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Original Article

Study of transesophageal echocardiography in young patients (<40 years) with acute arterial ischemic stroke: A pilot study

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ABSTRACT

Background: The aim is to study cardiac abnormalities as detected by transesophageal echocardiography (TEE) in young patients (<40 years) presenting with acute ischemic arterial stroke.

Methods: A cross-sectional observational study was conducted in young patients aged <40 years presenting with acute arterial ischemic stroke without any valvular heart disease, prosthetic valve, or previously diagnosed atrial fibrillation (AF). TEE was performed in all eligible patients preferably within the first week of the onset of ischemic arterial stroke. All patients with normal TEE underwent holter to rule out paroxysmal AF.

Results: Totally, 40 young patients were included in the study. Mean age was 35.17 (SD [standard deviation] $\pm$ 2.99) years. TEE abnormalities were noted in total 13 (32.5%) patients, of which patent foramen ovale was the most common cardiac abnormality in eight (20%) patients followed by left atrial appendage clot in three (7.5%) and atrial septal aneurysm in two (5%) patients. One patient (2.5%) was observed with atrial septal aneurysm along with a sieved septum. All the patients with normal TEE underwent holter, and four of 27 (14.8%) of these patients were noted to have paroxysmal AF.

Conclusion: Cardiac abnormalities on TEE and holter were detected in 42.5% of the young patients with idiopathic arterial stroke. TEE abnormality was noted in 33% (13/40), whereas AF on holter was seen in 14.8% (4/27) with normal TEE. Thus, probable cardioembolic stroke was responsible for acute ischemic stroke in 42.5% (17/40) of young patients in the absence of valvular heart disease, prosthetic valves, and persistent/permanent AF.

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Introduction

Ischemic arterial stroke in young remains a matter of concern as it occurs in the most productive age group and leads to significant long-term morbidity. Cardioembolic stroke and arterial dissection are the major causes of stroke in young individuals. But, finding the exact cause of embolism or stroke may sometimes be very challenging and difficult. It is very important to find the exact cause of stroke in young as it will help in planning the treatment of the patient and preventing the recurrences. Usually, the cardioembolic strokes in young are either related to a structural heart lesion such as valvular heart disease and prosthetic valve or due to rhythm disorders such as atrial fibrillation. It has been seen that even in the patients who do not have any known structural heart disease or rhythm disorder on a routine evaluation with transthoracic echocardiography (TTE) and electrocardiogram (ECG), chances of a cardioembolic event is a possibility that may be difficult to diagnose. As a screening tool, TTE is less sensitive in detecting the cardiac abnormalities. Transesophageal echocardiography (TEE) can improve detection of the cardiac lesions responsible for the cerebrovascular events in this subgroup of patients which can have a long-lasting and important therapeutic impact. Hence, we present here an observational study of TEE findings in young patients (<40 years), without valvular heart disease/prosthetic valves and atrial fibrillation at presentation, presenting with acute ischemic stroke (Tables 1 and 2).

Materials and methods

Inclusion criteria

1. All young patients aged <40 years presenting with acute ischemic arterial stroke to a tertiary care center

Exclusion criteria

1. Previously diagnosed cases of valvular heart disease or prosthetic heart valves
2. Patients with past history of stroke or transient ischemic attack (TIA) or established atrial fibrillation (AF) in the past or at presentation
3. Patients with hemorrhagic stroke on neuroimaging

4. History of illicit drug abuse
5. Patients with connective tissue disorders, human immunodeficiency virus (HIV) infection, and fever at onset suggestive of infective etiology
6. Patients with more than 50% stenosis on carotid Doppler
7. Patients with Glasgow Coma Scale of less than 8 or unwilling/uncooperative to undergo TEE

All consecutive young patients fulfilling the inclusion criteria who presented with sudden onset focal neurological deficit were enrolled in the study. Patients were enrolled from July 2014 to December 2016. All patients underwent urgent neuroimaging (non-contrast computed tomography of the brain) to rule out acute hemorrhage and a carotid Doppler to look for carotid artery stenosis. Patients with carotid artery stenosis of more than 50% were excluded from the study. Patients with established ischemic stroke were initially stabilized in the intensive care unit/high dependency units. A detailed history for associated comorbidities, family history of stroke, past history of similar episode, smoking, alcohol consumption, and other risk factors of stroke was taken. All patients underwent ECG at admission to rule out atrial fibrillation. Initially, a bedside TTE was performed to rule out any valvular heart disease or left atrial/ventricular clots. All patients with normal TTE underwent TEE after initial stabilization under local anesthesia. Patients with normal TEE underwent 24 h holter monitoring to look for any paroxysmal rhythm disorders. Findings of TEE and holter were recorded and analyzed. All patients were screened for risk factors of stroke in the form of hypertension, diabetes, dyslipidemia, antinuclear antibody testing, and vasculitis. Consent was obtained from the patients/next of kin to undergo TEE under local anesthesia. TEE was performed by a designated trained cardiologist using the iE33 Philips echocardiography machine. Ethical clearance was obtained from the institutional ethical committee.

Results

A total of 45 young male patients reported with sudden onset of neurological deficit in the study period. Five patients were excluded from the study, of which three had a valvular heart disease, one had intracerebral hemorrhage, and one had atrial fibrillation on the ECG at presentation. A total of 40 young male patients aged <40 years without valvular heart disease, prosthetic valves, significant atherosclerotic carotid artery disease, and atrial fibrillation at presentation were included in the study. Mean age of the patients was 35.19 (SD $\pm$ 2.99) years. Other baseline characteristics are noted in (Table 1). Of these forty patients, 36 (90%) had middle cerebral artery stroke, three (7.5%) had posterior circulation stroke, and one (2.5%) had anterior circulation stroke. All the patients with normal bedside TTE underwent TEE after stabilization. TEE was preferably performed within the first week of the stroke under local anesthesia by the cardiologist. The mean lag time from the onset of stroke to performing of TEE was 4.75 (SD $\pm$ 1.39) days. TEE abnormalities were noted in total 13 (32.5%) patients in which patent foramen ovale (PFO) was the most common cardiac abnormality in eight (20%) patients followed by left atrial appendage clot in three (7.5%) and atrial septal

Table 1 – Baseline characteristics.

Patient characteristics	Observation	Percentage
Mean age (years)	35.19 (SD $\pm$ 2.99)	
Mean lag time from the onset of stroke to TEE (days)	4.75 (SD $\pm$ 1.39)	
Hypertension	8/40	20%
Dyslipidemia	3/40	7.5%
Impaired glucose tolerance	2/40	5%
Onset at high altitude	8/40	20%
Smoker	26/40	67.5%

SD, standard deviation; TEE, trans-esophageal echocardiography.

Table 2 – Cardiac abnormalities detected on TEE and holter in young patients (<40 years) with acute ischemic strokes.

TEE findings	Patient characteristics	Observation	Percentage
Cardiac abnormalities in young idiopathic arterial stroke patients		17/40	42.5%
TEE findings	Total abnormalities in TEE	13/40	33%
	Patent foramen ovale	8/40	20%
	Left atrial appendage	3/40	7.5%
	Septal aneurysm	2/40	5%
Holter findings	Paroxysmal atrial fibrillation in holter	4/27	14.8%
TEE, trans-esophageal echocardiography.			

aneurysm in two (5%) patients. One patient with atrial septal aneurysm also had sieved septum. Twenty-seven patients (67.5%) were found to have a normal TEE. All the patients with normal TEE underwent holter monitoring, and four of 27 (14.8%) patients were noted to have paroxysmal atrial fibrillation (Table 2). Risk factors for stroke included smoking in 65% (26/40) followed by new onset hypertension and exposure to high altitude in 20% (8/40) each, impaired glucose tolerance in 5% (2/40), and dyslipidemia in 7.5% (3/40). History of alcohol consumption was present in 30% (12/40). No patient was noted to have renal dysfunction. Oral anticoagulation or novel anticoagulants were offered to all the patients with paroxysmal atrial fibrillation and left atrial appendage clot. All the other patients were offered antiplatelet agents. All patients were advised to undergo prothrombotic workup 3–6 months after the acute event was over.

Discussion

Ischemic arterial stroke in young adults is considered to be a catastrophic event, and identifying the etiology remains a diagnostic challenge in number of cases especially in the absence of valvular heart disease, prosthetic valve, and atrial fibrillation.¹ Although stroke in young comprises only 10–15% of all strokes, it has a tremendous economic impact as the victims are disabled in their most productive age group.² Recent studies have shown that there is increasing trend toward stroke in young.³ TEE is now considered a gold standard investigation in evaluation of young patients with embolic stroke of undetermined source (ESUS).⁴ With improvement in diagnostic modalities and widespread availability of echocardiography, PFO as a cause of ESUS is now an emerging area of clinical interest. In a study carried out by Mesa et al., it was noted that PFO was found on TEE in nearly half of the young patients with cryptogenic stroke in young.⁵ In our study too, PFO was the most common structural cardiac abnormality detected in young male patients with ESUS. Similar findings were noted in another study in which cardiac abnormalities on TEE were found in 21.2% of the patients and PFO was the commonest cardiac abnormality in 39.2% of these patients. It is now recommended to include TEE as a regular part of workup in ischemic arterial stroke in young population aged between 15 and 45 years.⁶

The association between ischemic stroke and PFO in young is not clear and is a matter of controversy, but studies have shown that it is much more common in younger patients with idiopathic ischemic arterial stroke.^{7,8} It was also noted that

smoking was the commonest risk factor of ischemic stroke in young patients (55.2%) followed by hypertension (31.4%) and dyslipidemia (27.6%).⁶ In our study also, smoking was the commonest associated risk factor comprising 65% of patients followed by new onset hypertension (20%) and dyslipidemia (7.5%). In a study conducted to compare TEE with TTE in patients with ischemic stroke in sinus rhythm, it was seen that TEE had additional therapeutic implications in about 32% of patients who otherwise had a normal TTE.⁹ Thus, TEE should be included in the regular workup of young patients with ischemic stroke especially in the absence of rheumatic heart disease, atrial fibrillation, and prosthetic valve. In a study carried out by Rus et al., it was noted that in young patients with cryptogenic stroke, TEE abnormality was found in 51% of the patients and led to change in therapeutic management in 47% of the patients.¹⁰ In another comparative study, it was noted that TEE was superior to TTE in detecting potential cardiac source of embolism, but requirement for change in therapy was required in only 7% of the patients.¹¹ In another study conducted on young patients, it was noted that the risk of spontaneous vascular thrombosis including acute arterial ischemic stroke was 30 times higher in high altitude area (HAA) defined as altitude more than 3000 m.¹² In our study, 20% of the patients with acute ischemic arterial stroke came from HAA; however, the association of high altitude and ischemic arterial stroke could not be studied in our patients. As per the existing literature, bubble contrast study using agitated saline under TTE can be used to demonstrate structural abnormalities with right to left shunts which may predispose to paradoxical embolism and cardioembolic stroke, but bubble study may rarely cause ischemic cerebrovascular complications.¹³ Hence, bubble contrast study was not used in our study. On the other hand, TEE is a relatively safe procedure but requires training and expertise. It has been seen that smoking is a very important risk factor for stroke, and the risk of stroke increases by threefold to fourfold in smokers as compared to non-smokers. Exposure to environmental stroke also increases the risk by twofold.¹⁴ In a study carried out by Balci et al., smoking was seen in 37% of patients with stroke in young.¹⁵ In our study, smoking was seen in 65% of patients with stroke in young. Besides smoking, other risk factors that can predispose to stroke in young include hypertension in 45%, dyslipidemia in 35%, and diabetes in 17%. In our study also, newly diagnosed hypertension was the commonest comorbidity noted in 20% of the patients followed by dyslipidemia in 7.5% and impaired glucose tolerance in 5%. None of the patients in our study were found to be diabetic. The incidence of these comorbidities was much less in our study as it was

conducted in young healthy patients who have a healthy lifestyle and undergo regular periodic annual medical checkup. As this study was conducted only in male patients, all other gender-based risk factors including pregnancy and oral contraceptive pills were excluded from this study. The association of high altitude and stress as a cause of arterial strokes could not be established as it is difficult to establish the causation with these factors.

The limitations of our study were non-availability of pro-coagulant workup in all the patients, small sample size, and absence of long-term follow-up. Another limitation was that high altitude as a cause of precipitant of stroke in the patients living at HAA could not be thoroughly evaluated as it is logistically and diagnostically challenging. All the patients with arterial stroke at HAA were immediately deinducted and were managed at an intermediate-level hospital before being further evacuated. The strength of the study is that only young patients with idiopathic arterial strokes were included in the study and that TEE was performed within the first 7 days of onset of the stroke. This was possible as most of the patients were referred early or evacuated by air to the tertiary care center.

Conclusion

Cardiac abnormalities on TEE were noted in 33% (13/40) of young males presenting with acute ischemic stroke. Paroxysmal atrial fibrillation was noted in 14.8% (4/27) of the patients with normal TEE. Thus, probable cardioembolic stroke was responsible for acute ischemic stroke in 44.3% of young patients in the absence of valvular heart disease, prosthetic valves, significant atherosclerotic disease of carotids, and persistent/permanent atrial fibrillation. Smoking was the most common modifiable risk factor noticed in 65% of the patients. Exposure to high altitude and new onset hypertension were noted in 20% of the patients. This study suggests that TEE and holter should be included in the standard protocol of ischemic arterial stroke in young patients without valvular heart disease/prosthetic valve and persistent or permanent atrial fibrillation. This may help in deciding the appropriate therapeutic modality and optimal treatment plan which can prevent recurrent strokes in young patients.

Conflicts of interest

The authors have none to declare.

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