



Risk stratification, an indispensable cogitation to avert stroke in patients with atrial fibrillation: Evidence from a prospective observational study from India

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ABSTRACT

The comprehensive management of AF aims not only at the restoration of the sinus rhythm but indulges itself in thromboprophylaxis for stroke prevention which remains inevitable. A prospective observational study was carried out. Newly diagnosed and existing cases with AF above the age of 18 years were reviewed for eligibility. Demographic details and complete history of the patients was obtained from medication charts and personal interview with patients and their attendants. This was succeeded by stratification of subjects using stroke risk calculators namely CHADS2 and CHA2DS2-VASc Score. Bleeding risk assessment was performed using HAS-BLED Score. Data from total of 130 patients were collected. At the outset, CHADS2 score was wielded to categorize the subjects based on their risk for stroke as a complication of AF and results revealed that 23% (n=12) were categorized as low risk, followed by 48 (36.92%) patients who were categorized to be intermediate risk. Higher proportion of the patients, i.e. 53.84% (n=70) were categorized to be at a high risk of developing stroke as a complication of AF. The same subjects were categorized for their stroke risk using the second risk stratification scheme, precisely CHA2DS2VASc score. The intermediate risk category comprises of 21.53% (n=28) with high risk category (81.53%, n=106) being the loftiest. CHADS2 score and CHA2DS2VASc score can be easily used to identify the patients at a risk for stroke. The study sketched a comprehensive description of incident AF patients and proffered estimates of the incidence of vascular and other outcomes in patients with AF.

INTRODUCTION

Atrial Fibrillation is one among the commonest heart rhythm disorders in which the normal organized rhythm contributed by the electrical impulses of the upper cardiac chambers, namely atria deteriorate to a rapid disorganized pattern and this disorganized pattern is classically referred to as “irregularly irregular”[1]. As the age of the population increases the amount of AF patients is expected to step up by 150% in the subsequent four decades with age over 80 years being a major risk factor for half of the patients. The elevated incidence of stroke augmented by the increasing load from AF stretches the risk to five-seven folds. Worse prognosis of stroke secondary to AF is discerned in patients with arrhythmia[2]. The comprehensive management of Atrial Fibrillation aims not only at

the restoration of the sinus rhythm but indulges itself in thromboprophylaxis for stroke prevention which remains inevitable. The key to thromboprophylaxis should be based on critical assessment of stroke as well as bleeding risk that warrants net clinical benefit[3].

Proposition to assess stroke risk in AF has been aided by an assortment of risk stratification models till date with an intension of helping clinicians in arriving at a sensible decision. The main focus of these risk stratification scores is to contemplate the risk and benefit before arriving at a decision for anticoagulation[4]. The essence from the AF Investigators and SPAF trial stroke risk stratification schemes supplemented by the data from the non-VKA arms of the historical trial cohorts lead to the evolution of CHADS₂ score. This scoring system emphasis mainly on 5 risk

factors namely congestive heart failure, hypertension, age ≥ 75 , diabetes, and prior stroke each set to a point of one each except for prior stroke which is allocated a point of 2. It was originally validated in the NRAF cohort (2001) of hospitalized AF patients and further more subjected to subsequent validation in numerous other cohorts[3]. An advancement of time and research lead the European Society of Cardiology Guidelines to assimilate the CHA₂DS₂-VASc score. Presently it is found to be the most robust in recognizing patients actually at risk of AF related stroke. Proposition in 2009 was preceded by validation in European cohort from the Euro Heart survey which was further succeeded by validation in multiple independent epidemiological and trial cohorts. Though constructed as an uncomplicated risk assessment tool this risk stratification scheme was worthy in that it was inclusive of additional risk factors not considered in the CHADS₂ score with a precise weight age given to age by classifying it into specific age groups and allocating a discreet value for the same[3]. Choice of prospective candidates for long term anticoagulation therapy should be preceded by careful assessment of patient specific risk and benefits before initiation. This could be accomplished by various bleeding risk score calculators namely HAS-BLED, HEMORR₂HAGES, ATRIA etc. For the purpose of estimating the risk for major bleeding in view of atrial fibrillation care HAS-BLED score has been widely used. The major factors considered in the HAS-BLED score includes hypertension (uncontrolled systolic blood pressure > 160 mmHg), abnormal renal and/or liver function, previous stroke, bleeding history or predisposition, labile international normalized ratios, elderly and concomitant drug and/or alcohol excess. The distribution of score ranges from 0-9. A caution and regular evaluation of patients is recommended for a score ≥ 3 [5]

With this study we aim to assess the risk for stroke in patients with Atrial Fibrillation with the future expectation of optimizing stroke risk assessment strategies in clinical settings that shuns the uncertainty.

METHODOLOGY

A prospective observational study was carried out in a 750 bedded tertiary care referral hospital in Perinthalmanna, Kerala for a period of one year. Official consent was obtained from the concerned authorities prior to the initiation of the study. Subject seeking services from the Cardiology department during the proposed time period were considered for the study. The criteria for selection of the subjects to be enrolled in the study were specified beforehand to data collection. The nature, type and intension of the study were explained to the patient by direct interaction in patient's vernacular language. After informing the participants about where and how the data will be used, sufficient time was given to decide whether or not to participate in the study. Written informed consent was then obtained from voluntary subjects. All newly diagnosed and existing cases with Atrial Fibrillation above the age of 18 years were reviewed for eligibility. Critically ill patients with high rate of mortality less than one month and patients with Acute Coronary Syndrome were excluded from the study. Transient Atrial Fibrillation due to reversible causes like infection, alcoholic intoxication and post operative Atrial Fibrillation and subjects with hyperthyroidism were not considered for the study. Reported cases confirmed with ECG by the physician were identified and critically analyzed to compile the requisite information. Specific data collection form was devised and stroke risk calculators were identified. Demographic details and complete history of the patients was obtained from medication charts and personal interview with

patients and their attendants. This was succeeded by stratification of subjects using stroke risk calculators namely CHADS₂ Score and CHA₂DS₂-VASc Score. The scoring pattern followed was 0 for low risk, 1 for intermediate risk and 2-6 for CHADS₂ and 2-9 for CHA₂DS₂-VASc Score to be classified as high risk respectively. The study subjects were categorized based on this score onto the latter groups with respect to the scores they received Bleeding risk assessment was performed using HAS-BLED Score. The score ranges from 0 to 9, with scores of ≥ 3 indicating high risk of bleeding, for which caution and regular review of the patient are recommended. Based on the collected information about the subject stroke risk was calculated for identifying the desideratum for thromboprophylaxis.

Data collected from the study was tabulated in Microsoft Excel 2010 and were keyed into the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) computer software version 20 for windows and analyzed by appropriate statistical methods. Statistical analysis was both descriptive at 95% confidence level (CI). Continuous variables were analyzed using the mean, percentage and standard deviation. Discrete variables were analyzed using proportions. Chi square test and repeated ANOVA was used for statistical analysis of follow up of clinical data variables.

RESULT

Data from a total of 130 patients were collected among which 72 males (55.38%) were followed by 58 females (44.61%). The subjects were categorized into various age groups for a better assessment of the risk for stroke. The detected mean $\pm$ SD of age of the study was found to be 67.64 ± 10.92 years. Minimum age was found to be 31 years and maximum age of the study population was 86 years. Among the subject under the study majority of patients lies in the age group above 70 years old ($n=60$) which constitutes 46.15%, followed by age group 61-70 which makes 32.37 % ($n=42$) and 15.38 % ($n=20$) of the study population comes under the age group 50-60 years. Minimum number of subjects ($n=8$) were observed in the age group below 50 years which makes 6.15%. According to the comparison performed based on the age wise distribution in males and females, the results revealed the presence of 20 females and 40 males in the age group above 70 years. The social history of the subjects when taken into account depicted that 33.8% ($n=44$) were found to be alcoholic and 41.5% ($n=54$) were established to be smokers. The segregation of study subjects into the three classifications of AF namely paroxysmal, persistent and permanent divulged that paroxysmal AF comprises of 56.9%, succeeded by permanent AF in 33.8% and persistent AF in 9.2%. Palpitation (75.4%), fatigue (69.2%), shortness of breath (52.3%), chest pain (23.1%), and syncope/ presyncope (7.7%) chronologically encapsulates the major symptoms observed. The concurrent diseases observed in the study subjects include hypertension (49%), coronary artery disease (27%), heart failure (18%), and valvular heart disease (6%). Among the patient population ($n=130$), the baseline mean heart rate observed was $125.4 \pm$ SD 16.1 and the minimum and maximum were observed as 106 and 170 respectively. The first and second follow up reported a mean of $109.0 \pm$ SD 9.8 with a minimum of 92 and maximum of 140 and a mean of $99.1 \pm$ SD 9.8 with a minimum of 82 and maximum of 123 respectively. The perceived baseline mean systolic blood pressure was $138.9 \pm$ SD 21.6. During the first follow up the mean was found to be $127.7 \pm$ SD 15.4. During the second follow up the mean was found to be $127.8 \pm$ SD 15.5. The baseline mean diastolic blood pressure

RISK STRATIFICATION USING CHADS₂ SCORE

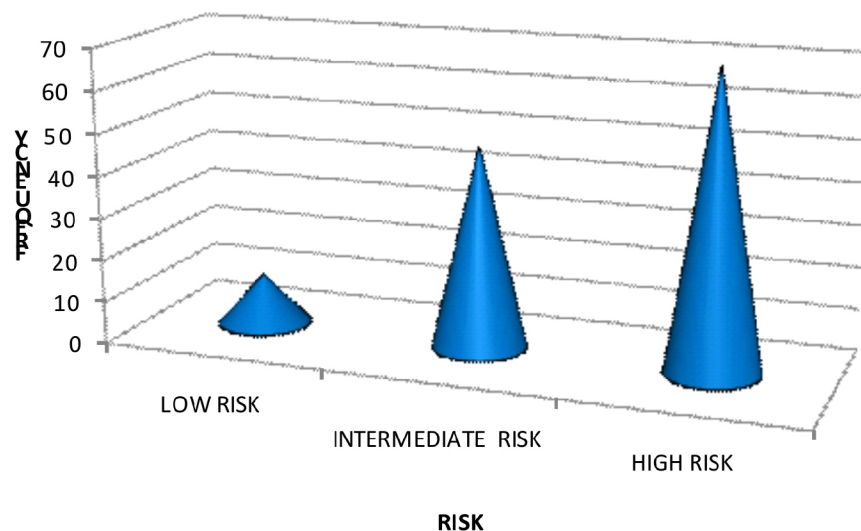


Fig. 1 : Risk stratification of stroke in study subjects using CHADS2 score

RELATIONSHIP BETWEEN AGE AND RISK FOR STROKE DEVELOPMENT STRATIFIED USING CHADS₂ SCORE

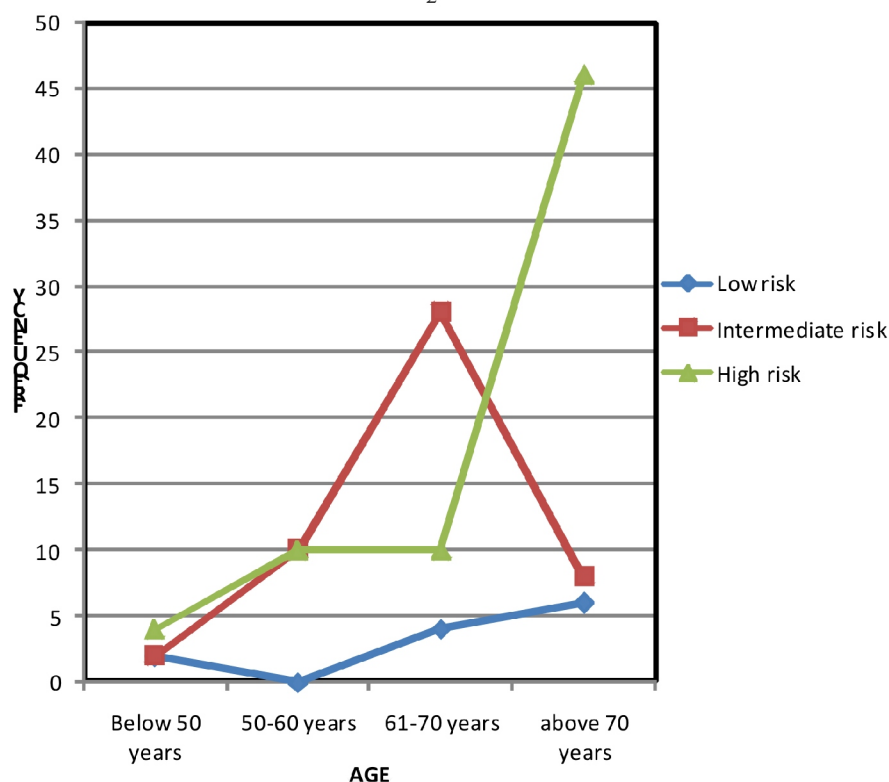


Fig. 2 : Distribution of CHADS2 score among various age groups

observed was $84.6 \pm \text{SD } 8.5$ with a mean of $84.8 \pm \text{SD } 7.1$ in the first follow up and $84.5 \pm \text{SD } 8.5$ in the second follow up.

At the outset, CHADS₂ score was wielded to categorize the subjects based on their risk for stroke as a complication of AF. Out

of 130 study subjects .23% (n=12) were categorized as low risk, followed by 48 (36.92%) patients who were categorized to be intermediate risk. Higher proportion of the patients, i.e. 53.84% (n=70) were categorized to be at a high risk of developing stroke as a complication of AF (Figure 1). Alongside they were also

sorted for risk for stroke development using CHADS₂ score based on their age, below the age of 50 years, 2 patients each were identified in both low risk and intermediate risk category and 4 patients were recognized to be high risk category. Within the age group 50-60 years no low risk patients were spotted, 10 each were identified in both intermediate risk and high risk category and in the age group between 61-70 years, 4, 28 and 10 patients were identified in low risk, intermediate risk and high risk respectively. In the age group above 70 years 6, 28 and 46 patients were identified in low risk, intermediate risk and high risk category respectively (Figure 2). In addition categorization was also executed with respect to gender and the results showed 8, 24, 40 males in low risk, intermediate risk and high risk respectively. Furthermore 4, 24 and 30 females were identified in low risk, intermediate risk and high risk category respectively (Figure 3).

The same subjects were categorized for their risk for stroke development using the second risk stratification scheme, precisely CHA₂DS₂VASc score. None of the study subjects were categorized as low risk according to CHA₂DS₂VASc score. The intermediate risk category comprises of 21.53% (n=28) with high risk category (81.53%, n=106) being the loftiest (Figure 4). The risk score. The risk score of the subjects were segregated with respect to the age based on which it was identified that none of the study subjects falls under the category of low risk. Below the age of 50 years, 2 patients were identified in intermediate risk category and 6 high risk patients were ascertained. In the age group between 50-60 years 8 patients were spotted in intermediate risk category and 12 patients were identified in high risk category. 12 and 30 patients were respectively identified in the age group of 61-70. Furthermore in the age group above 70

years none of the patients were categorized in low risk category, 6 and 54 patients were identified in intermediate risk and high risk category respectively (Figure 5). Withal segregation was also perpetrated with respect to gender. No low risk male and female patients were identified, 22 and 50 males were identified in intermediate risk and high risk category respectively and 6 and 56 females were identified in intermediate risk and high risk category respectively (Figure 6).

The risk for the development of bleeding as a consequence of anticoagulation was assessed using the HAS-BLED score. Among the study subjects who received anticoagulation 42% (n=54) had a low risk for development of bleeding whereas 58% (n=76) were at a high risk for bleeding (Figure 7). The study subjects (n=130) were categorized for their risk for stroke development using the HAS BLED score based on their age. Below the age of 50 years, 2 patients each were identified in both low risk and intermediate risk category and 4 high risk patients were identified. In the age group between 50-60 years none of the patients were identified in low risk category, 12 were identified in intermediate risk category and 8 in the high risk category and in between 61-70 years 0, 24 and 18 patients were identified in low risk, intermediate risk and high risk respectively. For bye the age group above 70 years identified 14 and 46 patients in intermediate risk and high risk category respectively.

DISCUSSION

The study aims to assess the risk for stroke in patients with Atrial Fibrillation and to characterize the efficacy of anticoagulants used for thromboprophylaxis in concerned patients. As per the inclusion and exclusion criteria, a total of 130 subjects were enrolled in the study on the basis of convenience

RELATIONSHIP BETWEEN GENDER AND RISK FOR STROKE DEVELOPMENT STRATIFIED USING CHADS₂ SCORE

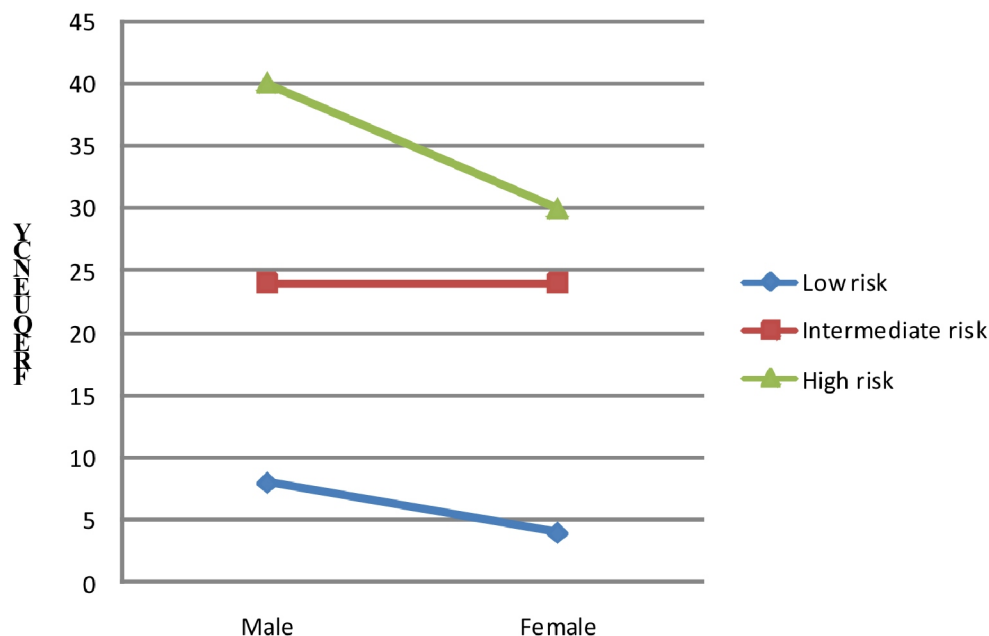


Fig. 3 : Distribution of CHADS2 score among males and females

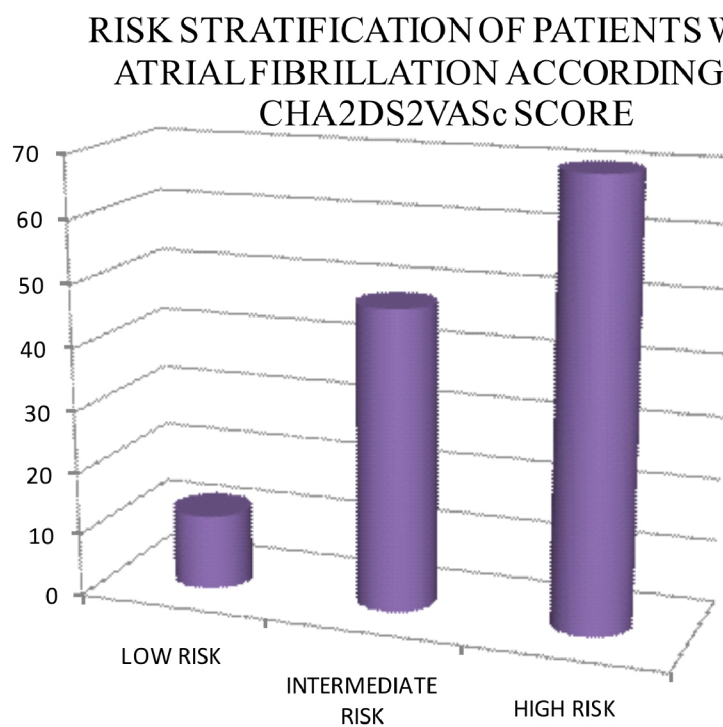


Fig. 4 : Risk stratification of stroke in study subjects using CHADS₂VASc score

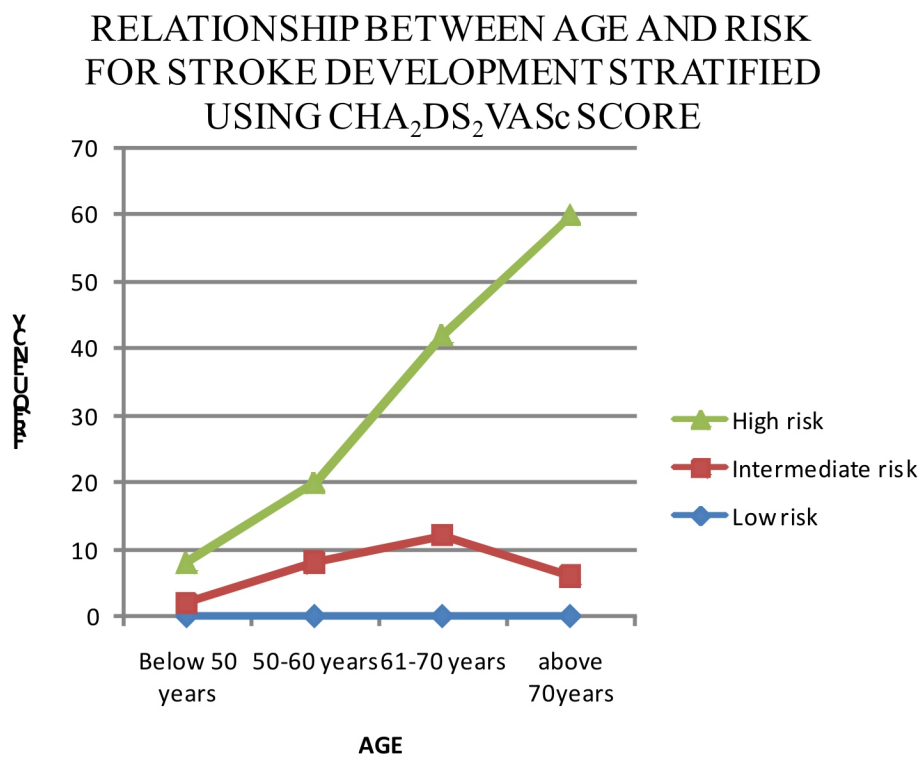


Fig. 5 : Distribution of CHADS₂VASc score among various age groups

RELATIONSHIP BETWEEN GENDER AND RISK FOR STROKE DEVELOPMENT STRATIFIED USING CHA₂DS₂VASc SCORE

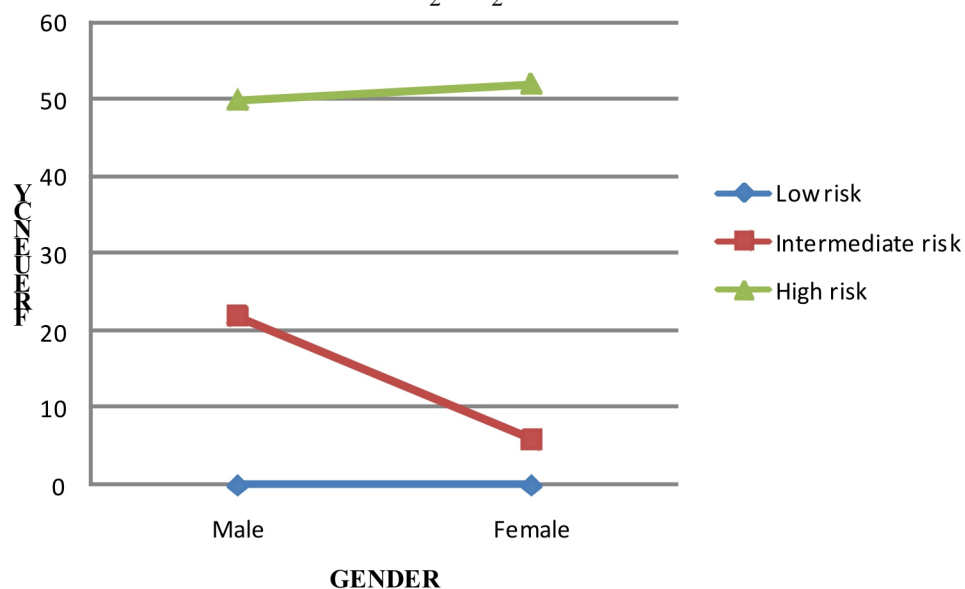


Fig. 6 : Distribution of CHADS2VASc score among males and females

RISK STRATIFICATION OF BLEEDING USING HAS- BLED SCORE

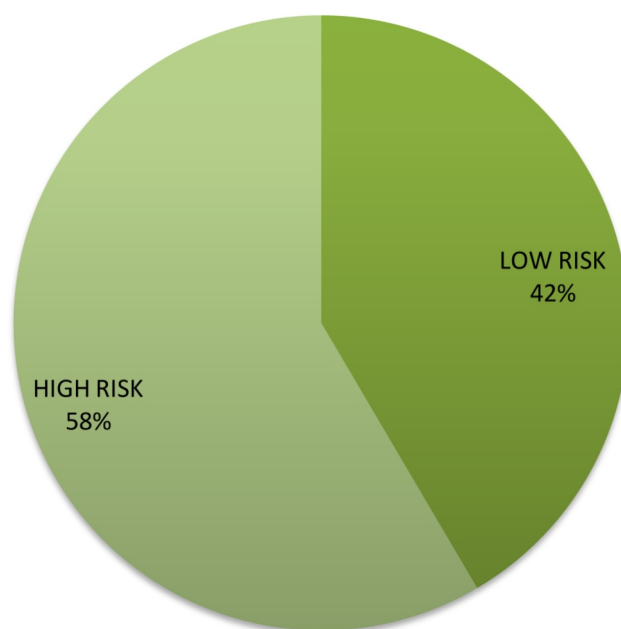


Fig. 8 : Risk for bleeding among the study subjects stratified using HAS-BLED score

sampling. The present study concludes a male predominance over female population with a male female ratio of 1.2:1 which overlaps the general statement of male gender at a higher risk for Atrial Fibrillation. Similar results were obtained in a study conducted by Massimo Zoni-Berisso et al[6] (2014). Studies conducted by Vicente Bertomeu-González[7] (2015) et al gave similar results with 57.5 % male supremacy. Reinforcing results were obtained regarding age above 70 years to be an independent risk factor for stroke. Through the study, it was perceived that mean age was 67.64 ± 10.92 years, similar to the outcomes of study conducted by Russo *et al*[8] (2015), where mean age of the population was 64.9 ± 8.8 years. The fact that the study population mostly included this age group cannot be ignored while deriving at a conclusion regarding age. Conclusive establishment of relationship between social habits and development of AF could not be extracted. Conflicting to the generally observed norm of increased incidence of permanent AF as in a study conducted by Eitaro Kodani et al[9] where permanent classification of AF predominates by 47.1%, our study revealed relatively towering incidence of paroxysmal AF. A possible explanation for this could be that the study population mainly included patients with paroxysmal AF. The pattern of symptoms observed in the study population was palpitation, fatigue, shortness of breath, syncope/presyncope, chest pain, shortness of breath etc. The perceived pattern was in accordance with the results observed in the study conducted by Massimo Zoni-Berisso et al[6], where the major symptoms observed were palpitation in 42-55% of patients, asthenia in 15-49% of the patients, dyspnoea in 24-49% of patients and angina in 10-20% of the patients.

Distribution of comorbidities contemplated during the study period identified that the major comorbidity as hypertension. Heart failure, Diabetes, Respiratory Disease and Renal Failure were the other described concomitant diseases. The results were similar to conclusions of study conducted by Massimo Zoni-Berisso et al[6], where the major comorbidity identified was hypertension 67-76%, followed by heart failure 22-42%, followed by diabetes 20-24%, respiratory disease 10-18%, renal failure 11-22%.

Elimination of thromboembolic complications is an indispensable dogma in the management of AF and should commence with individual risk assessment of each patient. CHADS₂ score can be easily used to identify the patients at a risk for stroke. Among the study subjects 9.23% (n=12) were categorized as low risk, followed by 48 (36.92%) patients who were categorized to be intermediate risk. Higher proportion of the patients, i.e. 53.84% (n=70) were categorized to be at a high risk of developing stroke as a complication of AF. The results were compared to a study conducted by Jonas Bjerring Olesen et al[10] (2011), and the results obtained were similar, with a low risk score of 21.6%, intermediate risk score of 31.4% and a high risk score of 47%.

As an attempt to improve the assessment of stroke risk, CHA₂DS₂-VASc score was developed as an amalgamation of risk factors that defined the CHADS₂ score together with additional risk factors. It is thought to simplify and precise the stroke risk identification. None of the study subjects were categorized as low risk according to CHA₂DS₂-VASc score. Of the study subjects 28 (21.53%) patients who were categorized to be intermediate risk. Higher proportion of the patients, i.e. 81.53% (n=106) were categorized to be at a high risk of developing stroke as a

complication of AF. The results were analogized to a study conducted by Abdulrahman M. Al-Turaiki et al[11] (2016), and the results obtained were homogeneous, with a low risk score of 1.5%, intermediate score of 6.4% and high risk score of 92%.

Among the study subjects who received anticoagulation 42% (54) had a low risk for development of bleeding whereas 58% (76) were at a high risk for bleeding. The percentage of patients who were at a high risk of bleeding was relatively high in the study sample (58%) compared to similar studies such as reported by Marcucci et al[12] (8.6%) and by Abdulrahman M. Al-Turaiki et al[11] (27.7%). This could also be attributed to the high prevalence of modifiable risk factors in the study sample. On the other hand, a high percentage of patients was using medications that may increase bleeding risk. The virtue of oral anticoagulants over aspirin in patients with Atrial Fibrillation emphasizes the necessity of anti coagulation. However it should be brought to concern that the recommendation for anticoagulation should not merely depend on risk but must also consider the risk for bleeding identified using various bleeding risk scoring schemes namely HAS-BLED score.

CONCLUSION

Atrial Fibrillation is considered to be a priority in the quality improvement areas due to the irrefutable clinical and financial impact it has on the patients prone to stroke. The study indulged itself to typify the risk of stroke in patients with Atrial Fibrillation to conclude that the use of risk stratification scheme plays a vital role in pinpointing patients with high risk of stroke. The study sketched a comprehensive description of incident AF patients and proffered estimates of the incidence of vascular and other outcomes in patients with AF.

The risk for stroke in Atrial Fibrillation is determined in both CHADS₂ and CHA₂DS₂-VASc score based on the contributions of risk factors composing the score specific to each patient. Though considered to be simple in assorting patients for need of anticoagulation, CHADS₂ is considered to provide modest predictability. Due to the considerations of additional risk factors in CHA₂DS₂-VASc score, the results are anticipated to better correlate with stroke risk. The discretion of necessity and agents to be used for antithrombotic therapy by the physician may fluctuate depending on which scheme is intimated for the patients.

The decision for anticoagulation should incorporate the risk of bleeding in potential subjects widely assessed using the HAS-BLED score to forecast the risk for major hemorrhage in vulnerable subjects. These tools can be employed to optimize clinical decision making and to address the foreseeable risks. It should be emphasized that exclusion of subjects from OAC therapy should not be based solely on outcomes of the score. With this study we advocate the mandate of risk stratification schemes in clinical settings in order to promote the judicious use of Oral Anticoagulant's in deserving patients.

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