Transesophageal Echocardiography Findings In A Series Of Patients With Brain Stroke Or Transient Ischemic Attack: A Descriptive Analytic Study

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***Abstract*—Background and objective:** brain ischemia is among the most important causes of hospitalization, morbidity and mortality. Brain stroke is a vascular event in brain in which tissue perfusion is impaired. Among cardiac etiologies for brain stroke, patent foramen ovale (PFO), cardiac emboli, atrial fibrillation (AF) and etc. are mentionable. Echocardiography is an applied technique for detecting cardiac etiologies of stroke. In this study we aimed to describe frequency of each abnormal echocardiographic finding in patients with stroke or transient ischemic attack (TIA) referred to Afshar heart center during 3 years.

Materials and methods: this study is a cross-sectional descriptive-analytic study. We enrolled 145 patients with stroke or TIA referred to Afshar heart center during 2014 to 2017 for transesophageal echocardiography (TEE). Patients demographic, past medical history and echocardiographic findings were recorded in a questionnaire. All collected data were entered SPSS 22 software for statistical analysis.

Results: our findings revealed that mean patients age was 50.53±13.01. Among 145 studied patients 88 (60.7%) of them were male. In our study the most common etiology for cardiac emboli was PFO (31%), mitral valve prolapse (19.3%), interatrial septum redundant (18.6%) and aortic atheroma (18.6%) respectively. In our study progressive MS was significantly more in women compared to men and mitral annular calcification, aortic valve sclerosis, aortic atheroma, aortic stenosis and interatrial septum redundant was significantly more frequent in patients above 55.

Conclusion: after this study we concluded that PFO and mitral valve prolapse are the most common cardiac etiologies for stroke detected in TEE.

Keywords: brain ischemia, transesophageal echocardiography, transient ischemic attack, stroke, cerebrovascular accident, patent foramen ovale

Introduction

Brain ischemia is one of the most common causes of hospitalization, morbidity and mortality. Brain ischemia may present as stroke or transient ischemic attack(TIA)(1). Brain stroke is a vascular event which occurs because of impaired brain tissue perfusion and clinical manifestations remain for longer than 24 hours. TIA term is used when the manifestations disappear before 24 hours which is an alarm event for possible brain stroke in future(2-4). Stroke or TIA is diagnosed through clinical presentations by a neurologist and imaging modalities such as brain computed tomography (CT-Scan) or magnetic resonance imaging (MRI)(5).

10% of brain strokes are hemorrhagic and 90% of them are ischemic. Among ischemic stroke cases, 30% of cases occur due to brain vasculature pathology, 30% are because of cardiac emboli and almost 40% are called cryptogenic in which no certain etiology can be defined(6). In so many of patients diagnosed with cryptogenic stroke, finally a cardiac etiology can be found but in recent guidelines there is no concordance about ratio of cardioembolic etiologies explained for cryptogenic stroke(7).

Interatrial communications (atrial septal defect or patent foramen ovale with or without atrial wall aneurysm) can cause stroke followed by paradoxical emboli and elevate the risk of recurrent thromboembolic events(8-10). In clinical evaluation it is not an easy task to diagnose paradoxical emboli(11). In autopsy, patent foramen ovale (PFO) prevalence was evidenced to be around 3.27%(12). In a study it was reported that PFO is more common in patients susceptible for cryptogenic stroke younger than 55, compared to control group(13). Based on this, PFO seems to be a risk factor for ischemic brain events in young patients. In older patients (older than 55) the association of PFO with brain stroke is less pronounced(14).

In this descriptive-analytic study we aimed to report prevalence of abnormal transesophageal echocardiography findings in patients with stroke or TIA in an Iranian population.

Materials and methods

This study is a cross-sectional descriptive-analytic study carried out on 145 consecutive patients with brain stroke or TIA referred to Afshar heart center for transesophageal echocardiography during 2014 till 2017. All patients diagnosed with TIA or stroke were included and only patients that were not available or their medical folder was not accessible were excluded. All patients were aware of the research and signed an informed consent to let their medical information be used for research purposes. This study was designed based on latest Helsinki declaration.

All patients underwent transesophageal echocardiography (TEE) by an expert echocardiography fellowship using Philips EPIQ 7 device and echocardiographic findings were collected in a questionnaire. Recorded echocardiographic findings were as: existence of clot, atrial fibrillation (AF) or flutter rhythm, evidences of myocardial infarction (MI) with regional wall motion abnormality (RWMA), cardiomyopathy (EF<40%), left ventricle (LV) aneurysm, non LV compaction, left atrium appendage (LAA) clot, LAA velocity less than 20cm/sec, smoky pattern, left side mechanical or biological valve, vegetation, non-bacterial thrombotic endocarditis (NBTE), mitral valve prolapse (MVP) (billowing or not), mitral annulus calcification (MAC), mitral stenosis (severe or progressive), aortic atheroma, aortic stenosis (AS), aortic valve sclerosis (AVS), Lambl's excrescence, intra cardiac devices, PFO (high risk, low risk or not), atrial septal aneurysm, atrial septal defect (ASD), interatrial septum redundant and intra cardiac tumors. Severe mitral stenosis (MS) was defined as mitral valve area (MVA) less than 1.5 cm^2 and progressive MS was defined as MVA between 1.5 cm^2 and 2 cm^2. High risk PFO was also defined as 1) severe bubble passage without maneuver, 2) severe bubble passage with maneuver along with one of these findings: Eustachian valve, Chiari network, PFO larger than 5 mm, evidences of septum redundant and atrial septal aneurysm, 3) mild bubble passage with maneuver along with 2 of mentioned findings and 4) no bubble passage with maneuver along with 3 of mentioned findings.

Other demographic and past medical information such as age, gender and atherosclerosis risk factors such as diabetes mellitus (DM), hypertension (HTN), hyperlipidemia (HLP), smoking and positive familial history (FH) were also recorded in a separate questionnaire.

All collected data were finally entered into SPSS Ver. 22 and for descriptive analysis, percentage, mean ± standard deviation and frequency were used. For analytic analysis Chi-Square test was used and in all tests P-Value<0.05 was considered as statistically significant. The results are presented in form of descriptive and frequency tables and supplementary information are presentable at any time by contacting corresponding author.

Results

This descriptive study of us was designed to publish statistical information about cardiac sources of emboli in patients with TIA or stroke undergoing transesophageal echocardiography in an Iranian population during 3 years.

In our study average age of participants was 50.53±13.01, ranged between 16 and 85. Among 145 studied patients 88 (60.7%) of them were male and 57 (39.3%) of them were female.

The complete percentage and number of each variable measured in our study is presented in table No.1 below:

Variable	Variable Status	
	YES	NO
DM	24 (16.6%)	121 (83.4%)
HTN	54 (37.2%)	91 (62.8%)
HLP	39 (26.9%)	106 (73.1%)
Smoking	20 (13.8%)	125 (86.2%)
FH	44 (30.3%)	101 (69.7%)
Existence of clot	3 (2.1%)	142 (97.9%)
AF or flutter rhythm	0 (0.0%)	145 (100%)
Evidences of MI with RWMA	6 (4.1%)	139 (95.9%)
Cardiomyopathy (EF<40%)	4 (2.8%)	141 (97.2%)
LV aneurysm	1 (0.7%)	144 (99.3%)
Non LV compaction	4 (2.8%)	141 (97.2%)
LAA clot	0 (0.0%)	145 (100%)
LAA velocity less than 20 cm/sec	0 (0.0%)	145 (100%)
Smoky pattern	3 (2.1%)	142 (97.9%)
Left side mechanical valve	1 (0.7%)	144 (99.3%)
Left side biological valve	0 (0.0%)	145 (100%)
Vegetation	0 (0.0%)	145 (100%)
NBTE	0 (0.0%)	145 (100%)
MVP	28 (19.3%)	117 (80.7%)
Mitral annular calcification	11 (7.6%)	134 (92.4%)
MS	7 (4.8%)	138 (95.2%)
Aortic atheroma	27 (18.6%)	118 (81.4%)
AS	4 (2.8%)	141 (97.2%)
AVS	3 (2.1%)	142 (97.9%)
Lambl's excrescence	2 (1.4%)	143 (98.6%)
Intra cardiac device	2 (1.4%)	143 (98.6%)
Atrial septal aneurysm	8 (5.5%)	137 (94.5%)
ASD	2 (1.4%)	143 (98.6%)
Intreratrial septum redundant	27 (18.6%)	118 (81.4%)
Cardiac tumor	2 (1.4%)	143 (98.6%)
PFO	45 (31%)	100 (69%)

Table 1 Frequency table of all measured variables in this study

In this population, 2 patients (1.4%) had smoky pattern in LV and this pattern was seen in left atrium (LA) or LAA only in 1 patient (0.7%) and 142 of participants (97.9%) did not have this pattern.

MVP was seen in 13 patients (9%) without billowing and 15 patients (10.3%) had MVP with billowing and 117 patients (80.7%) did not have any sign of MVP.
1 patient (0.7%) had severe MS, 6 patients (4.1%) of patients had progressive MS and 138 of patient (95.2%) did not have any sign of MS.
Based on PFO, in this study 28 patients (19.3%) were involved with high risk PFO, 17 patients (11.7%) of them had low risk PFO and 100 patients (69%) did not have PFO.
In this study we also evaluated the association between all measured variables with gender and age using Chi-Square test.
Based on the results of Chi-Square tests, smoking and MS both were significantly different between genders and it means that smoking was significantly more in men and progressive mitral stenosis was significantly higher in women compared to men.
In our study prevalence of DM, HTN, HLP, mitral valve calcification, aortic atheroma, AVS, AS and atrial septum redundant were significantly recorded to be higher in old patients (55-85) compared to young patients (16-54).
The results of assessing different variables based on age and gender are summed up in table No.2 below. Detailed descriptive statistics and frequency tables are available to be presented at any time to interested researchers by contacting corresponding author:

Variable Based on	Age	Gender
DM	P-Value=0.003	P-Value=0.842
HTN	P-Value=0.001	P-Value=0.786
HLP	P-Value=0.0001	P-Value=0.522
smoking	P-Value=0.359	P-Value=0.0001
FH	P-Value=0.934	P-Value=0.529
Existence of clot	P-Value=1.000	P-Value=0.279
Evidences of MI with RWMA	P-Value=1.000	P-Value=0.404
Cardiomyopathy (EF<40%)	P-Value=0.618	P-Value=0.154
LV aneurysm	P-Value=1.000	P-Value=1.000
Non LV compaction	P-Value=1.000	P-Value=1.000
Smoky pattern	P-Value=0.441	P-Value=0.520
Left side mechanical valve	P-Value=0.359	P-Value=1.000
MVP	P-Value=0.714	P-Value=0.682
Mitral annular calcification	P-Value=0.046	P-Value=0.201
MS	P-Value=0.480	P-Value=0.035
Aortic atheroma	P-Value=0.0001	P-Value=0.114
AS	P-Value=0.015	P-Value=0.154
AVS	P-Value=0.044	P-Value=1.000
Lambl's excrescence	P-Value=0.537	P-Value=1.000
Intra cardiac device	P-Value=0.537	P-Value=1.000
Atrial septal aneurysm	P-Value=0.921	P-Value=1.000
ASD	P-Value=0.537	P-Value=0.520
Interatrial septum redundant	P-Value=0.018	P-Value=0.418
Cardiac tumor	P-Value=1.000	P-Value=1.000
PFO	P-Value=0.998	P-Value=0.213

Table 2 Association of studied variables with age and gender

Discussion

Brain ischemia is one of the most common and most important causes of hospitalization, morbidity and mortality. Brain ischemia can happen in both stroke and TIA settings(1). Brain stroke is a vascular event in which brain tissue perfusion is impaired and the symptoms last for more than 24 hours. Based on available statistics, cardiac emboli and events are responsible for 30% of brain stroke cases(2). In numerous patients susceptible for cryptogenic stroke, finally a cardiac etiology can be explained but in recent guidelines there is no agreement on frequency of cryptogenic strokes followed by cardioembolic events(7). Interatrial communications (ASD and PFO, with or without atrial wall aneurysm) can lead to paradoxical stroke and increased risk of recurrent thromboembolic events(8-10). In Knebel et al. study, it was revealed that PFO was recorded more in patients with cryptogenic stroke compared to patients with a known etiology for stroke(15). Echocardiography is one of the most important evaluations in patients with stroke to find any possible cardiac source.
Considering antonymous results about prevalence of cardiac emboli and associated cardiac factors in patients with brain ischemia, in this descriptive study we aimed to report frequency of different cardiac etiologies detected via TEE in patients with stroke or TIA.
The average age of studied population was 50.53+13.01 ranged between 16 and 83 and 93 patients were aged between 16 and 54 (considered as young) and 52 patients aged between 55 and 85 (considered as old). Based on our results and other similar studies performed on patients with stroke and TIA, it can be interpreted that brain stroke mostly happens in 4th decade of life and frequency of patients below 55 is more compared to older patients(15-18).
Based on gender distribution, in our study which was performed on 145 patients, 88 (60.7%) of them were men and 57 (39.3%) of them were women. In a study performed by Dubrava et al. it was also reported that 70% of patients were men which is in accordance with our results(18) but in Shyu et al. study women were more compared to men (53% vs 47%)(16). It seems that stroke is more common in men but effect of regional and race differences between people should be in mind.
Considering the fact of higher sensitivity of TEE which was also performed by an echocardiography fellow ship in our study, we reported that the most common cardiac etiologies were PFO (31%), MVP (19.3%), interatrial septum redundant (18.6%) and aortic atheroma (18.6%), respectively. A previous autopsy-based study reported that PFO prevalence is 3.27% in general population(12).
In the study performed by Dubrava et al. it was reported that only in 21.6% of patients a source of emboli was detected and among those patients, PFO (53.7%) was the most common etiology and then aortic atheroma (53.7%) and other etiologies such as smoky pattern, atrial septum aneurysm and etc. were mentioned among etiologies. In this study TEE was

unable to detect source of emboli in 26.1% of patients(18).
In a study performed by Palazzuoli et al. it was also reported that PFO (19%) is the most frequent cardiac etiology for stroke(19).
Gutterman et al. on 1993 reported that they could find the source of emboli in 30% of patients. Cardiac etiologies that were explained using transthoracic echocardiography (TTE) and TEE were intra cardiac thrombosis, cardiac tumors, aortic atheroma and etc. They reported that TEE is prior to TTE in young patients, in patients without cerebrovascular disorders, in patients with recurrent embolic events and also when posterior chambers such as LA and LAA are susceptible(20). Priority of TEE over TTE was also confirmed in other studies(4, 16, 19, 21, 22).
There was a study performed on 2011 by Yoon et al. on treatment of PFO as the most common etiology of cardiac emboli in patients with stroke, and the researchers included 16 patients with PFO with at least one episode of cryptogenic stroke and they concluded that PFO repair is a safe treatment strategy in preventing thromboembolic events(23). Their study included a small study population and their follow up was not long enough, thus randomized clinical trials are needed for better evaluation.
In present study we did not find any difference in PFO prevalence based on age but other researchers have reported different results. A study reported that PFO is more common in patients susceptible for cryptogenic stroke and younger than 55(13), and PFO is considered as a risk factor for ischemic brain events in young patients. The association of PFO with stroke is less pronounced in older patients(14).
In a study performed by Mesa et al. it was evidenced that prevalence of PFO associated with atrial septal aneurysm in cryptogenic stroke patients older than 55 is similar to patients younger than 55. They concluded that prevalence of PFO associated with atrial septal aneurysm in patients older than 55 with a detected etiology for stroke was higher compared to cryptogenic stroke patients(17).
Knebel et al. reported that there is an association between PFO and cryptogenic stroke in both age groups and their data showed that paradoxical emboli is an important etiology in both age groups(15).
Overall it can be said that based on the results of our study and other investigations, PFO is the most common echocardiographic finding in patients with stroke, and TEE has a high accuracy in detecting PFO and other cardiac emboli etiologies.
It is suggested that in future studies researchers focus on diagnostic value of TEE (sensitivity, specificity, positive predictive value and negative predictive value) for detecting cardiac source of emboli in patients with ischemic brain stroke.

Conclusion

Based on the results we found, it can be concluded that the most common etiologies for cardiac emboli which are detected in TEE are PFO, MVP, interatrial septal redundant and aortic atheroma.
In our studied population, only MS was associated with gender and MS was more frequently recorded in women.
Based on our findings, Mitral annular calcification, AVS, aortic atheroma and interatrial septum redundant are associated with age and are recorded more in patients above 55 and it means that such patients should be evaluated more accurate to find any possible cardiac source of cardiac emboli in ischemic brain stroke.

References

1. Amarenco P. Cryptogenic stroke, aortic arch atheroma, patent foramen ovale, and the risk of stroke. Cerebrovascular diseases. 2005;20(Suppl. 2):68-74.
2. Sachdev PS, Brodaty H, Valenzuela M, Lorentz L, Looi J, Wen W, et al. The neuropsychological profile of vascular cognitive impairment in stroke and TIA patients. Neurology. 2004;62(6):912-9.
3. Sanna T, Diener H-C, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al. Cryptogenic stroke and underlying atrial fibrillation. New England Journal of Medicine. 2014;370(26):2478-86.
4. de Bruijn SF, Agema WR, Lammers GJ, van der Wall EE, Wolterbeek R, Holman ER, et al. Transesophageal echocardiography is superior to transthoracic echocardiography in management of patients of any age with transient ischemic attack or stroke. Stroke. 2006;37(10):2531-4.
5. Lamy C, Giannesini C, Zuber M, Arquizan C, Meder J, Trystram D, et al. Clinical and imaging findings in cryptogenic stroke patients with and without patent foramen ovale: the PFO-ASA Study. Stroke. 2002;33(3):706-11.
6. Homma S, Di Tullio MR, Sacco RL, Mihalatos D, Li Mandri G, Mohr J. Characteristics of patent foramen ovale associated with cryptogenic stroke. A biplane transesophageal echocardiographic study. Stroke. 1994;25(3):582-6.
7. Carroll JD, Saver JL, Thaler DE, Smalling RW, Berry S, MacDonald LA, et al. Closure of patent foramen ovale versus medical therapy after cryptogenic stroke. New England Journal of Medicine. 2013;368(12):1092-100.
8. Mas J-L, Arquizan C, Lamy C, Zuber M, Cabanes L, Derumeaux G, et al. Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both. New England Journal of Medicine. 2001;345(24):1740-6.
9. Ghosh S, Ghosh AK, Ghosh SK. Patent foramen ovale and atrial septal aneurysm in cryptogenic stroke. Postgraduate medical journal. 2007;83(977):173-7.
10. Wu LA, Malouf JF, Dearani JA, Hagler DJ, Reeder GS, Petty GW, et al. Patent foramen ovale in cryptogenic stroke: current understanding and management options. Archives of internal medicine. 2004;164(9):950-6.
11. Attaran RR, Ata I, Kudithipudi V, Foster L, Sorrell VL. Protocol for optimal detection and exclusion of a patent foramen ovale using transthoracic echocardiography with agitated saline microbubbles. Echocardiography. 2006;23(7):616-22.
12. Hagen PT, Scholz DG, Edwards WD, editors. Incidence and size of patent foramen ovale during the first

10 decades of life: an autopsy study of 965 normal hearts. Mayo Clinic Proceedings; 1984: Elsevier.

13. Lechat P, Mas J, Lascault G, Loron P, Theard M, Klimczac M, et al. Prevalence of patent foramen ovale in patients with stroke. New England Journal of Medicine. 1988;318(18):1148-52.

14. Overell J, Bone I, Lees K. Interatrial septal abnormalities and stroke: a meta-analysis of case-control studies. Neurology. 2000;55(8):1172-9.

15. Knebel F, Masuhr F, von Hausen W, Walde T, Dreger H, Raab V, et al. Transesophageal echocardiography in patients with cryptogenic cerebral ischemia. Cardiovascular ultrasound. 2009;7(1):15.

16. Shyu K-G, Chen J-J, Huang Z-S, Hwang J-J, Lee T-K, Kuan P, et al. Role of transesophageal echocardiography in the diagnostic assessment of cardiac sources of embolism in patients with acute ischemic stroke. Cardiology. 1994;85(1):53-60.

17. Mesa D, Ruiz M, Delgado M, de Lezo JS, Pan M, Tejero I, et al. Prevalence of patent foramen ovale determined by transesophageal echocardiography in patients with cryptogenic stroke aged 55 years or older. Same as younger patients? Revista Española de Cardiología (English Edition). 2010;63(3):315-22.

18. Dubrava J, Garay R. The role of transesophageal echocardiopgraphy in detection of cardiogenic and aortic sources of embolism in stroke and transient ischaemic attacks. Vnitrni lekarstvi. 2006;52(2):144-51.

19. Palazzuoli A, Ricci D, Lenzi C, Lenzi J, Palazzuoli V. Transesophageal echocardiography for identifying potential cardiac sources of embolism in patients with stroke. Neurological Sciences. 2000;21(4):195-202.

20. GUTTERMAN DD, AYRES RW. Use of echocardiography in detecting cardiac sources of embolus. Echocardiography. 1993;10(3):311-20.

21. Marx P, Schmacher H, Hartmann A, Blum S, Schultheiss H, Völler H, et al. Diagnostic advantage by transthoracic and transesophageal echocardiography in acute ischemic infarct. A contribution to indications for transesophageal echocardiography. Fortschritte der Neurologie-Psychiatrie. 1996;64(8):307-11.

22. Cujec B, Polasek P, Voll C, Shuaib A. Transesophageal echocardiography in the detection of potential cardiac source of embolism in stroke patients. Stroke. 1991;22(6):727-33.

23. Yoon JH, Kim JS, Lee DH, Shim EJ, Lee SY, Min KS, et al. Intermediate and long-term results of transcatheter closure of patent foramen ovale using the Amplatzer patent foramen ovale occluder: one case of pulmonary embolism irrespective of patent foramen ovale closure. Korean circulation journal. 2011;41(7):356-62.