

## Research Article

# Non valvular atrial fibrillation stroke risk stratification by CHA2DS2-VASc score and short term outcomes

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## ABSTRACT

**Background:** Atrial fibrillation confers a high risk of stroke and is associated with significant mortality and morbidity. Many scoring systems for have been proposed stroke risk stratification in atrial fibrillation. Peripheral thromboembolism, heart failure and death. The main objective of the study was to estimate CHA2DS2VASc score in cases of non valvular atrial fibrillation, to asses short term outcome in AF (stroke, thromboembolism, heart failure and death and to find out association of CHA2DS2VASc score with outcomes.

**Methods:** 64 cases (29 M, 35 F) of non valvular AF were included in this prospective observational study. CHA2DS2VASc score was calculated and cases were categorized into low (score 0), intermediate (score 1 ) and high risk (score 2 ) for development of stroke. Cases were clinically evaluated and investigated for type, etiology, complications and comorbidities.

**Results:** CHA2DS2VASc score was determined in 64 cases of non valvular AF. In 3 cases (4.6%) it was zero indicating low risk for stroke, 8 cases (12.5%) had CHA2DS2VASc score as 1 had intermediate risk, and 53 cases (82.8%) had score 2 or more indicating high stroke risk ( $p < 0.01$ ). 3 cases of non valvular atrial fibrillation (4.6%) presented with stroke and all of them had CHA2DS2VASc score  $> 2$ . At the end of 3 months, total no. of cases with stroke was reported to be 5 (7.8 %). Stroke risk was significantly higher in cases of CHA2DS2VASc score  $> 2$  ( $p < 0.01$ ). Congestive heart failure was reported in 32 (50%) cases. Peripheral embolism was documented in 1 case (1.5%). Overall Mortality at the end of 3 months was reported to be 7 (10.9%) and cases with CHA2DS2VASc score  $\geq 2$  had 13% mortality. CHA2DS2VASc score  $\geq 2$  was significantly associated with mortality ( $p < 0.01$ ). All 3 Cases with CHA2DS2VASc score as zero were uncomplicated. 8 cases (12.5%) had score as 1 and, out of these 8 cases, CHF was reported in 2 cases (25%), while 6 (75%) were uncomplicated. CHA2DS2VASc score  $\geq 2$  was reported in 53 cases (82.3%). This group had complications in the form of CHF in 30 cases (56.6 %), thromboembolism in 1 (1.8%), and stroke in 5 (9.4%) cases. Cases of AF with CHA2DS2VASc score  $> 2$  demonstrated significantly high incidence for stroke as compared to those with score as zero or one ( $p < 0.01$ ).

**Conclusions:** CHA2DS2VASc is a simple score to predict stroke risk in cases of non valvular atrial fibrillation and is easy to estimate. CHA2DS2VASc score  $\geq 2$ ; is associated with high incidence of stroke in cases of non valvular AF. CHA2DS2VASc score  $\geq 2$  is associated with mortality as a short term adverse outcome in non valvular atrial fibrillation.

**Keywords:** Atrial fibrillation, CHA2DS2-VASc score

## INTRODUCTION

Atrial fibrillation is the most common sustained tachyarrhythmia-affecting 1 to 2% of general population. Prevalence of AF increases with age and lifetime risk of developing AF is around 25% after the age of 40 years.<sup>1,2</sup> AF confers 5-fold risk of stroke, and one in five of all strokes is attributed to atrial fibrillation.

Strokes in association with AF are associated with significant mortality and morbidity.<sup>3</sup> Initially, CHADS2 score was used to stratify risk for stroke in non valvular AF. However, as it was demonstrated to have only a modest predictive value and it did not include many risk factors for stroke, viz. age >75 years, and vascular diseases, hence a new risk factor based approach expressed as CHA2DS2VASc score has been recommended for assessment of stroke risk, which includes additional stroke risk factors.

CHA2DS2VASc consists of congestive cardiac failure, hypertension, age >75 years (doubled), diabetes mellitus, stroke (doubled), vascular disease age 65-74 years and female gender.

This scheme is based on a point system in which 2 points are assigned for a history of stroke or TIA, or age  $\geq 75$  and 1 point each assigned for age 65-74 years, a history of hypertension, diabetes mellitus, recent cardiac failure, vascular disease (myocardial infarction, complex aortic plaque and peripheral arterial disease, prior revascularization, amputation due to peripheral vascular disease, or angiographic evidence of PAD) and female sex.<sup>4</sup> In cases of AF with CHA2DS2VASc score >2, anticoagulation therapy –OAC is recommended in a dose to achieve INR in the range of 2-3, unless contraindicated.<sup>5</sup>

Even if rheumatic AF is common in India, non valvular AF is also found in significant no. of cases. Very few centers are equipped with cardiac catheterization laboratories and ablation facilities and expertise and rate control is the predominant treatment practiced at many centers.

Even though OACs are recommended, many of the cases are non-compliant. Cost is the limiting factor for newer oral anticoagulants e.g. Dabigatran. Apart from stroke, patients of AF are prone for complications viz. congestive heart failure, thromboembolic episodes, and death.<sup>6-8</sup>

Aim and objectives of the study were to estimate CHA2DS2VASc score in cases of atrial fibrillation, to assess 3 month outcome (stroke, congestive cardiac failure, thromboembolism and death) in cases of atrial fibrillation, to find out association between CHA2DS2VASc score and short term outcomes (3 months) in cases of atrial fibrillation (stroke, death, heart failure, thromboembolism).

## METHODS

104 cases of atrial fibrillation were screened for the study. 64 (29 M, 35 F) cases of non valvular atrial fibrillation were enrolled for this prospective observational study. Permission from institutional ethics committee was obtained. Atrial fibrillation and types (first diagnosed, paroxysmal, persistent and permanent) was defined according to ESC guidelines.

Cases were evaluated for etiology and type of atrial fibrillation and CHA2DS2VASc score was calculated. Complications of AF at the time of recruitment and comorbidities were noted and anticoagulation therapy (low molecular weight heparin and/or VKA-warfarin was started if CHA2DS2VASc score 2 or more. Subjects having CHA2DS2VASc score as 1 were started on anticoagulation therapy if they have major risk factors. In cases of AF with CHA2DS2VASc score as 1 and minor risk factors, antiplatelets were prescribed.

Cases were followed up and at the end of three months; outcome was defined in the form of death, congestive heart failure, stroke and thromboembolism.

INR was maintained in the range of 2-3 and concomitant treatment (diuretics, ACE-inhibitors, antihypertensive drugs, Oral hypoglycaemic agents. Stroke was defined as a focal neurologic deficit of sudden onset as diagnosed by a physician, lasting >24 hours and caused by ischemia. Peripheral embolism was defined as Thromboembolism outside the brain, heart, eyes, and lungs.<sup>9</sup>

## RESULTS

CHA2DS2VASc score was determined in 64 (29 males, 35 females) cases of non valvular AF. In 3 cases (4.6%) it was zero indicating low risk for stroke. Eight cases (12.5%) had CHA2DS2VASc score as 1 had intermediate risk and 53 cases (82.8%) had score 2 or more indicating high stroke risk ( $p < 0.01$ ).

Present study demonstrated that significant no. of cases of non valvular AF fall in high risk group indicating the importance of risk stratification and stroke prevention by anticoagulant therapy.

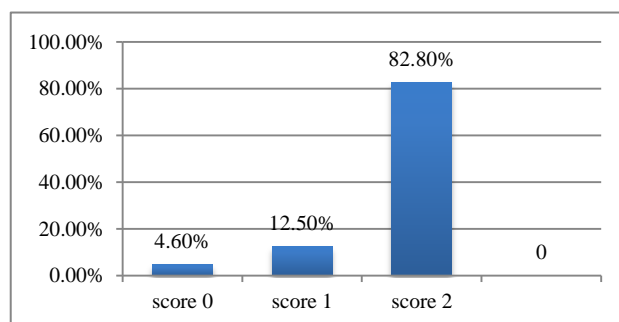


Figure 1: Distribution of CHAD2S2 score.

Three cases of atrial fibrillation (4.6%) presented with stroke and all of them had CHA2DS2VASc score >2. At the time of enrolment, stroke was not reported in any case with CHA2DS2VASc score as zero or one. Stroke risk was significantly higher in cases of CHA2DS2VASc score >2 (p<0.01). Frequency distribution of components of CHA2DS2VASc score has been shown in Table 1.

Other Complications of AF reported at the time of recruitment viz. CHF cardiogenic shock and peripheral thromboembolism have been shown in Table 2. At the end of 3 months, total no. of cases with congestive heart failure was reported be 32 (50%). Ischaemic stroke was present in 5 (7.8%) cases. Peripheral embolism was documented in 1 case (1.5%). Mortality at the end of 3 months in cases of non valvular AF was reported in 7 cases (10.9%).

**Table 1: Frequency distribution of components of CHA2DS2VASc score in non valvular AF.**

Component of CHA2DS2VASc score (at recruitment)	Frequency in non valvular AF (n=64)
Congestive heart failure	32 (50%)
Hypertension	50 (78%)
Age>75 years	7 (10.9%)
Diabetes mellitus	19 (29.6%)
Stroke	3 (4.6%)
Vascular disease	1 (1.56%)
Age 65 -74 years	16 (25%)
Sex category (female)	35 (54.6%)

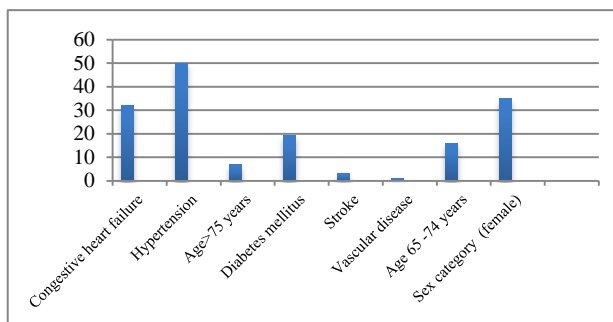
**Table 2: CHA2DS2VASc score and complications of AF at recruitment.**

Complications	CHA2DS2VASc score 0 (N=3)	CHA2DS2VASc score 1 (N=8)	CHA2DS2VASc score 2 (N=53)	Total (n=64)
Stroke	nil	nil	2 (3.7%)	2 (3.1%) p<0.01, s
CHF	nil	2 (25%)	27 (50.9%)	29 (45.3%)
Thromboembolism	nil	nil	1 (1.8%)	1 (1.56%)
cardiogenic shock	nil	nil	7 (13.2%)	7 (10.9%)
uncomplicated	3 (100%)	6 (75%)	16 (30.1%)	25 (39%)

**Table 3: CHA2DS2VASc score and complications of AF at the end of 3 months.**

Complications	CHA2DS2VASc score 0 (N=3)	CHA2DS2VASc score 1 (N=8)	CHA2DS2VASc score 2 (N=53)	Total (n=64)	P value
Stroke	Nil	Nil	5 (9.4%)	5 (7.8%)	<0.01,s
CHF	Nil	2(25%)	30 (56.6%)	32 (50%)	<0.001,s
Thromboembolism	Nil	Nil	1 (1.8%)	1 (1.56%)	NS
Death	Nil	Nil	7 (13.2%)	7 (10.9%)	<0.001,s
Uncomplicated	3 (100%)	6 (75%)	10 (18.8%)	19 (35%)	P<0.001,s

Hypertension (50, 78.1%) and/or ischaemic heart disease (44, 68.7%) were the common etiologic factors associated with non valvular atrial fibrillation. Thyrotoxicosis was documented in 8 (12.5%) cases and COPD in 4 (6.2%), Cardiomyopathy was present in 2 (3.1%) cases. Multiple etiologic factors (hypertension, IHD etc.) were reported in 42 (65.6%) cases. Diabetes mellitus as a comorbidity was present in 19 cases (29.6%). In non valvular type, AF was diagnosed for the first time in 17 (26.5%) cases at the time of recruitment and paroxysmal AF was reported in 3 (4.6%) cases. Persistent AF was present in 23 (35.8%) cases, and 21 (25%) cases had permanent type of AF. Echocardiography demonstrated LV EF<40 in 22 (34.3%) cases, Regional wall motion abnormality were documented in 43 (67.1%) cases. Ischaemic mitral regurgitation because of papillary muscle dysfunction was observed in 4 (6.2%) cases. Left atrial size >40mm was reported in 29 (45.1%) cases.

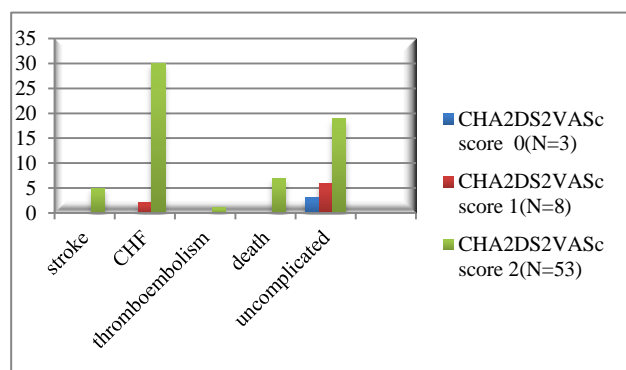


**Figure 2: Frequency distribution of components of CHA2DS2VASc score in non valvular AF.**

Cases with CHA2DS2VASc score as zero (n=3, 4.6%) were uncomplicated. Subjects with CHA2DS2VASc score as 1 (8, 12.5%) had complications in the form of congestive heart failure in 2 cases (25%), and 75% were

uncomplicated. However, stroke was not reported in these cases. CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$  was reported in 53 cases (82.3%). This group had complications in the form of CHF in 30 cases (56.6%), thromboembolism in 1 (1.8%), and stroke in 5 (9.4%) cases. Cases of AF with CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $> 2$  demonstrated significantly high incidence for stroke as compared to those with score as zero or one ( $p < 0.01$ ).

Overall mortality in non valvular group was reported in 7 (10.9%) cases and mortality in cases of AF with CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$  was 13%. CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$  was significantly associated with mortality ( $p < 0.01$ ) Table 3. It was observed in the present study that apart from stroke, other complications associated with AF (congestive heart failure, peripheral thromboembolism and death were also common in subjects with CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$ ).



**Figure 3: Association of CHAD<sub>2</sub>S<sub>2</sub> score with outcomes in non valvular AF.**

Graph (Figure 3) shows association of complications of atrial fibrillation and CHA<sub>2</sub>DS<sub>2</sub>-VASc score. Anticoagulants (LMWH/VKA -warfarin) were prescribed in 56 cases (87.5%) of non valvular AF. Non-compliance for anticoagulation was reported in 12 (18.7%) cases. All cases that were non-compliant had complications of AF. All 7 cases, which died had non-compliance for the anticoagulation therapy. Thromboembolism, ( $p < 0.02$ ), stroke ( $p < 0.01$ ), and death ( $p < 0.01$ ) were more common in cases who were non-compliant. One case on warfarin developed haemorrhagic stroke. However, INR was maintained in the range of 2.3 and patient also had hypertension. Cardiogenic shock was reported as the cause of death in 3 (42.8%) cases, acute decompensated heart failure in 2 (28.5%) cases and sudden cardiac death in 2 (28.5%) cases.

Univariate analysis revealed significant association of CHA<sub>2</sub>DS<sub>2</sub>-VASc score, CHF, stroke, EF $< 40\%$  type of AF with mortality in cases of atrial fibrillation. Multivariate analysis was performed to find out independent association of CHA<sub>2</sub>DS<sub>2</sub>-VASc score with CHF, stroke, EF $< 40\%$  type of AF with mortality, demonstrated significant association of CHA<sub>2</sub>DS<sub>2</sub>-VASc score with stroke and mortality in non valvular AF (OR 3.9, 95% CI

2.6 to 6.0,  $p < 0.002$ , OR 2.05, 95% CI 1.06 to 3.9,  $p < 0.05$  respectively).

## DISCUSSION

Contemporary clinical risk stratification schemata for predicting stroke and thromboembolism (TE) in patients with atrial fibrillation (AF) are largely derived from risk factors identified from trial cohorts. Framingham study reported the impact of atrial fibrillation for stroke incidence and mentioned that age adjusted incidence of stroke was near fivefold when AF is present, Euro heart survey refined the 2006 Birmingham/National Institute for Health and Clinical Excellence (NICE) stroke risk stratification schema into a risk factor-based approach by reclassifying and/or incorporating additional new risk factors.<sup>10</sup>

The CHA<sub>2</sub>DS<sub>2</sub>-VASc score has been validated in multiple cohorts and the accumulated evidence shows that CHA<sub>2</sub>DS<sub>2</sub>-VASc is better at identifying ‘truly low-risk’ patients with AF and possibly better than, scores such as CHADS<sub>2</sub> in identifying patients who develop stroke and thromboembolism.

Present study demonstrated a high stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $> 2$ ) in 53 (82.8%) cases of non valvular AF indicating need of anticoagulant therapy and stroke prevention. Roopindersingh K et al studied risk stratification schemes, anticoagulation use and outcomes in non valvular AF in 42834 cases by CHADS<sub>2</sub> risk score, and reported 22.7% as low risk, 27.5% in the intermediate group and 49.8% to be in high risk for stroke.<sup>11</sup>

CHA<sub>2</sub>DS<sub>2</sub>-VASc score reclassified 16,722 patients and found 7.8% in low risk, 13.8% in intermediate risk and 78.45% in high risk. Present study also demonstrated higher incidence of stroke (7.8%) in cases of non valvular AF. In subjects with CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $> 2$  incidence of stroke (9.4%) was significantly higher as compared to CHA<sub>2</sub>DS<sub>2</sub>-VASc score as 0 or 1,  $p < 0.01$ . ALFA study reported 10.8% incidence of stroke in AF and R Nieuwlaat et al reported the same as 9%.<sup>12,13</sup>

Cases with CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $> 2$  had higher incidence of CHF and peripheral embolism. RAFTING study reported thromboembolic events in 2.5% of cases of AF.<sup>14</sup> Tejinder k et al reported incidence of CHF in 67% cases of AF and ALFA study as 42.6%. Mortality in cases of AF with CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $> 2$  was significantly higher than those having score as 0 or 1, indicating that apart from predicting stroke and vascular events, CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $> 2$  may also indicate prognosis in non valvular AF.<sup>15</sup> Multivariate analysis revealed independent association of CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $>$  with mortality at the end of 3 months.

However, further long term, prospective large sample sized multicentric studies are needed to demonstrate

whether CHA<sub>2</sub>DS<sub>2</sub>VASc score can be used to predict mortality in non valvular AF. In ALFA study carried out on 726 cases of atrial fibrillation, Samuel et al reported that congestive heart failure in 4.1% of cases, embolic complications in 1.8% and mortality in 3.7%.<sup>16</sup> BAFTA study on 973 patients of age >75 years determined the use of aspirin versus warfarin in stroke prevention in elderly with atrial fibrillation.<sup>17</sup>

The primary end point was fatal or disabling stroke, (ischemic or haemorrhagic) intracranial haemorrhage, or clinically significant arterial embolism. Yearly risk cases on warfarin was 1.85 versus aspirin was 3.8% and absolute risk reduction as 2%. The Loire Valley Atrial Fibrillation Project done by Olesen JB et al revealed that in patients with CHADS<sub>2</sub> risk factors who were not treated with anticoagulation were associated with increased risk of stroke and presence of vascular disease further increased the risk of stroke.<sup>18</sup>

Present study also demonstrated that incidence of stroke in non valvular AF was significantly high in cases who were non-compliant for anticoagulant therapy than those who received anticoagulation therapy. It is also recommended that oral anticoagulants should be easily available, affordable and INR facilities made accessible for these cases of non valvular AF. It has also been demonstrated in the study that anticoagulation therapy is relatively safe, if INR is monitored.

Even if newer oral anticoagulants are approved for stroke prevention in non valvular AF, cost is the limiting factor for most of present patients. It was also observed that CHF was present in significant no. of cases in cases of AF. Even if AF is not the direct cause of CHF, it is one of the important precipitating factor and one of the adverse outcome associated with AF, and is an important aspect of management in cases of atrial fibrillation.

### Limitations

Cardiac catheterisation and catheter ablation facilities as well as newer oral anticoagulants are not available at our center and rate control strategy has been practised for treatment of atrial fibrillation. Short term outcomes have been assessed in the present study.

### CONCLUSION

CHA<sub>2</sub>DS<sub>2</sub>VASc is a simple score to predict stroke risk in cases of non valvular atrial fibrillation and is easy to estimate. Significant no. of cases of AF fall in high risk group and need oral anticoagulation therapy for stroke prevention. CHA<sub>2</sub>DS<sub>2</sub>VASc score  $\geq 2$ . Which is associated with high incidence of stroke in cases of non valvular AF? CHA<sub>2</sub>DS<sub>2</sub>VASc score  $\geq 2$  is associated with mortality as a short term adverse outcome in non valvular atrial fibrillation.

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