

Diagnostic Accuracy of MDCTA for Detection of Intracranial Aneurysm in Non Traumatic Subarachnoid Haemorrhage: A Cross-sectional Study

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ABSTRACT

Introduction: Non Traumatic Subarachnoid Haemorrhage (NTSAH) constitutes a neurological emergency. Multi-Detector Computed Tomographic Angiography (MDCTA) provides significant advantages over Digital Subtraction Angiography (DSA) owing to its immediacy, non invasiveness, and comparable diagnostic accuracy. This warrants exploration of its utility as a fully integrated component of routine imaging and therapeutic algorithm for NTSAH, replacing DSA.

Aim: To evaluate the potential of MDCTA of the Circle of Willis (COW) in the detection of causes of NTSAH and compare its diagnostic accuracy with DSA and/or intraoperative findings.

Materials and Methods: This cross-sectional study enrolled 45 patients with suspected or confirmed intracranial vascular abnormality or SAH, and subjected to non contrast enhanced Computed Tomography (CT) and MDCTA of the COW. MDCTA findings like aneurysms, Arteriovenous Malformations (AVM), their morphological characteristics and anatomical COW variations

were contrasted with DSA/operative findings in 24 patients and MDCTA's accuracy was calculated. The data was analysed using statistical software R (Ross Ihaka and Robert Gentleman) v.4.0.2, employing Kappa coefficient. The p-value ≤ 0.05 indicated statistical significance.

Results: Total of 45 subjects (mean age: 47.16 ± 17.4 years, 17 females and 28 males) were included in the study. The mean aneurysmal size was 7.6 ± 7.2 mm. Grade 3 or 4 (dense) SAH (48.88%) and aneurysms < 3 mm in size (48.89%) were most common. MDCTA showed sensitivity, specificity, and positive and negative predictive values of 89%, 79%, 84% and 85%, respectively. Kappa test revealed a substantial agreement between CTA and DSA (kappa coefficient=0.68).

Conclusion: MDCTA is a rapid, minimally invasive, and reliable substitute to DSA in diagnosing and characterising associated aneurysms and AVM, in most cases of NTSAH, aiding in further management of such patients.

Keywords: Arteriovenous malformations, Circle of willis, Computed tomography, Digital subtraction angiography, Multi-detector computed tomographic angiography

INTRODUCTION

Subarachnoid Haemorrhage (SAH) is a neurological emergency characterised by extravasation of blood into the subarachnoid space between the pial and arachnoid membranes, which are normally filled with cerebrospinal fluid [1]. The main cause of NTSAH in 80% of the cases is rupture of an intracranial aneurysm, an event accompanied by high morbidity and mortality [1]. The global incidence of SAH varies by region and has been approximately 10.5 cases per 100,000 inhabitants per year over the last 30 years [2,3]. The mean mortality rate for SAH patients is 51%, and one-third of the survivors require life-long medical assistance [2,3]. The main negative prognostic factors include poor level of consciousness, advanced age, and excess blood on initial head CT scan [2,3].

Subarachnoid haemorrhage should always be suspected in patients with a typical presentation of sudden and severe headache associated with nausea, vomiting, neck stiffness, or loss of consciousness [2-4]. Physical examination may reveal retinal haemorrhage, evidence of meningeal irritation, reduced level of consciousness, and/or focal or unilateral neurological deficit [2-4]. In the absence of the classical signs and symptoms, SAH can be confused with migraine and tension headaches in 50% of the cases [4]. This necessitates extensive utilisation of CT, which if correctly performed, is capable of identifying SAH in 100% of the cases within 12 hours and in 93% within 24 hours of symptom onset [5,6].

Despite being the gold standard for identifying and localising cerebral aneurysms, DSA remains an invasive, time-consuming technique which is more difficult to perform in SAH patients who may require sedation [7,8]. CT Angiography (CTA) is a non invasive method used in imaging in comparison with DSA, which has no need of arterial puncture or catheter manipulation. CTA can be effectively carried out instantly following the initial non enhanced CT having a single bolus of contrast medium intravenously which enables quick detection as well as therapy strategy in the acute setting. It also enables visualisation of the CTA data with unlimited projections which aids in aneurysm detection and characterisation [9]. There are several reports where the diagnosis precision has been observed to be compromised for single detector CTA in detecting aneurysms which are smaller than 3 mm [10,11]. In such cases, Multidetector Row CT (MDCT) is seen to conquer such shortcoming through volumetric acquisition which significantly improves the quality and spatial resolution [12].

Multi-Detector CT Angiography (MDCTA) is gaining consensus as an effective alternative to DSA owing to its immediacy (performed immediately after baseline CT, which significantly reduces the examination time and facilitates immediate treatment), non invasiveness, and specificity/sensitivity comparable to DSA. Hence, MDCTA of the COW holds promise to become a fully integrated component of routine imaging and therapeutic algorithm for NTSAH worldwide [13]. Therefore, the present study was designed to evaluate the role of MDCTA of the COW in the detection of NTSAH

causes and assess its diagnostic accuracy in comparison with DSA and/or intraoperative findings.

MATERIALS AND METHODS

This cross-sectional study was performed at the Radiodiagnosis Department, M.S. Ramaiah Medical College, Bengaluru, Karnataka, India, from November 2014 to April 2016. Ethical clearance was procured from the Institutional Review Board (Registration No.- ECR/215/Inst/Ker/2013). Voluntary written informed consent was obtained from the enrolled patients.

Sample size calculation: As per the previous study conducted by El Khalidi M et al., in which 109 patients out of 130 patients were diagnosed with cerebral aneurysms using multi-slice CTA [7]. Accordingly, for a confidence interval of 95% and a relative precision of 15%, the minimum required sample size was determined to be 35 participants.

Inclusion criteria: Those patients who were clinically suspected to have an intracranial vascular abnormality or SAH, were scheduled to undergo CTA of the COW, or had recently undergone non enhanced CT of the brain confirming the presence of SAH.

Exclusion criteria: Patients with SAH attributable to recent trauma, history of previous cranial surgery or endovascular therapy to the COW, and sub-optimal studies due to patient's movement or excessive venous contamination were excluded from the study.

The study enrolled total of 45 patients irrespective of their age and gender and relevant data was collected through patients' interviews.

Study Procedure

All the patients underwent non contrast-enhanced CT followed by CTA of the COW according to the institutional protocol, using a 128-slice CT scanner (Siemens Somatom Perspective, Siemens Healthcare Global, Germany) that utilised 64 detector rows with a collimation of 0.6 mm. The scan range extended from the foramen magnum to the cranial vault. Eighty mL of non ionic contrast medium Iopromide (Ultravist 300 mg I/mL, Bayer Healthcare) was injected through the right antecubital vein with an 18-20 mm gauge intravenous cannula with the help of a mechanical power injector at the rate of 4 mL/s followed by a saline chase of 50 mL. Arterial phase scanning was initiated by bolus tracking when a threshold enhancement of 100 Hounsfield units was reached in the arch of aorta. Delay in venous phase acquisition was 60-70 seconds after the injection of contrast. The scanning parameters are summarised in [Table/Fig-1]. Images were reconstructed with standard soft tissue algorithm. Source images were reformatted using Three-Dimensional (3D) Volume Rendering Technique (VRT) and Maximum Intensity Projection (MIP). Assessment of COW and associated vascular pathologies was done using the source images as well as the 3D VRT and MIP reformations [14].

Scan parameters	Pre-contrast phase	Arterial phase	Venous phase
Tube voltage (kVp)	130	130	130
Tube current	Varying from 80 to 250 mAs (Automatic Exposure Control)		
Detector pitch	0.75	1.1	1.05
Rotation speed (seconds)	0.48	0.48	0.48
Scan delay		Bolus tracking	60-70 seconds
Slice thickness	5 mm with post acquisition (0.6 mm reconstruction)		

[Table/Fig-1]: Findings of MDCTA.

kVP: Kilovoltage peak; mAs: Milliampere-seconds; MDCTA: Multi-detector computed tomographic angiography; mm: Millimeter

The images were transported to a free-standing workstation with 3D software (Syngo CT 2913A, Siemens) for further analysis. Image analysis was performed interactively by using the source images and various postprocessing techniques, including Two-Dimensional (2D) and 3D Multiplanar Reconstructions (MPR), MIP, and VRT. The parameters employed for evaluating the CTA findings are presented in [Table/Fig-2] [14].

Parameters		Description	
SAH	Grade 0	No SAH or IVH	
	Grade 1	Minimal/thin SAH, no IVH in either lateral ventricle	
	Grade 2	Minimal/thin SAH, with IVH in both lateral ventricles	
	Grade 3	Dense SAH (completely filling ≥ 1 cistern or fissure) with no IVH in either lateral ventricle	
	Grade 4	Dense SAH (completely filling ≥ 1 cistern or fissure) with IVH in both lateral ventricles	
Cerebral aneurysms	Site	Originating from anterior circulation	Internal carotid artery, ophthalmic artery, anterior communicating artery, anterior cerebral artery, pericallosal artery, callosal marginal artery, middle cerebral artery, Posterior Communicating Artery (PCOM)
		Originating from posterior circulation	Basilar artery, top of the basilar artery, posteroinferior cerebellar artery, anteroinferior cerebellar artery, anterosuperior cerebellar artery, posterior cerebral artery
	Size	≥ 25 mm	Giant aneurysms
		$\geq 13-24$ mm	Large aneurysms
		$\geq 5-12$ mm	Medium aneurysms
		3-4 mm	Small aneurysms
		< 3 mm	Very small aneurysms
	Neck	Narrow	Diameter neck/diameter sac $< 1/3$
Wide		Diameter neck/diameter sac $\geq 1/3$	

[Table/Fig-2]: Parameters employed to evaluate CTA findings.

CTA: Computed tomography angiography; IVH: Intraventricular haemorrhage; mm: Millimeter; SAH: Subarachnoid haemorrhage

Sites of cerebral aneurysms originating from the anterior circulation included internal carotid artery, ophthalmic artery, anterior communicating artery, anterior cerebral artery, pericallosal artery, callosal marginal artery, middle cerebral artery, Posterior Communicating Artery (PCOM). Sites of cerebral aneurysms originating from the posterior circulation included basilar artery, top of the basilar artery, posteroinferior cerebellar artery, anteroinferior cerebellar artery, anterosuperior cerebellar artery, posterior cerebral artery. Aneurysms were categorised into giant (≥ 25 mm), large ($\geq 13-24$ mm), medium ($\geq 5-12$ mm), small (3-4 mm) and very small (< 3 mm) [15].

Arteriovenous Malformations (AVMs) were assessed for location, size of the nidus, feeding arteries, and draining veins, and were graded based on the Spetzler and Martin scale [16]. Anatomical variations of the COW were also evaluated. The anterior and posterior parts of the circle were classified as per the modified morphological classification given by Li Q et al., [17]. Assessment was done for the absence or presence of each arterial segment in the COW. If an arterial segment was visible, the diameters of bilateral pre-communicating segments of the right and left anterior cerebral arteries (A1), pre-communicating segments of the right and left posterior cerebral arteries (P1) and left PCOM were determined. Normal arterial segments were those > 1 mm and hypoplastic arterial segments were < 1 mm. While investigating the posterior part of the COW, the P1 segment was assessed in relation to the ipsilateral PCOM. The posterior collaterals were categorised into three variants, namely, a foetal configuration, transitional configuration, and adult configuration. Branched vessels from the internal carotid artery having larger diameters than P1 and extending as posterior cerebral arteries were considered as foetal-type posterior cerebral artery. The transitional configuration was defined as a variant wherein equivalent diameters of the PCOM and the P1 segment were noted. In the adult configuration, the PCOM was smaller than the ipsilateral P1 [18,19].

During the DSA procedure, femoral catheterisation was done for all patients by employing the Seldinger technique with the help of a DSA unit (Innova IGS 540, single flat panel detector, GE healthcare) [20].

STATISTICAL ANALYSIS

Data was analysed using statistical software R version 4.0.2 and Microsoft excel. Categorical variables were presented in the form of frequency tables and continuous variables expressed as mean±Standard Deviation (SD). Predictive values, sensitivity, specificity, and other measures were represented in percentages. Kappa coefficient was employed to check the agreement between DSA and CTA. The p-value ≤0.05 indicated statistical significance.

RESULTS

The study consisted of 45 patients with suspected or confirmed SAH, subjected to MDCTA. The mean age of the patients was 47.16±17.4 years, and the male-female ratio was 1.6:1. The descriptive summary of variables is presented in [Table/Fig-3]. Most of the patients were aged between 41 and 60 years (42.2%) and had aneurysms of <3 mm in size (48.89%). The mean size of the aneurysms was 7.6±7.2 mm, the smallest being 2 mm and the largest measuring 39 mm. Two out of 45 patients had arteriovenous malformation whose findings have been represented in [Table/Fig-4]. Both these patients had CTA and DSA evaluation showing good agreement between two studies in regard to location, size of the nidus, feeding arteries, draining veins and also the spetzler and martin grades. [Table/Fig-5-7] help visualise the radiological manifestations of different causes of SAH as detected by CTA in a male and female patient, respectively.

Variable		Number of subjects n (%)
Gender	Female	17 (37.78)
	Male	28 (62.22)
Age (years)	<20	2 (4.44)
	20-40	15 (33.33)
	41-60	19 (42.22)
	61-80	7 (15.56)
	≥81	2 (4.44)
	Mean age	47.16±17.4
SAH Grade	0	21 (47)
	2	2 (5)
	3	11 (24)
	4	11 (24)
Anterior part of the circle	Type A Normal anterior circle	37 (82.22)
	Type C A1 hypoplasia	2 (4.44)
	Type D A1 aplasia	5 (11.11)
	Type E Absence of ACOM	1 (2.22)
Posterior part of the circle	Type A Normal adult type posterior circle	22 (48.89)
	Type B Transitional type	1 (2.22)
	Type D Bilateral FTP	2 (4.44)
	Type E Absence of bilateral PCOM	15 (33.33)
	Type G Unilateral PCOM absent	2 (4.44)
	Type H Unilateral PCOM hypoplasia	1 (2.22)
	Type I Full FTP	2 (4.44)
Number of aneurysms	0	20 (44.44)
	1	18 (40)
	2	6 (13.33)
	4	1 (2.22)

Size of aneurysms	<3 mm	22 (48.89)
	3 mm-5 mm	11 (24.44)
	>5 mm	12 (26.67)

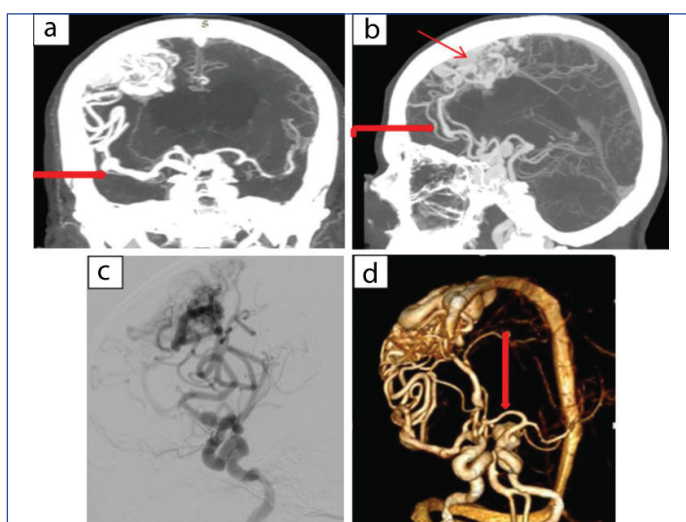
[Table/Fig-3]: Descriptive summary of variables.

ACOM: Anterior communicating arteries; FTP: Foetal-type posterior; mm: millimeter; PCOM: Posterior communicating arteries; SAH: Subarachnoid haemorrhage

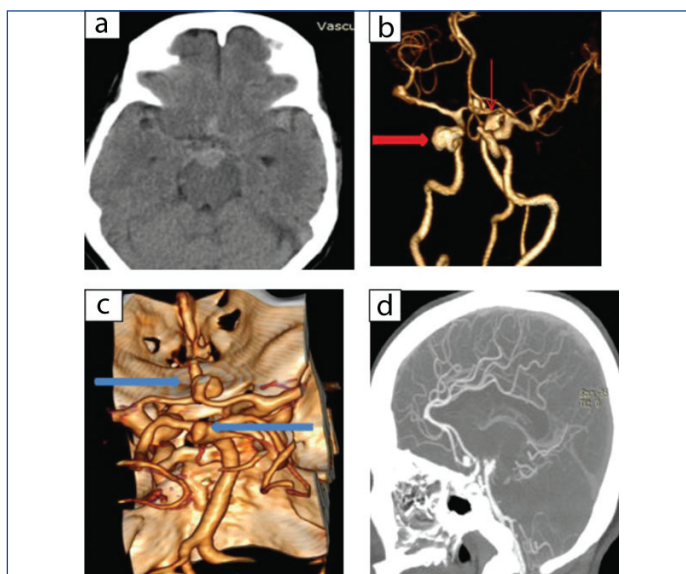
Arteriovenous Malformations (AVM)	Male patient	Female patient
Type	Classic pial AVM (compact type)	Proliferative type of brain AVM or Pial AVM (diffuse type)
Location	Right frontal lobe	Right fronto-parietal lobe
Size of nidus	4 cms	7 cms
Feeding arteries	Right MCA and right ACA	Right MCA and right ACA
Draining veins	Superior sagittal sinus	Superior sagittal sinus and thalamo-striate veins
Spetzler and martin grade	2	4
Associated aneurysms	Present (n=3)	Absent

[Table/Fig-4]: Summary of findings of AVMs.

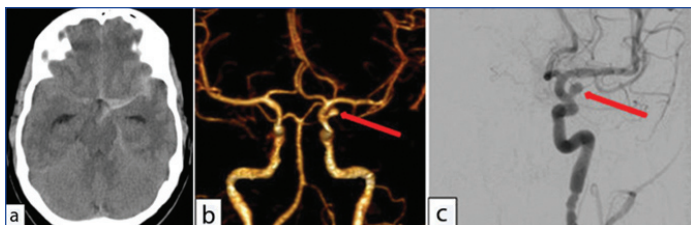
MCA: Middle cerebral artery; ACA: Anterior cerebral artery



[Table/Fig-5]: CTA of an 83-year-old male patient with unresponsiveness. (a) coronal and (b) sagittal arterial-phase MIP images showing right frontal AVM (thin arrow) with arterial feeders coming from right MCA (notched arrow) and right ACA (curved arrow); venous drainage into superior sagittal sinus; (c) Right ICA DSA and (d) VRT delineating the AVM and also the associated aneurysm in the supraclinoid segment of left ICA (block arrow)



[Table/Fig-6]: 55-year-old female with multiple intracranial aneurysms. (a) Axial precontrast CT showing subarachnoid haemorrhage (Spetzler and Martin grade 3). VRT (b), (c) Sagittal MIP (d) Showing saccular aneurysms at the right ICA (open arrow), ACOM (block arrow) and top of the basilar artery (notched arrow). Fusiform dilatation of the basilar artery (thin arrow) at the bifurcation is seen



[Table/Fig-7]: A 45-year-old female patient with sudden onset severe headache. (a) Unenhanced CT showing diffuse subarachnoid haemorrhage, Fisher's revised grade 3. (b) Anterior VRT and (c) Lateral DSA showing a saccular aneurysm at the supraclinoid segment of the left ICA.

[Table/Fig-8] depicts the comparison matrix of CTA over DSA. The total counts are not equal to 45 since some patients did not undergo DSA. Out of the total patients, 16 patients were positive whereas 11 patients were negative for both CTA and DSA diagnosis. There were two patients with negative CTA and positive DSA as well as three patients showed positive CTA and negative DSA.

CTA diagnosis	DSA diagnosis	
	Positive	Negative
Positive	16	3
Negative	2	11

[Table/Fig-8]: Comparison of CTA with DSA.

CTA: Computed tomography angiography; DSA: Digital subtraction angiography

Sensitivity and specificity of CTA over DSA were 89% and 79% with the positive and negative prediction values of 84% and 85% respectively. Area under receiver operating curve was 0.8441 kappa test showed a substantial agreement between DSA and CTA with kappa coefficient of 0.68 as represented in [Table/Fig-9].

Measures	Values
Sensitivity	89% (65%, 99%)
Specificity	79% (49%, 95%)
Positive predictive value	84% (60%, 97%)
Negative predictive value	85% (55%, 98%)
Area under ROC curve	0.8441 (0.7118, 0.9765)
Kappa coefficient	0.68 (0.4223, 0.9376)

[Table/Fig-9]: Sensitivity, specificity, and other measures of CTA over DSA.

DISCUSSION

Non Traumatic Subarachnoid Haemorrhage (NTSAH) is a neurological emergency with poor outcomes, and hence, requires immediate diagnosis and management [1,7,8]. Therefore, the present study was conducted to assess the role of MDCTA of the COW in the detection of causes of NTSAH and compare its diagnostic accuracy with that of DSA and/or intraoperative findings, wherever available.

The present study showed that MDCTA was technically feasible and well tolerated by all patients. All the images could be assessed, and there were no major motion artifacts owing to increased spatial resolution and shorter acquisition times afforded by the 64-detector-row CTA, contrary to DSA.

Similar to the present study, various other studies that employed 4-channel MDCT scanners demonstrated that the sensitivity of MDCTA in diagnosing intracranial aneurysms ranged from 85-96% and the specificity was 83-97% [8,17,21-23]. These studies also reported greater sensitivity, in comparison to previous single-detector row CTA studies, for the detection of small aneurysms [8,17,21-23]; however, they also stated that a number of small aneurysms could be missed even by MDCT [17,21-23].

In the current study, no difficulty was encountered in the evaluation of the aneurysms from the cavernous and supraclinoid segments of the internal carotid artery (nine out of 34) due to the advancements in postprocessing techniques such as VRT with bone removal algorithm and multi-planar reformations. In contrast, some studies

have shown decreased sensitivity in detecting these aneurysms due to their close proximity to bony structures of the skull base, and might be overlooked or their location misinterpreted on MDCTA [24]. Tipper G et al., used 16-channel MDCTA to monitor suspected intracranial aneurysms in 57 patients and detected 51 of 53 aneurysms, demonstrating sensitivity and specificity of 96% and 100%, respectively [24]. Additionally, a sensitivity of 91.7% was observed by two independent readers in the detection of 12 aneurysms <3 mm size, using an interactive VRT algorithm [24]. In the present study, the mean size of the aneurysms was 7.6 ± 7.2 mm, with the smallest being of 2 mm and the largest measuring 39 mm, which was similar to the findings of Tipper G et al., (mean size 6.3 ± 5.2 mm) [24]. No inter-examiner variability was taken note of in the present study. The results of this study were poorer than those reported by Tipper G et al., [24]. This might be due to the smaller sample size and lesser number of patients considered for both CT and DSA/intraoperative correlation (24 out of 45 patients).

Interestingly, the present study could identify all elusive aneurysms in retrospective review in line with DSA results. Therefore, perceptive errors in interpreting the results of MDCTA studies for intracranial aneurysms are expected to be reduced with expanding reader experience. All unnoticed aneurysms in the present study were of the small, unruptured type that are generally considered non causative and inconsequential in the acute setting since immediate treatment is often not required. Although the chances of small aneurysms rupturing are perceivably low, equivocal MDCTA findings should be complemented with DSA. The current study also demonstrated that MDCTA could accurately delineate the size of the nidus, associated aneurysms, as well as the feeding arteries and draining veins in the setting of arteriovenous malformations, thereby aiding in surgical management. Hence, MDCTA can be used as a complementary tool to DSA due to its ability of detecting AVMs.

Li Q et al., noted a complete anterior and posterior COW in 79% and 31% of the patients, respectively, compared to 82.2% and 51.1%, respectively, in the present study [20]. The complete COW in the current study was close to more than twice that reported by Li Q et al., (42% versus 27%) [17]. They observed a foetal-type posterior COW in 9.4% of the patients, which is more than that seen in the current study (6.6%) [20].

The present study demonstrates promising diagnostic accuracy of MDCTA, which is equivalent to that of DSA, in the detection of suspected intracranial aneurysms and AVMs, providing adequate anatomical guidance for formulating an appropriate treatment regimen in majority of the cases. Hence, it could serve as a potential substitute to DSA in most cases, except very small aneurysms <3 mm in size. Moreover, the anatomical variations of cerebral collaterals reported here with MDCTA may contribute to our understanding of collaterals as well as various underlying mechanisms of cerebrovascular diseases. MDCTA could also be a promising follow-up technique to verify exclusion of the aneurysmal sac after endovascular or surgical procedures.

Limitation(s)

The present study has its limitations as it was based on a small sample size and the association between the aneurysm size and diagnostic accuracy was not explored. Future multicentric, prospective studies with larger sample sizes and wider coverage of variations and anatomical analyses are encouraged to overcome these limitations.

CONCLUSION(S)

The MDCTA can be a rapid, minimally invasive, and reliable substitute to DSA in most cases of NTSAH. Due to its high sensitivity, specificity, and predictive values in diagnosing and characterising associated aneurysms and AVMs, it can facilitate better management of these patients.

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- For any images presented appropriate consent has been obtained from the subjects. Yes

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