

## Research Article

# Utility of Transthoracic Echocardiography and Carotid Doppler Ultrasound in Differential Diagnosis and Management of Ischemic Stroke in a Developing Country

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## Abstract

**Objective:** We sought to describe findings, diagnostic yield, cost effectiveness of transthoracic echocardiography (TEE) and Carotid doppler ultrasound (CDU) in ischemic stroke.

**Methods:** Cross sectional study at Mulago hospital, Uganda. Institutional ethical approval, patient consent was obtained. Patients eighteen years and above with ischemic stroke confirmed by brain computerized tomography (CT) scan and met inclusion criteria were selected. TTE and CDU were done as part of comprehensive assessment for stroke risk factors. Data was analyzed using SPSS 14. Univariate analysis was done for social-demographics, abnormalities on cardiac imaging and diagnostic yield using TOAST criteria. Bivariate analysis for association between stroke risk factors, cardio-embolic stroke and other ischemic subtypes (diagnosed using clinical and CT scan features). Statistical significance was set at  $P < 0.05$ .

**Results:** Of 139 screened patients with suspected stroke, 127 underwent brain CT scan as 12 died before CT. Eighty five were confirmed stroke by CT scan with 66 (77.6%) ischemic stroke, mean age 62 years (SD+16.6), 53% were male. Out of 66, 62 (93.9%) underwent both TTE and CDU. Although only 7 (11.3%) reported history of heart disease, 43 (69.3%) had abnormal findings on TTE with left atrial enlargement commonest in 21 (48.8%). Thirty eight (61.3%) had abnormal finding on CDU with atherosclerosis commonest in 28 (45.2%). Using clinical and CT scan features, atherosclerotic stroke was the commonest subtype in 29 (46.8%) then cardio-embolic 18 (27.3%). Only 6 (9.7%) patients had abnormal findings on TTE suggesting possible cardio-embolism by TOAST criteria. None had stenosis  $>50\%$  on CDU. Multiple valvular lesions  $P < 0.001$ , severe valvular lesions  $P = 0.001$  were associated with cardio-embolic stroke.

**Conclusions:** Majority of ischemic stroke patients without previous history of heart disease had abnormal findings on TTE and CDU. Diagnostic yield for cardio-embolic stroke by TOAST criteria was very low given the high cost involved for a developing country.

## ABBREVIATIONS

CT: Computerized Tomography; CDU: Carotid Doppler Ultrasound; DBP: Diastolic Blood Pressure; DCM: Dilated Cardio Myopathy; TTE: Trans Thoracic Echocardiography; SBP: Systolic Blood Pressure.

## INTRODUCTION

Stroke is one of the leading causes of morbidity and mortality worldwide [1-6] with developing countries accounting for 85% of global deaths from stroke [2,3,7,8]. Delayed hospital

presentation, lack of timely clinical evaluation in conjunction with diagnostic imaging, post stroke complications with lack of stroke units contribute to the high mortality rate, found to be as high as 62% at one year in developing countries [6,9-12]. Ischemic stroke accounts for 70-80% of strokes and is caused by embolic or thrombotic occlusions in the cerebral vessels [13,14]. The etiology of ischemic stroke is largely due to large artery atherosclerosis [13]. Up to 15 to 30% are caused by embolic occlusions which can be of arterial or cardiac origin and are associated with poor prognosis and high index of fatal recurrence [13,15-19].

TTE and CDU, now recommended as routine tests in stroke work up [20,21] search for the cardiac sources of stroke such as left atrial dilatation, poor left ventricular systolic function, valvular heart diseases, cardiac tumours and thrombi and patent foramen ovale, stenosis of extracranial internal carotid artery greater than 50%. This is a crucial part of the urgent ischemic stroke evaluation as it changes treatment decisions [17, 19]. Despite this, there is limited imaging of patients beyond brain CT scan for differential diagnosis and management of ischemic stroke in developing countries [22]. This is largely due to cost and its effectiveness followed by lack of access to echocardiography/ultrasound machines and the expertise to operate and interpret the results [22]. The purpose of this study was to describe the findings, diagnostic yield of TTE and CDU and cost effectiveness among patients presenting with ischemic stroke to Mulago Hospital in Kampala, Uganda.

## METHODS

We conducted a cross sectional study of an approved protocol by Makerere University College of Health Sciences' School of Medicine Research and Ethics committee.

We utilized quantitative methods for data collection at Mulago Hospital, one of Uganda's national referral hospitals and Makerere University College of health sciences' school of medicine teaching hospital. It has an estimated 1,500 hospital beds and among others a radiology department with highly trained personnel such as radiologists and cardiologists to interpret the findings of imaging investigations. It also houses the Uganda Heart Institute which is complete with a catheterization laboratory and operating rooms to carry out advanced cardiac procedures and operations.

### Study period

During a five month period from 1<sup>st</sup> July to 30<sup>th</sup> November 2006, 139 patients 18 years and above, presented to Mulago Hospital's emergency and general medical wards with neurologic deficits for acute stroke [23]. Study methods have been described before [14].

All patients were offered a free screening non-contrast head CT scan and informed consent for participation in the study obtained. Twelve patients died prior to screening, suspected but not confirmed to have intracranial hemorrhage. 127 patients underwent a head CT scan, typically performed on average two days following the onset of symptoms. Patients with a normal CT scan performed within 12 hours of symptom onset, a repeat CT scan was performed at 7 days to confirm diagnosis. Eighty five patients had stroke confirmed on brain CT scan and these were recruited consecutively into the study.

All patients were evaluated by the principal investigator and research assistants and underwent comprehensive assessment for stroke associated risk factors including; selected socio-demographics, present and past medical history of hypertension, Diabetes mellitus, heart disease, smoking, alcohol dependence, history of current medications such as antihypertensive, antiplatelet drugs and anticoagulants. A physician's diagnosis of hypertension and heart disease made during previous clinic visits or hospital admissions was accepted.

Physical examination included cardiovascular examination for irregularly irregular pulse, displaced apex beat, heart murmurs and carotid bruits. Blood pressure measurements were done twice at 5 minutes interval and the average values obtained classified according to the National Clinical Guidance Centre (NCGC) clinical guideline 127 [24].

Laboratory investigations included fasting serum glucose, fasting lipid profile, complete blood count and *Treponema pallidum* precipitation test.

TTE for cardio-embolic sources (for example akinetic wall segment, mural thrombi, vegetations, and an ejection fraction of < 35%) and CDU for presence and degree of extracranial internal carotid stenosis, were performed by cardiologists with experience in this field, using the Phillips Sonos 4500 machine.

For the purpose of this study, 66 patients with ischemic stroke were identified and findings of 62 patients who underwent both TTE and CDU were analyzed. Four patients did not have cardiovascular imaging done: one had a very poor echo window due to aspiration pneumonia and three patients had continuous convulsions before the imaging could be done. Despite the controlled convulsions, they died over the next few hours before the imaging was done.

The Trial of ORG 10172 in Acute Stroke Treatment or TOAST criteria's clinical and CT scan features were used to classify stroke subtypes as atherosclerotic, cardio-embolic, lacunar or unspecified etiology [25]. Diagnostic yield was determined using TTE and CDU abnormalities suggestive of cardio-embolic and atherosclerotic stroke subtypes by the TOAST criteria. These included: severe left ventricular systolic dysfunction, left ventricle thrombi, atrial myxoma, dilated cardiomyopathy, valve prosthesis, left ventricular segmental wall motion abnormalities with MI, left atrial dilatation with mitral stenosis to indicate cardio-embolic stroke; more than 50% extra cranial internal carotid artery stenosis by doppler ultrasound to indicate atherosclerotic stroke subtype.

Data was analyzed using the SPSS software version 14.0 statistical analysis package. Questionnaires were cross-checked daily for completeness of the data coding by the principal investigator and double entered into a computer to ensure consistency. Univariate analysis was done for social demographic variables, abnormalities on cardiac imaging and diagnostic yield of TTE and CDU abnormalities suggestive of cardio-embolism and atherosclerotic stroke subtypes using TOAST criteria. Bivariate analysis for the association between stroke associated risk factors, cardio-embolic stroke and other ischemic stroke subtypes (diagnosed using clinical and CT scan features) was done. Fisher's exact test was used in case of cells with numbers less than 5. Odds ratios and 95% confidence intervals are presented. Statistical significance was set at  $P < 0.05$ . Multivariate binary logistic regression could not be done because of the small numbers.

## RESULTS

Of 66 patients with ischemic stroke, the mean age was 62.0 years with a standard deviation of 16.6 years. Thirty five (53%) were male, 33.3% were subsistence farmers, 25.8% had

a small business, 18.2% performed housekeeping and 22.7% had other occupations or were not employed. Fifteen patients never attended school, 34 patients had only a primary level of education, 11 completed secondary education, and 6 completed college-level education.

Using clinical and CT scan features we classified 29 (46.8%), patients as atherosclerotic stroke subtype, 18 (29.0%) as cardio-embolic, 7 (11.3%) lacunar and 8 (12.9%) as unknown etiology.

On clinical evaluation, only seven (11.2%) patients reported a history of previously diagnosed heart disease. Thirteen (21.0%) patients had an irregularly irregular pulse and none of them was aware of a previous diagnosis of atrial fibrillation and therefore not taking warfarin.

On cardiovascular imaging, 43(69.3%) patients had abnormal findings on TTE with predominantly left atrial enlargement in 21 (48.8%), right atrial enlargement in 13 (30.2%) and left ventricular hypertrophy with diastolic dysfunction in 12 (27.9%) (Table 1) Only 6 (9.7%) patients, 3 of who reported prior history of heart disease had findings on TTE suggestive of possible cardio-embolism as defined by TOAST criteria (Table 2).

Thirty eight (61.3%) patients had abnormal findings on CDU including atherosclerosis in 28 (45.2%), atheromatous plaques in 24 (38.7%) and non-laminar velocity pattern in 6 (9.7%). None of the patients had >50% stenosis on CDU.

None of the patients presented with a mechanical prosthetic valve, left ventricle thrombus, atrial myxoma and left ventricular segmental wall motion abnormalities with myocardial infarction.

Table 3 shows bivariate analysis for association between stroke associated risk factors, cardio-embolic stroke and other ischemic stroke subtypes (using clinical and CT scan features). At bivariate analysis, multiple valvular lesions P < 0.001, severe valvular lesions P = 0.001, female sex P=0.02, irregularly irregular pulse P=0.03, were more common in cardio-embolic stroke compared to other ischemic stroke subtypes. The distribution

**Table 1:** Transthoracic echocardiographic findings (n=43)\*.

Findings	No (%)
Left atrial enlargement	21(48.8)
Right atrial enlargement	13(30.2)
Left ventricular hypertrophy with diastolic dysfunction	12 (27.9)
Mild left ventricular systolic dysfunction	3 (7.0)
Left ventricular dilatation	3(7.0)
Right ventricular dilatation	2(4.7)
Mitral myxoma	2(4.7)
Moderate ventricular systolic dysfunction	1(2.3)
Severe left ventricular dysfunction	1(2.3)
Left atrial enlargement with mitral stenosis	1(2.3)
Right atrium thrombi	1(2.3)
Mitral valve prolapse	1(2.3)
Constrictive pericarditis	1(2.3)

\*Since some patients had more than one significant finding on transthoracic echocardiogram, the cumulative percentage of abnormal findings is greater than 100.

**Table 2:** Transthoracic echocardiography findings consistent with TOAST criteria for possible cardio-embolism (n=6).

Findings	No
Severe left ventricle systolic dysfunction	2
Left ventricle dilatation	2
Left atrial dilatation with mitral stenosis	1
Mitral valve prolapse	1

**Table 3:** Bivariate analysis for association between stroke risk factors, cardio-embolic stroke, and other ischemic stroke subtypes.

Risk factor	Cardio-embolic stroke N=18, n	Other ischemic stroke subtypes N=44, n	OR (95%CI)	P-value
Sex, female	12	15	3.87(1.21-12.35)	*0.02
Age ≥ 62 years	9	26	0.69(0.23-2.08)	0.51
H/o of hypertension	10	26	0.87(0.29-2.62)	0.80
SBP ≥140mmHg	6	24	0.42(0.13-1.31)	0.13
DBP ≥90mmHg	3	19	0.26(0.07-1.01)	0.08
Irregularly irregular pulse	7	6	4.03(1.12-14.50)	*0.03
Waist hip ratio>0.9 in men, >0.85 in women	7	17	1.01(0.33-3.11)	0.99
Atherosclerosis of the carotid arteries	5	23	0.35(0.11-1.15)	0.08
Atheromatous plaques	4	20	0.34(0.10-1.21)	0.15
Left ventricular hypertrophy	9	18	1.44(0.48-4.35)	0.51
Multiple valvular lesions	12	2	42.00(7.49-235.52)	*<0.001
Severe valvular lesions	8	3	10.93(2.45-48.81)	*0.001

Given the small numbers in some of the cells, Fisher's exact test was used. Other ischemic stroke subtypes include: atherosclerotic, lacunar and unspecified stroke.

\*denotes statistically significant

of age >62 years, waist hip ratios, systolic and diastolic blood pressure, history of hypertension, atherosclerosis of carotid arteries, atheromatous plaques and hypertrophy of the left ventricle was the same among patients with cardio-embolic stroke compared to other ischemic stroke subtypes (P > 0.05).

## DISCUSSION

Transthoracic echocardiography and carotid doppler ultrasound are now part of routine diagnostic work up of cardiac sources of emboli in stroke patients in many centers across the world [20-22]. Various cardiac abnormalities were found on transthoracic echocardiogram in 43 (69.4%) patients in this study, with left atrial enlargement in half of the patients and left ventricular hypertrophy with diastolic dysfunction in a quarter of the patients. Almost an equal number of patients were found to have abnormal echocardiograms by a hospital-based study from Pakistan though in contrast, left ventricular hypertrophy with diastolic dysfunction was predominant in 57% of the patients [22]. According to TOAST criteria of abnormalities suggesting cardio-embolic etiology on TTE [25], the diagnostic yield in our study was only 6 (9.6%) raising the ongoing debate on the cost effectiveness of this diagnostic tool. An equally low diagnostic

yield of 4% was reported by a hospital-based study from Canada [26]. This is in contrast to a hospital based study from Pakistan and a single center study from Portugal that revealed higher yields of 16% and 37.2% respectively [22,27].

Majority of the patients with abnormal transthoracic echocardiograms presented with previously undiagnosed heart disease. Multiple valvular lesions, severe valvular lesions, were associated with cardio-embolic stroke similar to other studies [17,19]. This makes cardiogenic sources an under-recognized cause of cardiogenic stroke in our population and also emphasizes the failure by many to afford the high costs involved to access these diagnostic modalities.

Health facilities that offer tertiary level of care are very limited in our country and the diagnostic services offered at these hospitals are very costly. Analysis on the Neurology ward in our hospital revealed that hardly any ischemic stroke patient could afford a TTE and CDU after footing the bill for a CT scan of the brain that cost 120,000 Uganda shillings (47-50 US dollars).

Detection of significant abnormalities on TTE aided differential diagnosis of ischemic stroke subtype and influenced routine patient management on the neurology ward and follow up visits to the Neurology clinic, which previously done primarily by the neurology team were now done by both the Neurology team and the Cardiology team. Patients with cardio-embolic stroke were followed up primarily by the Cardiology team in the Cardiac clinic. However, recommendations regarding the routine use of TTE and CDU as part of diagnostic stroke work up are needed in our setting. The burden of cardiovascular disease and stroke continues to raise as western cultural adaptation and demographic transition increases [3]. However, barriers to cardio-embolic stroke recognition include difficulties in accessing these diagnostic modalities of care, cost of treatment, low educational levels and poverty, which factors lead to difficulty in establishing an adequate preventive strategy and management of cardio-embolic stroke. Recommendations should therefore keep all this in view.

## CONCLUSION

Transthoracic echocardiography revealed abnormal findings in majority of ischemic stroke patients most of who had previously undiagnosed cardiac disease likely due to failure to access and afford these investigations. However, the yield of echocardiographic abnormalities suggestive of cardio-embolic stroke according to TOAST criteria was low though it influenced medical treatment and follow up for patients with cardio-embolic stroke. Given the economic implications, routine cardiographic imaging in acute stroke requires further research to prioritize patients leading to high yield.

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