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ORIGINAL ARTICLE

COMPARISON BETWEEN DIGITAL SUBTRACTION ANGIOGRAPHY AND MAGNETIC RESONANCE ANGIOGRAPHY IN THE INVESTIGATION OF ACUTE ISCHEMIC STROKE IN A TERTIARY CARE HOSPITAL IN BANGLADESH

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Abstract:

Background: *Ischemic stroke is the most common type of stroke. Digital subtraction angiography (DSA) is a definite method for demonstrating vascular lesions, while High-resolution Magnetic Resonance Angiography (MRA) imaging has recently been introduced as a promising diagnostic modality in intra-cranial artery disease. This study aimed to compare between DSA and MRA as the modality of investigation of ischemic stroke.* ***Methods:*** *This quasi-experimental study was conducted at the department of Neurology, Sir Salimullah Medical College & Mitford Hospital, Dhaka, for one year following ethical approval. Total of 30 patients with acute ischemic stroke were enrolled in this study. DSAs and MRAs of all patients were analyzed and reported by two experienced neurologists. Collected data will be recorded into the separate case-record form and analyzed by SPSS 24.* ***Results:*** *The mean age of the studied respondents was 47.50±10.42 (SD) years with male predominance (63.3%).Among the male patients, 73.7% were smoker and female patients 81.8% were non-smoker. Among the total patients 80.0% had HTN and 73.3% DM, 24.1% had history of other cardio-vascular diseases and 36.7% of the patients had family history of stroke. Maximum patients had arm weakness (66.7%), leg weakness (60.0%), self-reported speech disturbance (53.3%) and dysphasia or dysarthria (53.3%). Hypertension and diabetes mellitus were present in 80% and 73.3% cases, respectively. For the majority of the patients the affected artery was MCA (Middle cerebral artery) and it was among 17 out of 30 patients. The aetiology based on TOAST diagnosis was similar by both MRA and DSA in 16 (out of 30). All the DSAs and 22 out 30 MRAs revealed abnormalities.* ***Conclusion:*** *MRA has significant agreement with DSA to identify etiology of acute ischemic stroke. Hence, it is better to use MRA in ischaemic stroke considering its non-invasiveness and cost-effectiveness.*

Key words: *Digital Subtraction Angiography, Magnetic Resonance Angiography, Acute Ischemic Stroke.*

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Introduction:

Over 10%, or 5.7 million deaths per year, are caused by strokes, which are the second biggest cause of mortality globally. Over the next several decades, more cases of stroke are expected to occur [1]. Vigorous control of blood pressure has reduced stroke mortality in affluent nations, but the burden of stroke is still increasing because of an aging population [1, 2]. Furthermore, the rising stroke prevalence in middle-income countries is a direct result of longer life expectancies in developing nations[1,2]. Among the two major types of stroke, hemorrhagic and ischemic. The ischemic stroke is more common, representing approximately 85 % of all stroke cases, and has a much lower 30-day mortality rate at approximately 12%.[3] In recent times, digital subtraction angiography (DSA) is being used for detection of type of lesion of ischemic stroke, but it is an invasive and time-consuming modality and the procedure needs to be performed by well experienced experts.[4]

DSA can detect intracranial branch arterial lesions even in the absence of identifiable sources of embolism. DSA is the most cases can identify stroke in the young patients and critically asses stroke etiology.[5] The popularity of DSA can be attributed to its good spatio-temporal resolution which is not easily matched by other acquisition techniques such as magnetic resonance imaging (MRI) and computed tomography (CT). Vascular abnormalities such as narrowing, blockage, or malformations can be visualized precisely in DSA.[6] In addition, DSA is invasive and is readily available in interventional suites of modern intensive care units (ICUs). Minimal cost, low risks, and rapid acquisition time are other features in favor of DSA.[5,7] DSA is a method of choice to visualize blood flow and guide endovascular interventions. DSA provides high-resolution spatio-temporal images that have mostly been used qualitatively through the manual review of raw gray scaled video.[8]

On the other hand, magnetic resonance-angiography (MRA) is a method that improves imaging protocol in both diagnosis and clinical management. MRA can track the changes in the vessel lumen with time.[9] Imaging of the vessels can reliably answer questions about the mechanism of the stroke, whether it is thrombotic, embolic or homodynamic. It also assesses the risk of future events by identifying whether there is occlusive arterial disease,

Localizing the exact site of occlusion and by determining the pathology underlying the stroke such as atherosclerosis or dissection.[10] MRA can also identify other vascular lesions such as malformation, aneurysms and arterial compression.[11]

In addition to that, DSA is an invasive procedure with the risk of neurologic complications and radiation exposure.[12] In contrast, MRA is an noninvasive, relatively less complicated method in acute phase of stroke, which provides early positive diagnosis of occlusive intracranial arterial disease that has a potentially important role in appropriate patient selection for intra-arterial fibrinolysis, by providing a relatively easy, non-invasive, time-efficient in screening procedure for the determination of the site of intracranial occlusion.[13] So this study is designed to compare the usefulness between Digital Subtraction Angiography and Magnetic Resonance Angiography in the investigation of acute ischemic stroke in a tertiary Care hospital in Bangladesh.

Methods:

Study design, population and settings:

This study was carried out in the Department of Neurology at Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh from July 2021 to June 2022. The study included 30 patients with acute ischemic stroke. According to inclusion and exclusion criteria, subjects were chosen. Following written consent, the patient was included. Aged e"18years or older, the included patients underwent a neurologist's examination, and acute ischaemia was clinically and CT scan / magnetic resonance imaging of the brain-evidently identified. Patients with Transient ischemic attack, intracerebral hemorrhage, primary or secondary brain tumor, any malignancy were all excluded from the study.

All of the patients had undergone clinical and neurological evaluation, electrocardiogram, hemogram, blood biochemistry, lipid profile, erythrocyte sedimentation rate, immunologic and coagulation testing and cranial computed tomography. These patients had also received high-resolution MRA and DSA within 7 days or less of the initial investigation. All collected information was stored in separate data record form.

The Sir Salimullah Medical College in Dhaka, Bangladesh, ethical committee gave its approval to the study protocol.

Data collection and laboratory procedures:
Standard imaging protocols was used where MRA was performed with a 1.5 T system with unenhanced 3D time-of-flight (TOF) multiple overlapping thin-slab acquisition (MOTSA) sequences, three-dimensional maximal intensity projection (MIP) images (TR/TE 33.3/3 ms, flip angle 20°, thickness=0.8 mm, matrix 256x192, field of view from 13x13 to 22x22 cm, 0 mm interval) with a smart preparation technique.

Intra-arterial 4-vessel selective DSA was performed via the femoral artery, starting with imaging of the aortic arch followed by selective injections of contrast material into both carotid and vertebral arteries. DSA (GE Medical Systems) was performed in the antero-posterior, lateral and oblique projections. Non-ionic contrast of low osmolarity (Iopamiro n®, Schering) was administered in the common carotid and subclavian arteries (volume: 8 ml) and a rate of 4 ml/ s in the internal carotid and vertebral arteries (6 ml). Hydrophilic coated guide wires res and 4 or 5-F sheaths will be used. Sheaths were intermittently flushed with heparinized saline (5000 IU of heparin in 1000 ml of normal saline). Manual compression at the puncture site was usually performed for 10 minutes after the end of the procedure.

Each patient was referred to an experienced neurologist for diagnosis of acute ischaemic stroke by symptom and CT scan and classified according to TOAST criteria. Results of DSA and MRA were given for each case; neurologists were blind to the modality of angiography and the order of DSA and MRA results were randomized. Treatment of each patient (anti-platelet drugs/ anticoagulants/ other) was defined, considering clinical and laboratorial investigation as well as results of MRA or DSA. Therefore, the two methods of neuro-imaging was compared the finding including arterial occlusions, stenosis, dissection, aneurysm in a descriptive way.

Data management and analysis:
After collection of all the required data, these were checked, verified for consistency and tabulated using the SPSS version 24. Statistical significance was set as 95% confidence level at 5% acceptable error level. Socio-demographic, clinical and neuroimaging profile were reported. Continuous data were expressed as mean and standard deviation and categorical data were expressed as frequency and percentage. To determine the level of agreement between MRA and DSA to detect stenosis, kappa statistic was done. Statistical significance was set as 95% confidence level at 5% acceptable error level ($p<0.05$). Data were analyzed by the SPSS 24.

Results:

The majority of the studied patients (66.7%) were belonged to 41-60 years of age group. The mean ages for the studied participants were 47.50±10.42 (SD) year's age. Regarding gender distribution, 63.3 %(n=19) of the studied patients were male and 36.7 %(n=11) were female.

Among the male patients, 73.7% were smoker and 26.3% were non-smoker whereas among the female patients 18.2% were smoker and 81.8% were non-smoker. A significant difference was seen in terms of smoking history when compared based on gender ($p<0.05$) (Table-I).

Table-I

Distribution of the studied patients by the smoking habit (n=30)

Smoking habit	Male (n=19)	Female (n=11)	p-value*
Smoker	14 (73.7)	2 (18.2)	0.007
Non-smoker	5 (26.3)	9 (81.8)	

*p-value was determined by chi-square test

In terms of co-morbidities and risk-factors, 80.0% of the total patients had HTN and 73.3% had DM, 24.1% had history of other cardio-vascular diseases. 36.7% of the patients had family history of stroke (Table II).

Table-II

Distribution of the studied patients by the co-morbidities and risk factors (n=30)

Co-morbidities and risk factors	Frequency (n)	Percentage (%)
HTN	24	80.0
DM	22	73.3
Other cardio-vascular diseases	7	24.1
Family history of stroke	11	36.7

Among the clinical presentations, arm and leg paresis was the most common and they were present among 83.3% of the total patients followed by decreasing order arm weakness (66.7%), leg weakness (60.0%), self-reported speech disturbance (53.3%), dysphasia or dysarthria (53.3%), facial weakness (36.7%), arm and leg paresthesia (23.3%), hemiparetic or ataxic gait (16.7%), eye movement abnormality (10.0%) and visual field defects (10.0%) (Table III).

Table-III : *Distribution of the studied patients by the clinical presentations (n=30)*

Clinical presentations*	Frequency (n)	Percentage (%)
Arm weakness	20	66.7
Leg weakness	18	60.0
Self-reported speech disturbance	16	53.3
Facial weakness	11	36.7
Arm paresthesia	7	23.3
Leg paresthesia	7	23.3
Headache	7	23.3
Non-orthostatic dizziness	9	30.0
Arm paresis	25	83.3
Leg paresis	25	83.3
Dysphasia or dysarthria	16	53.3
Hemiparetic or ataxic gait	5	16.7
Facial paresis	5	16.7
Eye movement abnormality	3	10.0
Visual field defects	3	10.0

*Multiple responses considered

Table: 4.4 showing the affected territories, MRA findings, DSA findings and TOAST diagnosis considering MRA and DSA findings according to cases. For the majority of the patients the affected artery was MCA (Middle cerebral artery) and it was among 17 out of 30 patients. TOAST diagnosis was similar for both MRA and DSA in 17 (out of 30). All the DSAs and 22 out 30 MRAs revealed abnormalities.

Table IV : *Distribution of the studied patients by the affected territories, MRA findings, DSA findings and TOAST diagnosis considering MRA and DSA findings (n=30)*

Case No.	Affected area	MRA findings	DSA findings	TOAST by MRA	TOAST by DSA
01.	R MCA	R MCA branch stenoses	R MCA branch occlusion#	1	2
02.	R MCA	R cICA dissection	R cICA dissection, R iICA occlusion	4(D)	4 (D)
03.	L MCA	L MCA stenoses	L iCA, LAC stenosis, LMCA occlusion#	1	5
04.	LICA	L cICA occlusion	L cICA FMD, LiICA, LS occlusion	1	4 (FMD)
05.	R ICA, L PCA	Normal	Diffuse lesion in cortical arteries	5	4 (V)
06.	BA	L MCA branch stenoses	LVA dissection	5	4 (D)
07.	L MCA	L MCA stenoses	L cICA dissection and LMCA branch occlusion	1	4 (D)
08.	L MCA	L cICA dissection, L iICA occlusion	L cICA dissection, L iICA occlusion	4 (D)	4 (D)
09.	R MCA	R cICA dissection	R cICA dissection, R iICA occlusion	4 (D)	4 (D)
10.	R PICA	Normal	R PICA occlusion#	4 (D)	4 (D)
11.	L MCA	L cICA dissection, L iICA occlusion	L cICA dissection, L iICA occlusion	4 (D)	4 (D)
12.	L PCA, R MCA, L MCA	Normal	R MCA posterior parietal branch occlusion#	2	2
13.	R PICA	Normal	R PICA occlusion#	4 (D)	4 (D)
14.	BA	R/L VA and BA occlusion	R/L VA dissection and BA occlusion	4 (D)	4 (D)
15.	L MCA	R/L ACA, L MCA stenoses	LACA and LMCA stenoses	5	5
16.	R PCA	Normal	R calcarine artery occlusion#	5	5
17.	R ICA	Normal	R ICA dissection and stenosis at LVA	5	4 (D)
18.	L MCA	L MCA stenoses	L MCA angular branch occlusion#	1	2
19.	MCA	L MCA branch stenoses	LVA dissection	5	5
20.	L MCA	LMCA stenoses	L iICA, LAC stenoses, L MCA occlusion	5	5
21.	L MCA	L MCA stenosis	LMCA angular branch occlusion#	1	2
22.	R PICA	Normal	R PICA occlusion	5	5
23.	BA	Normal	L MCA parietal branch occlusion#	5	2
24.	R ICA, L ICA	Stenosis of R ICA	90% stenosis R ICA and 70% stenosis at LICA	1	1
25.	L MCA	L MCA stenoses	LVA dissection	1	5
26.	RICA and LICA	Stenosis at both ICA	40% Stenosis at R ICA, 30% stenosis L ICA and occlusion at LVA	1	5
27.	L MCA	LMCA stenoses	L MCA branch occlusion#	5	5
28.	R MCA	R MCA branch stenoses	R MCA branch occlusion	2	2
29.	L PCA, L MCA, R MCA	L MCA stenosis	R MCA posterior parietal branch occlusion#	1	2
30.	R ICA	R ICA stenoses	>95% stenosis of R ICA after bifurcation	1	1

L- Left, R-Right, MCA- Middle Cerebral Artery, PICA- Posterior inferior cerebellar artery, BA- Basilar artery, PCA- Posterior Cerebral artery, ICA- Internal Carotid Artery, cICA- Cervical ICA, iICA- Intracranial ICA, ACA- Anterior Cerebral Artery, FMD- Fibromuscular dysplasia, V- vasculitis, #Lesion suggestive of embolism

Discussion:

Currently, cerebrovascular disease is the third most commonest causes of death following malignant tumors and cancer, especially ischemic cerebrovascular disease, which has a high risk of paralysis.[14] There are nearly 7.5 million Transient Ischemic attacks (TIAs) worldwide each year.[15] TIA carries a particularly high short-term risk of stroke, and approximately 15% of diagnosed strokes are preceded by TIAs. Due to the negligence of TIA management, TIAs eventually evolved to stroke, which has brought huge economic losses and left the patients with disability and dependence.[16, 17] Clinicians tend to diagnose TIA with the collection of imaging evidence and duration of cerebral ischemia. With the increased recognition of TIA, update diverse imaging techniques have been used to improve the early diagnosis rate and location of TIA.40 The largest obstacle for the clinicians must to overcome is how to confirm the evaluation and management of TIA with multiple neuroimaging technologies.[18] For example, cranial Doppler ultrasonography can be used for the acute attack as a minimally invasive method to identify large vessels occlusion or monitor stroke response. Compared with Digital subtraction angiography, four-dimensional CTA and MRA provide a less invasive alternative to determine the degree of vascular obstruction and collateral blood flow during macrovascular obstruction[19]. When there is substantial disagreement regarding TIA diagnosis, patients may miss the best treatment window and get the unnecessary treatment. This study aimed to Compare Digital Subtraction Angiography and Magnetic Resonance Angiography in the Investigation of Acute Ischemic Stroke in A Tertiary Care Hospital in Bangladesh

This current study found that nearly two-thirds of the studied patients (66.7%) belonged to 41-60 years of age group followed by decreasing order 26.7% were with 21-40 years age group and only 6.6% were from 61-80 years age group. The mean age for the studied participants was 47.50±10.42 (SD) years in this current study. A study by Cotter et al. found that the mean age for the stroke patients was 63.2 [20] and another study of 679 patients done by Bhowmick et al. found the mean age 60.4 years.[21] In Nepal, Shakya et al, conducted a study where the mean age was 63.2 years.[22] However, in Europe Caso et al, found the mean age 72.68±13.27 (SD) years.[23]

In terms of gender distribution, this study found that 63.3% of the studied patients were male and 36.7% were female. A study was done by Palm et al., to see the gender differences for ischemic stroke; they also found the male predominance in the ischemic stroke although the difference wasn't significant.[24].

Among the male patients of this present study, 73.7% were smoker and 26.3% were non-smoker whereas among the female patients 18.2% were smoker and 81.8% were non-smoker. A significant difference was seen in terms of smoking history when compared based on gender ($p<0.05$). Ischemic stroke is a complex disease state with structural and functional perturbations at the tissue, cellular and molecular levels. The vascular pathophysiological mechanism involved in ischemic stroke include peripheral thrombus formation, changes in cerebral blood flow, breakdown of the blood-brain barrier, and alterations in the cerebrovascular endothelium and it is evident that smoking adversely affects all of these characteristics and that nicotine is a major contributing factor in some of these effects.[25]

In terms of co-morbidities and risk factors, 80.0% of the total patients had HTN and 73.3% had DM, 24.1% had a history of other cardiovascular diseases. 36.7% of the patients had a family history of stroke. A study by Fekadu et al., showed that, patients with ischemic stroke, 83.7% of them had HTN, 10% of them had a family history of stroke and 75% of them had Diabetes Mellitus.[26]

In this present study, for the majority of the patients the affected artery was MCA (Middle cerebral artery) and it was for 17 patients out of 30. The final diagnosis was completely in concordant for 10 patients out of 30 in this present study.

The aetiologies according to TOAST diagnosis were similar by both MRA and DSA in 18 (out of 30) cases and different in 12 cases. In case 1, diagnosis was large-artery atherosclerosis by MRA but DSA showed cardioembolism. In case 3, MRA diagnosed large artery atherosclerosis but DSA showed undetermined aetiology. In case 4, MRA found large artery atherosclerosis but DSA revealed fibro-muscular dysplasia (FMD). Case 18 showed large artery atherosclerosis by MRA and undetermined aetiology by DSA findings. In case 21 large artery atherosclerosis was diagnosed by MRA and cardioembolism by DSA was found. For case 23, undetermined aetiology by MRA and cardioembolism by DSA, for 25 and 26, large artery atherosclerosis was diagnosed by MRA but for 25 undetermined aetiology and for 26 cardioembolism was diagnosed by DSA. For case 29, large artery atherosclerosis was diagnosed by MRA but cardioembolism by DSA. All the DSAs and 22 out 30 MRAs revealed abnormalities in this present study. This study

showed that, MRA didn't reveal a posterior cerebellar inferior artery (in case 10, 22) lesion, Fibro-muscular dysplasia (FMD) in case 4.

Digital subtraction angiography (DSA) is the gold standard for evaluating arterial stenosis but it has some disadvantages like it's an invasive procedure, costly and complicated.[27] On the other hand, MRA is non-invasive and cost-effective for the patients. This was a single-centered study so the findings may not represent the true scenario. Multi-centered studies are recommended to corroborate these research findings.

Conclusion:

This study found that both MRA and DSA can effectively identify etiology of acute ischemic stroke. However, DSA is an invasive, costly and complicated procedure. Therefore, the application of MRA is suggested as practical tools to evaluate the etiology of ischaemic stroke individuals as MRA is non-invasive and cost-effective, especially for third world countries, like Bangladesh.

Limitations:

Small sample size and this single hospital based study did not reflect exact scenario of the whole community. Patients from all socioeconomic status and all parts of the country did not come to seek medical attention in the study place.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

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Ethical consideration:

The study was conducted after approval from the ethical review committee of Sir Salimullah Medical College.. The confidentiality and anonymity of the study participants were maintained.

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