Original Article

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Differential Associations Between Left Atrial Volume Parameters and Ischemic Stroke Subtypes

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Abstract

Aim: An increase in left atrial diameter (LAD) is commonly used to differentiate cardioembolic stroke from other ischemic stroke subtypes. We investigated whether echocardiographic volume-indexed parameters beyond the routinely used LAD could also be used to differentiate cardioembolic from atherothrombotic ischemic stroke.

Methods: In this single-center retrospective cross-sectional study, 74 patients with confirmed ischemic stroke were classified as having cardioembolic (n=33) or atherothrombotic stroke (n=41) based on neuroimaging, clinical assessment, and cardiac rhythm monitoring. Baseline demographics, National Institutes of Health Stroke Scale (NIHSS) scores, modified Rankin Scale (mRS) outcomes, and echocardiographic measurements—including left atrial diameter/height (LAD/H), left atrial diameter/body surface area (LAD/BSA), left atrial volume index (LAVi), interventricular septal thickness, and left ventricular (LV) posterior wall thickness—were recorded. Receiver operating characteristic curve analysis was conducted to assess the discriminative performance of left atrial (LA) parameters.

Results: The cardioembolic group demonstrated significantly higher NIHSS scores and worse follow-up mRS outcomes compared with the atherothrombotic group (p=0.011). Echocardiography revealed elevated values of LAD (p<0.001), LAD/H (p<0.001), LAD/BSA (p=0.004), and LAVi (p=0.004) in patients with cardioembolic stroke, while interventricular septum and LV posterior wall thicknesses showed no significant intergroup differences. Receiver operating characteristic analysis identified LAVi, LAD/H, LAD/BSA, and LAD as significant discriminators. Optimal thresholds included LAVi >42 mL/m², LAD/BSA >21.59 mm/m², and LAD/H >0.23 mm/cm. Pairwise comparisons showed no significant differences between LAD and these echocardiographic markers in discriminating cardioembolic from atherothrombotic stroke (p>0.05).

Conclusion: Indexed LA measurements, particularly LAVi, LAD/H, and LAD/BSA enhance discrimination between cardioembolic and atherothrombotic stroke and may improve routine echocardiographic evaluation.

Keywords: Stroke, cardioembolic, ischemic, echocardiography, left atrium, left atrial volume

Introduction

Ischemic stroke is a heterogeneous clinical entity comprising several subtypes, most prominently cardioembolic and atherothrombotic strokes, each with distinct pathophysiological mechanisms and therapeutic implications (1). Accurate identification of stroke subtype is essential, as secondary prevention strategies—particularly antithrombotic and anticoagulant therapies—are largely determined by the underlying etiology (1,2). Cardioembolic stroke is commonly related to structural or functional

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cardiac abnormalities, whereas atherothrombotic stroke is typically associated with advanced vascular stenosis. In recent years, the concept of atrial cardiomyopathy has emerged, emphasizing the role of atrial structural and functional remodeling as a potential contributor to ischemic stroke, independent of atrial fibrillation (AF) (3).

Left atrial (LA) enlargement, a hallmark of atrial remodeling, has been consistently associated with adverse cardiovascular outcomes, including stroke and all-cause mortality, independent of traditional vascular risk factors (2,3). Transthoracic echocardiography remains the most widely available imaging modality for the assessment of LA size in routine clinical practice (4,5). Although cardiovascular magnetic resonance is considered the gold standard for quantifying cardiac chamber volumes, echocardiographic indices, such as left atrial diameter (LAD) and left atrial volume index (LAVi), serve as readily identifiable and practical markers of atrial cardiomyopathy (6). Left atrial volume index, in particular, reflects the severity and chronicity of diastolic dysfunction and has been linked to increased risks of AF, heart failure, and ischemic stroke (7-10). However, the comparative value of indexed LA measurements—including left atrial diameter/height (LAD/H), left atrial diameter/body surface area (LAD/BSA)—in discriminating between ischemic stroke subtypes remains insufficiently defined. We hypothesized that indexed LA measurements, particularly increased LAVi, LAD/H, and LAD/BSA, would be more strongly associated with cardioembolic stroke than with atherothrombotic stroke.

Based on this hypothesis, the present study aimed to compare the most commonly used echocardiographic parameter, LAD with indexed LA parameters (LAD/H, LAD/BSA, and LAVi) in differentiating cardioembolic from atherothrombotic ischemic stroke and to evaluate their associations with stroke severity and prognosis. Elucidating the relationships between indexed LA measurements and stroke etiology may enable improved risk stratification and implementation of more targeted preventive strategies in clinical practice.

Materials and Methods

Compliance with Ethical Standards

This study was performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from every participant. Ethical approval for the study was granted by the University of Health Sciences Türkiye, Bakirkoy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (approval no.: 2023-21-23, date: 06.11.2023).

Study Design and Patient Selection

This retrospective cross-sectional study was conducted in the Clinic of Neurology at University of Health Sciences Türkiye, Bakirkoy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital. A total of 74 patients diagnosed with acute ischemic stroke between September 2021 and September 2022 were enrolled. Patients with known coronary or congenital heart disease, left ventricular (LV) systolic dysfunction (ejection fraction <50%), acute heart failure, acute coronary syndrome, hepatic or renal failure, malignancy, or inadequate echocardiographic imaging windows were excluded. Patients with evidence of hemorrhagic stroke; those with hematologic, neoplastic, infectious, or inflammatory etiologies; and patients with stroke due to any other subtype (e.g., cryptogenic stroke, known hypercoagulable state, or arterial dissection) were also excluded.

Demographic data (age and gender), body mass index, comorbidities, smoking status, alcohol use, medical history, laboratory results, imaging findings, ultrasound parameters, and discharge medications were collected. Ischemic stroke etiologic subtypes were classified using the Trial of Org 10172 in Acute Stroke Treatment (11) criteria by two neurologists during routine clinical practice before study conception. The present study retrospectively analyzed these pre-existing classifications, with stroke subtype assignment performed independently of echocardiographic data. Patients were categorized as having cardioembolic or atherothrombotic stroke based on completed imaging studies and 24-72-hour Holter rhythm monitoring. Stroke severity and functional outcome were assessed at stroke onset and after at least three months' follow-up, respectively, using the National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS) (12). Based on their NIHSS scores, patients were classified as having a mild stroke (0-5) or a moderate-to-severe stroke (≥6). Based on the mRS scores, functional outcome was defined as good (0-2) or poor (>2) (Figure 1).

Echocardiography Measurements

Transthoracic echocardiography was performed on all participants during hospitalization by two experienced cardiologists who were blinded to the clinical information, using a GE Vivid 7 Dimension system. Standard imaging planes were obtained in the left lateral decubitus position, in accordance with the recommendations of the American Society of Echocardiography (13). Left atrial diameter was measured using two-dimensional echocardiography in the parasternal long-axis view at end-ventricular systole, extending from the posterior aortic wall to the posterior LA wall. Left atrial diameter was indexed to the patient's height and BSA (4,14).

Left ventricular ejection fraction was assessed using either the Teichholz method or the biplane Simpson

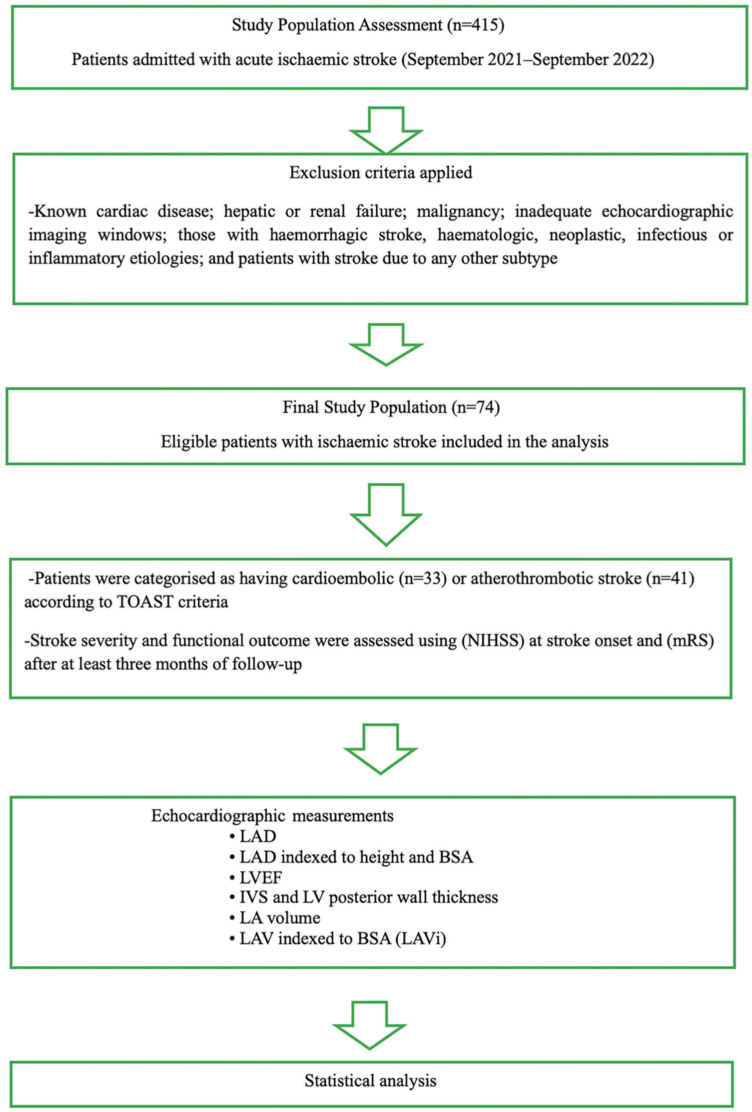

Figure 1. Flowchart of the study

BSA: Body surface area, LA: Left atrial, LAD: Left atrial diameter, LAVi: Left atrial volume index, LV: Left ventricular, LVEF: Left ventricular ejection fraction, IVS: Interventricular septum, TOAST: Trial of Org 10172 in Acute Stroke Treatment

method, depending on image quality. The interventricular septal thickness (IVS) and the LV posterior wall thickness were also recorded.

Given that a single linear LA dimension may be insufficient when atrial enlargement is non-uniform, additional volumetric assessment was performed. Left atrial volume was calculated using the area-length method with planimetry on apical four-chamber (A1) and two-chamber (A2) views at end-ventricular systole. Left atrial volume was obtained using the area-length method, calculated as 0.85 × (A1×A2) / L, and indexed to BSA to derive the LAVi (14,15).

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 25. Categorical variables are reported as counts and percentages. The normality of continuous variables was examined with the Shapiro-Wilk test. Since these variables did not follow a normal distribution, they are summarized as median values with corresponding ranges (minimum-maximum). In comparisons of demographic, clinical, and echocardiographic variables between atherothrombotic and cardioembolic groups, the independent sample t-test was used if the data conformed to normal distribution, and the Mann-Whitney U test was used if the data did not conform to normal distribution. The ability of echocardiographic measurements to discriminate cardioembolic stroke was evaluated through receiver operating characteristic (ROC) analysis. Parameters demonstrating statistically significant ROC curves were further subjected to pairwise comparisons. A two-tailed p-value <0.05 was considered statistically significant.

Results

The demographic and clinical characteristics of the study population are presented in Table 1. A total of 74 patients were included, including 49 males (66.2%) with a median age at stroke onset of 59 years (range, 31-76) and 25 females (33.8%) with a median age at stroke onset of 61 years (range, 37-76). There was no statistically significant difference in age between the groups (p>0.05). Of the 74 patients, 41 (55.4%) were categorized as having atherosclerotic ischemic stroke and 33 (44.6%) as having cardioembolic ischemic stroke. No significant differences were observed between groups with respect to age, age at stroke onset, or median follow-up duration.

The median NIHSS score was significantly higher in the cardioembolic group than in the atherosclerotic group [3 (1-16) vs. 2 (1-6), p<0.001]. During a median follow-up of 45.5 (34-50) months, recurrent ischemic stroke occurred in 10 (13.5%) patients, including 3 patients in the atherothrombotic group and 7 patients in the cardioembolic group. The two groups also differed significantly in follow-up mRS scores, with median mRS scores of 0 (0-3) and 1 (0-4) in the atherothrombotic and cardioembolic groups, respectively (p=0.011).

Baseline characteristics and echocardiographic parameters are summarized in Table 2. Patients in the cardioembolic group demonstrated significantly higher LAD values than those in the atherothrombotic group [38 (29-50) mm vs. 36 (26-42) mm, p<0.001]. Similarly, LAD/H was significantly elevated in the cardioembolic group [0.23 (0.18-0.31) mm/cm vs. 0.21 (0.15-0.26) mm/cm, p<0.001]. Left atrial diameter/body surface area was significantly higher in patients with cardioembolic stroke than in patients with atherothrombotic stroke [20.6 (16.2-31.5) mm/m² vs. 18.9 (13.46-26.8) mm/m², p=0.004].

Left atrial volume index values were likewise significantly higher in the cardioembolic group than in the atherothrombotic group [33.5 (17-62) mL/m² vs. 23 (16-59) mL/m²; p=0.004]. The two groups did not differ significantly in median IVS thickness [12 (10-17) mm vs. 10 (9-15) mm] or in LV posterior wall thickness [11 (9-18) mm vs. 10 (9-17) mm] (p>0.05 for both).

As shown in Table 3, ROC curve analysis demonstrated that LAD (p=0.001), LAD/BSA (p=0.004), LAD/H (p<0.001), and LAVi (p=0.004) were significant markers for distinguishing cardioembolic stroke. The risk of cardioembolic stroke increased with LAVi values above 42 mL/m², LAD/BSA above 21.59 mm/m², and LAD/H above 0.23 mm/cm.

Pairwise comparisons based on ROC curve analysis revealed no significant differences between LAD and

Table 1. Demographics and clinical characteristics of study patients

	n (%)
Gender	
Female	25 (33.8)
Male	49 (66.2)
Smoking	
No	63 (85.1)
Yes	11 (14.9)
Alcohol use	
No	72 (97.3)
Yes	2 (2.7)
Hypertension	
No	42 (56.8)
Yes	32 (43.2)
Diabetes	
No	53 (71.6)
Yes	21 (28.4)
History of stroke or TIA	
No	57 (77)
Yes	17 (23)
NIHSS	
<6	65 (87.8)
≥6	9 (12.2)
mRS	
<3	60 (81.1)
≥3	14 (18.9)
Recurrent ischemic stroke	
No	64 (86.5)
Yes	10 (13.5)
Treatment at baseline	
None	54 (73.0)
Antiplatelet	17(23.0)
Dual antiplatelet	3 (4.0)
Treatment at discharge	
Antiplatelet	14 (19)
Anticoagulant	28 (38)
Dual antiplatelet	27 (36)
Anticoagulant+antiplatelet	5 (7)

NIHSS: National Institutes of Health Stroke Scale, mRS: modified Rankin Score, TSI: Transient ischemic attack

LAD/BSA (p=0.393), between LAD and LAD/H (p=0.803), or between LAD and LAVi (p=0.464) in discriminating cardioembolic stroke from the atherothrombotic group, as shown in Table 4.

Discussion

The present study reinforces and expands the evidence linking LA structural remodelling with both the occurrence and prognosis of ischemic stroke across etiological subtypes. Consistent with prior research, we observed that, similar to LAD, left atrial enlargement (LAE) parameters, including LAD/BSA, LAD/H, and LAVi, were significantly higher in patients with cardioembolic stroke than in those with atherothrombotic stroke. These findings are consistent with earlier population-based and clinical cohort studies identifying LAE as an independent predictor of cardioembolic stroke and stroke recurrence (5,14,16-18).

In the cardioembolic group, our data further show that increased LA size and volume correlate with greater stroke severity, as reflected by higher NIHSS scores and poorer functional outcomes (mRS). This supports prior studies reporting that LAE is associated with more severe neurological deficits, particularly in embolic stroke subtypes (19-21). The pathophysiological mechanisms likely involve the close association between LAE and AF, a major embolic stroke risk factor, and structural changes in the LA appendage that promote thrombus formation by causing blood stasis and reduced appendage flow velocity (21-24). Recent imaging-based studies have provided further insight into these mechanisms. In a study it is demonstrated that impaired LA functional parameters predicted AF development independently of LA volume, highlighting the clinical relevance of atrial structural-functional coupling (25).

Importantly, the ROC curve analysis demonstrated that LAD, LAD/H, LAD/BSA, and LAVi were significant discriminators of cardioembolic stroke, with the established thresholds that support improved risk stratification. These indexed measurements showed prognostic utility comparable to LAD, corroborating findings from large cohorts, including the Atherosclerosis Risk in Communities Study (5,14,26,27). Because the left atrium is an asymmetrical cavity, volume-based measurements provide a more accurate assessment of its size compared to area or linear dimensions (28). While LAVi is widely regarded as a robust cardiovascular risk marker, in our study pairwise comparisons revealed no significant superiority of one echocardiographic parameter over another, suggesting

Table 2. Demographic and echocardiographic parameters of ischemic stroke patients

	Med (min-max)
Age	62 (34-79)
Follow-up period (months)	45.5 (34-50)
Age at stroke onset	59 (31-76)
BSA	1.82 (1.43-2.26)
LAD (mm)	36 (26-50)
LAD/BSA (mm/m²)	19.7982 (13.46-31.5)
LAD/H (mm/cm)	0.2174 (0.15-0.31)
IVS (mm)	10 (9-17)
LV posterior wall thickness (mm)	10 (9-18)
LAVi (mL/m²)	26.5 (16-62)
A1	16.6 (10.6-32.4)
A2	16.5 (12-30.7)

A1: Apical 4-chamber view, A2 and apical 2 chamber view
BSA: Body surface area, LAD: Left atrial diameter, LAD/H: Left atrial diameter/height, LAD/BSA: Left atrial diameter/body surface area, LAVi: Left atrial volume index, IVS: Interventricular septal wall thickness

Table 4. Pairwise comparisons between LAD and echocardiographic markers in discriminating cardioembolic from atherothrombotic stroke

	LAD p-value
LAD/BSA	0.393
LAD/H	0.803
LAVi	0.464

LAD: Left atrial diameter, LAD/H: Left atrial diameter/height, LAD/BSA: Left atrial diameter/body surface area, LAVi: Left atrial volume index
ROC curve analysis

Table 3. ROC curve analysis of echocardiographic parameters for discriminating cardioembolic from atherothrombotic stroke

	AUC	SE	p-value	95% CI	Cut-off	Sensitivity	Specificity
LAD	0.734	0.061	0.001*	0.614-0.854	>38	45.45	95.12
LAD/BSA	0.703	0.063	0.004*	0.579-0.827	>21.59	42.42	95.12
LAD/H	0.746	0.059	<0.001*	0.631-0.861	>0.23	42.42	95.12
LV posterior wall thickness	0.594	0.069	0.175	0.459-0.729	>11	48.39	70.00
LAVi	0.703	0.064	0.004	0.578-0.828	>42	36.36	97.56
IVS	0.618	0.068	0.091	0.485-0.75	>13	25.81	95.00

*p<0.05
ROC: Receiver operating characteristic, AUC: Area under the curve, SE: Standard error, CI: Confidence interval, LAD: Left atrial diameter, LAD/H: Left atrial diameter/height, LAD/BSA: Left atrial diameter/body surface area, LAVi: Left atrial volume index, IVS: Interventricular septal wall thickness

that these measures may be used interchangeably in clinical practice.

Our findings also support the emerging concept of atrial cardiopathy as an independent embolic substrate beyond clinically detected AF. Elevated LAVi, a marker of chronic diastolic dysfunction and atrial remodeling, was associated with more disabling strokes, including cryptogenic presentations, which indicates its utility in identifying subclinical atrial pathology and embolic risk (8,28,29). Zhang et al. (30) further demonstrated that LAE is associated with ischemic stroke severity even in the absence of overt AF, reinforcing the clinical value of LA indices in detecting subclinical atrial pathology.

However, therapeutic implications remain complex. The ARCADIA randomized clinical trial failed to demonstrate the superiority of apixaban over aspirin for secondary prevention of stroke in patients with cryptogenic stroke and atrial cardiopathy (31). These findings underscore that, while LA structural markers provide valuable risk stratification and etiologic insight, they may not yet be sufficient to serve as the sole determinants of anticoagulation strategies. Ongoing and future studies integrating LA structural, functional, and biomarker-based parameters may help refine patient selection and optimize secondary prevention.

Study Limitations

This single-center study had a limited sample size, which may affect the generalizability of the results. The retrospective design limited data availability, contributing to the absence of significant differences in pairwise comparisons of parameters. Additionally, the small sample size precluded multivariable modeling to evaluate combined echocardiographic predictors for cardioembolic stroke. Larger prospective multicenter studies are needed to confirm these findings.

Despite these limitations, a major strength of this study was the meticulous etiological evaluation performed for all participants, which enhanced the accuracy of stroke subtype classification. Additionally, extended Holter monitoring—prolonged up to 72 hours when clinically indicated—and a detailed echocardiographic examination allowed a more comprehensive assessment of occult arrhythmias and reduced the likelihood of missed paroxysmal AF.

Conclusion

Our findings suggest that, similar to LAD, LAVi and LAD adjusted for height and BSA may provide incremental value in the etiologic classification and risk stratification of patients with ischemic stroke. Systematic integration of these measures into routine echocardiographic reporting could improve clinical decision-making, facilitate more precise identification of cardioembolic risk, and support the implementation of targeted secondary prevention strategies, ultimately enhancing patient outcomes.

Ethics

Ethics Committee Approval: The study received ethical approval from the University of Health Sciences Türkiye, Bakirkoy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (approval no.: 2023-21-23, date: 06.11.2023).

Informed Consent: Written consent was obtained from every participant.

Footnotes

Authorship Contributions

Surgical and Medical Practices: I.Y.G., E.O., A.K., K.N.B., D.A., A.Se., A.S., Concept: I.Y.G., E.O., A.K., K.N.B., D.A., A.Se., A.S., Design: I.Y.G., E.O., A.K., K.N.B., D.A., A.Se., A.S., Data Collection or Processing: I.Y.G., E.O., Analysis or Interpretation: I.Y.G., K.N.B., Literature Search: I.Y.G., E.O., A.K., K.N.B., D.A., A.Se., A.S., Writing: I.Y.G., E.O., A.K.

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