Clinical and Etiological Profile of Patients Admitted with Non-Valvular Atrial Fibrillation

Authors
Dhinakaran Krishnamurthy[1], Ramprakash B[2]
[1]DNB (Med), DNB (Cardiology), Registrar, GKNM Hospital, Coimbatore, Tamil Nadu
[2]MD (Med), DM (Cardiology), Senior Cardiologist and Electrophysiologist, GKNM Hospital, Coimbatore
Corresponding Author
Dr Dhinakaran Krishnamurthy, DNB (Med), DNB (Cardiology)
Consultant Cardiologist, AMC Super Speciality Hospital, Tirupur, Tamil Nadu, India

Abstract
Background: *Atrial Fibrillation (AF) is a common, growing and serious cardiac rhythm disturbance that is responsible for considerable morbidity and mortality. Due to rising prevalence of hypertension and diabetes the number of patients presenting with non-valvular atrial fibrillation is increasing.*
Aim: *To study the etiology and clinical presentation of patients admitted with non-valvular atrial fibrillation.*
Methods: *This is a retrospective observational study of non-valvular atrial fibrillation (NVAF) patients admitted under cardiology unit during the period July 2017 to December 2018. Diagnosis of atrial fibrillation was made by 12-lead ECG. Patients underwent thorough physical examination, routine laboratory testing, Echocardiogram and other relevant investigations based on comorbid conditions.*
Results: *A total of 75 patients with non-valvular atrial fibrillation were enrolled in the study. Many patients had more than one risk factors for AF, which included obesity (69.4%), hypertension (53.3%), diabetes (42.7%), age more than 65 years (41.3%) and coronary artery disease (CAD) (22.7%). Echocardiographic mean left atrial size was 40.2 mm and many patients had elevated LA volume. Septal E/E' was elevated in 65.3% of patients in this study, and the majority of the patients (89.3%) had a CHA2DS2-VASc score of 2 or more requiring anticoagulation.*
Conclusion: *Hypertension, obesity, diabetes and age more than 65 years are observed to be major risk factors for non-valvular atrial fibrillation in this study. Enforcing healthy lifestyle, early screening, appropriate evaluation and control of modifiable risk factors can reduce the risk of non- valvular atrial fibrillation and its consequences*
Keywords: *Non-valvular atrial fibrillation, left atrial volume, Diastolic dysfunction, Anticoagulation.*

Introduction

Atrial fibrillation (AF) is a common, growing, and serious cardiac rhythm disturbance that is responsible for considerable morbidity and mortality in the population. Atrial fibrillation is a major risk factor for stroke, congestive heart failure, and mortality. Cardiovascular Health Study and Framingham study data indicate that the incidence of AF per 1000 person – years in those younger than the age 64 years is 3.1 in men and 1.9 in women, increasing sharply to approximately 19.2 per 1000 person – years in those aged 65 to 74 years and to as high as 31.4 to 38 in octogenarians[1].

A global burden of disease 2010 study on the worldwide epidemiology of AF gives important insights into the changing trends in the incidence, prevalence and gender relation of AF. Patients with AF are hospitalized twice as often as patients without AF and are 3 times more likely to have multiple admissions. 2.1% of patients with AF died in the hospital compared to 0.1% without it [2, 3].

Most reports on the epidemiology of AF are based on white North Americans or Europeans. In our country, there is very little data on AF, most of the data that has been derived is from international studies with the Indian cohort[4]. However with the knowledge about the Indian cohort from the REALIZE-AF and RELY-AF studies and the IHRS-AF registry, more insight is now available on AF data amongst Indian patients.

The RELY-AF registry reported that amongst the AF patients, Valvular heart disease (VAD) was most common in India (46.7%) and Africa (32.6%) and much less common in Eastern Europe (10.7%) and Western Europe (8.8%)[5]. Due to lack of quality epidemiological and detailed echocardiographic data it is difficult to determine the exact burden of population with AF & its etiology in India. Multiple clinical risk factors, echocardiographic parameters and other investigations have been shown by many studies, to increase the risk of AF. They also have an influence on morbidity and mortality.

There are only very few studies on Non-valvular atrial fibrillation in India. Most of the studies done earlier had more information and research on atrial fibrillation of Rheumatic etiology.

Aim

To study the etiology & clinical presentations of patients admitted with non-valvular atrial fibrillation

Objectives

1. To study the various etiologies of Atrial fibrillation of non-valvular etiology in admitted patients.
2. To study the clinical & echocardiographic profile of non-valvular AF in hospitalized patients
3. To assess the risk of thromboembolic stroke in patients admitted with non-valvular AF using the CHA2DS2-VASc score

Materials and Methods

All patients admitted in our Hospital, under Cardiology unit with atrial fibrillation during the period July 2017 to December 2018 were the potential subjects. 75 patients were included in the study. Diagnosis of AF was based on the routine 12- lead electrocardiogram (ECG) report during the hospitalization. Past medical records including ECG's, echocardiogram & laboratory investigations were used in determining the duration & cause of AF & underlying comorbid conditions.

Data is entered into Microsoft Excel and analyzed using SPSS software (version 26.0, IBM Corporation). Standard statistical procedures of descriptive and inferential statistics were used for the analysis of the data. Following are the statistical tools used to analyze and interpret the data to arrive at a conclusion. Descriptive analyses such as mean, standard deviation, and percentage are used to express quantitative variables of clinical parameters considered in research interpretation. After the data were tested for Independent sample t-test will be used to compare the groups. For interpretation of the results, a p value 0.05 was considered statistically significant. Qualitative data will be described as frequencies (number of cases) and percentages.

Inclusion Criteria

1. All adult patients (age above 18 years) admitted with clinical diagnosis of atrial fibrillation of non-valvular etiology
2. Patient's or patient's relatives signing the informed consent.

Exclusion Criteria

1. Atrial fibrillation of rheumatic and valvular etiology

2. Patients or relatives not giving consent for the study

Initial Evaluation

The initial evaluation of a patient presenting with AF involves characterizing the pattern of the arrhythmia, determining its cause, defining associated cardiac and extra cardiac disease, and assessing thromboembolic risk. Symptoms, prior treatment, family history, and a review of associated conditions and potentially reversible risk factors will be meticulously documented.

Investigations

Routine investigations like complete blood counts, blood urea, serum creatinine, blood sugar, serum electrolytes and chest x-ray examination were carried out. Special investigations like cardiac biomarkers like troponin I (Quantitative) were done as necessary by clinical presentation. Thyroid function test was done for all patients admitted with AF.

ECG was analyzed for the presence of LV hypertrophy, evidence of Myocardial infarction, bundle branch blocks & other features. Presence of LV hypertrophy was assessed by Cornell's ECG criteria. Echocardiogram was used to assess the presence of LV hypertrophy, chamber dimensions (LA size, LA volume, RA size), regional wall motion abnormalities, LV function (Ejection fraction, Diastolic function). LA volume was measured using disc summation technique. Doppler assessment of valvular pathology was done. Diastolic function was assessed by E/E' (Tissue doppler), by taking an average of 3 different measurements.

Patients presenting with clinical features of acute coronary syndrome underwent coronary angiogram for assessment of coronary lesions. The findings on coronary angiogram were noted. CHA2DS2-VASc score was used to assess the risk of stroke in patients with AF. It includes congestive heart failure, hypertension, age ≥75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack (TIA) or thromboembolism (doubled), vascular disease age 65 to 74 years and sex category point score systems.

Results

Common risk factors for atrial fibrillation in our study were obesity (69.4%), hypertension (24.0% and 29.3%), diabetes (16.0% and 26.7%), age more than 65 years (58.7%), CAD (14.7%), and smoking (6.7%).
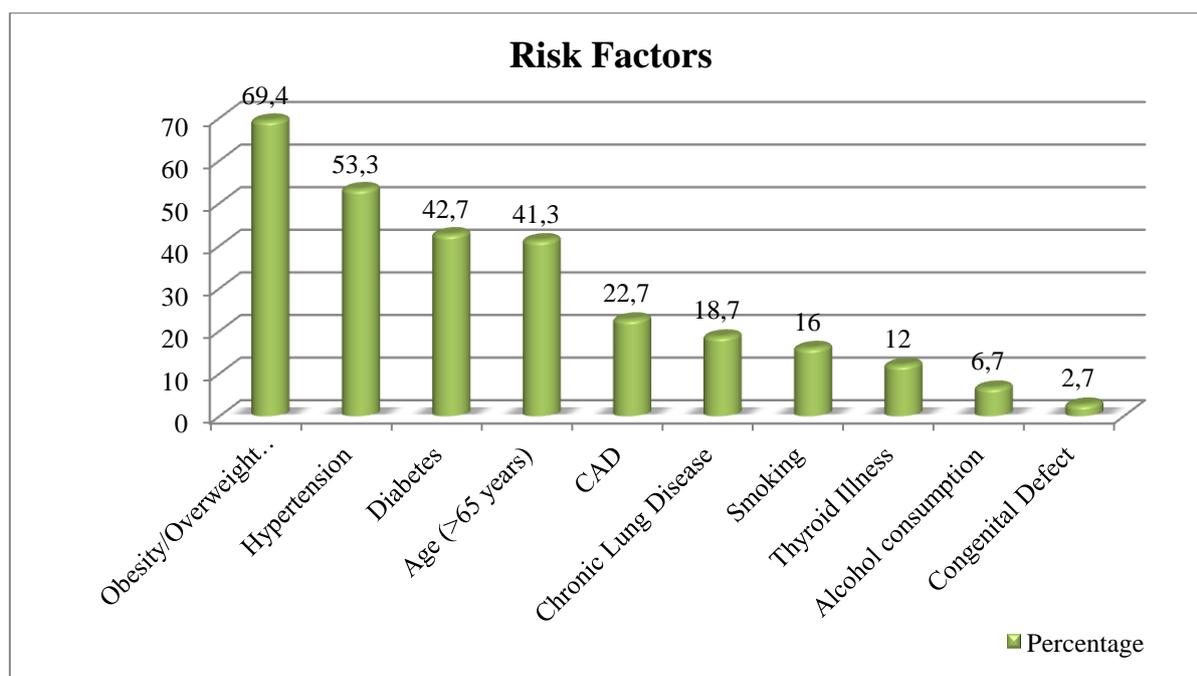

Figure 1: Risk Factors Present in the Study Populations

75 patients included in the study were grouped based on age into Group A (below 65 years) and Group B (above 65 years). The mean age was 56.55±7.84 in Group A and 75.48±6.58 in Group B. In the above 65 years age group (Group B), 44 patients had significant relation to body mass index (BMI) categories (p=0.041). There were no significant differences in the other characteristics of the patients between the two groups, such as age, hemoglobin, creatinine, thyroid stimulating hormone (TSH), random blood sugar, heart rate, systolic blood pressure, and diastolic blood pressure values (Table 1).

Table 1: Demographic and Laboratory Characteristicsof the Study Populations

Variables	Group A (n-31) Below 65 Years	Group B (n=44) Above 65 Years	P Value
Age	56.55±7.84	75.48±6.58	0.814
BMI	27.13±4.35	25.05±3.98	0.041**
Hemoglobin	13.70±1.82	12.50±2.10	0.561
Creatinine (mg/dl)	0.95±0.32	0.98±0.28	0.408
TSH	2.91±2.64	2.31±1.79	0.124
Random blood sugar	131.26±57.48	136.09±50.70	0.539
Heart Rate	111.74±29.44	117.20±35.80	0.472
Systolic blood pressure	121.29±20.29	120.71±24.53	0.243
Diastolic blood pressure	75.81±15.01	72.38±15.27	0.648

** Significant at the 0.05 level.

Table 2. Study involving 75 patients, major risk factors for non-valvular atrial fibrillation were
.
diabetes, hypertension, alcohol intake, LV EF, LA size and LA Volume are significant (p>0.050)

Table 2: Risk Factors and Echocardiographic of the Study Populations

Variables	Group A (n-31) Below 65 Years	Group B (n=44) Above 65 Years	P Value
Smoking	7 (9.3)	5 (6.7)	0.192
Alcoholism	4 (5.3)	1 (1.3)	0.003*
Diabetes	12 (16.0)	20 (26.7)	0.006*
Hypertension	18 (24.0)	22 (29.3)	0.044**
CAD	6 (8.0)	11 (14.7)	0.565
AF	5 (5.3)	10 (13.3)	0.282
CVA	1 (1.3)	2 (2.7)	0.774
Thyroid	6 (8.0)	3 (4.0)	0.100
LV EF (%)	54.03±15.68	59.48±9.75	0.000*
LA size (cms)	4.04±0.72	4.02±0.60	0.040**
LA Volume (ml)	82.87±48.35	70.97±17.04	0.016**
E/E'	16.49±7.07	17.56±6.29	0.592

* Significant at the 0.01 level. ** Significant at the 0.05 level.

As illustrated in figure 1, the ROC curve analysis revealed that Area Under Curve (AUC) was LV EF=0.608, p=0.330; LA size=0.512, p=0.912; LA Volume=0.466, p=0.757; E/E'=0.608, p=0.330. When AUC, which measures sensitivity and specificity, is less than 0.7, the ROC curve will likely fall on the diagonal indicating that the diagnostic test lacks discriminating power. It demonstrates a negative actual state group for LV EF, LA size, LA Volume and E/E'. Therefore, these Echocardiographic markers have significant association with atrial fibrillation.
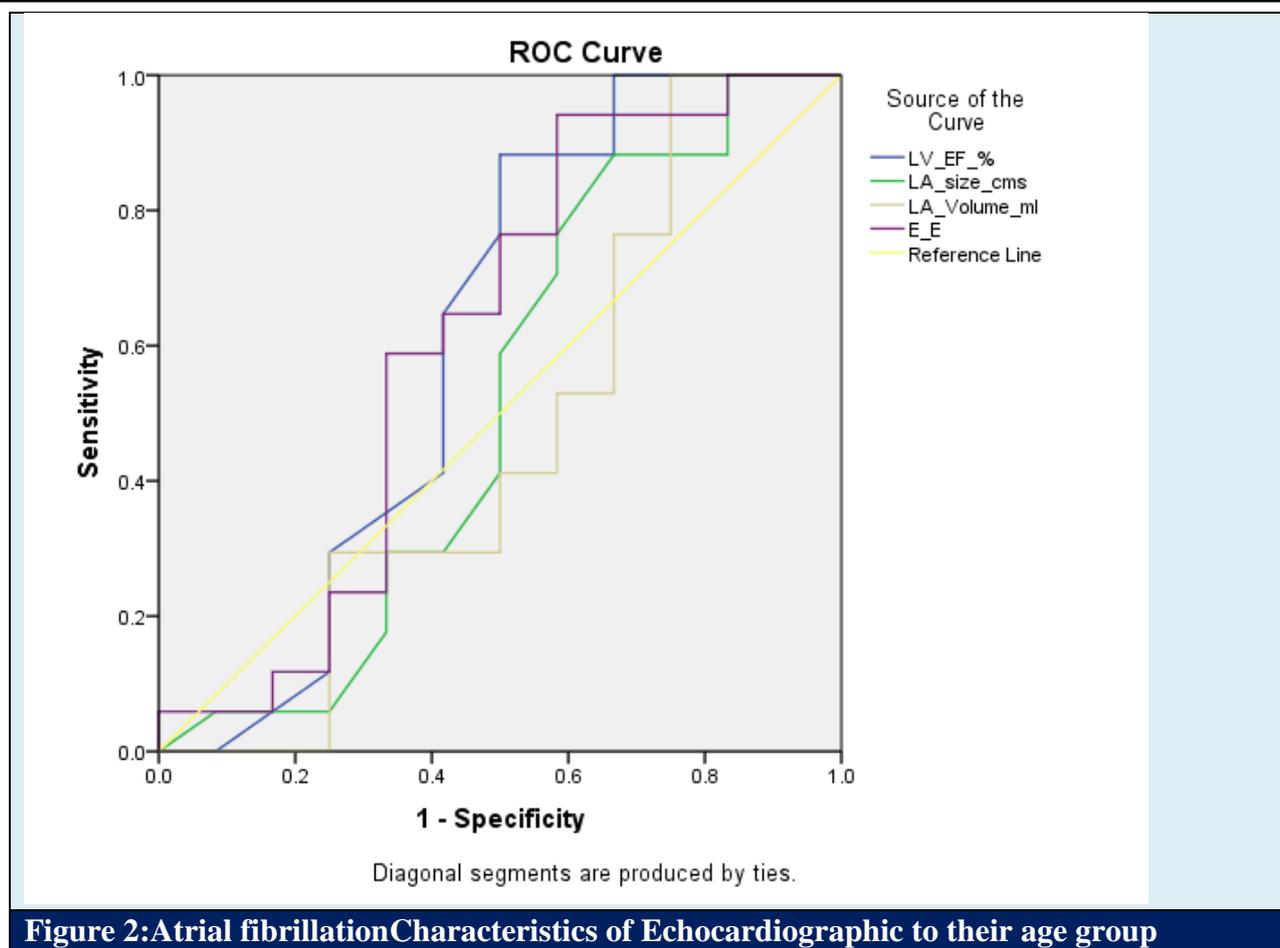
Figure 2:Atrial fibrillationCharacteristics of Echocardiographic to their age group

Discussion

Atrial fibrillation (AF) is a common and serious cardiac rhythm disturbance that is responsible for considerable morbidity and mortality in the population and is increasing in frequency nowadays. Atrial fibrillation is common in the elderly people particularly above 65 years. Approximately one third of all patients who have AF are aged 80 years or older [16]. The mean age of patients in our study was 67.6 years. In a study of non-valvular AF by Boriani et al, the mean age was 71 years[7].

According to the statistical data from the Framingham study, the occurrence rate of NVAF is 0.5% at ages 50-59, 1.8% at 60-69, about 4.8% at ages 70-79 and 8.8% at ages 80-89 [6]. In our study, the age-wise distribution of NVAF was 41.3% in the age group of less than 65 years, 32% in the age group of 65-74 years, 26.7% in the age group of above 75 years.

In a study of Sachindhungel et al, the age-wise distribution of NVAF was 30.5% in age group of less than 65 years, 26.6% in the age group of 65-74 years & 42.9% in the age group above 75 years [8]. In the study of non-valvular atrial fibrillation by Sachindhungel et al, among 154 patients,89 (57.8%) were male and 65(42.2%) were female [8]. The risk of AF increases progressively with rising body mass index (BMI). Compared to the normal weight population, over weight and obese individuals have up to a 2.4 -fold increased AF risk [9]. A meta-analysis reported that obese individuals have a 49% increased risk of AF compared to non-obese [12]. In our study36% patients were in the overweight category &33.4% patients were in the obese category. Obesity is one of the modifiable risk factors of AF.

Multiple clinical risk factors, electrocardiographic and echocardiographic features are associated with an increased risk of AF. One epidemiologic analysis found that 56% of the population attributable risk of AF could be explained by ≥1 common risk factor [15]. Many patients have more than one risk factor for atrial fibrillation.

Common risk factors for atrial fibrillation in our study were obesity (69.4%), hypertension (53.3%), diabetes (42.7%), age more than 65 years (41.3%), CAD (22.7%), chronic lung disease (18.7%) and smoking (16%). In a study by Mayank Jain et al, study involving 165 patients, common risk factors for non-valvular atrial fibrillation were hypertension (70.9%), heart failure (61.81%), CAD (25.54%), dilated cardiomyopathy (18.18%), COPD (16.36%) and diabetes mellitus (5.45%)[13].

In our study, the presenting complaints at admission were dyspnea (52%), chest pain (40%), palpitations (25.3%), sweating (20%) and fatigue (12%). Most of the patients had multiple complaints at presentation. In the study on non-valvular atrial fibrillation by Sachindhungel et al, common presentations at admission were dyspnea (42.9%), palpitation (27.3%) and stroke (17.2%)[10].

Among 75 patients in our study the mean left atrial dimension was 40.2mm. Left atrial dimension was less than 40mm in 57.3% patients,40-50mm in 32% patients and more than 50mm in 10.7% patients. In a study by Sachindhungel et al, left atrial dimension was less than 40mm in 42.2% patients, 40-50mm in 45.5% patients and more than 50mm in 13.3% patients.

In our study, LA volume was measured for 38.6% patients. Out of these patients, 75.8% had increased LA volume. A study by Tsang TS et al, showed that larger LA volume was associated with the higher risk of AF[15]. LV hypertrophy and LV dilatation cause an increase in end diastolic pressure followed by enlargement of left atrium and hence associated with subsequent development of AF. Among 75 patients 21.3% patients had increased LV diastolic diameter. A study by Yuta Seko et al, showed that the prevalence of AF was increasing according to LV geometric remodelling patterns in association with LA size and LVEF. In our study 32% of patients had low ejection fraction.

Septal E/E '(>15) was independently associated with mortality, both in patients with impaired and preserved LV ejection fraction. Elevated E/E'(>15) in AF also associated with functional capacity and quality of life[17]. E/E' was elevated in 65.3% of patients in our study. A study by Okura H et al, on 230 non-valvular AF patients identified that septal E/e '(>15) was independently associated with mortality, both in patients with impaired and preserved LVEF[18].

Among 75 patients, 19 (25.3%) patients had mild mitral regurgitation (MR), 12 (16%) patients had moderate MR. mild aortic regurgitation (AR) was present in 4(5.3%) patients and moderate AR was present in 1(1.3%) patients moderate tricuspid regurgitation (TR) was present in 2(2.7%) patients. Valvular pathology was not present in 32(42.7) patients. Cardiac troponins are elevated in a significant proportion of patients with AF. Troponin elevations do not necessarily represent the expression of an ongoing acute coronary event. In our study, out of 75 patients, Troponin I was done for 43 patients. Troponin I was done for 43 patients. Troponin I was positive for 32% of patients and negative for 25.3% of patients. In a study of atrial fibrillation by Ewout J. van den bos et al, involving 407 patients 39% patients had elevated troponin I levels.

In echocardiography, regional wall motion abnormality was present in 34.7% of patients. Among 75 patients, coronary angiogram was done for 41 patients in view of cardiac ischemia and presence of regional wall motion abnormality in echocardiogram. 20% of patients had normal coronaries and 16% of patients had triple vessel disease.

For patients with non-valvular AF with prior stroke, transient ischemic attack (TIA), or a CHA2DS2-VASc score of 2 or greater, oral anticoagulants are recommended. In a study by Sachindhungel et al, CHA2DS2-VASc score was >1 in 63.6% of patients with non-valvular AF (11). Among 75 patients in our study, 89.3% patients had CHA2DS2-VASc scores of 2 or more. All patients with CHA2DS2-VASc score of 2 or more were started on oral anticoagulants.

Conclusion

In this hospital based study of non-valvular atrial fibrillation, the common risk factors present in admitted patients were hypertension, obesity, CAD, diabetes, age more than 65 years and smoking. This was consistent and comparable to other published western studies.

Echocardiographic parameters of enlarged LA size, LA volume, elevated septal E/E' and low LVEF were present in most of the patients. There was an increased risk of cerebrovascular accident as evidenced by elevated CHA2DS2-VASc score, in the majority of admitted patients. Enforcing healthy lifestyle, early screening, appropriate evaluation and control of modifiable risk factors can reduce the risk of Non-valvular atrial fibrillation and its consequences.

Study Limitations

1. It is an observational study. Patients with non-valvular atrial fibrillation were studied and comparison with age matched controls were not done due to time constraints
2. Since it was an observational study, risk factor assessment cannot be done. Hence a cohort study is a better one

References

1. William B. Kannel, Emelia J. Benjamin, Current Perceptions of the Epidemiology of Atrial Fibrillation. Cardiology Clinics 27 (2009) 13-24.
2. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American heart association. Circulation.2014; 129; e28-e292
3. Kim MH, Johnston SS, Chu BC, et al. estimation of total incremental health care costs in patients with atrial fibrillation in the United States. Circ Cardiovasc Qual Outcomes.2011; 4: 313-20
4. Hori M, Connolly SJ, Zhu J, Liu LS, Lau CP, Pais P, et al. Dabigatran versus warfarin: effects on ischemic and hemorrhagic strokes and bleeding in Asians and non-Asians with atrial fibrillation. Strokes and bleeding in Asians and non-Asians with atrial fibrillation. Stroke 2013; 44:1891-6.
5. Oldgren J, Healy JS, Ezekowits M, et al. variations in cause and management of atrial fibrillation in a prospective registry of 15,400 emergency department patients in 46 countries: the RELY-Atrial fibrillation registry. Circulation 2014:129: 1568-76
6. Wolf PA, Abott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The Framingham study. Stroke. 1991: 22: 983-988.
7. Boriani G, Cimaglia P et al. non valvular atrial fibrillation: potential clinical implications of the heterozenous definitions used in trials on new oral anticoagulants. J Cardiovasc Med. 2015; 16:491-6
8. Sachin Dhungel, Shankar Laudari. Clinical profile of atrial fibrillation in a Tertiary Hospital in Central Nepal; J Nepal med Assoc 2017;56(207):335-40
9. Frost L, Hune LJ, Vestergaard P. overweight and obesity as risk factors for atrial fibrillation or flutter: The Danish diet, cancer, and health study. The American journal of medicine. 2005; 118:489-495.
10. Mayank Jain et al, Non-valvular atrial fibrillation: a study of epidemiology, demography and clinicoetiological profile in Central India :DOI: http://dx.doi.org/10.18203/2349-3933.ijam 20184754.

11. Das SS, Dutta SN, Chattopadhyay BP: Atrial fibrillation: a 5-year follow-up study. Indian Heart J 2002 Sep.

12. Wanahita N, Messerli FH, Bangalore S, et al. atrial fibrillation and obesity results of a meta-analysis. American Heart Journal. 2008; 155:310-315.

13. Go AS, Hylek EM et al. prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: The Anticoagulation and risk factors in Atrial Fibrillation (ATRIA) study. J Am Med Assoc 2001; 285:2370-5

14. Huxley RR, Lopez FL et al. absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: The Atherosclerosis Risk in Communities (ARIC) study. Circulation. 2011; 123:1501-8.

15. Tsang TS Barnes ME et al, left atrial volume: important risk marker of incident atrial fibrillation in older men and women. Mayo clinic proc.2001 May:76(5):46-75.

16. Yutoseko, Takaokato et al, association between atrial fibrillation, atrial enlargement, and left ventricular geometric remodelling. Nature.23 April 2018;8:6366

17. Dipak Kotecha, Mohamed et al, Is echocardiography valid and reproducible in patients with atrial fibrillation? A systematic review, europace (2017) 19, 1427-1438.

18. Okura H, Takada Y, et al. Tissue Doppler-derived index of left ventricular filling pressure, E/E', predicts survival of patients with non-valvular atrial fibrillation. Heart 2006; 92:1248-52.

19. Ewout J. van den Bos, Alina A. Constantinescu et al; Minor elevations in troponin I are associated with mortality and adverse cardiac events in patients with atrial fibrillation. European Heart Journal (2011) 32, 611-617

20. Tongers J, Schwerdtfeger B et al. Incidence and clinical relevance of supraventricular tachyarrhythmias in pulmonary hypertension. Am heart journal 2007; 153: 127-32.