Original Research Article

Clinical Factors associated with Atrial Fibrillation in Congestive Heart Failure patients admitted to the University Teaching Hospital, Lusaka, Zambia

Abstract

Introduction: Atrial fibrillation (AF) and Congestive Heart failure (CHF) have emerged as major global epidemics. Each of these conditions predisposes to the other, and their concomitant presence has additive adverse effects. This study examined the clinical factors associated with AF in CHF patients admitted to the University Teaching Hospital (UTH), Lusaka, Zambia.

Methods: This was a hospital-based cross-sectional study done in the admission wards of the UTH involving adult patients with the primary diagnosis of congestive heart failure. The data was collected from July 2014 to September 2014. A structured interview schedule was used to capture the socio-demographic and related historical data. Then all patients had a standard 12-lead ECG done on them to check for AF. Those participants with no AF on a standard 12-lead ECG had 24-hours ECG DR180+ Digital Recorder applied to try to pick-up paroxysmal AF. Finally all participants with AF were assessed for clinical factors (i.e. sex, age, BMI, smoking, excessive alcohol intake, hypertension, coronary artery disease, dilated cardiomyopathy, diabetes mellitus, and chronic lung disease). Pearson chi-square of independence of the data was used to analyze the data in SPSS® 20.0 to determine clinical factors of AF in CHF patients.

Results: A total of 49 patients were included in the study and 13 (26.5%) of them had AF, 7 diagnosed by standard ECG and 6 diagnosed by holter ambulatory ECG monitoring. The prevalence of AF in CHF was found to be strongly associated with age 65 years and above, obesity, smoking, excessive alcohol intake, hypertension, dilated cardiomyopathy, diabetes mellitus and chronic lung disease. These findings suggest the need for clinicians to consider full scale use of ambulatory ECG monitors in all CHF patients with the above conditions.

Keywords: ECG DR180+ Digital Recorder, smoking, cardiomyopathy, diabetes, lung disease, .

1.0. INTRODUCTION

1.1. Background

Atrial fibrillation (AF) and Congestive Heart failure (CHF) have emerged as major global epidemics [1]. These two conditions share similar risk factors, frequently coexist, and have additive adverse effects when occurring in conjunction [2]. The risk factors include hypertension (HTN), coronary artery disease (CAD), structural heart disease (non-ischaemic, valvular), diabetes mellitus (DM), obesity and obstructive sleep apnoea [3]. The co-prevalence also increases with advancing age and each predicts/compounds the course of the other [1,4].

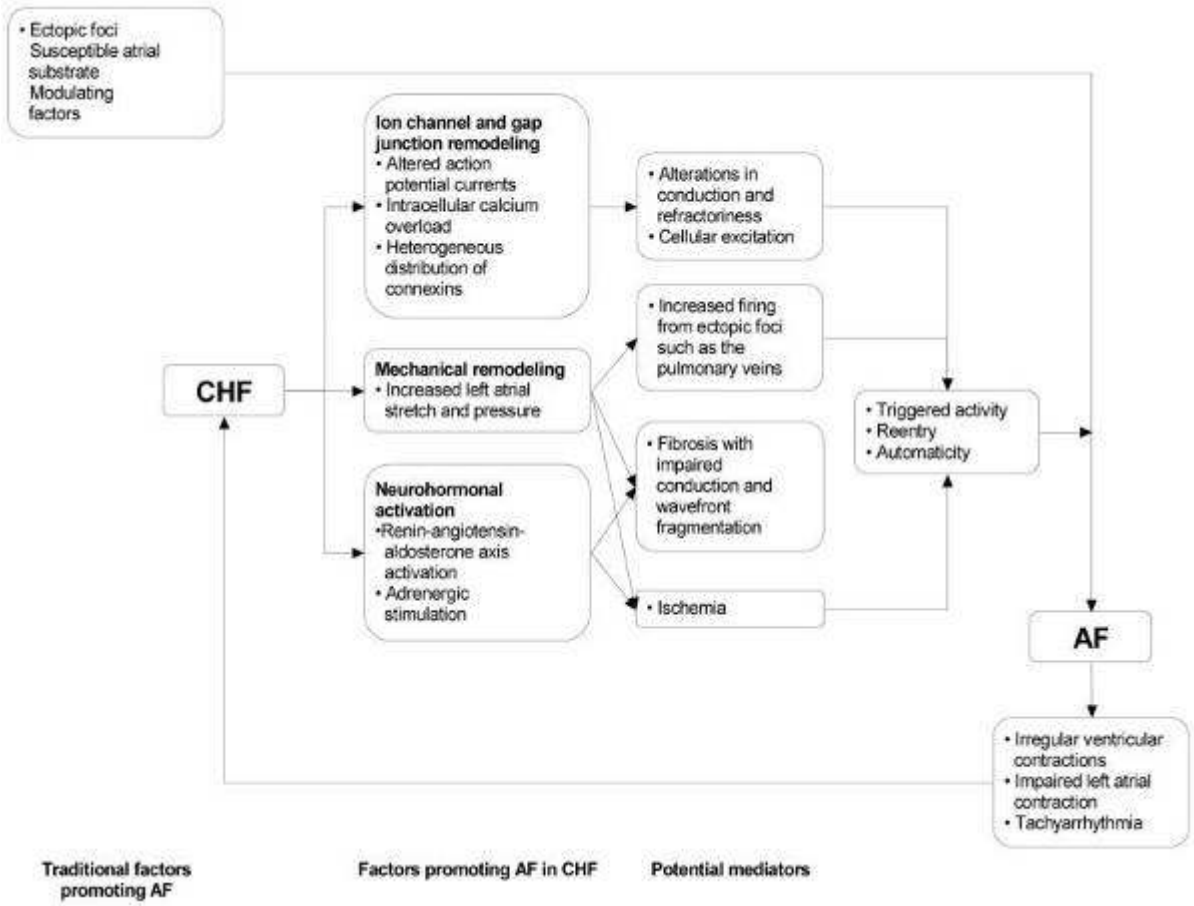
There has been increasing evidence regarding the adverse role of AF in patients with CHF both in terms of morbidity as well as prognosis [1]. Most of the studies done have revealed that AF through the loss of organized atrial activity and absence of coordinated atrial mechanical function, is associated with clinical and hemodynamic deterioration which may predispose the patient to systemic thromboembolism and poorer prognosis [1]. Impaired contraction of the atria may cause blood stasis and the potential for thrombus formation, particularly in the left atrial appendage, especially in CHF as there is already presumed stagnation of blood [5].

1.1.1. Pathoetiology of Atrial Fibrillation in Congestive Heart Failure

The pathoetieological interplay between CHF and AF is complex. CHF predicts the development of AF and conversely AF predisposes to CHF [1]. The mechanisms, through which CHF provides arrhythmogenic atrial substrate include: elevated left-sided filling pressures, mitral regurgitation, atrial enlargement, interstitial fibrosis and electromechanical remodelling [4]; activation of autonomic and renin-angiotensin axis; as well as changes in the intracellular calcium [6].

Conversely, AF can lead to CHF through multiple adverse effects including loss of atrial systole, functional mitral/tricuspid regurgitation, tachycardiomyopathy, and reduced ventricular diastolic filling time

[1]. Irregularity in the RR interval can also have a potentially deteriorating influence on cardiac output irrespective of the heart rate [7]. Moreover, deterioration of sinus rhythm in AF patients with CHF can lead to acute decompensation.



Source: **Lubitz, Benjamin & Ellinor (2010)**

Figure 1: Pathoetiological inter-relationship between AF and CHF

1.1. Clinical factors known to be associated with AF in CHF

Body Mass Index [23] is said to be associated with AF and may impact on outcomes. This is probably due to its association with cardiovascular conditions like hypertension. The severity of heart failure as determined by the New York Heart Association (NYHA) classification has also been reported to be a factor in AF whose prevalence is said to increase with increased severity of the NYHA class[49], [50], [51], [52], [53].

Persistent or sustained elevation of blood pressure (Hypertension) with the systolic pressure of equal or above 140mmHg and diastolic of equal or above 90mmHg, affecting one or both pressures based on two or more consecutive readings [17] is also a known factor. Hypertension is implicated in the initiation and maintenance of AF through structural changes, neurohormonal activation, fibrosis, atherosclerosis seen in this condition [18]. Coronary artery disease is implicated in atrial fibrillation in that a partially blocked artery might cause an imbalance of nutrient flow to an area of downstream heart muscle causing ischemia[11]. Ischemia can cause electrical irritability in the ventricle leading to the initiation and perpetuation of atrial fibrillation [12].

Dilated Cardiomyopathy**,** a progressive disease of heart muscle that is characterized by ventricular chamber enlargement and contractile dysfunction with normal left ventricular (LV) wall thickness [15], has been associated with occurence of AF as well. Electrophysiological features associated with left atrial dilation in dilated cardiomyopathy include shortening of the refractory period and prolongation of conduction time. These alterations may both lead to development of multiple reentrant wavefronts starting and possibly perpetuating AF in dilated cardiomyopathy [16].

In diabetes mellitus both glucose and insulin disturbance may directly affect the myocardium in atrium and ventricle, leading to AF. Left ventricular (LV) hypertrophy has been associated with DM and abnormal glucose tolerance in several epidemiology studies and LV hypertrophy has been said to be a significant risk factor for AF. Analysis of the Framingham study subjects showed that LV mass increased with the worsening of glucose tolerance and the trend was more striking in women than in men. There was also a close relationship between insulin resistance and LV mass, as well as LV wall thickness, in women both with normal and abnormal glucose tolerance [14]. The supraventricular and ventricular arrhythmias are common in chronic obstructive lung disease[8],[9]. The reasons are thought to be due to hypoxia, hypercarbia, pulmonary hypertension, and myocardial ischemia, which are easily provoked by this limited ventilatory condition [10].

Smoking and heavy alcohol intake are also a factors in the occurrence of AF[19]. Smoking may harm the heart through causing or aggravating endothelial dysfunction and atherosclerosis as well as causing cardiac rhythm disorders through the combined effects of nicotine, carbon monoxide, and polycyclic

aromatic hydrocarbons. Thus, smoking may change the myocardial substrate as well as action potentials, both processes that may provoke and/or facilitate AF [20]. Heavy alcohol drinking is described as the drinking of 5 or more glasses of alcohol on the same occasion on each of 5 or more days in the past 30 days [21]. It is understood that alcohol consumption acutely affects catecholamine release, causes metabolic acidosis and electrolyte disturbances, and increased oxidative distress[21]. In the long term, this results in myocardial fibrosis/dilatation, structural heart disease, metabolic disturbances, and increased sympathetic tone. The combination of these effects contributes to the increase in atrial arrhythmias including AF[22].

1.2. Statement of the problem

Studies done have revealed that AF through the loss of organized atrial activity and absence of coordinated atrial mechanical function, is associated with clinical and hemodynamic deterioration which may predispose the patient to systemic thromboembolism and poorer prognosis [1,2,4,5,6,7]. Impaired contraction of the atria may cause blood stasis and the potential for thrombus formation, particularly in the left atrial appendage, especially in CHF as there is already presumed stagnation of blood [5].

Furthermore, in clinical practice, the use of clinical risk factors in predicting disease development, prognosis as well as the probability of death is said to be very important; because early recognition and treatment of reversible factors indicative of poor outcome could aid in early identification and better management of patients [6]. Therefore, the ability to define clinical factors associated with AF in CHF patients has important clinical relevance.

2.0. MATERIALS AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

2.1. *Population and sampling procedures*

This was a hospital based cross-sectional study carried out in adult medical wards run at the UTH, Lusaka, Zambia. The UTH is the national referral health centre that treats and reviews patients with various diseases, including CHF.

2.1.1. Inclusion criteria

All known congestive heart failure patients aged 18 years and above who consented to take part in the study were included.

2.1.2. Exclusion criteria

However, CHF patients below the age of 18 years, acute patients who were not able to get out of bed, congestive heart failure patients who refused to consent to the study and those who were recruited in the previous month(s) were excluded from the study.

2.2. *Data collection*

A structured interview schedule was used to capture data on demographic characteristics, clinical factors and laboratory measurement results. The interview schedule was developed based on the World Health Organization (WHO) stepwise survey (STEPS) instrument [24]. The same instruments were used on all the patients to ensure reliability and validity. The data on demographic and clinical factors were obtained by interview, review of medical records and anthropometric measurements.

The weight and height of the patients were measured using a ZT-160 adult weighing mechanical scale model with a height rod (Wuxi Weigher Factory Co., Ltd, Zhejiang, China) whose values were used to compute the body mass index (BMI) taken as proportion of weight(in kilograms) and square height (in metres). Blood Pressure and pulse rate were measured on the left hand of the patient in a lying position using an Omron HEM 780 automated Blood Pressure machine (Omron HEALTHCARE Co. Ltd, Vietnam). A standard 12-lead Electrocardiogram (ECG) was done using Schiller AT-102 ECG machine on all participants to identify those with and without atrial fibrillation. Then those who had no atrial fibrillation on Schiller AT-102 ECG machine, had a holter monitor (DR180+ Digital Recorder, Northeast Monitoring Inc, USA) applied for 24 hours in trying to pick up some paroxysmal arrhythmias which were not detected on a standard 12-lead ECG. Data was analysed using IBM® SPSS® version 20.0. The analyses included descriptive statistics and Pearson chi square of independence tests. A 95% confidence interval (CI) and *P*-value of < 0.05 were set.

2.3. *Ethics approval*

This non-interventional study was approved by ERES CONVERGE IRB (Reference number 2014-Mar-003) and permission was granted by the Hospital authority to carry out the study. All subjects were older than 18 years and gave written consent prior to their participation.

3.0. RESULTS

3.1. Socio-demographic data

Table 1: Socio-demographic characteristics of CHF patients recruited (N=49)

Variable	**Frequency**	**Per cent**
Sex		
Female	25	51
Male	24	49
Total	**49**	**100**
Age		
35 - 44 Years	2	4.1
45 - 54 Years	10	20.4
55 - 64 Years	16	32.7
65 Years and above	21	42.9
Total	**49**	**100**
Body Mass Index		
18.5 - 24.9	26	53.1
25 - 29.9	11	22.4
30 and above	12	24.5
Total	**49**	**100**
Smoking		
No	39	79.6
Yes	10	20.4
Total	**49**	**100**
Alcohol consumption		
No	34	69.4
Yes	15	30.6
Total	**49**	**100**

Table 1 shows the socio-demographic characteristics of congestive heart failure patients admitted to the UTH who consented to participation in the study. A total of 49 black African Congestive Heart Failure patients who met the inclusion criterion were enrolled into the study. There were almost equal number of men and women; 49% vs. 51% respectively. Most of the patients (42.9%) were aged 65 years and above. The majority (53.1%) of the patients had a normal BMI (18.5 – 24.9). About 20.4% of the patients were tobacco smokers; and 30.6% of the patients were consumers of alcohol.

3.2. Clinical Factors Data

Table 2: Clinical characteristics of CHF patients (N=49)

Variable	Frequency	Per cent
NYHA Class		
Class III	9	18.4
Class IV	40	81.6
Total	**49**	**100**
Hypertension		
No	36	73.5
Yes	13	26.5
Total	**49**	**100**
Coronary Artery Disease		
No	46	93.9
Yes	3	6.1
Total	**49**	**100**
Dilated Cardiomyopathy		
No	40	81.6
Yes	9	18.4
Total	**49**	**100**
Diabetes Mellitus		
No	42	85.7
Yes	7	14.3
Total	**49**	**100**
Chronic Lung Disease		
No	42	85.7

Yes	7	14.3
Total	**49**	**100**

Table 2 shows the clinical characteristics of the CHF patients included in the study. The majority of the patients (81.6%) were in the New York Heart failure Association (NYHA) class IV; 26.5% of the patients had hypertension; 18.4% had dilated cardiomyopathy; 14.3% had chronic lung disease; 14.3% had diabetes mellitus; and 6.1% had coronary artery disease.

3.3. Electrodiagnosis of Atrial Fibrillation in CHF patients

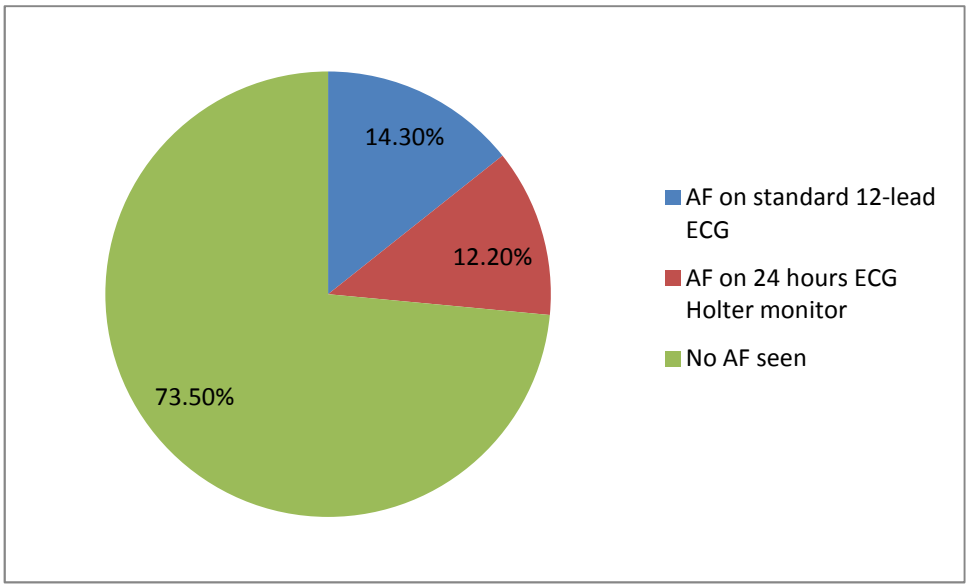


Figure 2: Electrodiagnosis of Atrial Fibrillation (N=49)

Figure 2 shows the electrographic modality utilised to diagnose AF. Standard 12-lead ECG done on the patients showed that 7 (14.3%) of them had atrial fibrillation. The ambulatory ECG monitor showed atrial fibrillation in another 6 (12.2%) patients, giving a combined prevalence of AF of 26.5% in this study population.

3.4. Association between AF in CHF and the Socio-Demographic Characteristics

Using Pearson chi-square of independence test, the association between atrial fibrillation in congestive heart failure patients and the socio-demographic characteristics. The results obtained are presented in tables 3.

Table 3: Atrial Fibrillation by the socio-demographic factors

	Atrial Fibrillation			
	No AF seen	AF seen		
Clinical Factor	**N (%)**	**N (%)**	**X^2**	**P-value**
Sex[a]				
Female	20 (80.0)	5 (20.0)	1.12	NS
Male	16 (66.7)	8 (33.3)		
Age[a]				
35 - 44 Years	2 (100.0)	0 (0.0)		
45 - 54 Years	10 (100.0)	0 (0.0)		
55 - 64 Years	12 (75.0)	4 (25.0)	5.03	**<0.05***
65 Years and above	12 (57.1)	9 (42.9)		
Body Mass Index[a]				
18.5 - 24.9	26 (100.0)	0 (0.0)		
25 - 29.9	8 (72.7)	3 (27.3)	22.59	**<0.001***
30 and above	2 (16.7)	10 (83.3)		
Smoking[a]				
No	33 (84.6)	6 (15.4)	9.54	**<0.01***
Yes	3 (30.0)	7 (70.0)		
Alcohol intake[a]				
No	33 (97.1)	1 (2.9)	27.88	**<0.001***
Yes	3 (20.0)	12 (80.0)		

[a]**Fisher's Exact Test. *Indicates significant *p*-value at $p < 0.05$.**

Table 3 shows the cross tabulations of AF by the socio-demographic factors. The incidence of AF was higher in males 8 (33.3%) than in the females 5 (20.0%), although no statistical significance was noted in relation to gender. The presence of AF in CHF patients increased with age from 4 (25%) below 65 years to 9 (42.9%) in those above 65 years, although Fisher's exact test did not attain statistical significance. Furthermore, the incidence of AF increased with the increase in the BMI from 3 (27.3%) in the overweight to 10 (83.3) in the obese. 7 (70%) of the 10 smokers in CHF had AF and Fisher's exact test showed that there is a statistically significant association between atrial fibrillation in congestive heart failure and smoking. The majority 12 (80.0%), of the patients who reported taking alcohol had atrial fibrillation.

3.5. Association between AF in CHF and the Identified Clinical Factors

Table 4: Atrial Fibrillation by the Clinical Factors

	Atrial Fibrillation			
	No AF seen	AF seen		
Clinical Factor	**N (%)**	**N (%)**	**X^2**	**P-value**
NYHA Class[a]				
Class III	7 (77.8)	2 (22.2)	0.00	NS
Class IV	29 (72.5)	11 (27.5)		
Hypertension[a]				
No	34 (94.4)	2 (5.6)	26.71	**<0.001**
Yes	2 (15.4)	11 (84.6)		
Coronary Artery Disease[a]				
No	35 (76.1)	11 (23.9)	0.90	NS
Yes	1 (33.3)	2 (66.7)		
Dilated Cardiomyopathy[a]				
No	34 (85.0)	6 (15.0)	11.81	**<0.001**
Yes	2 (22.2)	7 (77.8)		
Diabetes Mellitus[a]				
No	35 (83.3)	7 (16.7)	11.35	**<0.001**
Yes	1 (14.3)	6 (85.7)		
Chronic Lung Disease[a]				
No	35 (83.3)	7 (16.7)	11.35	**<0.001**
Yes	1 (14.3)	6 (85.7)		

[a]Fisher's Exact Test. *Indicates significant *p*-value at $p < 0.05$.

Table 4 above shows the Pearson chi-square of independence test of AF in CHF by the clinical factors. While 11 (27.5%) of the 40 patients in NYHA IV had AF, only 2 (22.2%) of the 7 patients in NYHA III had AF. However, this difference did not attain statistical difference. Of the 13 hypertensive patients in the study population, 11 (84.6%) had AF. Only 3 patients were reported to have coronary artery disease. And of these, 2 (66.6%) had AF. Of the nine (9) patients who had Dilated Cardiomyopathy, 7 (77.8%) had AF. Six (6, 85.6%) of the seven patients with diabetes mellitus and similar proportion with chronic lung disease had AF. The test showed that there was a statistically significant association between AF in CHF and hypertension, dilated cardiomyopathy, diabetes mellitus as well as chronic lung disease.

4.0. DISCUSSION

Atrial fibrillation is said to be the most common arrhythmia seen in clinical practice and is responsible for significant morbidity [25]. The presence of AF is said to confer a five-fold increased risk of stroke [26], a significantly increased risk of dementia [27] and an almost two-fold increased risk of death [26]. The clinical consequences of AF are derived from the loss of organized atrial activity and absence of coordinated atrial mechanical function. Impaired contraction of the atria may cause blood stasis and the potential for thrombus formation, particularly in the left atrial appendage, with a resultant risk of stroke.

This risk of stroke is said to be increased in patients with CHF [28]. The concomitant presence of AF and CHF identifies individuals with a higher risk for death than with either condition alone [2].

4.1. Prevalence of Atrial Fibrillation in Congestive Heart Failure

There were 49 participants in the study. The prevalence of AF in the CHF patients admitted to UTH during the period of the study was 26.5%. This prevalence was quiet high; though almost half of the patients in this group were missed by routine ECG. The routine standard 12-lead ECG missed some of the cases of AF probably because these cases may have had paroxysmal AF which may not have been active at the time a standard 12-lead ECG was being taken. Indeed this underlies the recommendations that came out of the Cryptogenic Stroke and Underlying Atrial Fibrillation (CRYSTAL-AF) trial [69] and the 30-Day Cardiac Event Monitor Belt for Recording Atrial Fibrillation After Cerebral Ischemic Event (EMBRACE) trial [70] which demonstrated the effectiveness of extended cardiac monitoring when compared to the routine electrocardiographic recording done. This demonstrates the need for use of ambulatory diagnostic equipment such as ECG Holter monitors and now the insertable cardiac monitors (ICM) in the diagnostic investigations so that even those with paroxysmal AF may also be picked. With prolonged monitoring we may have obtained a higher yield of individuals with AF. However, the prevalence rate recorded on this study is similar to the 30% prevalence rate reported in the Acute Decompensated Heart Failure National Registry [29] in the United States in 2005.

This high prevalence rate may be attributed partially to the advancing age of the Zambian population [30]; increase in prevalence of the non-communicable diseases such as hypertension, and diabetes mellitus; as well as the increase in the chronic lung diseases [31].

4.2. Socio-demographic Characteristics of the patients

There were almost equal numbers of males 24 (49%) and females 25 (51%) in the study population. Although, we did not find any statistical difference (X^2= 1.12, p= .291) between males and females, in the prevalence of AF in CHF, the majority 8 (61.5%) of patients with AF in CHF were males. Among the male CHF patients, the prevalence of AF was higher (33.3%) compared to 20% among the female CHF patients. Similarly, Lloyd-Jones AM at al [32] reported that AF after the age of 40 in the United States is

26% for men, and 23% for women and Humphries KH [33] also reported that in all age groups, men have a higher incidence of AF than women. Furthermore, Nazario B[3] also reported that males are more likely to suffer from AF than their female counterparts. It is postulated that this may be so because males are more exposed to other risk factors for AF like smoking and excessive alcohol intake. However, although women have a lower incidence of AF, other studies have shown a worse outcome and a higher rate of recurrence after cardioversion [32], [33].

Most 21 (42.9%) of the patients in the study were aged 65 years and above. Of those who had AF in CHF, the majority 9 (69.2%) were within the 65 years and above age group, 4 (30.8%) were with the 55 years – 64 years age group, while no cases of AF were recorded in the age groups below 55 years. The study also revealed that age 65 years and above was statistically (X^2= 5.03, p= 0.025) associated with AF in CHF. This result was similar to what was reported by Benjamin EJ et al[34] in a cohort study which found that the development of AF increases with advancing age. Nazario B[3] also reported that advancing age is a risk factor for the development of AF. Advancing age is implicated in the development of AF probably because pre-existing alterations, such as autonomic dysbalance, degenerative tissue changes and fibrosis, can provide an electrophysiological and morphological substrate, which increases the likelihood of AF. In particular, alterations of the interstitial matrix in atrial tissue seem to be significant contributory factors [35].

The majority 26 (53.1%) of the patients in the study had a normal body mass index (18.5 – 24.9) (Table 2). Of the 13 (26.5%) patients who had AF, the majority 10 (76.9%) were obese with a body mass index of 30 and above, 3 (23.1%) were overweight and no case was found among the CHF patients who had a normal body mass index. The study also revealed that body mass index is significantly (X^2= 22.59, p < 0.001) associated with AF in CHF. Similarly, Psaty BM et al[36] and Nattel S[37] reported that obesity is associated with the development of AF and may impact AF-related outcomes. However, it is worthy to note that it is very difficult to calculate body mass index in CHF patients because of the exaggerated patient's weight resulting from fluid retention.

There were 10 (20.4%) patients who were smokers in the study, and 7 (70%) of them had AF compared to 6 (15.4%) among the 39 non-smokers. The study also showed that smoking is statistically (X^2= 9.54,

p< 0.01) associated with AF in CHF. This result is in agreement with what was reported by Guillan L et al [38] in their prospective, population-based study where current and former cigarettes smokers were associated with increased risk of AF; as well as Overvad TF et al[39] who also reported that smoking was associated with higher incidence of AF, with more than a two-fold increased risk of AF attributed to current smoking. Smoking may harm the heart through causing or aggravating endothelial dysfunction and atherosclerosis as well as causing cardiac rhythm disorders through the combined effects of nicotine, carbon monoxide, and polycyclic aromatic hydrocarbons [20]. Thus, smoking may change the myocardial substrate as well as action potentials; of which both processes may provoke and facilitate AF.

Compared to non-consumers of alcohol where only 1 (2.9%) patient had AF, the majority 12 (80%) of the consumers of alcohol in CHF had AF. These patients reported taking more than 5 glasses of alcohol on each of the 5 days of the week, thus easily described as having excessive alcohol intake .The current study has shown that excessive alcohol intake is strongly (X^2= 27.88, p= <0.001) associated with AF in CHF. Similarly several case-control studies[40], [41], [42], [43] reported a relatively lower odds of developing AF among abstainers and significantly higher odds of developing AF among heavier drinkers. Furthermore, Koskinen P et al[44] in the Copenhagen City Heart Study and Rich EC et al[45] also found that the risk of developing AF increased with increasing levels of alcohol consumption. Although, this result was anticipated there has been much controversy over the exact mechanism by which alcohol induces AF. Mukamal KJ et al[46] postulated that alcohol-induced atrial arrhythmias were related to intramyocardial catecholamine release in response to the toxic effects of acetaldehyde. Other studies [47], [48], have suggested that an increase in sympathetic reaction could be related to the production of AF based on the increased density of beta-adrenergic receptors in lymphocytes. Balbao CE et al[22] proposed multiple mechanisms for the acute and long-term consumption of alcohol resulting in AF. They thought that alcohol consumption acutely affected catecholamine release, metabolic acidosis, electrolyte disturbances, and increased oxidative distress. In the long term, this resulted in myocardial fibrosis/dilatation, structural heart disease, metabolic disturbances, and increased sympathetic tone. The combination of these effects contributed to the increase in atrial arrhythmias.

4.3. Clinical Factors

The patients in this study were in NYHA classes III/IV because this study was conducted at a tertiary hospital where critically ill patients (usually in NYHA class III/IV) are referred from primary health care centres and second-level hospitals. The majority 40 (81.6%) of the patients were in NYHA class IV. Compared to patients with NYHA class IV 11 (84.6%), the incidence of AF was lower 2 (15.4%) in patients with NYHA class III. Although, there was no statistical difference (X^2= 0.00, p= 1.000) between the two groups, there were more AF cases in NYHA class IV compared to the cases in NYHA class III. Findings from previous studies[49], [50], [51], [52], [53] have revealed that the prevalence of AF increases significantly with the increase/severity in the NYHA class. Our small sample size may have influenced the results in this study. Congestive heart failure has been implicated in the initiation and perpetuation of AF through elevated left-sided filling pressures, mitral regurgitation, atrial enlargement, interstitial fibrosis and electromechanical remodelling [4]; activation of autonomic and renin-angiotensin axis; as well as changes in the intracellular calcium [6].

Slightly over a quarter 13 (26.5%) of the patients had hypertension in the study population. The majority 11 (84.6%) of these patients had AF compared to the non hypertensive group where only 2 (5.6%) of 36 patients had AF. This study revealed that hypertension in congestive heart failure is strongly associated (X^2 = 26.71, p<0.001) with AF. Similar reports have affirmed that hypertension is a strong independent risk factor for AF[36] [54]. Hypertension may be implicated in the initiation and maintenance of AF through structural changes, neurohormonal activation, fibrosis, atherosclerosis, etc. Untreated or suboptimally treated hypertension leads to the development of Left Ventricular Hypertrophy (LVH), which is one of the most important expressions of subclinical organ damage, and is an independent risk factor for cardiovascular events, including the development of AF. In the presence of LVH, left ventricular compliance is reduced, left ventricular stiffness and filling pressure increase, coronary flow reserve is decreased, wall stress is increased and there is activation of the sympathetic nervous system and of the renin–angiotensin–aldosterone system. In the atria, proliferation and differentiation of fibroblasts into myofibroblasts and enhanced connective tissue deposition and fibrosis are the hallmarks of this process. Structural remodelling results in electrical dissociation between muscle bundles and in local conduction heterogeneities facilitating the initiation and perpetuation of AF. This electroanatomical substrate permits

multiple small re-entrant circuits that can stabilize the arrhythmia. Over time tissue remodelling promotes and maintains AF by changing the fundamental properties of the atria [18].

The current study showed that only 3 (6.1%) of the patients had coronary artery disease and out of these 2 (66.8%) had AF. Fofana M[55] reported that transient ischemic attack as may be found in coronary artery disease is a risk factor for AF. However, Lokshyn S, Mewis C and Kuhlkamp V [12] reported, that in patient with coronary artery disease, systolic heart failure may be more important than atrial ischemia in causing AF. They explained that coronary artery disease is thought to cause AF in that a partially occluded artery might cause an imbalance of nutrient flow to an area of downstream heart muscle (ischemia). Atrial ischemia plays an important pathophysiological role in the genesis of AF. Hence, significant stenosis in the proximal right coronary artery and the circumflex artery prior to the takeoff of the atrial branches increase the likelihood of AF in these patients [56].

Only 9 (18.4%) of the patients had dilated cardiomyopathy and the majority 7 (77.8%) of these patients had AF. The study revealed that dilated cardiomyopathy in CHF is strongly (X^2 = 11.81, p= 0.001) associated with AF. Similarly, Thakkar S & Bagarhatta R[57] and Anter E[6] reported that AF is relatively frequent in patients with idiopathic dilated cardiomyopathy. Garlinho A et al[58] also reported that Tachycardia-induced cardiomyopathy may be a more common mechanism of LV dysfunction in patients with atrial arrhythmia than expected, and aggressive treatment of this arrhythmia should be considered. Electrophysiological features associated with left atrial dilation in dilated cardiomyopathy include shortening of the refractory period and prolongation of conduction time [59]. Both these alterations may lead to development of multiple reentrant wave fronts starting and possibly perpetuating AF in dilated cardiomyopathy [60].

Like most of the studies [16], [61] have implicated diabetes mellitus in the initiation and perpetuation of AF, this study also revealed that most 6 (85.7%) diabetic patients with CHF had AF. The study revealed that diabetes was strongly (X^2 = 11.35, p< 0,001) associated with AF when compared to non-diabetics in CHF. Diabetes mellitus may be implicated as an independent risk factor for AF in that glucose and insulin disturbance can directly affect the myocardium in atrium and ventricle, by causing atrial and ventricular hypertrophy leading to AF. Prospective data from large population based studies established the

relationship between LA size and risk of developing AF [62]. Analysis of the Framingham study subjects showed that left ventricular (LV) mass increased with the worsening of glucose tolerance and the trend was more striking in women than in men. There were also close relationship between insulin resistance and LV mass, as well as LV wall thickness, in women both with normal and abnormal glucose tolerance [14]. Furthermore, several observations suggest that the autonomic nervous system plays an important role in both the initiation and/ or the maintenance of AF in humans. In the animal model of diabetes mellitus, the occurrence of AF was enhanced by adrenergic activation in the diabetic heart. The intra-atrial conduction delay and fibrotic deposition in atria play a major role in producing atrial tachyarrhythmia in diabetes animal model. The heterogeneous increase in sympathetic innervations has proved to be associated with the promotion of AF in several studies [63], [64].

6 (85.7%) of patients with chronic lung disease in CHF had AF. The current study revealed that chronic lung disease in CHF is strongly (X^2 = 11.35, p< 0.001) associated with AF in CHF. This is in agreement with what was reported by Shibata Y et al[65], who reported that impaired pulmonary function was an independent risk factor for AF in the Japanese general population. Furthermore, Kang H et al[66] reported that reduced FEV_1%, which represents the severity of airway obstruction, was associated with chronic AF and the greater the pulmonary function impairment, the greater the co-existence with AF. Atrial fibrillation in chronic lung disease is thought to result from changes in blood gases, abnormalities in pulmonary functions, and hemodynamic changes resulting from pulmonary hypertension [67] as well as structural remodelling. Hypoxemia and hypercapnia are associated with over-compensatory fluctuations in autonomic tone, intrathoracic pressures and cardiac haemodynamics, with possible atrial stretch and remodeling, each of which could lead to AF, particularly when hypercapnia causes a significant decrease in pH values [68]. Morphological abnormalities associated with chronic obstructive pulmonary disease (COPD) include signs of right atrial enlargement, and right ventricular hypertrophy. Structural remodeling results in an electrical dissociation between muscle bundles and local conduction heterogeneities, facilitating the initiation and perpetuation of AF. This electro-anatomical substrate allows multiple small re-entrant circuits that may trigger the arrhythmia [69].

5.0. CONCLUSION

This study objectively evaluated clinical factors associated with AF in CHF patients admitted to UTH, Lusaka, Zambia. Atrial fibrillation at UTH is often diagnosed by routine ECG examination, in the course of investigating and/or managing other cardiovascular disorders, as most of the patients with AF are usually asymptomatic or may have very few symptoms if at all they have symptoms.

In the small patient population of 49 comprising slightly more men than women, the prevalence of AF in CHF patients was 26.5%. The prevalence was this high due to the use of ambulatory ECG monitor which captured almost half of the cases that were missed by routine ECG. The prevalence of AF was slightly higher in males compared to females. The study revealed that obesity, smoking, excessive alcohol intake, hypertension, dilated cardiomyopathy, diabetes mellitus and chronic lung disease in CHF were strongly associated with AF. There was also a weak statistical difference between AF in CHF among different age groups, with those 65 years and above being more predisposed to AF.

This study highlights the importance of electrocardiographic evaluation of patients with chronic heart failure and enlightens the physicians to be more vigilant in searching for AF in particular subpopulations. These findings will guide the physicians in risk stratification and in initiating appropriate treatment for prevention and control of AF in CHF thus enhancing the physicians' clinical practice.

REFERENCES

1. Caldwell JC, & Mamas MA., ***Heart failure diastolic dysfunction and atrial fibrillation; mechanistic insight of a complex inter-relationship***, Heart Failure Review Journal 2012; No. **17**: 27-33

2. Lubitz SA, Benjamin EJ, and Ellinor PT., ***Atrial Fibrillation in Congestive Heart Failure.*** Heart Fail Clin. Apr 2010. 6(2): 187-200.

3. Nazario B., ***Atrial Fibrillation and Stroke – Symptoms of Atrial Fibrillation***. Cardiology Journal. 2013, Vol. 18, No. 3, pp. 356–364.

4. Deedwania PC, & Lardizabal JA., ***Atrial fibrillation in heart failure: a comprehensive review.*** American Journal of Medicine 2010; No. 123: 198-204

5. Wang TJ, Larson MG, Levy D, Vasan RS, Leip EP, Wolf PA, D'Agostino RB, Murabito JM, Kannel WB, Benjamin E, ***Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study.*** Circulation. 2003;107:2920–5. [PubMed]

6. Anter E, Jessup M and Callans DJ., ***Atrial Fibrillation and Heart Failure Treatment Considerations for a Dual Epidemic,*** Circulation. 2009; 119: 2516-2525.

7. Clark DM, Plumb VJ, Epstein AE, Kay GN., ***Hemodynamic effects of an irregular sequence of ventricular cycle lengths during atrial fibrillation.*** J Am Coll Cardiol. 1997;30:1039–1045. [PubMed]

8. http://www.thoracic.org/copd-guidelines/for-patients/what-is-chronic-obstructive-pulmonary-disease-copd.php accessed on 22/07/15 12:35Hours

9. Kothari SA, Apiyasawat S, Asad N, Spodick DH. **Evidence supporting a new rate threshold for multifocal atrial tachycardia.** Clin Cardiol. 2005 Dec;28(12):561-3.

10. Khokhar N. **Cardiac arrhythmias associated with acute respiratory failure in chronic obstructive pulmonary disease. Mil Med. 1981 Dec;146(12):856-8.**

11. http://www.nhlbi.nih.gov/health/health-topics/topics/cad accessed on 22/07/15 12:40hours

12. Lokshyn S, Mewis C and Kuhlkamp V. ***Atrial Fibrillation in Coronary Artery Disease***, Int J Cardiol. 2000 Jan 15;72(2):133-6

13. Green, Flatt & Bailey 2006

14. Rutter MK, Parise H, Benjamin EJ, Levy D, Larson MG, Meigs JB, Nesto RW, Wilson PW, Vasan RS. **Impact of glucose intolerance and insulin resistance on cardiac structure and**

function: sex-related differences in the Framingham Heart Study. Circulation. 2003 Jan 28;107(3):448-54.

15. http://www.webmd.com/heart-disease/guide/dilated-cardiomyopathy accessed on 22/07/15 12:50 Hours

16. Murphy NF, Simpson CR, Jhund PS, et al. ***A national survey of the prevalence, incidence, primary care burden and treatment of atrial fibrillation in Scotland.*** *Heart. 2007 May;93(5):606-12. Epub 2007 Feb 3.*

17. www.merckmanuals.com

18. Healey JS and Connolly SJ. **Atrial fibrillation: hypertension as a causative agent, risk factor for complications, and potential therapeutic target.** Am J Cardiol. 2003 May 22;91(10A):9G-14G

19. www.Tobacco.com

20. Ambrose JA, Barua RS.; **The pathophysiology of cigarette smoking and cardiovascular disease: an update.** J Am Coll. Cardiol. 2004 May 19;43(10):1731-7.

21. www.SAMHSA.com

22. Balbão CE, de Paola AA, Fenelon G. ***Effects of alcohol on atrial fibrillation: myths and truths.*** Ther Adv Cardiovasc Dis. 2009;3(1):53–63. [PubMed]

23. www.BMI.com

24. World Health Organization. ***World Health Organization STEPwise approach to chronic disease risk factor surveillance (STEPS) instrument. Version 3. 2007***. Geneva. World Health Organization. **Google Scholar**

25. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzey JY, Kay GN, Lowe JE, et al. ***ACC/AHA/ESC 2006 Guidelines for the Management of Patients***

with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation. 2006;114:e257–e354. [PubMed]

26. Kannel WB, Benjamin EJ. **Status of the epidemiology of atrial fibrillation.** Med Clin North Am. 2008 Jan;92(1):17-40, ix. [PMC free article] [PubMed]

27. Otto ME, Belohlavek M, Romero-Corral A, et al. Comparison of cardiac structural and functional changes in obese otherwise healthy adults with versus without obstructive sleep apnea. Am J Cardiol 2007; 99:1298–302.

28. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. ***Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation.*** JAMA. 2001;285:2864–70. [PubMed]

29. Adams KF, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, Berkowitz RL, Galvao M, Horton DP. ***Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE)***. Am Heart J. ; 2005, No.149: 209-216. [PubMed]

30. Mapoma CC (2013), **Population Ageing in Zambia: Magnitude, Challenges and Determinants**, Lusaka, Zambia

31. Ministry of Health – Zambia and World Health Organization Country Office (Zambia) (2008), ***STEPS Report Zambia: Prevalence rates of the common non-communicable diseases and their risk factors in Lusaka district, Zambia 2008***, Ministry of Health World Health Organization. Survey

32. Lloyd-Jones DM, Larson MG, Leip EP, Beiser A, D'Agostino RB, Kannel WB, Murabito JM, Vasan RS, Benjamin EJ, Levy D. ***Lifetime risk for development of atrial fibrillation: the Framingham Heart Study***. Circulation. 2004 Aug 31;110(9):1042-6. Epub 2004 Aug 16.

33. Humphries KH, Kerr CR, Connolly SJ, et al. New-onset atrial fibrillation: sex differences in presentation, treatment and outcome. Circulation 2001;103:2365–70.

34. Benjamin E.J., Wolf P.A., D'Agostino R.B. et al. ***Impact of atrial fibrillation on the risk of death: the Framingham Heart Study***. Circulation 1998;98:946—952.

35. Suttorp MJ, Kingma JH, Koomen EM, van't Hof A, Tijssen JG, Lie KI. Recurrence of paroxysmal atrial fibrillation or flutter after successful cardioversion in patients with normal left ventricular function. Am J Cardiol 1993;71:710 –3.

36. Psaty BM, Manolio TA, Kuller LH, Kronmal RA, Cushman M, Fried LP, White R, Furberg CD, Rautaharju PM; ***Incidence of and risk factors for atrial fibrillation in older adults***, Circulation. 96 (1997), pp. 2455–2461

37. Nattel S. ***New ideas about atrial fibrillation 50 years on***. Nature. 2002;415:219–26. [PubMed]

38. Guilian L, Jinchuan Y, Rongzeng D, Jun Q, Jun W, Wenqing Z. ***Impact of body mass index on atrial fibrillation recurrence: a meta-analysis of observational studies***. Pacing Clin Electrophysiol. 2013 Jun;36(6):748-56. doi: 10.1111/pace.12106. Epub 2013 Feb 25.

39. Overvad TF, Rasmussen LH, Skjøth F, Overvad K, Albertsen IE, Lane DA, Lip GYH, Larsen TB: **Alcohol intake and prognosis of atrial fibrillation patients.** *Heart doi:10.1136/heartjnl-2013-304036*

40. Heeringa J, Kors JA, Hofman A, van Rooij FJ, Witteman JC. ***Cigarette smoking and risk of atrial fibrillation: the Rotterdam Study***. Am Heart J. 2008 Dec;156(6):1163-9. doi: 10.1016/j.ahj.2008.08.003. Epub 2008 Oct 14. [PubMed]

41. Chamberlain AM, Agarwal SK, Folsom AR, Duval S, Soliman EZ, Ambrose M, Eberly LE, Alonso A. **Smoking and incidence of atrial fibrillation: results from the Atherosclerosis Risk in Communities (ARIC) study.** Heart Rhythm. 2011 Aug;8(8):1160-6. doi: 10.1016/j.hrthm.2011.03.038. Epub 2011 Mar 15. [PubMed]

42. Djoussé L, Levy D, Benjamin EJ, Blease SJ, Russ A, Larson MG, Massaro JM, D'Agostino RB, Wolf PA, Ellison RC.. ***Long-term alcohol consumption and the risk of atrial fibrillation in the Framingham Study.*** Am J Cardiol. 2004 Mar 15;93(6):710-3. [PubMed]

43. Ruigomez A, Johansson S, Wallander MA, et al; ***Incidence of chronic atrial fibrillation in general practice and its treatment pattern.*** J Clin Epidemiol. 2002 Apr;55(4):358-63.

44. Koskinen P, Kupari M, Leinonen H, et al. ***Alcohol and new onset atrial fibrillation: a case-control study of a current series.*** Br Heart J v.57(5); 1987 May PMC1277202

45. Rich EC, Siebold C, Campion B. ***Alcohol-related acute atrial fibrillation. A case-control study and review of 40 patients.*** Arch Intern Med. 1985 May;145(5):830-3.

46. Mukamal KJ, Tolstrup JS, Friberg J, et al. ***Alcohol consumption and risk of atrial fibrillation in men and women: the Copenhagen City Heart Study.*** Circulation. 2005 Sep 20;112(12):1736-42. Epub 2005 Sep 12.

47. Satoru K, Kazumi S, Shiro T, Chika H, Aki S, Yoriko H, et al: ***Alcohol Consumption and Risk of Atrial Fibrillation: A meta-Analysis,*** J Am Coll Cardiol. 2011 Jan 25;57(4):427-36. doi: 10.1016/j.jacc.2010.08.641.

48. Engel TR, Luck JC. ***Effect of whiskey on atrial vulnerability and "holiday heart."*** J Am Coll Cardiol. 1983;1(3):816–818. [PubMed]

49. Mäki T, Toivonen L, Koskinen P, Näveri H, Härkönen M, Leinonen H. ***Effect of ethanol drinking, hangover, and exercise on adrenergic activity and heart rate variability in patients with a history of alcohol-induced atrial fibrillation.*** Am J Cardiol. 1998;82(3):317–322. [PubMed]

50. Steinbigler P, Haberl R, König B, Steinbeck G. ***P-wave signal averaging identifies patients prone to alcohol-induced paroxysmal atrial fibrillation.*** Am J Cardiol. 2003;91(4):491–494. [PubMed]

51. Wright SP, Verouhis D, Gamble G, Swedberg K, Sharpe N and Doughty RN**; *Factors influencing the length of hospital stay of patients with heart failure.*** Eur J Heart Fail. 2003 Mar;5(2):201-9.

52. Nicol E D, Fittall B, Roughton M, Cleland J G F, Dargie H and Cowie M R. ***Heart failure and cardiomyopathy: NHS heart failure survey: a survey of acute heart failure admissions in England, Wales and Northern Ireland.*** *Heart.* 2008*;* 94:172-177.

53. Rogers A, Julia MA, McCoy ASM, Edmonds PM, Abery AJ, Coats AJS, et al. ***Qualitative study of chronic heart failure patients, understanding of their symptoms and drug therapy:*** Eur J Heart Fail. 2002 Jun;4(3):283-7.

54. Mwandolela H (2007), ***Types of cardiac diseases in women presenting with features suggestive of cardiac disease in peripartum period and their pregnancy outcomes in MNH***. MMed Thesis, MUHAS.2007.

55. Fofana M, Toure S, Dadhi Balde M, Sow T, Yassima Camara A, Damby Balde O, Toure A, Conde A.. ***Etiologic and nosologic considerations apropos of 574 cases of cardiac decompensation in Conakry.*** Ann Cardiol Angeiol (Paris). 1988 Oct;37(8):419-24.

56. Hennersdorf MG, Schueller PO, Steiner S, Strauer BE.. ***Prevalence of Paroxysmal Atrial Fibrillation Depending on the Regression of Left Ventricular Hypertrophy in Arterial Hypertension,*** Hypertens Res. 2007 Jun;30(6):535-40. [PubMed]

57. Thakkar S and Bagarhatta R; **Detection of paroxysmal Atrial Fibrillation or Flutter in Patients with Acute Ischemic Stroke or Transient Ischemic Attack by Holter Monitor**; Indian Heart Journal 66 (2); March – April 2014; 188-192

58. Galrinho A, Gomes JA, Antunes E, *et al.* ***Atrial fibrillation and coronary disease*** Rev. Port. Cardiol. 12 (1993), pp. 1037–1040

59. Aleksova A, et al. ***Impact of Atrial Fibrillation on Outcome of Patients with Idiopathic Dilated Cardiomyopathy: Data from the Heart Muscle Disease Registry of Trieste***, Clin Med Res. Dec 2010; 8(3-4): 142–149. doi: 10.3121/cmr.2010.908

60. Luchsinger JA and Steinberg JS **Resolution of cardiomyopathy after ablation of atrial flutter.** J Am Coll Cardiol. 1998 Jul;32(1):205-10.

61. Lindsay BD and Smith JM (1996), **Electrophysiologic aspects of human atrial fibrillation.** In: DiMarco JP, ed. *Cardiology Clinics*. Philadelphia, Pa: WB Saunders; 483–505.

62. Movahed MR, Hashemzadeh M, Jamal MM. ***Diabetes mellitus is a strong, independent risk for atrial fibrillation and flutter in addition to other cardiovascular disease****. Int J Cardiol. 2005 Dec* 7;105(3):315-8.

63. Schmid H, Forman LA, Cao X, et al; ***Heterogeneous cardiac sympathetic denervation and decreased myocardial nerve growth factor in streptozotocin induced diabetic rats: implications for cardiac sympathetic dysinnervation complicating diabetes.*** Diabetes. 1999 Mar;48(3):603-8.

64. Olgin JE, Sih HJ, Hanish S, et al. ***Heterogeneous atrial denervation creates substrate for sustained atrial fibrillation.*** Circulation. 1998; 98: 2608-14.

65. Shibata Y, Watanabe T, Osaka D, Abe S, Inoue S, Tokairin Y, Igarashi A, Yamauchi K, Kimura T, Kishi H, Aida Y, Nunomiya K, Nemoto T, Sato M, Konta T, Kawata S, Kato T, Kayama T, Kubota I.; ***Impairment of pulmonary function is an independent risk factor for AF: the Takahata study***, Int J Med Sci. 2011;8(7):514-22. Epub 2011 Aug 29.

66. Kang H, Bae BS, Kim JH, Jang HS, Lee B, and Jung B,: ***The Relationship Between Chronic Atrial Fibrillation and Reduced Pulmonary Function in Cases of Preserved Left Ventricular Systolic Function*****.** Korean Circ J. 2009 Sep; 39(9): 372–377.

67. Lopez CM and House-Fancher MA. ***Management of atrial fibrillation in patients with chronic obstructive pulmonary disease.*** J Cardiovasc Nurs. 2005 Mar-Apr;20(2):133-40.

68. Stevenson IH, Roberts-Thomson KC, Kistler PM, Edwards GA, Spence S, Sanders P, Kalman JM; **Atrial electrophysiology is altered by acute hypercapnoea but not hypoxiemia: implications for promotion of atrial fibrillation in pulmonary disease and sleep apnea.** Heart Rhythm. 2010 Sep;7(9):1263-70. doi: 10.1016/j.hrthm.2010.03.020. Epub 2010 Mar 22.

69. Sanna T, Diener HC, Passman RS, Di Lazzaro, Bernstein RA, Morillo CA et al; CRYSTAL AF Investigators. Cryptogenic stroke and underlying. New England Journal of Medicine. 2014; 370:2478-2486.

70. Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J, et al;EMBRACE Investigators and Coordinators, Atrial Fibrillation in Patients with Cryptogenic stroke. New England Journal of Medicine. 2014; 370:2467-2477.

71.