

ORIGINAL PAPER

# FREQUENCY OF RISK FACTORS IN PATIENTS WITH ATRIAL FIBRILLATION, HEART FAILURE, CORONARY ARTERY DISEASES, AND VALVULOPATHIES

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## ABSTRACT

**Introduction.** Atrial fibrillation (AF) is frequently linked to various risk factors and comorbidities and closely connected to cardiovascular diseases (CVDs) like coronary artery disease (CHD), heart failure (HF) and valvular heart disease. The concomitant presence of AF with one or more of these CVDs increases the risk of stroke and requires a different clinical management.

**The objective of the study** was to analyse the differences between risk factors and comorbidities, depending on the presence/absence of three cardiac comorbidities (HF, coronary heart disease, valvopathies).

**Materials and methods.** 4216 patients with primary or secondary diagnosis of AF on discharge were selected from the database of the County Emergency Clinical Hospital Oradea, Romania, and included in a retrospective study. Specific data on demographic information and comorbidities were gathered and organized in a digital form. Patients were divided into three groups: low risk group (LRG) – 1404 participants who did not have any of the three cardiac conditions; the medium risk group (MRG) – 2760 participants who had at least one and most two cardiac conditions, and

## RÉSUMÉ

**Fréquence des facteurs de risque chez les patients atteints de fibrillation auriculaire, d'insuffisance cardiaque, de maladies coronariennes et de valvulopathies**

**Introduction.** La fibrillation auriculaire (FA) est fréquemment liée aux divers facteurs de risque et comorbidités et étroitement liée aux maladies cardiovasculaires (MCV) telles que les maladies coronariennes (CHD), l'insuffisance cardiaque (IC) et les valvulopathies. La présence concomitante d'une FA avec une ou plusieurs de ces maladies cardiovasculaires augmente le risque d'AVC et nécessite une prise en charge clinique différente.

**L'objectif de l'étude** était d'analyser les différences entre facteurs de risque et comorbidités, en fonction de la présence/absence de trois comorbidités cardiaques (IC, coronaropathie, valvulopathies).

**Matériaux et méthodes.** 4216 patients avec un diagnostic primaire ou secondaire de FA à la sortie de l'hôpital ont été sélectionnés à base de données de l'hôpital clinique d'urgence du comté d'Oradea, en Roumanie, et inclus dans une étude rétrospective. Des données

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the high-risk group (HRG) –52 participants who had all three cardiac conditions.

**Results.** A higher incidence of hypertension (HT), smoking, alcohol consumption, and peripheral arterial disease can be seen in the LRG compared to MRG and HRG. In the MRG, in contrast to LRG and HRG, there was a higher incidence of HT, sedentary lifestyle, smoking, alcohol consumption and peripheral arterial disease; increased incidence of diabetes, family history of AF, family history of CHD, and dyslipidemia were noted in HRG as compared to LRG and MRG.

**Conclusions.** The present research reveals a strong association between AF alone or concomitant with one or two of HF, CAD and valvulopathies and several risk factors like HT, adverse lifestyle and diabetes.

**Keywords:** atrial fibrillation, risk factors, comorbidities, cardiovascular diseases

#### Abbreviations list

BMI – body mass index

BP – blood pressure

CHD – coronary heart disease

COPD – chronic obstructive pulmonary disease

CVD – cardiovascular disease

HF – heart failure

HRG – high risk group

HT – hypertension

LRG – low risk group

MRG – medium risk group

OSA – obstructive sleep apnea

RA- rheumatoid arthritis

VHD – valvular heart disease

#### INTRODUCTION

A health issue with growing incidence, atrial fibrillation (AF), is frequently linked with various complications and comorbidities<sup>1,2</sup>. About 3% of Western people older than 20 years are nowadays affected by this disease, and it is estimated that the number of AF patients will grow from approximately 7 million to about 13 million by 2030 in the European Union<sup>3-5</sup>. Among the main causes of this widespread disease, besides ageing, are cardiovascular (CV) risk factors and several chronic cardiovascular diseases (CVDs), partly consequences of an unhealthy lifestyle<sup>5-7</sup>.

The risk of stroke is greater in patients suffering from AF, this arrhythmia being considered responsible for 25% of strokes<sup>8</sup>. Besides being a considerable risk factor for stroke, in case of strokes associated with AF, patients present higher rates of disability, with prolonged hospitalization, mortality and morbidity in contrast to patients with stroke who do not suffer

spécifiques sur les informations démographiques et les comorbidités ont été recueillies et organisées sous forme électronique. Les patients ont été divisés en trois groupes : groupe à faible risque (LRG) – 1 404 participants qui ne souffraient d'aucune des trois affections cardiaques ; le groupe à risque moyen (MRG) – 2760 participants qui avaient au moins un et surtout deux de ces problèmes cardiaques, et le groupe à haut risque (HRG) –52 participants qui avaient les trois problèmes cardiaques.

**Résultats.** Une incidence accrue d'hypertension (HT), de tabagisme, de consommation d'alcool et de maladie artérielle périphérique peut être observée dans le groupe LRG par rapport aux MRG et HRG. Dans le MRG, contrairement au LRG et au HRG, il y avait une incidence plus élevée d'HT, de mode de vie sédentaire, de tabagisme, de consommation d'alcool et de maladie artérielle périphérique : une incidence accrue de diabète, d'antécédents familiaux de FA, d'antécédents familiaux de coronaropathie et de dyslipidémie a été notée dans le HRG par rapport aux LRG et MRG.

**Conclusions.** La présente recherche révèle une forte association entre la FA seule ou concomitante avec un ou deux des HF, CAD et valvulopathies et plusieurs facteurs de risque comme l'HT, un mode de vie nocif et le diabète.

**Mots-clés:** fibrillation auriculaire, facteurs de risque, comorbidités, maladies cardiovasculaires

from AF<sup>8</sup>. AF is closely connected to CVDs like HT, coronary artery disease (CHD), heart failure (HF), valvular heart disease (VHD) and diabetes mellitus<sup>9,12</sup>.

When HF and AF co-occur, they are linked to serious outcomes. The risk of stroke is enhanced in the presence of these two illnesses, in many cases being necessary oral anticoagulant treatment<sup>13</sup> or even left atrial appendage closure in some cases. Therapy success in controlling the AF rhythm and rate in HF is limited by side effects, intolerance, and fluctuating efficiency<sup>14</sup>.

Compared to the general population, patients suffering from CHD are more likely to be affected by AF, and patients with AF are more likely to develop CHD, as well. The incidence of several types of AF in men was doubled by CHD, while in women the risk of transient AF increased four times, as highlighted by the Framingham Study<sup>15</sup>. AF patients commonly present VHD (up to 60%), that determines an increased risk of stroke when combined with AF<sup>6,7</sup>. Stroke is more frequent among patients with VHD and AF.

As a general principle, it is recommended to prevent the occurrence of AF than its complications. In most patients, AF is a consequence of atrial remodeling (also known as atrial cardiomyopathy) determined by risk factors and comorbidities, which can be subclinical<sup>16,17</sup>. Moreover, this arrhythmia may overlap with other CVDs that have the same common risk factors.

**THE OBJECTIVE OF THE STUDY**

This research intended to analyse the differences between risk factors and comorbidities, depending on the presence/absence of the three cardiac comorbidities (HF, CHD, VHD).

**MATERIALS AND METHODS**

A retrospective, single centre, observational study was performed between 2017-2020 in the County Emergency Clinical Hospital, Oradea, Romania. A number of 4216 patients were selected from the hospital database, based on the I48.0 AF (I International Classification of Disease 10th Revision) diagnostic code. Specific data on family history of AF or CHD, adverse lifestyle (alcohol consumption, smoking, obesity, sedentary lifestyle), demographic information and comorbidities were gathered and organized in a digital form.

The patients were divided into three groups: low risk group (LRG) - 1404 participants who did not have any of the three cardiac conditions; the medium risk group (MRG) - 2760 participants who had at least one and at most two cardiac conditions, and the high-risk group (HRG) -52 participants who had all three cardiac conditions.

The study was approved by the Ethics Commission of the County Emergency Clinical Hospital of Oradea (no. 11943/ 12.05.2021) and the Ethics Commission

of Faculty of Medicine and Pharmacy, University of Oradea (no. 1/31.05.2021), and was carried out in agreement with the WMA Declaration of Ethics in Helsinki<sup>18</sup>. When hospitalized, the subjects signed an informed consent form.

For the statistical analysis, the JASP v16 and IBM SPSS Statistics 20 programs were used. At the beginning of the evaluation, the records were described by measuring the dispersion and central tendency parameters for numerical variables; frequency tables were determined for ordinal and nominal variables. Corresponding diagrams were plotted using the most significant results. The Shapiro - Wilk distribution test revealed that the numerical data are not normally dispersed ( $p < 0.001$ ), thus for the evaluation other non-parametrical tests (Kruskal - Wallis or Mann - Whitney) were used. The odds ratio (OR) and the 95% confidence interval were calculated for the risk analysis and the Chi-Square test was used to determine the statistical significance. The  $p - value = 0.05$  was set as threshold for the entire research.

**RESULTS**

The mean age of the patients was 72.52 years,  $SD \pm 10.63$  and from the total of 4216 subjects, 2261 (53.7%) were women. 2110 (50.05%) subjects were from rural areas.

Dyslipidemia, CHD, peripheral artery disease, rheumatoid arthritis (RA), HT, chronic obstructive pulmonary disease (COPD), HF, VHD and obstructive sleep apnea (OSA) are the most frequent comorbidities in the study group.

Evaluating the research variables in the three groups described in Table 1, it was observed that in the HRG, men and patients from urban areas predominated, and in the MRG predominated women and patients from rural areas. Diabetes, and dyslipidemia are more prevalent in HRG patients, while HT

**Table 1.** Statistical description of the study parameters according to risk groups (N=4216)

Parameters		LRG	%	MRG	%	HRG	%
Sex	Male	711	50.6	1213	43.9	31	59.6
	Female	693	49.4	1547	56.1	21	40.4
Area of origin	Urban	777	55.3	1202	43.6	27	51.9
	Rural	627	44.7	1558	56.4	25	48.1
High blood pressure	No	11	0.8	816	29.6	23	44.2
	Yes	1393	99.2	1944	70.4	29	55.8
Heart failure	No	1404	100.0	1046	37.9	0	0.0
	Yes	0	0.00	1714	62.1	52	100.0
Coronary diseases	No	1404	100.0	1384	50.1	0	0.0
	Yes	0	0.0	1376	49.9	52	100.0
Diabetes	No	939	66.9	1399	50.7	12	23.1
	Yes	465	33.1	1361	49.3	40	76.9

**Table 1.** Statistical description of the study parameters according to risk groups (N=4216) (*continuare*)

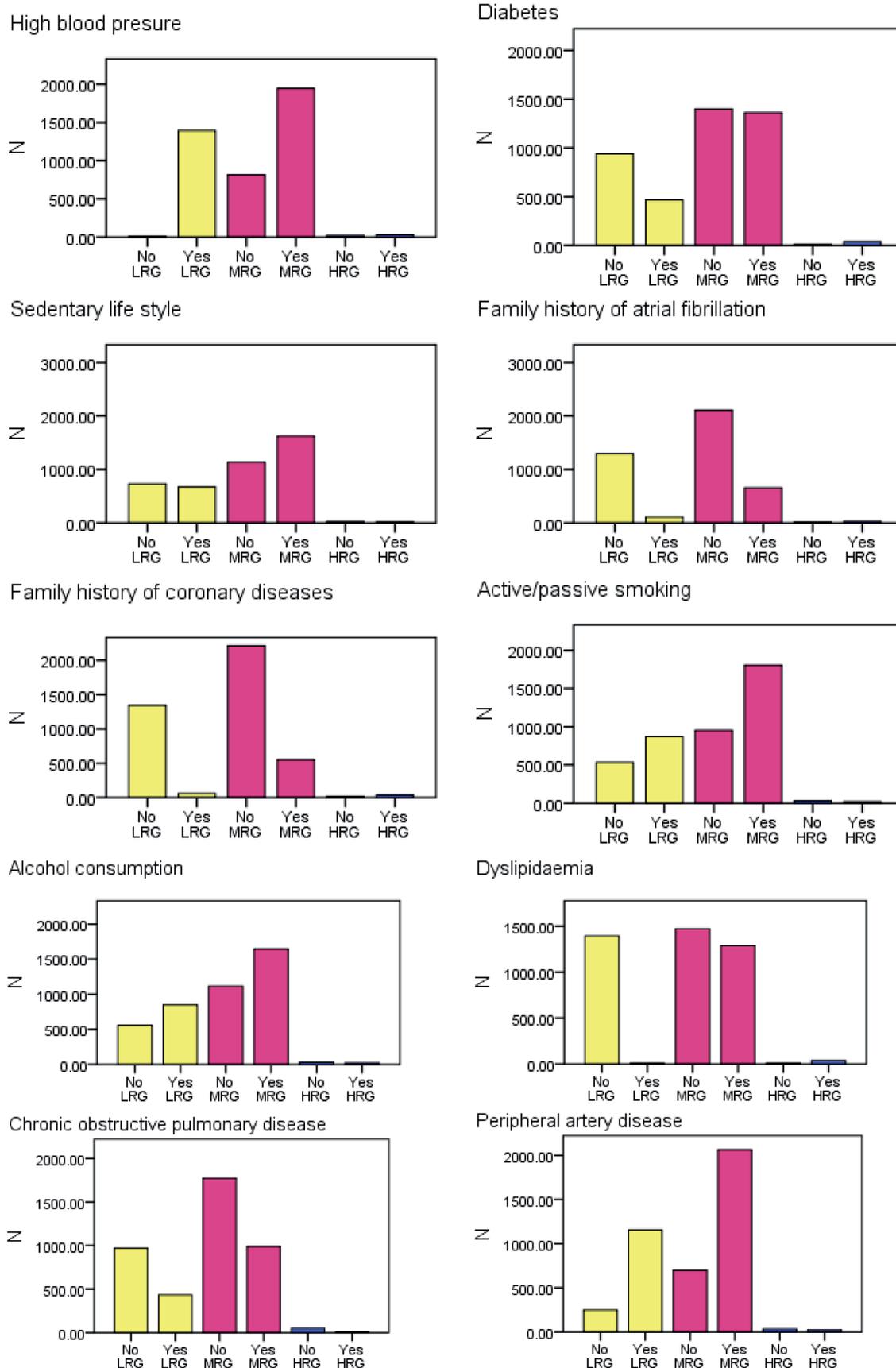
Parameters		LRG	%	MRG	%	HRG	%
		Sedentary lifestyle	No	729	51.9	1136	41.2
	Yes	675	48.1	1624	58.8	23	44.2
Family history of atrial fibrillation	No	1294	92.2	2106	76.3	20	38.5
	Yes	110	7.8	654	23.7	32	61.5
Family history of coronary disease	No	1343	95.7	2210	80.1	16	30.8
	Yes	61	4.3	550	19.9	36	69.2
Active / passive smoking	No	533	38.0	953	34.5	32	61.5
	Yes	871	62.0	1807	65.5	20	38.5
Alcohol	No	557	39.7	1114	40.4	30	57.7
	Yes	847	60.3	1646	59.6	22	42.3
Valvopathies	No	1404	100.0	2346	85.0	0	0.0
	Yes	0.0	0.0	414	15.0	52	100.0
Dyslipidemia	No	1393	99.2	1471	53.3	12	23.1
	Yes	11	0.8	1289	46.7	40	76.9
Obstructive sleep apnea	No	1382	98.4	2623	95.0	52	100.0
	Yes	22	1.6	137	5.0	0	0.0
Chronic obstructive pulmonary disease	No	970	69.1	1773	64.2	48	92.3
	Yes	434	30.9	987	35.8	4	7.7
Peripheral artery disease	No	248	17.7	697	25.3	32	61.5
	Yes	1156	82.3	2063	74.7	20	38.5
Rheumatoid arthritis	No	1333	94.9	2594	94.0	52	100.0
	Yes	71	5.1	166	6.0	0	0.0

LRG, low risk group; MRG, medium risk group; HRG, high risk group.

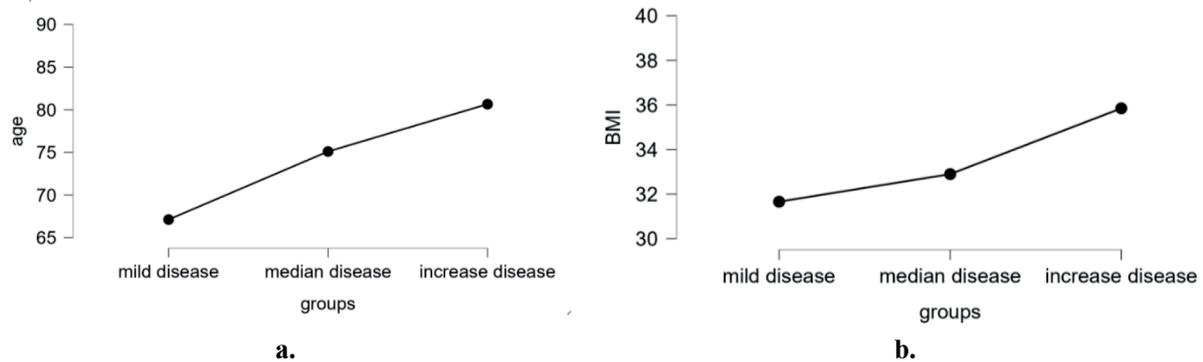
**Table 2.** Chi-Square statistical test and statistical significance in the 3 research groups

Parameters	Test Statistics	Groups		
		LRG	MRG	HRG
High blood pressure	Chi-Square	1360.345 <sup>a</sup>	461.009 <sup>b</sup>	.692 <sup>c</sup>
	Asymp. Sig.	0.001	0.001	0.405
Diabetes	Chi-Square	160.026 <sup>a</sup>	.523 <sup>b</sup>	15.077 <sup>c</sup>
	Asymp. Sig.	0.001	0.469	0.000
Sedentary lifestyle	Chi-Square	2.077 <sup>a</sup>	86.284 <sup>b</sup>	0.692 <sup>c</sup>
	Asymp. Sig.	0.150	0.001	0.405
Family history of atrial fibrillation	Chi-Square	998.473 <sup>a</sup>	763.878 <sup>b</sup>	2.769 <sup>c</sup>
	Asymp. Sig.	0.001	0.001	0.096
Family history of coronary disease	Chi-Square	1170.601 <sup>a</sup>	998.406 <sup>b</sup>	7.692 <sup>c</sup>
	Asymp. Sig.	0.001	0.001	0.006
Active / passive smoking	Chi-Square	81.370 <sup>a</sup>	264.245 <sup>b</sup>	2.769 <sup>c</sup>
	Asymp. Sig.	0.001	0.001	0.096
Alcohol consumption	Chi-Square	59.900 <sup>a</sup>	102.545 <sup>b</sup>	1.231 <sup>c</sup>
	Asymp. Sig.	0.001	0.001	0.267
Dyslipidemia	Chi-Square	1360.345 <sup>a</sup>	12.001 <sup>b</sup>	15.077 <sup>c</sup>
	Asymp. Sig.	0.001	0.001	0.001
Chronic obstructive pulmonary disease	Chi-Square	204.627 <sup>a</sup>	223.839 <sup>b</sup>	37.231 <sup>c</sup>
	Asymp. Sig.	0.001	0.001	0.001
Peripheral artery disease	Chi-Square	587.225 <sup>a</sup>	676.071 <sup>b</sup>	2.769 <sup>c</sup>
	Asymp. Sig.	0.001	0.001	0.096

Legend: LRG, low risk group; MRG, medium risk group; HRG, high risk group. a. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 702.0. b. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 1380.0. c. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 26.0.



**Figure 1.** Graphical representation of the average values of the research variables according to the risk group. The parameters evaluated as risk factors in the studied patients are expressed as the incidence number of people in the study groups (N = 4216). LRG, low risk group; MRG, medium risk group; HRG, high risk group.



**Figure 2.** The differences obtained after applying the Kruskal-Wallis test based on the disease severity on a. age, b. BMI

sedentary lifestyles, active smoking, alcohol use, and circulatory disease are more prevalent in the MRG.

According to the Chi-Square statistical analysis, significant results were obtained, following the differences of the three research groups (LRG, MRG and HRG), at HT, at the level of the following parameters: diabetes, sedentary lifestyle, family history of AF, family history of CHD, active / passive smoking, alcohol consumption, dyslipidemia, COPD, and peripheral atrial disease (Table 2).

A higher incidence of HT, smoking, alcohol consumption and peripheral arterial disease can be seen in the LRG compared to the other two groups; in MRG in contrast to LRG and HRG, there was a higher incidence of HT, sedentary lifestyle, smoking, alcohol consumption and peripheral arterial disease; higher incidence of diabetes, family history of AF, family history of CHD, and dyslipidemia were noted in HRG compared to LRG and MRG (Figure 1).

A Kruskal Wallis test on age and body mass index (BMI) was applied and we obtained significant differences ( $p < 0.001$ ). The number of comorbidities is increasing proportionally with BMI and age. The main results are plotted in Figure 2.

## DISCUSSION

AF is the most common sustained cardiac arrhythmia. It is expected that by 2050, in the USA, 6 to 12 million people will suffer from AF, and in Europe, by 2060, 17.9 million people will be affected by it, as the population is ageing, worldwide<sup>1,5,19</sup>. The incidence of AF is linked to several CV risk factors and diseases, as highlighted by various studies, whereas lone AF is rare. The risk of CV complications and mortality in individuals with AF and comorbidities is higher than in those with AF alone<sup>20</sup>. The results of the present study indicated the presence of at least one of the three cardiovascular comorbidities in 66.7% of patients diagnosed with AF.

AF and HF develop either simultaneously or separately, being favoured by neurohormonal changes, general risk factors and comorbidities, and structural and electrophysiological alterations<sup>21</sup>. In this study, the combined prevalence of the two pathologies was identified in 41.9% of cases. The combined prevalence of HF and AF and their temporal connection was revealed by the Framingham Heart Study. Of the 931 subjects presenting HF, 24% suffered from prior or concurrent AF and 17% developed AF after the diagnosis of HF. 20% of the subjects included in the study presented both HF and AF, identified in the same day<sup>22</sup>. The prevalence of initial HF in subjects with AF was 33 out of 1000, which is equivalent to that identified in the Danish nationwide cohort trial<sup>23</sup>. In a Framingham Heart Study group, the prevalence of HF was considerably increased in subjects with AF compared to the prevalence of AF in subjects without a history of HF. Otherwise stated, HF generates AF less than AF generates HF<sup>24</sup>.

The prevalence of CHD combined with HF was identified in 11.3% patients, and with VHD in 11.1% patients. According to World Health Organization (WHO) data, the main cause of death worldwide is CHD, growing from 27.3% to 31.4% in the last decades<sup>15,25</sup>. Considering the everyday life habits, the prevalence of CHD is expected to grow. There is an increasing tendency for patients with CHD to develop AF<sup>15,26</sup>, particularly for new AF occurrence, succeeded by myocardial infarction<sup>27</sup>. Subjects suffering from AF were indicated to be more susceptible to present coronary artery lesions<sup>28</sup>. The longevity of the subjects is negatively influenced if CHD and AF coexist<sup>29</sup>. The therapy for subjects suffering from both AF and CHD should be focused on efficient management of AF rhythm using various procedures in combination with CHD therapy. When these procedures are not successful, the use of antithrombotic treatment may be efficient in these diseases by delaying or preventing their complications.

In our study, the prevalence of the risk factors was significantly different between the three groups. HT, diabetes, and dyslipidemia were more prevalent in HRG patients, while sedentary lifestyles, active smoking, alcohol use, and circulatory disease were more prevalent in MRG. The number of comorbidities increased proportionally with BMI. These results emphasize the importance of maintaining an adequate lifestyle in case of patients with AF.

## CONCLUSIONS

The present research reveals a strong association between AF alone or concomitant with HF, CHD and VHD and several risk factors like HT, adverse lifestyle and diabetes. Besides stroke prevention, rhythm and rate control, efficient medical and therapeutical management needs to comprise the treatment of underlying cardiovascular morbidities and associated risk factors proper follow-up, the adequate care for AF patients determining better results for these patients.

## Author Contributions:

Conceptualization, T.M.M., and D.M.T.; methodology, T.M.M. and D.M.T.; software, D.M.T. and A.F.B.; validation, T.B., and D.M.T.; formal analysis, T.M.M. and D.M.T.; investigation, T.M.M. and D.M.T.; resources, T.M.M. and D.M.T.; data curation, T.M.M., A.F.B., A.G.F. and D.M.T.; writing—original draft preparation, T.M.M. and D.M.T.; writing—review and editing, T.M.M., A.F.B., A.G.F, T.B and D.M.T.; visualization, D.M.T.; supervision, D.M.T.; project administration, D.M.T. All authors have read and agreed with the final version of this article.

## Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article“

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study“

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