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Aging, Diabetic Nephropathy and Multiple Macrovascular Involvement are Associated with Atrial Fibrillation in Type 2 Diabetes Mellitus

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Authors' contributions

Author GP participated in the overall design, data collection, statistical analysis, data interpretation, writing and critical review of the manuscript. Authors MPI, CL and RM participated in data collection, data interpretation and critically revised the manuscript before final approval. Authors CF and VP supervised the design and conduction of the study, participated in data interpretation and critically revised the manuscript before final approval. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Background: Atrial fibrillation (AF) is the most common arrhythmia in the world and a recognized risk factor for stroke and death.
Aims: To establish the association between atrial fibrillation and markers of glucose homeostasis as well as anthropometric, laboratory and clinical variables in type 2 diabetes.
Study Design: Cross-sectional retrospective study.
Place and Duration of Study: Unit of Metabolic and Endocrine Diseases, "Centro Catanese di Medicina e Chirurgia" Clinic, Catania, Italy, between January 1, 2008, and January 1, 2014
Methods: We included 6,920 type 2 diabetic (T2D) patients (mean age 66.4±11.4 years, 50.4% men) treated in specialist diabetes center. Persistent AF was assessed by clinical history and confirmed (by a single cardiologist) by a resting 12-lead electrocardiogram.

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Demographic, clinical and laboratory parameters were included in the analyses, as well as vascular laboratory studies. Standardized procedures were used to assess microvascular complications and Metabolic Syndrome (MetS).
Results: In total, 6,455 (93.3%) patients had no evidence of atrial arrhythmia and the remaining 465 (6.7%) had AF. The prevalence of AF increased with age (peak of prevalence after 75 years in both sexes) and it was significantly greater in men (p=0.02). AF was significantly associated with hypercreatininemia, eGFR (and more advanced stage of Chronic Kidney Disease, CKD) and albuminuria (p<0.0001) as well as the diagnosis of cardio-vascular disease (CVD, p<0.0001). In a multivariate logistic regression analysis, age (OR 1.08, 95% CI 1.05-1.11, p<0.0001), male sex (OR 2.46, 95% CI 1.5-3.9, p=0.0002), estimated Glomerular Filtration Rate (eGFR) (OR 0.99, 95% CI 0.98-0.99, p=0.02) and the presence of CVD (OR 1.65, 95% CI 1.01-2.75, p=0.04) were all independent factors related to AF. When we subgrouped patients according to cardiovascular patterns, an adjusted analysis revealed a significant difference only in the poly-vascular subgroup (OR 2.24, 95% CI 1.26-3.99, p=0.006).
Conclusion: Aging, CKD and cardiovascular disease (particularly poly-vascular involvement) were the most significant AF-related factors. In T2D patients, the identification of factors predisposing individuals to AF may facilitate an early diagnosis and stroke prevention therapy.

Keywords: Type 2 diabetes mellitus; atrial fibrillation; cardiovascular disease; risk factors.

ABBREVIATIONS

AF, Atrial fibrillation; AH therapy, Antihypertensive therapy; BMI, Body mass index; CAD, Coronary artery disease; CBVD, Cerebrovascular disease; DBP, Diastolic blood pressure; DUS, Duplex ultrasonography; eGFR, Estimated glomerular filtration rate; FPG, Fasting plasma glucose; LVH, Left ventricular hypertrophy; MVD, Macrovascular disease; MDIs, Multiple daily injections; MetS, Metabolic syndrome; NMVD, No macrovascular disease; NOAC, Novel oral anticoagulant; NSCS, Non-significant carotid stenosis; OAC, Oral anticoagulant; PAD, Peripheral artery diseases; PVD, Polyvascular disease; SBP, Systolic blood pressure; T2DM, Type 2 diabetes mellitus; VKA, Vitamin K antagonist; WC, Waist circumference.

1. INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in the world causing persistent disturbances of cardiac rhythm observed in clinical practice [1-3]. The prevalence of such arrhythmia increases with age, reaching nearly 9% of subjects aged 80 years and older [4-5]. Due to the aging population, a 2.5-fold increase in the AF prevalence is expected in the next 50 years. In the U.S. alone, AF affects approximately 2.2 million adults, and the number is expected to increase to 5.6million by 2050 [1]. AF appears to be a strong risk factor for stroke as a result of thromboembolisms typically originating from the left atrial appendage [6]. Furthermore, AF is associated with an increase in the relative risk of death, ranging from 1.3 to 2.0, independent of other risk factors. The doubled mortality rate of AF is often linked to the severity of underlying heart disease [7-9]. Certain risk factors for AF are represented by cardiovascular diseases, in particular hypertension, coronary artery disease, cardiomyopathy and valvular disease (particularly mitral) [10]. Other predisposing conditions include excessive alcohol intake, hyperthyroidism, pulmonary disorders and diabetes. The

prevalence of AF in type 2 diabetes is greater than expected. The association between the two diseases has been confirmed by several epidemiologic studies [10]. A recent meta-analysis that evaluated seven prospective cohort studies and four case/control studies, which included 108,703 cases of AF, demonstrated that diabetes was associated with a relative risk of 1.34 of developing arrhythmia [11]. The same authors confirmed these results in the ARIC study, a community-based prospective cohort study with 15,792 participants aged 45-64 years at baseline and recruited from four communities in the U.S. [12]. Furthermore, the contribution of diabetes to the prevalence and incidence of AF was evaluated by a recent observational, longitudinal study (34,744 patients), demonstrating that diabetes was an independent determinant of this arrhythmia [13]. Although the link between AF and diabetes is now well recognized, the pathogenetic factors of this arrhythmia have not been fully investigated in the diabetic population.

The aim of our retrospective observational study was to assess the prevalence of AF in our type 2 diabetic population and extensively evaluate its associations with markers of glucose homeostasis and anthropometric, laboratory and clinical variables.

2. MATERIALS AND METHODS

2.1 Study Population and Subjects

This observational, cross-sectional survey, consisted of 7,365 consecutive patients with type 2 diabetes who had been referred to us by general practitioners or other specialists for diabetes management and/or chronic complication assessment between January 1, 2008, and January 1, 2014. The study was approved by the ethics committee of our institution and informed consent was obtained from all participants. We studied 6,920 subjects (445 excluded on the basis of criteria listed below) and the data were collected from a diagnostic Day-Hospital in our center (Unit of Metabolic and Endocrine Diseases, “Centro Catanese di Medicina e Chirurgia” Clinic, Catania, Italy) and were retrospectively analyzed. Persistent AF was assessed by clinical history and confirmed at admission in our ward by a single cardiologist on the basis of a resting 12-lead electrocardiogram (ECG) that was recorded in a supine position after a 5 min rest. Subjects were divided into 2 groups according to the diagnosis of AF. The exclusion criteria were as follows: acute illnesses, acute heart failure, acute renal failure, chronic active hepatitis (liver transaminases $\geq$2-fold higher than the normal range and/or positive viral hepatitis B or C serology), other unstable medical condition and glucocorticoid therapy. Furthermore, we excluded patients who had a history of previous moderate-to-severe aortic or mitral valvular disease.

2.2 Clinical and Laboratory Measurements, Definition of Terms

Body weight was measured in light clothing without shoes to the nearest half kilogram. Height was measured to the nearest half centimeter. Body mass index (BMI) was calculated as Kg/m^2. Waist circumference (WC, to the nearest half centimeter) was measured in a standing position at the umbilicus. Arterial blood pressure was taken with a standard mercury blood pressure meter. Three blood pressure readings were obtained at 1-minute intervals, and the systolic and diastolic pressure readings were averaged and used for the analysis. Venous blood was drawn in the morning at ward admission after a 10-12 h overnight fasting. All of the biochemical parameters were evaluated with standard laboratory procedures. All of the patients were tested for viral hepatitis B and C. LDL cholesterol was calculated by the Friedewald formula ([LDL-Chol]=[Total Chol]-[HDL-chol]-([TG]/5])), except when the serum

triglyceride concentration was >400 mg/dL. HbA_{1c} was measured by high-performance liquid chromatography (HPLC); the upper normality limit for the laboratory was 5.9%. A daily glycemic profile with 6 finger-prick tests (One Touch Ultra, LifeScan, Milpitas, California, USA) was also obtained from all of the patients. Metabolic syndrome (MetS) was diagnosed using the AHA-NHLBI criteria [14], by the presence of diabetes and ≥2 of the following components: 1) WC >102cm in men and >88cm in women; 2) triglycerides >1.7mmol/L (150 mg/dL) or fibrate/fish oil users; 3) HDL <1.0mmol/L (40mg/dL) in men and <1.29mmol/L (50mg/dL) in women; and 4) blood pressure ≥130/85 mmHg or receiving blood pressure reduction treatment.

A macrovascular complication evaluation was conducted by a thorough cardiovascular history, as documented by previous medical records (including medical and hospital records), and vascular laboratory studies (all patients underwent a standardized electrocardiogram, an echocardiogram, the ankle/brachial index, the duplex ultrasonography (DUS) of the carotid and lower limbs and, if clinically indicated, provocative tests for cardiac ischemia and CT or MRI-scan of brain). The diagnosis of left ventricular hypertrophy (LVH) was made by a single cardiologist on the basis of echocardiographic data.

Patients were also divided into 6 macrovascular subgroups according to the vascular areas that were involved (as previously reported by our group [15]): *NMVD*, no macrovascular disease; *NSCS*, non-significant carotid stenosis; *CBVD*, cerebrovascular disease; *CAD*, coronary artery disease; *PAD*, peripheral artery disease; and *PVD*, polyvascular disease (two or more of the above conditions present at the same time). In addition, the MVD group included any patient with macrovascular disease.

Microvascular complications were evaluated using fundus oculi and/or fluorescence angiography to assess retinopathy, urinary albumin excretion, eGFR calculation and CKD staging to assess nephropathy, and the 10 g monofilament test and vibration perception threshold analysis to assess peripheral neuropathy. Albuminuria was defined as urinary albumin excretion between 30 and 299 mg/day (microalbuminuria) or ≥300 mg/day (macroalbuminuria) on at least 2 of 3 occasions. The eGFR was calculated using the *MDRD* formula [estimated GFR (ml/m/1.73m^2) =186xcreatinine (mg/dl)$^{-1.154}$ x age (yy)$^{-0.203}$ x 0.742 (if female) x 1.210 (if of black ethnicity)] [16]. Patients were then assigned to one of the following categories of eGFR (mL/min/1.73m^2): 1 (≥90); 2 (60-89); 3 (30-59); 4 (15-29); and 5 (<15). Finally, patients were classified as having no CKD (stage 0) or CKD stages 1-5, based on the presence of absence of micro or macroalbuminuria and the value of eGFR calculated by the MDRD Study equation, according to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative [17]. Diabetic retinopathy was defined as any diabetes-linked retinal injury. Diabetic peripheral neuropathy was diagnosed based on neuropathic symptoms, insensitivity to a 10g monofilament and an abnormal vibration perception threshold.

2.3 Statistical Analysis

Mean and standard deviation were determined from data and presented as means ± SD or proportions. Skewed variables were logarithmically transformed to improve normality before analysis. Patients were grouped as no AF or AF based on the diagnosis of AF. Continuous variables were analyzed using the unpaired *t* test, and categorical variables were analyzed using the chi-square test. The independence of the associations of significant variables (in a univariate analysis) with AF was assessed using a multivariate logistic regression model and expressed as an odds ratio (OR). In the fully adjusted regression model, age, sex (M), eGFR

(as a marker of nephropathy), fibrinogen, AH (anti-hypertensive) therapy, neuropathy and presence of cardiovascular diseases were included. A separate model (adjusted for age, sex, eGFR, fibrinogen, neuropathy, AH therapy) was also tested with the individual components of cardiovascular groups included as categorical measures. All analyses were performed by Statistical package, SPSS (version 16, Chicago, IL, USA) and StatView (version 5.01, SAS institute, Cary, NC). *P<.05* was considered statistically significant.

3. RESULTS

The patients' clinical and biochemical characteristics are presented in Table 1 (*continuous variables and categorical variables*). The mean age of the study sample was 66.4 ± 11.4 years, and 50.4% were men. In total, 6,455 (93.3%) patients had no evidence of atrial arrhythmias, and the remaining 465 (6.7%) had AF. The mean age of patients with AF was significantly greater (see Fig. 1, panel A). The prevalence of AF increased with age in the male sex (with the highest prevalence in subjects older than 75 years). In women, we observed no such trend, except a peak of prevalence after 75 years (Fig. 1, panel B). The prevalence of AF was significantly greater in men (290 patients, 8.3% of the entire male sample) compared to women (175 patients, 5.0% of the entire female sample, p=0.01). No significant differences were found in weight, BMI or WC between the two groups. Similar glycometabolic parameters were also observed in the two groups; in fact, HbA1c levels, FPG levels and post-prandial glucose levels were comparable.

The diagnosis of MetS did not affect the prevalence of AF in our series (AF was present in 5.9% of patients without MetS and in 7.3% with MetS, p=0.6).

We instead found that AF was significantly associated with altered values of serum creatinine, eGFR and albuminuria. By dividing patients into subgroups on the basis of CKD classification, subjects with AF showed more advanced stages of renal disease compared with patients without AF (Fig. 2). As expected, patients with AF were the greatest antihypertensive drug users and were more frequently treated with multiple daily insulin injections.

AF was significantly associated with the diagnosis of MVD (10.5% vs. 3.4%, p<0.001). The highest frequency of AF was recorded in the PVD subgroup (15.3%). The frequency of AF in the other subgroups was 3.8% in NSCS, 7.2% in CBVD, 6.9% in CAD and 7.0% in PAD. Multivariate logistic regression analysis was used to determine the independent contribution of significant factors (identified with a univariate analysis) associated with AF. In this analysis, age, male sex, eGFR and the presence of MVD were all independent factors related to AF (Table 2). When we divided the patients into cardiovascular subgroups (according to the vascular areas involved), the analysis (model adjusted for age, sex, fibrinogen, eGFR, neuropathy and AH therapy) revealed a significant OR only in the PVD subgroup (p=0.006, Table 3).

Table 1. Clinical and metabolic continuous and categorical variables stratified by atrial fibrillation (AF) status in 6920 subjects with type 2 diabetes mellitus

	No AF	**AF**	
n (%)	**6,455 (93.3%)**	**465 (6.7%)**	
Continuous variables			**P value[a]**
Age (yy)	65.8±11.3	75.0±8.2	<.0001
DMT2 duration (yy)	14.0±10.0	19.3±11.2	<.0001
Weight (Kg)	81.8±18.5	84.8±19.5	ns
BMI (Kg/m^2)	32.0±6.7	32.9±7.4	ns
WC (cm)	107.8±16.1	110.5±16.2	ns
SBP (mmHg)	131.4±15.5	126.9±15.9	.007
DBP (mmHg)	76.4±8.6	74.9±9.2	ns
Total-C (mg/dl)	182.3±47.1	171.4±49.1	.03
HDL-C (mg/dl)	47.4±15.6	44.8±11.5	ns
LDL-C (mg/dl)	105.9±40.2	98.3±38.7	ns
Triglycerides (mg/dl)	145.0±90.8	140.7±97.9	ns
FPG (mg/dl)	190.5±73.4	177.8±69.1	ns
2 h-BG (mg/dl)	211.1±75.5	204.8±75.0	ns
HbA1c (%)	8.4±1.9	8.3±1.8	ns
Creatininemia (mg/dl)	0.98±0.5	1.3±0.9	<.0001
eGFR (ml/min/1.73 m^2)	82.4±28.1	65.8±27.9	<.0001
C-RP (mg/dl)	0.70±1.05	0.75±0.85	ns
Fibrinogen (mg/dl)	401.0±106.9	427.8±102.8	.02
Categorical Variables			**P value[b]**
Sex %M	49.6	62.4	.02
Smoking history %	29.4	29.0	ns
MetS %	86.5	88.2	ns
Albuminuria %	26.7	45.1	.0003
Diabetic retinopathy	36.5	37.6	ns
Diabetic neuropathy	48.7	59.1	.004
Statin users %	65.4	62.4	ns
AH users %	80.2	90.3	.017
ACE-I or ARBs %	73.8	80.6	ns
CC blockers %	30.1	29.0	ns
Alpha blockers %	6.7	10.7	ns
Beta blockers %	16.9	23.7	ns
OHA users %	38.6	28.0	ns
OHA+BI users %	14.3	10.8	ns
MDI users %	47.1	61.3	.03
History of CVD %	45.1	73.1	<.0001

Continuous Variables: data are means±SD; [a]unpaired t-test. FPG, fasting plasma glucose; 2 h-BG, 2 h blood glucose after meals; ns, not significant. Categorical Variables: data are percentages; [b]chi-square test. AH, antihypertensive; OHA, oral hypoglycemic agent; BI, basal insulin; MDI, multiple daily insulin injections.

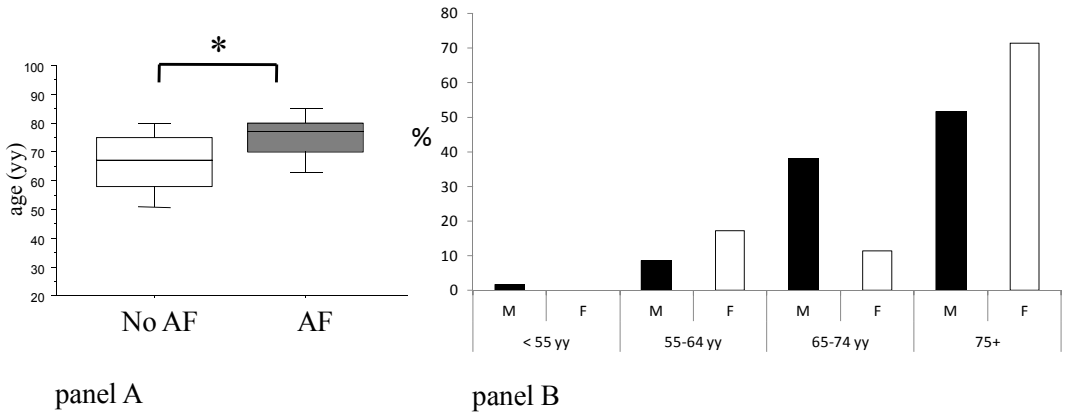

Fig. 1. Panel A: Age of patients with and without atrial fibrillation (AF) (*box plot*)
**p<0.001*
Panel B: Distribution of patients (%) with AF divided by age decade and sex; *sex M, chi-square test for trend p <0.0001*

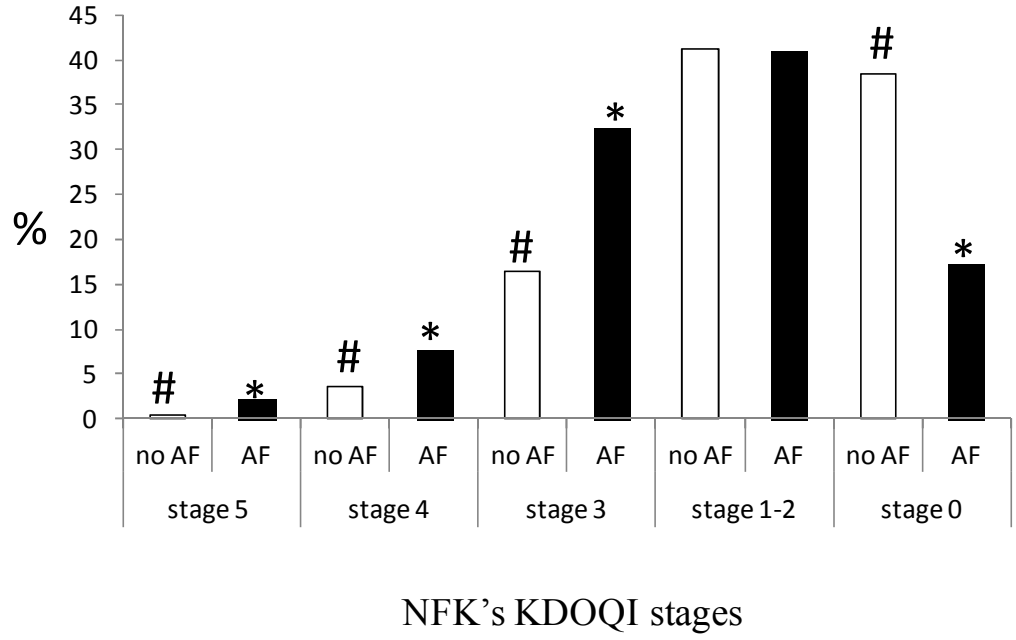

Fig. 2. Distribution of patients (%) with and without atrial fibrillation (AF) divided by CKD stages
** vs. # p<0.05*

Table 2. Logistic regression model for significant factors (identified by a univariate analysis) as predictors of AF in patients with type 2 diabetes

	OR	95% CI	*P* value
Age	1.08	1.05-1.11	<.0001
Sex (male)	2.46	1.5-3.9	.0002
Fibrinogen	1.0	0.99-1.0	.75
eGFR	0.99	0.98-0.99	.02
AH therapy	1.63	0.52-2.33	.81
Neuropathy (Yes)	1.09	0.66-1.78	.74
MVD	1.65	1.01-2.75	.04

Relationship among selected variables and the presence of AF. Data are expressed as odds ratios ± 95% confidence intervals

Table 3. Logistic regression model for MVD (divided in subgroups) as a predictor for the development of AF

	OR	95% CI	P
Non-significant carotid stenosis	1.0	0.29-3.45	ns
Cerebrovascular disease	1.14	0.46-2.81	ns
Coronary artery disease	1.38	0.54-3.56	ns
Peripheral artery disease	1.0	0.36-2.88	ns
Polyvascular disease	2.24	1.26-3.99	.006

Relationship among cardiovascular subgroups (model adjusted for age, sex, fibrinogen, eGFR, neuropathy, AH therapy) and the presence of AF. Data are expressed as odds ratios ± 95% confidence intervals

4. DISCUSSION

Diabetes has been associated with an approximately 35% greater risk of AF compared to unaffected individuals (RR 1.35, 95% confidence interval [CI]: 1.14-1.60) after adjustment for confounders [12]. Furthermore, diabetes has also been shown to significantly contribute to the prevalence and incidence of AF, independent of other established risk factors such as hypertension and congestive heart failure [13]. Poor glycemic control has also been independently associated with an increased risk of AF. However, the underlying mechanisms responsible for this relationship are unknown [12]. The hemodynamic consequences of AF are related to the loss of atrial mechanical function, irregularity of the ventricular response, and a high heart rate. These consequences are magnified in the presence of impaired diastolic ventricular filling, hypertension, mitral stenosis, left ventricular hypertrophy, and restrictive cardiomyopathy. In clinical practice, the prevention of stroke is of the utmost importance in the management of AF. The new CHA2DS2-VASc [Congestive heart failure/left ventricular dysfunction, Hypertension, Age≥75 (doubled), Diabetes, Stroke (doubled) – Vascular disease, Age 65-74, and Sex category (female)] score is inclusive of the most common stroke risk factors in everyday clinical practice [18-19]. All diabetic patients (by definition they have a CHA2DS2-VASc score ≥1) with AF are recommended to receive effective stroke prevention therapy, which is essentially an oral anticoagulant (OAC) with either well-controlled vitamin K antagonist (VKA) therapy (INR 2-3, with a high percentage of time in the therapeutic range, for example, at least 70%) [18-19] or one of the NOACs (novel oral anticoagulants); the 2012 update committee recommends NOACs “as broadly preferable” to vitamin K active substances in the vast majority of patients with non-valvular AF [19].

In the present study, we recorded the prevalence of AF in our diabetic population and extensively investigated correlations between anthropometric, laboratory and clinical variables and the presence of AF.

We identified 465 patients with chronic AF in our sample (6.7% of the entire population). The majority of patients with AF were older than 65 years, with the highest prevalence in the population aged over 75 years. It is well known that the prevalence of AF doubles with each decade of age in the elderly [10,20]. Currently, AF affects approximately 8% of subjects aged 65 years and older [5]. In our series, considering this age cut-off, the prevalence of AF was 10.1% (81 of 804 patients). The prevalence of diagnosed AF in the diabetic population has not been well established in previous reports. In a recent prospective cohort study, individuals with diabetes had an age-adjusted incidence rate of AF that was twice that of individuals without diabetes (9.02 vs. 4.51 per 1,000 person-years) [12]. As expected, in our study, the average age of patients with AF was significantly greater than individuals with sinus heart rhythm (75.0 vs. 65.8 years, $p < 0.0001$). The increase in incidence with age may involve age-related cardiac abnormalities, including a gradual loss of nodal fibers and increased fibrous and adipose tissue in the sinoatrial node, decreased ventricular compliance from myocardial fibrosis, resulting in atrial dilatation that predisposes individuals to AF, and extensive senile amyloid infiltration of the sinoatrial node [21-24]. In our study, we observed a higher prevalence of AF among males. There is a male preponderance of risk for currently unknown reasons. Based on the Framingham Study, men have a 1.5-fold (age and risk factor adjusted) greater risk of AF than women [10]. In our population, the distribution by age decade showed a trend to increased AF in males. In females, we only found a peak of prevalence over 75 years. These epidemiologic data should be confirmed by further trials with larger diabetic populations.

Neither obesity nor smoke history appeared to be associated with AF in our patients. The diagnosis of MetS also did not affect the prevalence of AF in our series (AF was present in 5.9% of patients without MetS and in 7.3% with MetS, $p=0.6$). These data appear to contradict other reports showing that obesity and MetS were strongly associated with AF in patients without heart disease [25-26]. However, in our series of only diabetic subjects with a high prevalence of both these conditions (88% of patients were overweight or obese and 86.6% had MetS), it is likely that MetS was no longer a discriminant.

Hypertension appears responsible for AF in the general population more than any other risk factor [10,27]. In our series, we also observed an increased use of antihypertensive drugs in patients with AF (probably for this reason we found SBP values reduced in this group), confirming that the majority of patients in this group have hypertension.

In the univariate analysis, the variables more closely associated with AF were those related to the presence of nephropathy (serum creatinine, eGFR and albuminuria). Recently, several studies have found a high incidence and prevalence of AF among patients with chronic kidney disease (CKD) not yet requiring dialysis [28-32]. One recent study estimated that the prevalence of AF was 18% in a multicenter cohort with a wide range of kidney function [32]. In our study, eGFR was significantly different in the two groups of patients (i.e., those with and without AF), with lower values in patients with AF (65.8 vs. 82.4 ml/min/1.73 m^2). The analysis of CKD stages demonstrated that patients with AF were those with the most impaired renal function. In the multivariate regression analysis, eGFR was an independent risk factor for AF.

One could speculates that aging, chronic exposure to high glucose (duration of diabetes) and electrolytic and metabolic abnormalities secondary to CKD are very strong factors that determine structural heart modifications predisposing to development of AF.

It is well known that the presence of AF is closely linked to cardiovascular diseases, particularly left atrial enlargement, left ventricular hypertrophy (as also confirmed by our data), coronary artery disease, valvular heart disease, heart failure and previous myocardial infarction. To study the association between AF and MVD, we divided our patients into six groups according to the type of macrovascular involvement.

We found that patients with AF were more likely to have cardiovascular disease. Moreover, patients at higher risk of AF appeared to be those with a polyvascular atherosclerotic disease. In fact, the association between AF and MVD (after adjusting for confounders) was confirmed in the multivariate analysis only for patients with polyvascular diseases (OR 2.24, 95% CI 1.26-3.99).

Only a few studies have examined the association between markers of glucose homeostasis and AF. In a recent prospective cohort study setting, i.e., the atherosclerosis risk in communities (ARIC) study, the authors concluded that diabetes, HbA1c levels and poor glycemic control were independently associated with an increased risk of AF [12]. In our series, by contrast, analyzing glycometabolic parameters (HbA1c, fasting glucose and postprandial glucose) demonstrated that no differences existed between patients with and without AF. Hence the unsatisfactory glycaemic control seems not responsible for AF because FPG, PPG and HbA1c values were not different between the two group. However, diabetic patients with poor metabolic control had been referred to us for the first time, and therefore, we were unable to clarify the causal or temporal relationship between the presence of AF and glycemic control over time.

Several limitation of the present study deserves comment. First, the number of subjects with AF was small to ensure our findings. Second the retrospective cross-sectional design precluded the establishment of causal or temporal relations among AF and other features in our diabetic population. In addition, this study mainly included older diabetic subjects who had unsatisfactory glycaemic control, who may not have been representative of the general population. Further large-scale prospective studies are required to confirm our results.

5. CONCLUSION

AF is a common and potentially serious arrhythmia that confers significant risks for stroke and death. In addition, an underlying coronary disease (as frequently observed in the type 2 diabetic population) may bring on or aggravate angina because of an associated high heart beat frequency. In our study, we found that advanced age, chronic kidney disease and cardiovascular diseases (particularly polyvascular involvement) were the most significant AF-related factors. Our study supports the approach of diagnosing AF before the occurrence of the first complication for the better prevention of strokes. In type 2 diabetic patients at high risk for AF, the identification of factors predisposing individuals to AF could allow a more accurate selection of patients for screening by pulse palpation, followed by ECG recording, aimed at the early diagnosis of AF and stroke prevention therapy through an increased follow-up frequency.

ETHICAL APPROVAL

All authors declare that the study was approved by the ethics committee of our institution and informed consent was obtained from all participants.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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