A Study on Etiology, Echocardiographic Parameters, and Stroke Risk Assessment Using CHAD2DS2-VASc Score in Atrial Fibrillation

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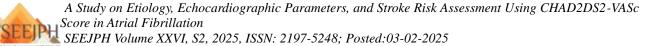| KEYWORDS	ABSTRACT
Atrial fibrillation, Valvular Heart disease, Left atrial size, Stroke, CHA2DS2-VASc score.	Atrial fibrillation is the most common sustained arrhythmia and its incidence is associated with ischemic stroke, heart failure, and other cardiovascular diseases. It is more common in the patients who are elderly, hypertensive, diabetics, obese or valvular heart disease. In AF patients, the CHA2DS2-VASc score is used to estimate stroke risk, and more recently, LA size has also been suggested as a potential additional factor for stroke in the patients. In this study, the etiology of AF is investigated by the comorbidities and their effect on development of AF, LA size and AF severity and the predictive power of the CHA2DS2-VASc score for stroke risk in 102 AF patients of ASRAM Medical College, Eluru who were evaluated for various comorbidities, echocardiographic parameters (LA size) and CHA2DS2-VASc score to see if there is any correlation with stroke risk. Hypertension, vascular disease (CAD and PAD) and type 2 diabetes mellitus (DM) were the most common comorbidities. LA size was correlated with AF severity and was greater in permanent AF (4.93 cm). In patients with persistent and long standing AF, the CHA2DS2-VASc score was positively correlated with the incidence of stroke. Further additional echocardiographic parameters such as LA size can improve stroke risk stratification, and CHA2DS2-VASc was useful in predicting stroke risk.

Introduction

"'Atrial fibrillation' (AF) is the most common arrhythmia in the world with high morbidity and mortality. AF markedly increases 'Congestive heart failure' (CHF), ischemic stroke, and other cardiovascular problems (Kang et al., 2017). AF is more common with age and in people with comorbidities such as hypertension, diabetes, obesity, and other forms of CVD such as valvular heart disease, 'peripheral artery disease' (PAD), and 'coronary artery disease' (CAD) (Batta et al., 2023). Peripheral artery disease (PAD) is another important vascular condition with an associated increased cardiovascular morbidity. Like CAD, it has similar risk factors and is associated with increased risk of atrial fibrillation and stroke from systemic atherosclerosis and endothelial dysfunction. Prevention of adverse outcomes and improvement of patient management requires effective risk stratification of stroke, one of the most devastating complications of AF (Lip et al., 2015). The main progress in coping with AF has been to show risk stratification routines. For example, AF patients' risk of stroke is measured by the CHA2DS2-VASc score, which takes into account factors including age, hypertension, diabetes, and past stroke (Galvin, 2018). Treatment decisions, in particular, initiation of anticoagulation therapy, are frequently determined using the CHA2DS2-VASc score. Even though it is the gold standard for predicting stroke risk in people with AF, the growing research also suggests a role for LA size as a separate predictor of stroke and other unfavorable outcomes in individuals with atrial fibrillation (Siddiqi et al., 2022).

AF is a well-known feature of left atrial enlargement. The size of the left atrium has been studied about stroke risk many times, and many studies have shown that a large left atrium increases thromboembolic risk (Xu et al., 2020). Habibi et al. (2015) state that in patients with AF, left atrial enlargement is a significant predictor of stroke. AF is characterized by elevated atrial pressure, stasis of blood, atrial remodeling and thrombus formation in the left atrium (Sulague et al., 2023). Patients with larger left atrial size are at increased risk of stroke due to clot development in the left atrial appendage and embolization into the cerebral circulation (Fang et al., 2022). However, Leung et al. (2018) showed that left atrial size is a risk factor for stroke but does not reflect the burden of the AF illness. Left atrial dimensions and valvular heart diseases are larger in AF patients. LA size can be measured with 2D echocardiography and the structural changes that are related to AF can also be determined (Vieira et al., 2014). LAVI is a standard method of measuring atrial enlargement

and the risk of stroke, as stated by Waldenhjort et al. (2016). Another common clinical risk assessment method for stroke in patients with AF is CHA2DS2-VASc with AF and other factors such as congestive heart failure, hypertension, age, diabetes, history of stroke and vascular disease including CAD and PAD, and sex (Gažová et al., 2019; Nai et al., 2024). The more the CH2DS2-VASc score increases, the more likely one has had a stroke. In addition, it has been used in a wide variety of clinical samples including the general population and patients with various cardiac diseases and is the most widely used tool for stroke risk assessment in patients with AF (Lahad et al., 2022). The CHA2DS2-VASc score is beneficial, but it has been observed in the recent past that left atrial enlargement is a good predictor of stroke risk independent of clinical variables. LA size can also predict thromboembolic risk in patients with low CHA2DS2-VASc scores and, therefore can be used to risk-stratify stroke (Jagadish et al., 2019). In large cohorts, the correlation between LA size and stroke incidence has been validated, and essentially, all studies have reported that larger atrial sizes are linked to a higher risk of stroke once other comorbidities have been taken into account (Xu et al., 2020).

An established method for assessing stroke risk in AF patients is the CHA2DS2-VASc score; however, the role of left atrial size prediction in AF patients in clinical practice has not been well-studied. Since early stroke prevention in AF patients is so important, it is not clear whether LA size measurements will improve the ability to identify stroke risk in individuals with mild to moderate AF. In addition, the relationship of AF type (paroxysmal, persistent, long-standing, permanent) to stroke risk by LA size and CHA2DS2-VASc score has not been fully characterized in diverse populations. This study seeks to fill in the gaps in the etiology of AF, LA size by echocardiography, Using the CHA2DS2-VASc score for predicting AF patients' risk of stroke. This study aims to understand the etiology of 'atrial fibrillation' (AF), specifically concerning comorbidities that contribute to the development of AF. In addition, the study seeks to inspect the relationship between echocardiographic constraints, specifically LA size, and AF severity and their potential use in determining stroke risk. The study also examines the use of the CHA2DS2-VASc score in the prognosis of stroke in AF patients and to reduce the risk of stroke in AF patients, and provides information to improve risk assessment and management.

Materials and Methods
Study design
"This was a cross sectional study to find out the cause of AF, correlation between AF and left atrial size and the accuracy of CHA2DS2-VASc score in predicting stroke in patients with AF. This study was conducted in ASRAM Medical College, Eluru, India from July 2023 to June 2024, and 102 consecutive AF patients were included from cardiology outpatient department, emergency department, and ICU.

Inclusion Criteria
Patients of 18 years and above with confirmed diagnosis of atrial fibrillation by ECG were included in the study. All participants had different types of AF, paroxysmal, persistent, long standing, or permanent, and all were selected on their willingness to participate in the study.

Exclusion Criteria
The study also excluded patients with other severe forms of arrhythmia, such as ventricular tachycardia or fibrillation, or other diseases that could affect the diagnosis of AF. Participants were also excluded from the study if they had pregnancy, active substance use or dependence, severe mental illness, terminal illness, or end stage renal disease. The study also did not include patients with incomplete reported or clinically implausible data.

Data Collection
Symptomatology and Diagnosis of AF
Clinically and by 12 lead ECG, AF was established. AF was considered to be present in patients with palpitations, dizziness, fatigue or syncope, and abnormal rhythm on the ECG. The most important ECG changes that indicated AF were the absence of clear P waves and irregular R-R intervals. Coming up with the diagnosis of AF was useful with the ECG characteristics.

Echocardiographic Assessment

All the participants were subjected to a comprehensive 2D echocardiography of the cardiac parameters. In particular, the major outcomes were the echocardiographic dimensions of left atrium, LVEF and valvular disorders. Left atrial size was measured and indexed for body surface area in the parasternal long axis view. Patients with AF also have LA size as a predictor of thromboembolic events and stroke. LVEF is an established marker of worse prognosis, especially heart failure, and the overall function of the left ventricle was evaluated. The study also included valvular heart disease (VHD), including mitral and aortic valve disorders, which are known to be associated with the development of AF.

CHA2DS2-VASc Score Calculation

AF is a clinical risk stratification tool used to estimate the risk of stroke in patients with AF. The score for each patient was computed using the following parameters: congestive heart failure (C), hypertension (H), age (A), diabetes mellitus (D), history of stroke or transient ischemic attack (S2), vascular disease (V) and sex category (Sc). C (1 point), H (1 point), A ($\geq$75 years = 2 points, 65-74 years = 1 point), D (1 point), S2 (2 points), V (1 point), and Sc (female = 1 point). The total score was used to divide the patients into low risk, moderate risk and high risk for stroke. With a higher CHA2DS2-VASc score of 6 or more, the risk of stroke is increased; with a lower score, the risk of stroke is decreased.

Statistical analysis

The data were made appropriate for statistical analysis and correlation of the echocardiographic parameters including left atrial size, LVEF, CHA2DS2-VASc scores and stroke risk. Mean $\pm$ standard deviation was used to express continuous variables, and frequencies and percentages were used to express categorical variables. Normality was tested with the Shapiro-Wilk test. Data was analyzed using Pearson's or Spearman's correlation coefficients based on the distribution of the data. Echocardiographic parameters and CHA2DS2-VASc scores were compared between different AF types using one-way analysis of variance (ANOVA) and the Kruskal-Wallis test for nonparametric data. Kaplan-Meier survival curves were used to compare stroke incidence between subjects with higher and lower scores to assess the predictive ability of CHA2DS2-VASc score to predict stroke using the log-rank test. The independent risk factors for stroke in AF patients were determined using a logistic regression model.

Result

Etiology of Atrial Fibrillation (AF)

Several comorbidities mainly contributed to the etiology of atrial fibrillation (AF) in the cohort. Atrial pressure increase and myocardial injury were caused by hypertension and vascular disease (CAD and PAD). It also promoted inflammation and atrial remodeling in type 2 diabetes mellitus (DM). Altered clinical history of stroke, transient ischemic attacks (TIA), and cerebrovascular accidents (CVA) with a history of thromboembolic risks to AF was noted. AF was due to atrial dilation and fibrosis from congestive heart failure (CHF). In addition, age, valvular heart disease, and pulmonary arterial hypertension (PAH) were present. Persistent AF was the most common type of AF, followed by long-standing AF, and fewer patients had paroxysmal or permanent AF."

Table 1: Etiology of Atrial Fibrillation

Comorbidity	Percentage of Patients (%)
Age >/= 75	13.73%
Stroke/TIA/Thromboembolism	14.71%
Coronary Artery Disease (CAD)	55.88%
Cerebrovascular Accident (CVA)	10.78%
Hypertension	66.67%
Type 2 Diabetes (DM)	47.06%
Vascular Disease (including PAD)	56.86%

Table 1 shows the prevalence of different comorbidities in the study cohort. The most common comorbidity was hypertension in 66.67% of patients and vascular disease (PAD) in 56.86%. Second, the prevalence of 'coronary artery disease' (CAD) was 55.88%. Among patients, type 2 diabetes (DM) affected 47.06%, and

14.71% had stroke/TIA/thromboembolism. 13.73% of patients were aged≥75, and 10.78% had a cerebrovascular accident (CVA), indicating a significant overlap of cardiovascular and metabolic conditions.

Table 2: Atrial Fibrillation (AF) Types and Their Most Common Etiologies (Ranked)

AF TYPE	MC Etiology (Ranked)
Long-Standing	1. CAD > 2. CRHD > 3. Non-Ischemic DCMP
Paroxysmal	1. Post-Operative > 2. CAD (AF after PTCA)
Permanent	1. CRHD > 2. CAD > 3. CKD > 4. CVA
Persistent	1. CAD > 2. Non-Ischemic DCMP > 3. CVA

The most common contributing factors for this study cohort are presented in Table 2, which ranks the etiologies for each type of AF. The most common cause across all AF types, and in particular in Long-standing, Persistent, and Permanent AF, was CAD. Permanent AF had predominant Chronic Rheumatic Heart Disease (CRHD), while Paroxysmal AF was noted with Post Operative AF. Moreover, Chronic Kidney Disease (CKD) and Cerebrovascular Accident (CVA) were also important in Permanent AF, supporting their role in AF progression.

Left Atrium Size and Atrial Fibrillation
Size of left atrium (LA size) is a substantial parameter for assessing the severity of atrial fibrillation (AF). The investigation results showed a good relationship between the enlargement of the left atrium and the presence of AF, and the typical size of the left atrium was 4.8 cm, but the larger left atrial sizes were often associated with more severe forms of AF, such as permanent, long standing and persistent AF. LA size was then correlated with AF severity and it was found that patients with larger LA sizes are more prone to thromboembolic events and stroke. Both are also a contributing cause of AF and stroke risk linked with marked left atrial enlargement in patients with severe valvular heart disease and ischemic heart disease.

Table 3: Average Left Atrial Size and Patient Distribution Across AF Types

AF Type	Average LA Size (cm)	Number of Patients
Long-Standing	4.77	26
Paroxysmal	4.01	27
Permanent	4.93	22
Persistent	4.57	27

The average left atrial (LA) size and the number of patients for each atrial fibrillation (AF) type are presented in Table 3. Mean LA size was substantially larger in patients with long-standing AF and was 4.77 cm in 26 patients, and paroxysmal AF was 4.01 in 27 patients. Permanent AF had an average LA size of 4.93 cm in 22 patients; persistent AF had a moderate LA size of 4.57 cm in 27 patients. AF type and LA size are correlated with long-standing and permanent AF having larger atrial dimensions.

Figure 1: Distribution of Left Atrium Size and frequency
Figure 1 presents the distribution of left atrial (LA) size across different ranges in the cohort. The majority of patients had LA sizes between 4.1 and 5.0 cm, and the most common size was in the 4.5–5.0 cm range. LA sizes between 3.5 cm and 4.0 cm and 4.1 cm and 4.5 cm had the largest number of patients. Few patients had LA sizes greater than 5.5 cm, and there were fewer LA sizes between 5.1 cm and 5.5 cm, which might suggest a concentration of patients with moderate atrial enlargement.

CHA2DS2-VASc Scores and Stroke Risk
The CHA2DS2-VASc score was used to evaluate each patient's risk of stroke and the results were good correlation between higher scores and higher probability of stroke. In particular, the risk of stroke was significantly increased for those with CHA2DS2-VASc scores of more than six compared to those with scores less than 3. The CHA2DS2-VASc scores of the cohort were extremely wide, with most patients having scores of 3–7. Higher CHA2DS2-VASc score was associated with a rapid increase in stroke risk even in the presence of hypertension, diabetes, valvular heart disease, and vascular conditions such as CAD and PAD, and the distribution of CHA2DS2-VASc scoring was higher. This study shows that the CHA2DS2-VASc

score predicts stroke or transient ischemic episodes (TIA) incidence in patients with scores below 6, and hence, the assessment of stroke risk is predictive.

Table 4: CHA2DS2-VASc Score Distribution and Stroke Risk

CHA2DS2-VASc Score	Stroke Risk (%)
0-2	30.39%
3-4	59.80%
5-6	8.82%
≥6	3.92%

The distribution of stroke risk according to CHA2DS2-VASc scores in the cohort is presented in Table 4. The majority of patients (59.80%) are moderate risk (scores 3-4), while 30.39% are low risk (scores 0-2). About 8.82% of patients are in the high-risk category (scores 5–6), and only 3.92% have a score of ≥6, which means that they have a very high stroke risk. The skewed risk towards moderate risk scores and the majority of patients having a moderate risk according to their CHA2DS2-VASc score for stroke are highlighted in this distribution.

Group Analysis: Atrial Fibrillation Types and Risk Factors
The learning divided patients into four types of atrial fibrillation such as paroxysmal, persistent, long-standing, and permanent. The association between AF type, etiology, left atrial size, and CHA2DS2-VASc scores was then examined using a correlation analysis. Patients with paroxysmal AF had smaller left atrial sizes. They scored lower on the CHA2DS2-VASc than those who had persistent or long-standing AF. This group had a lower risk of stroke. The persistent AF group was associated with valvular heart disease and coronary artery disease and had moderate to large left atrial sizes. This group had higher CHAS2DS2-VASc scores and higher stroke risk correlated with higher CHA2DS2-VASc scores. Permanent AF patients had the largest left atrial sizes and the highest CHA2DS2-VASc scores, indicating higher stroke risk. Congestive heart failure was also common in this group. Older patients with significant comorbidities such as hypertension, diabetes, or valvular heart disease with very high CHA2DS2-VASc scores and stroke risk were mostly seen with permanent AF.

Table 5: Correlation Between AF Type, LA Size, and CHA2DS2-VASc Score
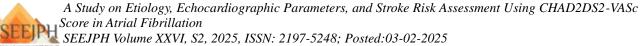
AF Type	Average LA Size (cm)	Average CHA2DS2-VASc Score	Stroke Incidence (%)
Long-Standing	4.77	3.27	11.54%
Paroxysmal	4.01	2.37	3.70%
Permanent	4.93	2.95	27.27%
Persistent	4.57	3.63	18.52%

The relationship between AF type, LA size, CHA2DS2-VASc score, and stroke incidence is summarized in Table 5. In patients with long standing AF, LA size (4.77 cm), CHA2DS2-VASc score (3.27), and stroke incidence (11.54%) . Paroxysmal AF had the smallest LA size (4.01 cm) and the lowest stroke incidence (3.70%). Permanent AF had an LA size of 4.93 cm and a stroke incidence of 27.27%. LA size (4.57 cm) and stroke incidence (18.52%) were for persistent AF.

Discussion
This study aimed to identify the cause of atrial fibrillation (AF) and its relationship with echocardiographic parameters, specifically left atrial (LA) size, Considering the reliability of the CHA2DS2-VASc score in predicting AF patients' risk of stroke. The cohort was well chosen of adult patients with various AF types, and the study measured key comorbidities, echocardiographic parameters, and stroke risk factors and examined their relation in the cohort.
The study findings confirm the well-established role of some comorbidities in the development and severity of 'atrial fibrillation' (AF). It illustrates the distribution of the most common etiologies across different AF types, highlighting CAD as the predominant cause in Long-standing, Persistent, and Permanent AF. Notably, CRHD was a key contributor in Permanent AF, while post-operative AF was more frequent in Paroxysmal AF. Hypertension was the most prevalent comorbidity in 66.67% of patients, vascular disease (CAD and

PAD) in 56.86% of patients, and type 2 diabetes mellitus (DM) in 47.06%. These conditions were shown to induce atrial remodeling and AF development. The fact that stroke risk in AF patients was substantially linked with the CHA2DS2-VASc score and that the higher the score, the greater the stroke risk validates the predictive value of the score as a stroke risk stratification. Patients in the moderate-risk group (CHA2DS2-VASc score 3–4) constituted 59.80%, low-risk group (scores 0–2) 30.39%, and high-risk patients (scores ≥6) 3.92%. Additionally, the study discovered a favorable relationship between the risk of stroke and the severity of AF and left atrial size (LA size) in terms of echocardiographic parameters. Patients with permanent AF had the biggest average LA size (4.93 cm) and the smallest in patients with paroxysmal AF (4.01 cm), an established risk factor for thromboembolic incidents. The literature suggests that LA enlargement is a marker of AF severity and stroke risk, and this relationship was consistent with it. In patients with larger left atrial size and higher CHA2DS2-VASc score, stroke incidences were higher in long standing (11.54%) and permanent (27.27%) AF, compared to paroxysmal (3.70%) AF. This emphasizes the significance of patient LA size and CHA2DS2-VASc score in evaluating the risk of stroke in AF patients.

The result is consistent with previous studies that found a greater LA size associated with higher risk of stroke in patients with atrial fibrillation. LA enlargement was confirmed to be a significant predictor of thromboembolic events, and LA enlargement is clinically relevant to identify high risk individuals (Radwan, 2017). This is in agreement with Van et al. (2017) who showed that the CHA2DS2-VASc score is a good indicator of stroke risk in patients with atrial fibrillation, especially in patients with other comorbidities such as hypertension, diabetes, and valvular heart disease. Delgado et al. (2017) also support the AF type to stroke risk link, but they go on to say that persistent and long standing AF is associated with a larger LA size and increased risk of stroke. This was consistent with the study which showed that long standing AF has the largest LA size (4.77 cm) and the highest stroke incidence (11.54%). Botto et al. (2021) showed that a small LA size, low stroke risk and paroxysmal AF and a large LA size, high stroke incidence and persistent and long standing AF. It is important to note that late detection and risk stratification were crucial in AF patients. Thus, the combination of echocardiographic parameters of LA size and CHA2DS2-VASc scoring can improve stroke risk prediction (Overvad, 2016). These methods can identify patients at risk of stroke and hence guide the anticoagulation therapy approach to improve patient safety and outcomes. Moreover, LA size may be another predictor of AF severity and may provide useful information on long-term AF management. As more and more AF is diagnosed and managed in clinical practice, echocardiographic findings could be combined with clinical risk scores to become a standard of care for AF management and stroke prevention (Kirchhof, 2017).

It is important to consider the limitations of this study. The study's observational design does not allow for the firm establishment of causality between comorbidities, AF type, LA size, and stroke risk. Secondly, although the sample size of 102 patients is adequate for some of the analyses, the sample size might not fully capture variability observed in larger populations; multicenter studies with larger cohorts are necessary for confirming the findings. Furthermore, the study was conducted at only one center, and it is uncertain whether these results can be generalized to other populations. A limitation is that some variables are analyzed cross-sectionally. There has been refinement of clinical data for CHA2DS2-VASc scores, and future research might determine the longitudinal effects of these scores over time and the influence of different treatments on stroke outcomes. Additional research can attempt to validate the power of the predictive LA size and CHA2DS2-VASc scores in larger and more diverse populations. Therefore, longitudinal studies could assess how changes in LA size over time influence stroke incidence in AF patients. Moreover, studies of the effects of certain comorbid conditions, such as valvular heart disease and coronary artery disease, on AF progression and stroke risk, for example, would also allow the relevant management of such comorbidities about AF. More accurate assessments of atrial size and function may be possible with the use of sophisticated imaging methods like cardiac MRI and might be incorporated into clinical guidelines. Genetic research could also reveal underlying genetic markers that predispose individuals to both AF and stroke, allowing for more personalized approaches to treatment.

Conclusion

This study's goals were to determine the various causes of atrial fibrillation, to assess if there is any association between left atrial size and the severity of AF, and to evaluate whether the CHA2DS2-VASc score is suitable for predicting the risk of stroke. It is evident from the results that hypertension, vascular disease and the onset and course of AF are influenced by type 2 diabetes mellitus. These situations contribute to atrial remodeling, one of the causes of AF, and so these risk factors should be controlled to avoid AF. The study

also displayed a positive correlation between LA size, the severity of AF, and the incidence of stroke. Patients with larger LA size, especially with permanent and persistent AF, were found to have more incidence of stroke and thromboembolic events. These results imply that measuring LA size with echocardiography is a therapeutically helpful way to identify stroke risk factors. The results are in line with earlier research that has consistently shown that LA enlargement is a significant risk factor for thromboembolic events in patients with atrial fibrillation. Additionally, it was demonstrated that the CHA2DS2-VASc score was significantly stratifying in favor of setting stroke risk in AF patients. Higher CHA2DS2-VASc scores were substantially linked to a higher chance of stroke, confirming the predictive validity of the measure for stroke risk assessment. CHA2DS2 -VASc scoring integration into clinical practice reinforces the necessity of including the score when stratifying the stroke risk to offer the best therapeutic decision, especially the use of anticoagulation therapy. Therefore, this study concluded by illustrating that LA size should also be considered when using CHA2DS2-VASc scores in conjunction with stroke risk assessment for AF patients. The potential impact of these parameters on stroke incidence and progression of AF, if present, needs further research, which can only be done using larger multicenter cohorts.

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