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ORIGINAL ARTICLE

Accuracy of combined Carotid/ Transcranial color coded duplex Compared with Magnetic Resonance Angiography in the Diagnosis of Extracranial and Intracranial Artery Stenosis

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ABSTRACT

Keywords: acute cerebral infarction, extracranial artery stenosis, intracranial artery stenosis , Carotid duplex, transcranial color coded Duplex , magnetic resonance angiography.

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Background: Stroke is the second leading cause of mortality. Nearly 90% of strokes are ischemic, and large artery atherosclerosis is one of the main causes of ischemic stroke. **Objective:** The goal of this study was to compare the accuracy of combined Carotid duplex/ Transcranial color coded Duplex versus magnetic resonance angiography (MRA) in detecting extracranial and intracranial stenosis among acute ischemic stroke patients . **Methods**: Consecutive patients with acute ischemic stroke (AIS) recruited from the ward and outpatient clinics of neuropsychiatric department, during the period from August 2017 to July 2018, underwent both MRA and combined carotid duplex/TCCD examination, To calculate the agreement between the results of MRA and TCD, kappa coefficient test was calculated in comparison with MRA **Results:** A total of 250 patients with AIS were included in this study. Their ages ranged from 38 to 87 years old with a mean ± S.D; 59.9 ±11.2 years. The overall agreement between MRA and carotid duplex was in 95.4% of cases and discordant results were 4.6% of cases, weighted kappa agreement 0.906, p-value< 0.001, which is a high agreement. The overall agreement between MRA and transcranial color coded duplex (TCCD) was in 80.0% of cases and discordant results were 20.0% of cases, weighted kappa agreement 0.614, p-value < 0.001, which is a moderate agreement. **Conclusion:** Moderate agreement was found between TCCD and MRA and higher level of agreement was found between carotid duplex and MRA in the evaluation of AIS patients.

INTRODUCTION

Stroke epidemiology is evolving rapidly and the global incidence of stroke continues to rise worldwide.[(1)] The number of new strokes in Egypt per year may be around 150 000–210 000, in addition stroke accounts for 6.4% of all deaths and thus ranks third after heart disease and gastrointestinal diseases.[(2)] Carotid atherosclerosis is one of the well-known risk factors for ischemic stroke.[(3)] Carotid artery stenosis is responsible for 8% of all strokes. [(4)] It is also a cause of transient ischemic attack (TIA).[(5)] Duplex ultrasound (DUS) has received special attention for the detection of carotid stenosis because it is accessible, non-invasive, cheaper, and without the additional risks of digital subtraction angiography (DSA), MRA, and CTA.[6] It is establishing its role in screening and diagnosis of carotid pathology because of patient comfort, lack of risks, low cost and accuracy in detecting carotid atherosclerosis.[7] Intracranial Atherosclerosis(ICAS) is a high-risk factor for TIA and ischemic stroke. [8] The estimated prevalence of symptomatic ICAS ranges from 20% to53% with higher risk in Asian, Hispanic, and African American ancestry.[9] Stroke patients manifesting symptomatic ICAS may have a poor prognosis including worsened functional outcome and even increased morbidity and mortality.[10] Ultrasound scans (TCD and TCCD) are noninvasive ultrasonic techniques and a quick and simple way to detect the blockage of blood vessels in the brain.[11] It could measure the blood flow velocities in the basal intracranial arteries of the brain. An advantage of TCD is that it can be performed at the bedside and repeated as needed or applied for continuous monitoring.[12] For people with acute ischaemic stroke, TCD or TCCD can provide clinically helpful information for detecting blockage of large arteries in the brain compared with DSA , CTA and MRA.[11] A few studies have focused on the correlation between TCD and MRA to the diagnosis of ICAS.[12]

AIM OF THE WORK

The purpose of this study was to compare the diagnostic accuracy of Carotid duplex and Transcranial color coded Duplex (TCCD) versus magnetic resonance angiography (MRA) in detecting extracranial and intracranial stenosis among acute ischemic stroke patients.

MATERIALS AND METHODS

Study design

This work was a cross-sectional study conducted on 250 patients with acute ischemic stroke.

Patients &Methods

250 consecutive patients with Acute Ischemic Stroke (AIS) were participated in this study. The subjects' age ranged from 38 to 87 years old with a mean of 59.9 ± 11.2 years , and were recruited from inpatients and outpatients clinics of neuropsychiatric department, from August 2017 through July 2018.

Inclusion criteria: patients were eligible for study if they had recent AIS (confirmed by CT and /or MRI) not more than one week, had stroke affecting anterior circulation and their ages were above 18 years.

Exclusion criteria: AIS patients who had the following criteria were excluded:

1) hemorrhagic stroke , 2) any medical illnesses as anemia, hepatic/renal impairment or other systemic illnesses that could affect TCD results, 3) Autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, and scleroderma, 4) History of acute/chronic inflammatory diseases, malignancy, trauma, surgery, known diagnosis of vacuities, 5) Malignancy elsewhere in the body or brain, 6) a poor TCD acoustic temporal window.

Study tools

All patients were submitted for the following evaluation:

1. Full neurological history, complete neurological examination where the following clinical and demographical data were collected: age, sex, and presence of stroke risk factors (as smoking history, hyperlipidemia, diabetes mellitus, history of hypertension, history of transient ischemic attacks, history of myocardial infarction, or any cardiac problems).
2. Stroke etiology was classified according to the criteria of Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification.
3. Stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS)[(13)] measured at the time of admission. A value of 0 is normal; so, the higher the score, the worse the neurological deficit (the highest possible score is 42), (mild stroke 1—4, moderate stroke 5—15, moderate to severe 16—20, severe stroke 21—42).[(14)]
4. Electrocardiography and echocardiography were conducted for all patients.
5. Laboratory investigations including routine parameter estimation (random blood glucose, renal and liver function tests, and lipid profile)and Vacuities workup (erythrocytic sedimentation rate (ESR), rheumatoid factor (RF), antinuclear factor)

6. Neuro-Imaging:

A) Computed tomography (CT) brain to exclude intracranial hemorrhage or other diseases that could have caused the neurologic deficit.
B) Magnetic resonance imaging and magnetic resonance angiography (MRI and MRA) of the brain for assessment of brain and cerebral vasculature (Closed MRI machine, Toshiba, 1.5 Tesla). Axial three-dimensional time of flight MRA of the circle of Willis was obtained, with no evidence of intracranial bleeding and no contraindication for MRA. Two neuroradiologists without knowledge of the clinical findings independently interpreted MRA studies and agreement was obtained for the final analysis.

7. Neurosonological assessment:

A) Carotid duplex:

LOGIQ V5 Duplex ultrasonography apparatus equipped with a 5–10 MHz linear-array transducer was used for carotid and vertebrobasilar systems examination. Initially, the common and internal carotid arteries were scanned transversally and longitudinally, with subject lying in the supine position and the head slightly tilted to opposite side. During the initial scanning, optimal insonation angles were determined for the estimation of respective plaque heights, and the measurements were performed on the frozen frame, perpendicular to the vascular walls. Bilateral carotid and vertebral arteries were examined. Carotid stenosis/occlusion was diagnosed by the commonly used criteria. Peak systolic velocities (PSVs) and end diastolic velocities (EDVs) were measured in the common, external, and internal carotid arteries and when stenosis was detected the velocities were measured at the maximally stenotic area. Extracranial atherosclerotic carotid artery disease was considered significant if either stenosis of ≥ 70% or an occlusion was present. Carotid artery stenosis of ≥ 70% was defined as an increase of the PSV of ≥ 250 cm/s or as a ratio of the internal carotid artery (ICA) PSV to the common carotid artery (CCA) PSV of ≥ 4.5. Quantification of the intima media thickness (IMT) at the distal far wall of the CCA was done for both sides for each patient and the highest value of the 2 sides was used.

B) **Transcranial Color Coded Duplex (TCCD)**

Trans Cranial Color coded Duplex (TCCD) was done using the available TCD apparatus (LOGIQ V5, Alkan Medical, GE-Ultrasound Solution) having 2-4 MHZ phase array probe. TCCD was used for assessment of intracranial cerebral vasculatures, while the patient in the supine position through different bone windows (transtemporal and, suboccipital). The following vessels were examined: The middle cerebral arteries (MCA), anterior cerebral arteries (ACA), pre communicating (P1), and post communicating (P2) posterior cerebral arteries (PCA). Each insonated artery was investigated by: Peak systolic velocity (PSV) used for the presence of stenosis or occlusions, flow direction (antegrade or reversed). The quantification of intracranial stenosis was calculated according to criteria by Baumgartner et al. [15]

Ethical consideration

The current study was approved by the Institutional Ethics Committee, Faculty of Medicine, Aswan University. All patients were provided with complete information about the study objectives, methods, and risk/benefit assessment. A written consent was obtained from each participant upon acceptance to take part in the study. The study was conducted in accordance with the principles of Declaration of Helsinki.

Statistical analysis

Data were verified, coded by the researcher, and analyzed using SPSS version 24. Descriptive statistics: Means, standard deviations, and percentages were calculated. Test of significances: chi-square test was used to compare the difference in distribution of frequencies among different groups. The clinical and demographic factors with proven statistical significance from the univariate analyses were further included in the multivariate logistic regression models. Agreement between MRA and Duplex in diagnosis of extracranial stenosis/intracranial stenosis was examined using weighted Cohen's kappa coefficient (κ). P-value equals or less than 0.05 was considered significant.

RESULTS

250 patients with AIS were included in this study, 175 of them (70%) were males and 75 (30%) were females. Their ages ranged from 38 to 87 years old with a mean±S.D of 59.9 ±11.2 years. There was no significant difference between the mean age of the male and female groups. Median National Institute of Health Stroke Scale score was 14, range, 3 to 25 points **(as shown in Table 1)**.

Table (1): Demographic characteristics and vascular risk factors of the study population (n = 250)

Variable	Total = 250
Age, y (mean ± SD)	59.9±11.2
Gender, male	175 (70%)
HTN	144 (57.6%)
Dyslipidaemia	126 (50.4%)
Smoking	117 (46.8%)
DM	96 (38.4%)
IHD	74 (29.6%)
Median admission NIHSS, range (mean ± SD)	3-25 (11.5 ± 4.91)

Abbreviations: IHD, Ischemic heart disease; DM, diabetes mellitus; HTN, hypertension; NIHSS, National Institute of Health Stroke Scale; SD, standard deviation.

The frequency of different risk factors among our study group is shown in (**Table 1)**. 144, 126, 117 and 96 patients were hypertensive, dyslipidemics , diabetic, , and smokers (57.6%, 50.4%, 46.8% and 38.4%, respectively). Additionally, 74 (29.6%) of patients had ischemic heart disease.

Kappa coefficient values were calculated to determine the agreement between TCD and MRA for assessment of carotid and ICA atherosclerosis . The overall agreement (matching) between MRA and carotid duplex was in 95.4% of cases and discordant results were 4.6% of cases, weighted kappa agreement was significant agreement **(as shown in Table 2).**

Table (2): Agreement between MRA and duplex in extracranial stenosis

	MRA		**Total**
	Extracranial stenosis <70%	Extracranial stenosis ≥ 70%	
Carotid Duplex			
Extracranial stenosis <70%	59 (54.6%)	5 (4.6%)	64 (59.3%)
Extracranial stenosis ≥70%	0 (0%)	44 (40.8%)	44 (40.8%)
Total	59 (54.6%)	49 (45.4%)	108 (100%)
Weighted Kappa Agreement		0.906	P < 0.001
Chi-square test		89.403	P < 0.001

The overall agreement between MRA and transcranial color coded duplex (TCCD) was in 80.0% of cases and discordant results were 20.0% of cases, weighted kappa agreement was significant agreement **(as shown in Table 3)**.

Table (3): Agreement between MRA and duplex in intracranial stenosis

	MRA		Total
	Intracranial stenosis < 50%	Intracranial stenosis ≥ 50%	
TCCD			
Intracranial stenosis <50%	24 (36.9%)	13 (20%)	37 (56.9%)
Intracranial stenosis ≥50%	0 (0%)	28 (43.1%)	28 (43.1%)
Total	24 (36.9%)	24 (63.1%)	65 (100%)
Weighted Kappa Agreement		0.614	P < 0.001
Chi-square test		28.794	P < 0.001

DISCUSSION

Several noninvasive diagnostic tools were used for diagnosis of intracranial and extracranial atherosclerosis. MRA, CTA, and TCD methods are commonly used. TCD is one of the most frequently used tests due to its simplicity and affordability. Moreover, it permits monitoring of bedside in critical condition.(16) Ultrasound of carotid and vertebral arteries coupled by transcranial doppler sonography are essential parts of the diagnostic workflow in every acute stroke unit.(17) The gold standard for diagnosing extracranial arterial stenosis and intracranial stenosis is digital subtraction angiography.(18) However, it is invasive, pricey, and linked to serious “peri-procedural” problems.(19) MRA produces angiogram-like images that can be processed in many planes using three-dimensional post-processing.(20) Time-of-flight MRA uses 3-dimensional post processing to provide angiogram-like pictures in many planes. Furthermore, when it comes to detecting MCA stenosis, the combination of carotid duplex/TCCD and MRA is more reliable than DSA alone.(21) In carotid stenosis, it's also useful for determining the border zone infarction stroke mechanism. (22)

Our study reported moderate agreement between MRA and duplex in intracranial stenosis. Our result agrees with a previous study, that detected a moderate agreement between CT angiography, transcranial color-coded sonography, and digital subtraction angiography in the evaluation of intracranial stenosis.(23)

Furthermore, similar results were previously obtained by Navarro et al, who compared 573 patients referred for TCD with contrast angiography or MRA and found the sensitivity and specificity of TCD was 90% and 83% respectively.(24) Jaiswal et al., showed that the diagnostic accuracy of TCD is higher, particularly in anterior circulation where sensitivity is 85.9% and specificity is 90.0%.(25) Moreover, Xiao et al., stated that Color-coded duplex sonography is a more suitable approach for the evaluation of cerebrovascular diseases than MRA.[26] Our findings contradict the results of Gujjar and co-workers that stated a poor correlation between TCD and MRA in Omani patients with acute ischemic stroke.[27] They performed TCD studies within 5 days after MRA . The mean time interval between MRA and TCD was 24-48 hours in our study. Discrepancy between the studies could be attributed to the long time delay between TCD and MRA that can provide sufficient time for the termination of thrombus extent.

In regard to agreement between MRA and carotid duplex in extracranial stenosis, we stated that the overall agreement was in 95.4% which is a high agreement, and that is in line with a previous study done by Back and co-workers.[28] They compared sensitivity, specificity, positive predictive and negative predictive values between ultrasound scan and MRA for detection of > 70% ICA stenosis. They established 100%, 77%, 76%, and 100% for MRA and 90%, 74%, 72%, and 91% for duplex ultrasound scan, respectively. In contrast to our results, an earlier meta-analysis published by Blakeley et al., concluded that DUS and MRA had similar diagnostic performance in predicting carotid artery occlusion and 70% stenosis. [29] Kallmes et al., found lower sensitivity for MRA in recognizing severe carotid artery stenosis.[30]

Of note, our study had some limitations. First, the small sized sample because some patients were excluded poor acoustic bone window and others had contraindications for MRA. Second, it was a single-center study. Third, TCD is an operator-dependent technique that requires considerable experience in intracranial arterial anatomy and understanding.

CONCLUSION

In the assessment of cerebral atherosclerosis, there was moderate agreement between TCCD and MRA for intracranial stenosis, and a higher agreement between carotid duplex and MRA for extracranial stenosis, The combined carotid duplex/TCCD is a less expensive, noninvasive, portable, and technically less difficult instrument. Carotid duplex/TCCD validates extracranial and intracranial vascular anatomy less than MRA, but It gives real-time information on cerebral blood flow velocities, whereas MRA simply provides morphological characteristics.

List of abbreviations

ACA	:	Anterior Cerebral Arteries
ACA	:	Anterior Cerebral Artery
ACAS	:	Asymptomatic Carotid Atherosclerosis Trial
AF	:	Atrial Fibrillation
CCA	:	Common Carotid Artery
CEA	:	Carotid Endarterectomy
CRP	:	C-Reactive Protein
CTA	:	Computed Tomography Angiography

DSA	:	Digital Subtract Angiography
ECAS	:	Extracranial Atherosclerosis
EDVs	:	End Diastolic Velocities
HR-MRI	:	High-Resolution Magnetic Resonance Imaging
ICA	:	Internal Carotid Artery
ICAS	:	Intracranial Atherosclerosis
ILA	:	Intracranial Large Artery
IMT	:	Intima Media Thickness
IMT	:	Intima Media Complex Thickness
INR	:	International Normalized Ratio
MCA	:	Middle Cerebral Artery
MRA	:	Magnetic Resonance Angiography
MRI	:	Magnetic Resonance Imaging
NIHSS	:	National Institutes Of Health Stroke Scale
TOAST	:	Trial Of Org 10172 In Acute Stroke Treatment
P1	:	Pre Communicating branch of Posterior cerebral artery
P2	:	Post Communicating branch of Posterior cerebral artery
PCA	:	Posterior Cerebral Artery
PI	:	Pulsatility Index
PPV	:	Positive Predictive Value
PSV	:	Peak Systolic Velocity
SBP	:	Systolic Blood Pressure
SVD	:	Small Vessel Disease
TCCD	:	Transcranial Color Coded Duplex
TCCS	:	Transcranial Color-Coded Duplex Sonography
TCD	:	Transcranial Doppler
TIA	:	Transient Ischemic Attacks
TOF-MRA	:	Time-Of-Flight Magnetic Resonance Angiography

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