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Left atrial dilatation in undetermined group according to TOAST classification: echocardiographic assessment of stroke patients

Ahu TAKOĞLU[1,*] , Ufuk CAN[2]

[1]Department of Neurology, Keçiören Hospital, Ankara, Turkey

[2]Department of Neurology, Faculty of Medicine, Başkent University, Ankara, Turkey

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Aim: To investigate the left atrial dilatation in an undetermined etiological group according to Trial of Org 10172 in Acute Stroke Treatment (TOAST) and to evaluate the relationship between left atrial dilatation and stroke volume and localization.

Materials and methods: Files of patients admitted to our hospital (2000–2010) with acute ischemic stroke diagnosis were investigated. The size of their left atrium was registered using the data from transthoracic echocardiogram. Lesion size and localization were registered using brain MRI. Stroke etiology was categorized according to TOAST classification. The relationship between left atrial dilatation and stroke volume and localization in the undetermined group was investigated.

Results: It was detected that 47% patients had left atrial dilatation. A significant difference was observed in the occurrence of left atrium dilatation for the undetermined group compared to the other groups and infarct volume was found to be larger in patients having left atrial dilation ($P < 0.038$).

Conclusion: Left atrial dilatation is an important etiological factor in the undetermined-cause group and it also affects stroke volume.

Key words: Left atrium, stroke, echocardiography

1. Introduction

Cerebrovascular diseases constitute the most common category of neurological diseases. Large vessel atherosclerosis, arterial thrombus formation, cardioembolism, and atherosclerosis in small vessels take place in ischemic stroke etiology. For less than 5% of ischemic stroke cases, etiological factors like hereditary diseases, congenital vessel diseases, primary and secondary vasculitis of central nervous system, cerebral amyloid angiopathy, mitochondrial diseases, and blood diseases are detected.

Cardiac strokes constitute 15%–20% of all ischemic strokes (1). Cardioembolic strokes have a higher repetition and mortality rate considering the long-term results in comparison to other stroke subcategories.

In various studies, the requirement to examine especially the left appendix for spontaneous echo contrast and thrombus has been stated (2). It was also noted that transesophageal echocardiogram has an important role in the detection of those (3). It has been found that the left atrial dilation is more common in patients with atrial fibrillation (AF) (4). The annual risk of stroke caused by AF varies between 3% and 8% (5).

Certain clinical features are suggestive of cardioembolic infarction, including sudden onset to maximal deficit, decreased level of consciousness at onset, Wernicke's aphasia or global aphasia without hemiparesis, a Valsalva maneuver at the time of stroke onset, and cooccurrence of cerebral and systemic emboli (6,7).

The goal of this study is to determine the frequency of left atrial dilatation in stroke patients and to search for the effect of atrial dilation on stroke volume and localization.

2. Materials and methods

Files of 2380 patients who were admitted to the Neurology Department of Başkent University Hospital between 2000 and 2010 were investigated. Of those, 330 were included in the study since their medical charts included the required amount of medical data for the target study, brain images, and echocardiography data.

Patient complaints, personal history and family history, previous stroke history, risk factors, and electrocardiography (ECG), echocardiography, and Holter findings were taken into consideration while patient files were being investigated.

* Correspondence: ahukoctas@yahoo.com

All neuroradiological analyses that were related with diagnosis and etiology (brain computed tomography (CT), brain magnetic resonance imaging (MRI), diffusion MRI, brain MRI angiography, carotid MRI angiography), blood tests (lipid profile, homocysteine levels), ECGs, echocardiographies, carotid Doppler ultrasonographies, and 24-h ECGs (Holter) in selected patients were evaluated.

Radiographies of patients with stroke diagnosis were examined. Patients with brain MRI and diffusion MRI were included in the study. Patients with only brain CT results were excluded.

Patients with ischemic stroke were taken into the study by examining brain MR images. Volumes of the biggest lesions were measured by examining axial cross-sections on the printed copies of diffusion MR images by using the rectangular estimation of morphometric volume (largest diameter × depth × section thickness (0.5 cm)) (8). Infarct locations were classified as anterior cerebral artery (ACA), middle cerebral artery (MCA), posterior cerebral artery (PCA), thalamic, anterior choroidal, cerebellar, and brain stem.

Using clinical data and radiological images, patients were classified into 5 groups following the TOAST classification system: large-artery atherosclerosis (LAAS), cardioembolic infarct (CEI), lacunar infarct (LAC), stroke of other determined origin (ODE), and stroke of undetermined origin (UDE) (9). Patients having stenosis in the carotid vertebral system according to carotid Doppler and carotid MR angiography findings were included in the atherosclerosis group. Patients with atrial fibrillation according to Holter and ECG results were included in the cardioembolic group. Patients having no atrial fibrillation or atherosclerotic vascular disease were included in the undetermined group. Patients showing no stroke symptoms and having small infarcts (0.2 to 20 mm in diameter) were included in the lacunar group. Patients having other stroke etiology like hematological disease, congenital vessel disease, primary and secondary vasculitis of the central nervous system, cerebral amyloid angiopathy, and mitochondrial diseases were included in the other determined origin group.

Echocardiography results of patients were analyzed to determine whether left atrial expansion existed. Left atrium diameter were assessed statistically. Left atrial enlargement was classified as mild (left atrial diameter: 4.1–4.6 cm in men or 3.9–4.2 cm in women), moderate (4.7–5.1 cm in men or 4.3–4.6 cm in women), or severe (≥5.2 cm in men or 4.7 cm in women) in accordance with the recommendations of the American Society of Echocardiography (10). The cut-off threshold value was found to be 4 cm and diameter values above that threshold were considered to represent left atrium expansion.

The study was presented to the ethics board and the board gave approval for the study.

SPSS 11.5 was used for statistical analysis. Continuous variables were represented as mean ± standard deviation and median; categorical variables were represented as numbers and percentages. The Mann–Whitney U Test was used to compare continuous variables and the Kruskal–Wallis Test was used to compare categorical variables. The chi-square test was used to define the differences between groups. Statistical significance level was set to $P < 0.05$.

3. Results

In this study, 330 (167 male, 163 female) patients treated in our department were evaluated. It was seen that the most common risk factor was hypertension, with a rate of 74.5% when the risk factors of patients were analyzed. The second most common risk factor was diabetes mellitus, at 28.2%. and the third was coronary arterial disease, at 25.5%.

When distribution of patients according to infarct localization was investigated, it was seen that 7 people had ACA (2.1%), 210 people had MCA (63.6%), 25 people had PCA (7.6%), 9 people had thalamic (2.7%), 7 people had anterior choroidal (2.1%), 20 people had cerebellar (6.1%), 31 people had brain stem (9.3%), and 21 people (6.3%) had infarct in more than 1 area (Figure 1).

According to the investigation done by TOAST classification, LAAS in 48 patients (14.5%), CEI in 83 patients (25.2%), and LAC in 49 patients (14.8%) were noted. Cause could not be determined in 125 patients (37.9%) and multiple causes were determined in 25 patients (7.6%) (Figure 2).

According to transthoracic echocardiogram (TTE) findings, the cause of cardioembolic stroke was primarily left ventricular dysfunction at a rate of 51.6% (patient group whose ejection fraction was below 50%), while 14.5% of patients had AF, 2.1% of patients had thrombus, and 1.2% of patients had valve replacement (Figure 3).

According to TTE findings on middle and undefined risk factors, 79% of patients had left ventricular concentric hypertrophy, 46.7% of patients had left atrial dilation, 43% of patients had calcified aorta, 18.2% of patients had mitral annular calcification, and 1.2% of patients had septal hypertrophy (Figure 4).

In our study, it was seen that 154 patients had left atrial dilation when the relationship between left atrial dilation and infarct volume (which is defined as middle/undefined risk factor) was analyzed. Infarct volume was found to be larger on a statistically significant level for the patients with left atrial dilation ($P < 0.038$) (Table 1).

When the frequency of left atrial dilatation in the undetermined group was analyzed (Table 2), the existence of left atrial dilatation in the cardioembolic and undetermined groups was found to be significantly high ($P < 0.0001$) compared to other groups according to TOAST classification.

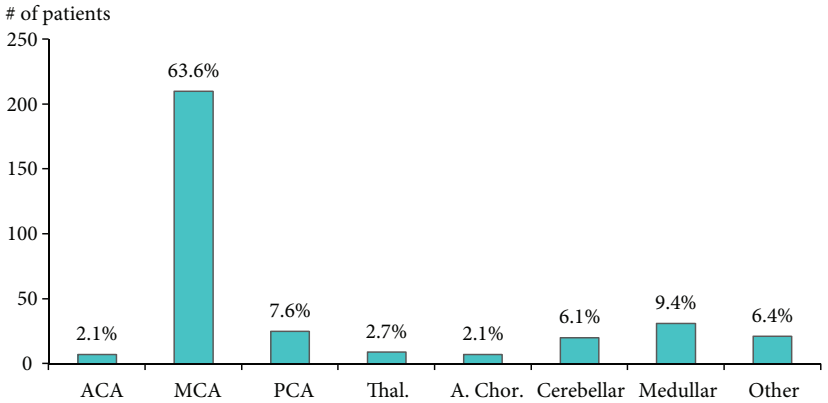

Figure 1. Distribution of patients according to infarct localization. ACA: Anterior cerebral artery, MCA: middle cerebral artery, PCA: posterior cerebral artery, Thal.: thalamic , A. Chor.: anterior choroidal.

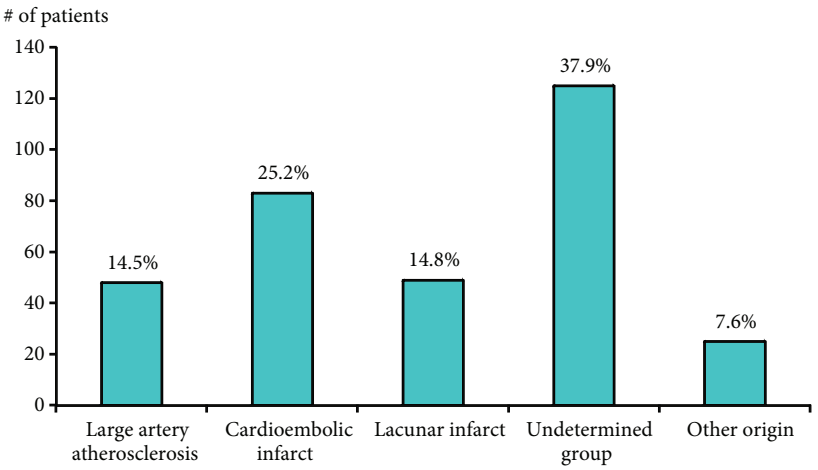

Figure 2. Distribution of patients according to TOAST classification.

No difference was detected statistically for infarct localization in patients who had left atrial dilatation (χ^2 = 4.405, P = 0.732) (Table 3).

According to TOAST classification, left atrium dilation was most frequent in the cardioembolic group, followed by the undetermined cause group.

4. Discussion

Stroke is the world's third most common cause of death behind diseases of the heart and cancer (11). Ischemic stroke, which has an increasing incidence rate with age, is a complex multifactorial disorder that is affected by environmental and genetic factors (12). Considering the biological and socioeconomic damage of stroke, it is essential to determine stroke risk factors in detail and take precautions to decrease the prevalence and incidence of stroke.

Twenty percent of ischemic strokes have cardiological origins. Cardioembolic strokes usually have more severe clinical status and a higher risk of recurrence in the short term compared to other stroke groups (13,14). Echocardiography serves as the cornerstone in evaluating patients who may have had a cardioembolic stroke (15).

Although there are many studies on echocardiogram findings and acute stroke diagnosis, they were all focused on echocardiogram findings and cause of stroke (16,17). Relationship between echocardiogram findings and infarct localization and volume has been investigated for the first time in this study. In addition, while there are many studies on atrial septal defect (18,19) and patent foramen ovale (20–22), which are echocardiogram findings, and strokes with undetermined cause, the number of studies on the relationship between medium uncertain risk factors and acute strokes of undetermined cause is very small.

The reason for having a high number of patients in the undetermined stroke group in our study is the inclusion of patients without AF and LAAS to this group. In these patients there are additional etiological risk factors.

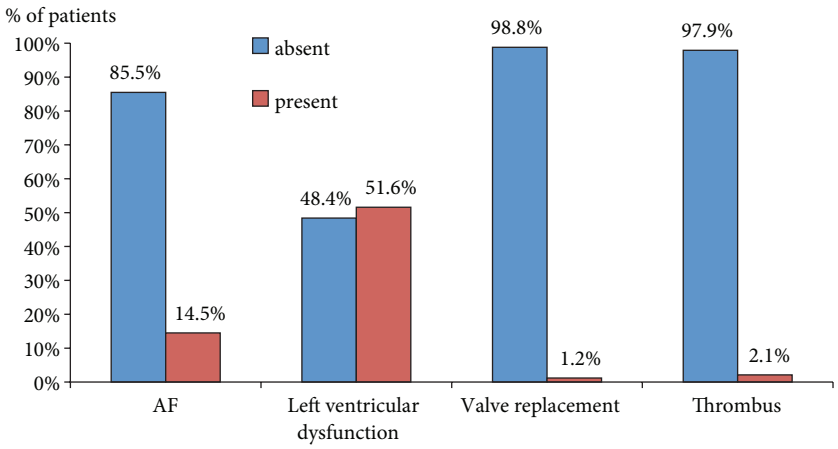

Figure 3. Cause of cardioembolic stroke according to TTE. AF: Atrial fibrillation.

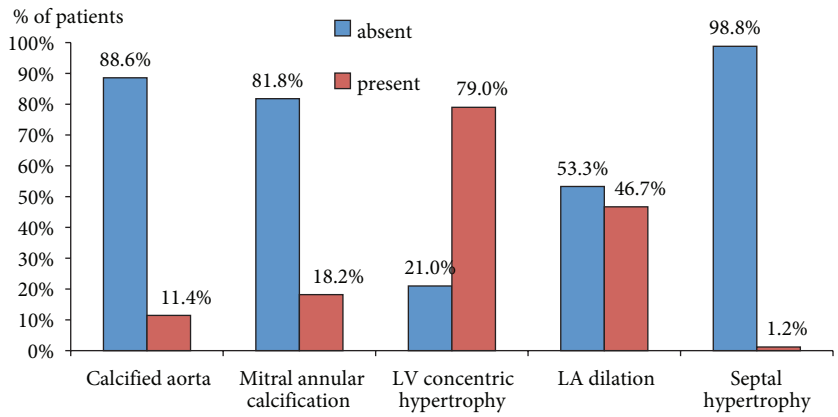

Figure 4. Distribution of patients with middle/undefined risk factors. LV: Left ventricular, LA: left atrial.

It is thought that left atrial dilatation is related with poor clinical course such as cardiac failure, AF, or stroke development (23–25). The relationship of left atrial dilatation and stroke has been supported by some studies, although in some studies no relationship with stroke was found.

Patients that were involved in the Atherosclerosis Risk in Communities (ARIC) study were taken into the scope of study that was done by Nagarajarao et al. (26). The study was done among 1886 patients. At the end of the study, it was found that left atrial dilatation increased stroke and death risk, besides many other cardiovascular risks. Meanwhile, 472 people were included in the study done by Kim et al. Seventy-five people had experience a stroke for the first time and 397 healthy people were taken as he control group. At the end of the study, a significant relationship between stroke frequency and left atrial dilatation existence was found. It was emphasized that left atrial dilatation existence should be underlined in patients with sinus rhythm (27).

A study done by Barnes et al. involved 1554 patients retrospectively. Patients did not have previously known AF. As a result of this study, left atrium volume was found to be an independent risk factor in patients not having AF previously and having stroke for the first time. In addition, it was reported as an independent risk factor for risk of death (28).

Table 1. Infarct volumes according to left atrium diameter.

	Infarct volume Mean ± SD [Median (min–max)]
With atrial dilatation (left atrium diameter of >4 cm)	177.16 ± 29.36 [4.91 (0.02–278.4)]
Without left atrial dilatation (left atrium diameter of <4 cm)	155.3 ± 29.41 [1.96 (0.03–158.4)]

Table 2. Frequency of left atrial dilatation occurrence according to TOAST. LAAS: Large-artery atherosclerosis, CEI: cardioembolic infarct, LAC: lacunar infarct, UDE: undetermined origin.

	LAAS	CEI	LAC	UDE
Number of patients that do not have left atrial dilatation	36	17	35	82
% of total	10.9%	5.1%	10.6%	24.8%
% in TOAST group	75%	20.5%	71.4%	65.6%
Number of patients that have left atrial dilatation	12	66	14	43
% of total	3.6%	20%	4.2%	13%
% in TOAST group	25%	79.5%	28.6%	34.4%

Table 3. Infarct location in patients with and without left atrial dilatation. ACA: Anterior cerebral artery, MCA: middle cerebral artery, PCA: posterior cerebral artery.

Infarct location	Left atrial dilatation			
	Absent		Present	
	Number of patients	%	Number of patients	%
ACA	4	2.3%	3	2.0%
MCA	110	62.1%	100	65.4%
PCA	15	8.5%	10	6.5%
Thalamic	7	4.0%	2	1.3%
Choroidal	3	1.7%	4	2.6%
Cerebellar	11	6.2%	9	5.9%
Medullar	18	10.2%	13	8.5%
Other	9	5.1%	12	7.8%
Total	177	100.0%	153	100.0%

A study by Benjamin et al. included 1371 male patients and 1728 female patients. Stroke was encountered in 64 males and 73 females at the end of 8 years of observation. At the end of the study, it was stated that the diameter of the left atrium had a correlation with stroke risk in males and was also correlated with death risk in both sexes. The mechanism of this increased risk could not be determined precisely; it was assumed to be multifactorial (29).

In our study, different than these other studies, infarct volume and location were examined in patients with left atrial dilatation, and it was seen that infarct volume was higher in patients that had left atrial dilatation. Left atrial dilatation should be checked in infarcts without any known cause and left atrial dilatation should be considered as a cardioembolic risk factor.

When TOAST classification was followed, it was seen that left atrial dilatation was most frequent in the cardioembolic group. This was an expected situation since left atrial dilatation was observed together with AF in the cardioembolic group. However, left atrial dilatation had the second highest frequency in the undetermined cause group, after the cardioembolic group, which was a surprising finding and implies that having only left atrial dilatation in the undetermined cause group should be evaluated as a risk factor.

Studies investigating the relationship between left atrial dilatation and stroke can be performed on larger patient groups and for longer time periods in the future; thus, it might be possible to start protective treatment earlier. It is important to know under which risk conditions the treatment process should be started in order to decrease the death and disability incidences caused by stroke.

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