT scan of brain; most of them revealed SAH. In the department of Radiology, the patients were explained about the study process and after written informed consent, MRA was done at *3.0 Tesla MRI machine, GE Healthcare, Signa3THDxt*, as a screening tool for diagnosing intracranial aneurysms. After MRA, those patients with diagnosed aneurysm were referred to DSA unit, *DSA machine, Philipsalleuraxper FD20 biplane*; for confirmation and better characterization of aneurysms. Patients with non traumatic SAH/ICH were included. Few of the patients with strong clinical suspicion but undiagnosed on MRA also undergone DSA for any missing aneurysm on MRA taking DSA as gold standard tool. 38 patients with strong clinical suspicion were not diagnosed as intracranial aneurysms either in MRA or DSA; were labeled as control group for comparison and statistical calculation

Each of the diagnosed aneurysms were characterized based on their number, location, shape, identification of the neck, origin of artery and maximum diameter in both MRA at 3T and DSA with 3D reconstruction. For each of the above mentioned variable, findings of MRA were compared with those of DSA taking DSA as gold standard tool in diagnosing intracranial aneurysm.

Intra-arterial digital subtraction angiography (IA-DSA) was performed within 24 hours (n=25) to one week (n=5) of 3D-TOF MRA. Intra-arterial digital subtraction angiographic examinations were performed using digital subtraction system with standard Seldinger technique via transfemoral route using 6F arterial sheath and catheter systems. 5-6 ml of non-ionic contrast medium (Ultravist 300 mg I/mL) was injected in a dilution of 1:1 at a rate of 3-4 ml per second. For 3D image acquisition, undiluted 10 ml of contrast agent was injected (fig 7).

Out of total sample size ($N_{total} = 85$); 47 patients were diagnosed as having 53 intracranial aneurysms either on MRA or DSA or both; they were labeled as cases ($N_{cases} = 47$). However remaining 38 patients suspected of cerebral aneurysm did not reveal any aneurysm either on MRA or DSA; they were labeled as control group ($N_{control} = 38$).

For each of the diagnosed aneurysm, data was collected separately for MRA and DSA based on following characteristic variable

1. Detection of aneurysm (+/-)
2. Location of aneurysm (anterior/posterior circulation)
3. Nature of aneurysm (unruptured/ ruptured)
4. Identification of shape of aneurysm
5. Identification of neck of aneurysm
6. Identification of artery of origin
7. Maximum diameter of the aneurysm

Inclusion criteria:

1. Patients with non traumatic SAH/ICH
2. Patients presenting at neuromedicine /neurosurgery OPD/Emergency at BIN/SSKM hospital Kolkata with suspected features of intracranial aneurysms like headache, convulsions and other compressive symptoms
3. Patients referred to department of Neuroradiology for DSA and diagnosed intracranial aneurysm
4. No contraindication to MRI

Exclusion criteria:

1. Patients presented with traumatic SAH
2. Patients not giving consent

3. Patients with history of contrast allergy
4. Patients with contraindications to MRI

Statistical analysis

Statistical Software used : Graph Pad prism ver 7.02, Graph Pad Software, Inc. 7825 Fay Avenue, Suite 230 La Jolla, CA 92037 USA. For each of the above mentioned characteristic variable; contingency table was made separately and sensitivity, specificity, positive and negative predictive values were calculated for MRA taking DSA as gold standard test using statistical software Graph Pad(Table 5). Fischer’s exact test was done to test the significance of the results and level of significance calculated (p value<0.0001).Cohen’s kappa coefficient(k) was calculated (Table 6) in Graph Pad statistical software to measure the agreement between MRA and DSA taking DSA as gold standard test for different variables using their respective contingency tables.

III. Result

Most of the patients (46.8%) presented in 5th decade, youngest patient was of 12 years and oldest patient was of 72 years with mean age of 45.8±10.6 years. Nineteen patients (40%) were males and 28 patients (60%) were females. Twenty two (47%) patients presented with subarachnoid hemorrhage, 2(4%) patients with focal neurological deficits and 23(49%) patients had only severe headache. Most of the aneurysms were found to be in anterior circulation (Table 1), with most common site being the anterior communicating artery(ACOM) i.e. 26.4% (Fig 1,2&3).In six patients, two aneurysms were present. Only one out of 53 aneurysms were very small in size(<3mm); 5 aneurysms were between 3mm to 6mm; forty four aneurysms between 6-15mm; 2 were between 15-25mm and only one giant aneurysm(>25mm) as shown below (Table 2). Using all 3 sequences of 3D-TOF, PC-MRA and CE-MRA; 52(98.1%) of 53 aneurysms were visualized. Minimum diameter of aneurysm detected on CE-MRA was 4.8mm and that on DSA was 1.8mm size (Table 3). Only one aneurysm missed on MRA but diagnosed in DSA was very small of size 1.8mm. Overall sensitivity and specificity, as well as the positive and the negative predictive values for MRA, were calculated. The sensitivity of MRA in detecting intra cerebral aneurysms was 0.98, and specificity was 1. The positive and negative predictive values for MRA were 1 and 0.97 respectively (Table 4 & 5). When findings of 3D-TOF, PC-MRA and CE-MRA combined; MRA produced only one false-negative reading in which the aneurysm was very small in size (1.8mm) and located in PCOM artery. Each of the aneurysms detected on MRA and DSA was characterized based on their number, location, nature, shape, identification of neck and artery of origin. Sensitivity, specificity as well as positive and negative predictive values were calculated for each of the characteristic variable for MRA taking DSA as gold standard and tabulated below (Table 4 & 5).Also the reliability of MRA in diagnosing and characterizing intracranial aneurysms was tested using *kappa statistics* and *Cohen’s kappa(k)* value came out to be between 0.85-1.0 inferring very strong strength of agreement between the two tests(Table 6).

Table 1: Location and frequency of Intracranial aneurysms

Artery	ANTERIOR CIRCULATION							POSTERIOR CIRCULATION		
	ACOM	A1	DACA	M1	M1-M2	ICA	PCOM,PARA PCOM	BA	PCA	PICA
No;n=53	14	1	2	4	13	7	6	4	1	1
(%)	26.4	1.8	3.7	7.5	24.5	13.2	11.3	7.5	1.8	1.8

Table 2: Size wise distribution of intracranial aneurysms

Max. Diameter (mm)	No. Of aneurysms
Very Small (<3)	1
Small (3-6)	5
Intermediate (6-15)	44
Large (15-25)	2
Giant (>25)	1

Table 3:Size of aneurysm by both methods

Size(mm)	MRA	DSA
Min. diameter	4.5	1.8
Max. diameter	25.5	25.5
Mean±SD	8.06±3.3	8.08±3.2

Table 4: Validation analysis of MRA for detection and characterization of intracranial aneurysms by keeping IA-DSA as gold standard (n=85).

	sensitivity	specificity	Positive predictive value	Negative predictive value
Detection of aneurysms	98.1%	100%	100%	97.1%
Location of aneurysm	100%	100%	100%	100%
Nature of aneurysm	95.6%	93.1%	91.6%	96.4%
Identification of shape of aneurysm	92.3%	100%	100%	90.4%
Identification of neck of aneurysm	84.6%	100%	100%	82.9%
Identification of artery of origin of aneurysm	90.5%	100%	100%	88.3%

Table 5: Diagnostic accuracy of CE-MRA according to size of aneurysm

Size	Sensitivity	Specificity	PPV	NPV
>5mm	100%	100%	100%	100%
<5mm	96.9%	95%	90%	92.5%
<3mm	91.7%	88.9%	79.1%	86%

Table 6: INTER TEST AGREEMENT USING “KAPPA STATISTICS”

	KAPPA	SE	95% CI	STRENGTH
DETECTION OF ANEURYSM	0.977	0.022	0.934-1.00	Very good
LOCATION	1.000	0.00	1.00-1.00	Perfect
ARTERY OF ORIGIN	0.889	0.048	0.795-0.983	Very good
NATURE	0.884	0.065	0.756-1.00	Very good
SHAPE	0.910	0.044	0.824-0.996	Very good
NECK	0.825	0.058	0.711-0.939	Very good
LENGTH	0.810	0.062	0.710-0.921	Very good

FIGURES

Fig 1: CE-MRA source image showing a large left distal ACA aneurysm.

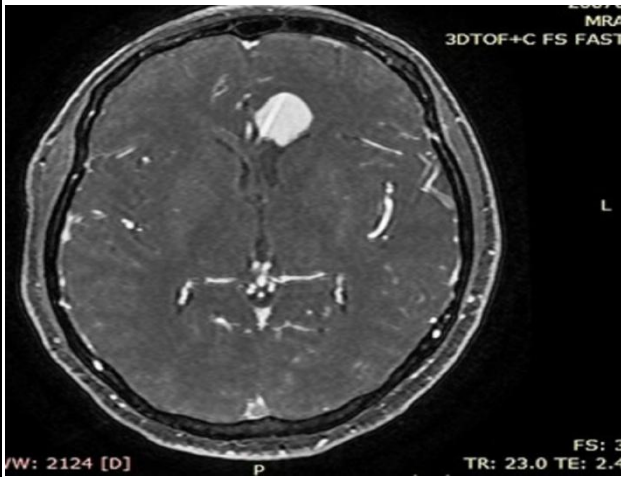


Fig 2: PC-MRA of the same patient source image showing a large aneurysm with its artery of origin as left distal ACA.

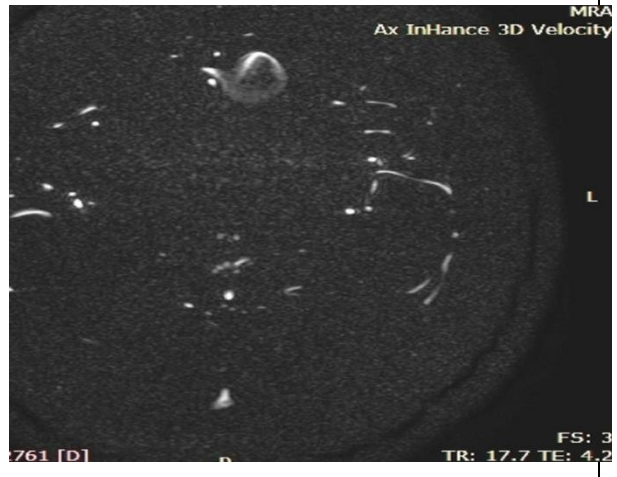


Fig 3: volume rendered 3D image of MRA showing a large aneurysm in left distal ACA(DACA)

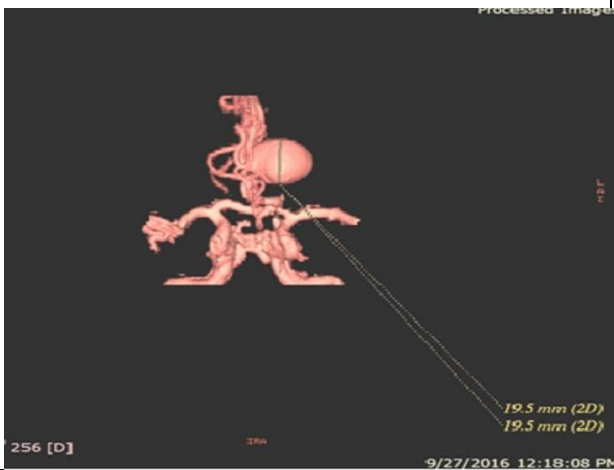


Fig 4: Axial MIP MRA shows an aneurysm at the basilar tip with its characteristics

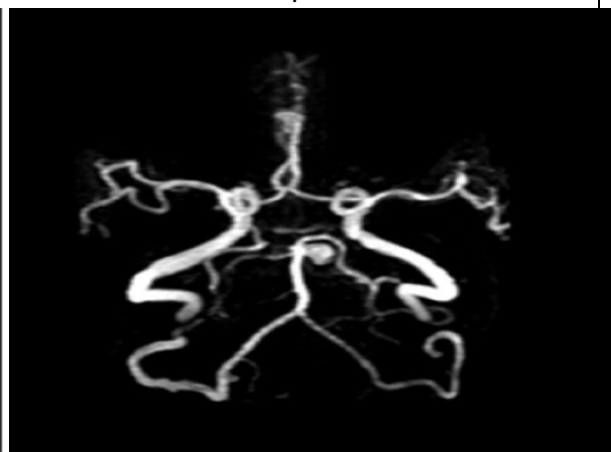


Fig 5(a): AP source image DSA from left VA injection reveals the aneurysm at the top of basilar artery



Fig 5(b): oblique view source image of DSA from left VA injection reveals the basilar top aneurysm.

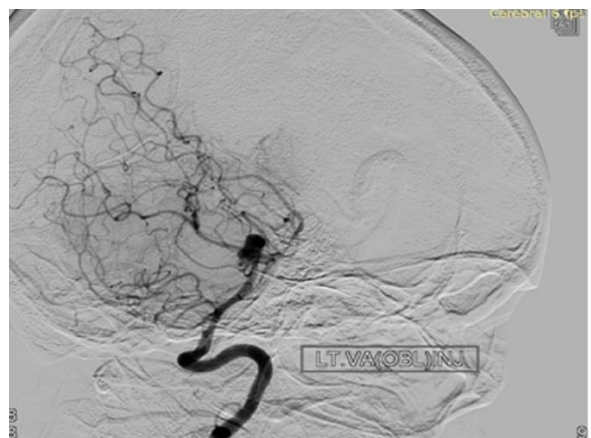
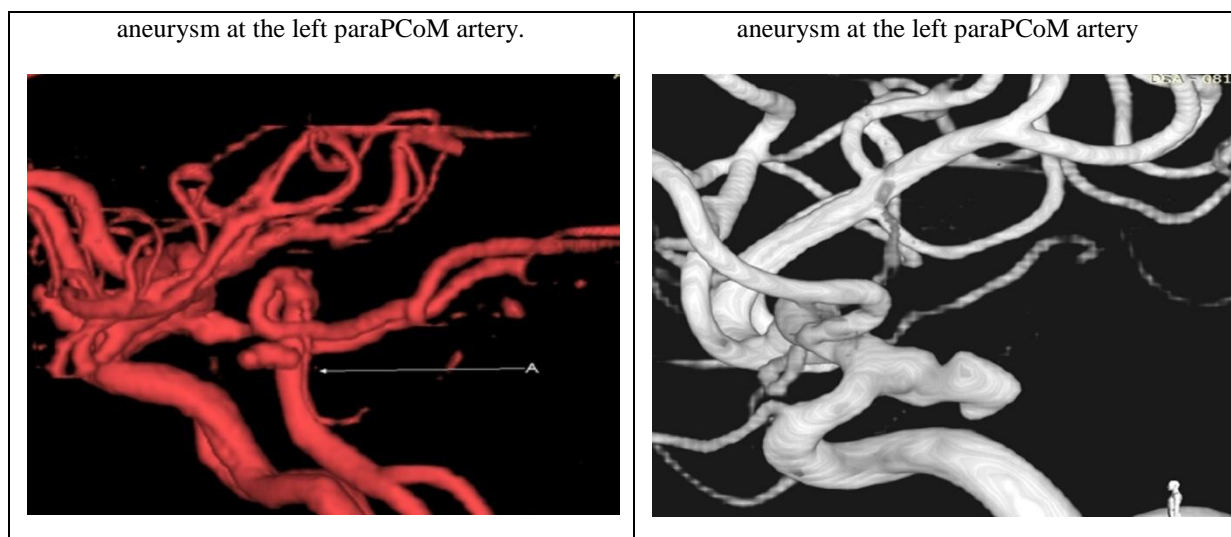


Fig 6: 3D reconstructed MIP-MRA image showing an

Fig 7: 3D reconstructed image of DSA showing an



IV. Discussion

Intracranial aneurysms are common in the general population with the reported prevalence of 3.6 percent, predominantly in women. A ruptured aneurysm is considered to be the main cause of a non-traumatic SAH. Seventy-seven percent of cases of SAH are due to an aneurysmal rupture. The incidence of intracranial aneurysm rupture is approximately 12/100,000 population/year.²⁴ There are usually no symptoms caused by an unruptured aneurysm. Likewise, asymptomatic patients that need to be investigated for the presence of an intracranial aneurysm should undergo a minimally invasive diagnostic procedure, as CTA or MRA. A lot of controversy still exists regarding the treatment of incidentally identified intracranial aneurysms. According to the International Study of Unruptured Intracranial Aneurysms Investigators (ISUIAI), the rupture rate of small aneurysms (<1 cm) is 0.05%/year, while that of aneurysms larger than 1 cm or aneurysms that have previously ruptured is 0.5%/year.²⁵ The optimal management of an unruptured aneurysm remains ill-defined, and definitely the therapeutic decision depends on several parameters. Furthermore, the necessity of screening the general population for an intracranial aneurysm is disputable. Specific patient populations present an increased risk for intracranial aneurysms. These are patients with polycystic kidney disease, Marfan syndrome, coarctation of the aorta, fibromuscular dysplasia, family history of saccular aneurysm, and Ehlers-Danlos syndrome. In such patients, a minimally invasive, sensitive, and highly accurate method needs to be available for their investigation. The symptoms occur when aneurysms rupture or if they cause a compression of the adjacent neural structures which results in focal neurological deficits.²⁶ Several case reports denote the disease in early years of life¹⁰ but maximum cases are seen in 4th and 5th decade of life. Gender distribution pattern of female pre-dominance has also been noted in other studies. In another study incidence of SAH in women was 1.24 times higher than in men starting at the age of 55 years and increased thereafter. Female gender is a recognized risk factor for occurrence of aneurysmal SAH along with other risk factors including age, smoking, hypertension, excessive alcohol intake and familial preponderance.²⁷ There has been a significant increase in the incidental detection of unruptured intracranial aneurysm due to the recent advances in the imaging techniques and the common use of noninvasive imaging methods such as CT or MR angiography.²⁸ Since there is no exposure to radiation nor the iodinated contrast agent is used, MRA may be the method of the first choice for the screening setting.²⁹ MRA is a fast, accurate and non-invasive method for the detection of aneurysms with none of the risks that may be involved in the conventional angiography. Since the aneurysms may overlap with adjacent arteries and the signal is reduced by the flow patterns, the detection of small (5-7 mm) or very small (<3mm) aneurysms on maximum-intensity projection images can often be difficult. A sensitivity of detection of aneurysms by the use of 3D-TOF, PC-MRA and CEMRA; as shown by our study, is up to 98.1%, which is comparable with that of DSA. Based on the comparison of 3T with 1.5T 3D TOF MRA, in their study, Willinek et al. concluded that an improved spatial resolution as well as better evaluation of the peripheral segments of intracranial vessels is obtained by 3T. Intra-arterial DSA is the gold standard for evaluating intracranial vessels, but this procedure is invasive, involving risks of complications such as arterial puncture, emboli, dissection, hemorrhage and septicemia, which can be prevented by using noninvasive imaging tools.³⁰ Magnetic resonance angiography offers benefits such as its lower cost and the absence of procedure-associated risk of stroke and arterial injury. Another benefit of MRA is that views can be stored and used by technicians and physicians after the patient has left, and interactive viewing among different users is possible. A distinct advantage of MRA is that it can be used for patients with a critical status in conjunction with anesthetic equipment. Gibbs et al. reported that 3D TOF MRA at 3T had more clear depiction of intracranial aneurysms compared to 1.5 T, even

though all aneurysms were detected on 1.5T.³¹ As above mentioned, 3D TOF MRA may miss aneurysms with slow or turbulent flow. Contrast-enhanced MRA provides better depiction of this aneurysm, being less prone to signal intensity losses due to turbulence or flow saturation. However, it is more invasive, requiring an ultrafast, bolus injection of intravenous contrast media.³² Contrast enhanced MRA was also improved from high-field MRI at 3T, due to improved spatial and temporal resolution. Increased gadolinium effect at 3T can also result in reduced contrast volume, is easier to be performed, and may cover larger areas extending from the aortic arch to the intracranial vessels, simultaneously. Additional imaging of giant or slow-flow aneurysms may be performed with PC MRA.³³ Moreover; evaluation of SE T1 weighted images nicely delineates thrombosed aneurysms and may provide complementary information regarding the size of the thrombus. It is generally accepted that meticulous knowledge of the flow dynamic characteristics of an aneurysm is of paramount importance for assessing the possibility of rupture in cases of unruptured aneurysms and also for the treatment planning, either microsurgical or endovascular.³⁴ Adequate depiction of the regional blood flow and its dynamics becomes essential for evaluating intracranial aneurysms and also for minimizing the chance of aneurysmal recanalization in cases of endovascular treatment.³⁵ Phase-contrast MRI is the method of choice since it can depict dynamics of flow in the vessels. Phase-contrast MRA may theoretically measure flow velocity at the neck of an aneurysm. However, it has to be emphasized that these methods are investigational and require further evaluation and validation before being implemented into the clinical practice. For identification of aneurysmal neck and estimation of relationship between aneurysmal neck and parent vessel MRA also showed reasonable sensitivity. 3D-TOF MRA and CEMRA is equally good in detection and characterization of intracranial aneurysms as the IA-DSA and can be used as a non-invasive screening test for intracranial aneurysms and it can be a suitable alternative to IA-DSA as a primary examination for aneurysmal surgery.

There were certain limitations of this study like small sample size (N=85). Imaging at 3T presents several limitations and drawbacks generated by the prolonged acquisition time and the high magnetic field. The incidence of susceptibility artifacts at 3 T is double of that at 1.5 T. The occurrence of susceptibility artifacts and missing of Small-sized aneurysms (<3mm) appear to be higher at the skull base and near the bone-air interphase. Moreover, CE-MRA may not be performed in patients with renal failure due to the increased risk of nephrogenic systemic fibrosis.³⁶ Further studies can be carried out with larger sample size.

V. Conclusion

The prevalence of intracranial aneurysm is more common in females compared to males. 3D TOF, MRA AND CE MRA when combined can detect even very small sized aneurysm (<3mm), delineating their exact shape, size and relationship to the adjacent vessels. The application of 3T MRA further improves sensitivity by increasing the SNR and the spatial resolution, while minimizing the examination time.

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Dr. KashiSarkar. "Detection and characterization of intracranial aneurysms: 3T magnetic resonance angiography versus digital subtraction angiography with 3D and reconstruction." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 18, no. 6, 2019, pp43-50.