PLOS ONE

RESEARCH ARTICLE

Association between atrial fibrillation and risk of end-stage renal disease among adults with diabetes mellitus

Yu-Kang Chang[1,2,3], Hueng-Chuen Fan[4,5], Chi-Chien Lin[2,6], Yuan-Hung Wang[7], Wan-Ni Tsai[8☯], Paik-Seong Lim[9☯] *

1 Department of Medical Research, Tungs' Taichung MetroHarbor Hospital, Taichung, Taiwan, 2 Department of Post-Baccalaureate Medicine, College of Medicine, National Chung Hsing University, Taichung, Taiwan, 3 Department of Nursing, Jenteh Junior College of Medicine, Nursing and Management, Miaoli, Taiwan, 4 Department of Pediatrics, Tungs' Taichung MetroHarbor Hospital, Taichung, Taiwan, 5 Department of Rehabilitation, Jenteh Junior College of Medicine, Nursing and Management, Miaoli, Taiwan, 6 Institute of Biomedical Science, iEGG and Animal Biotechnology Center, National Chung-Hsing University, Taichung, Taiwan, 7 Department of Medical Research, Shuang Ho Hospital, Taipei Medical University, New City, Taiwan, 8 Department of Endocrinology and Metabolism, Tungs' Taichung MetroHarbor Hospital, Taichung, Taiwan, 9 Division of Renal Medicine, Tungs' Taichung MetroHarbor Hospital, Taichung, Taiwan

☯ These authors contributed equally to this work.
* jamespslim@gmail.com.

Abstract

Diabetes mellitus (DM) is an important risk factor in patients with end-stage renal disease (ESRD). DM is associated with the development of cardiovascular diseases, such as atrial fibrillation (AF), due to poor glycemic control. However, few studies have focused on the risk of developing ESRD among DM patients with and without AF. This study evaluated ESRD risk among DM patients with and without AF in Taiwan. Data were retrieved from one million patients randomly sampled from Taiwan's National Health Insurance Research Database, including 6,105 DM patients with AF propensity score–matched with 6,105 DM patients without AF. Both groups were followed until death, any dialysis treatment, or December 31, 2013, whichever occurred first. AF was diagnosed by a qualified physician according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), using the diagnostic code 427.31. Patients aged <20 years or diagnosed with ESRD before the index date were excluded. A Cox proportional hazard regression model was used to calculate the relative ESRD risk. Among DM patients, those with AF have more comorbidities than those without AF. We also found a 1.18-fold (95% confidence interval [CI]: 1.01–1.46) increase in ESRD risk among patients with AF compared with those without AF. In addition, DM patients with hypertension, chronic kidney disease (CKD), or higher Charlson Comorbidity Index scores also have significantly increased ESRD risks than those without these complications. A 1.39-fold (95% CI: 1.04–1.86) increase in risk was observed for patients with AF among the non-CKD group. Our findings suggest that patients with DM should be closely monitored for irregular or rapid heart rates.

Introduction

Diabetes mellitus (DM) is a major public health priority worldwide, and the global prevalence of DM is projected to increase from 463 million (9.3%) in 2019 to 700 million (10.9%) in 2045 [1]. Patients with DM have high risks of cardiovascular morbidity and mortality [2], and DM is a leading cause of end-stage renal disease (ESRD), as approximately 40% of all patients with ESRD also have DM [3]. According to the United States Renal Data System annual report, Taiwan has the highest ESRD incidence and prevalence rates worldwide [4], leading to a heavy financial burden on Taiwan's health care systems. Thus, preventive strategies that reduce the risks of developing ESRD should be implemented among patients with DM.

Among patients with ESRD, cardiovascular disease is considered a leading cause of mortality [5], accounting for 48% of total deaths [6]. The most common cardiac arrhythmia is atrial fibrillation (AF), characterized by rapid and irregular atrial activation and associated with increased risks of poor outcomes, such as stroke, heart failure, and mortality [7]. AF and ESRD share risk factors, such as age, hypertension, obesity, DM, vascular heart disease, and heart failure [8], and patients with ESRD on dialysis have a higher AF prevalence (13%–27%) than the general population (approximately 1%), suggesting that uremia may be associated with AF [9–11]. In addition, previous studies have shown that AF is associated with increased risks of stroke and mortality among patients with ESRD on dialysis [12, 13]. The risk of developing AF is even higher among patients with ESRD on dialysis who have one or more of the following risk factors: advanced age, hypertension, heart failure, coronary artery disease (CAD), peripheral vascular disease, and chronic obstructive pulmonary disease (COPD) [14, 15].

AF is associated with poor outcomes among patients with ESRD [16], and the incidence of AF was approximately 40% among patients with DM, which is higher than the incidence in patients without DM [17]. Patients with DM who also present with AF have increased risks of stroke, cardiovascular disease, mortality, and heart failure [18, 19]. However, the potential bidirectional association between AF and ESRD has not been evaluated, and the role of AF incidence on the progression from DM to ESRD has not been elucidated. Therefore, this study examined the association of AF incidence with the risk of developing ESRD among patients with DM by conducting a retrospective population-based cohort study using claims data from the National Health Insurance Research Database (NHIRD) of Taiwan.

Materials and methods

Data source

The National Health Insurance (NHI) program of Taiwan started in 1995 and currently covers nearly 99% of Taiwan's population of approximately 23 million people [20]. Since 1999, the NHI program has made data available to researchers through the NHIRD, which contains registration files and claims data for NHI beneficiaries, including diagnoses, demographics, medication types, prescription dates, dosages, and prescription durations [21]. In the present study, we reviewed claims data for 1 million randomly sampled NHI beneficiaries. The datasets analyzed in the current study are available in the longitudinal health insurance database **(LHID) 2000** repository. The National Health Research Institutes oversees all claims data and generates random identification numbers for insured patients to protect their privacy. Because the NHIRD contains deidentified and anonymously analyzed secondary data, the need for informed consent in this study was waived. This study was approved by the institutional review board of Tungs' Taichung MetroHarbor Hospital in Taichung, Taiwan (106206N). All protocols used in this study were performed in accordance with relevant guidelines and regulations.

From among the 1 million NHI beneficiaries who were randomly sampled from the NHIRD, we first selected those diagnosed with DM according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM; code 250, n = 98,213) and prescribed at least one antidiabetic drug between 2000 and 2013. We divided these patients into those with (n = 8,886) and without AF (n = 89,327) according to ICD-9-CM code 427.31. After excluding those aged <20 years (n = 611) and those diagnosed with ESRD before the index date (n = 1,456), 6,819 patients with DM and AF remained. The AF group was matched on a 1:1 basis from among the 89,327 patients without AF. The date of AF diagnosis among the AF group was defined as the index for both the patients with AF and propensity score–matched non-AF counterparts. All patients were followed until death, any diagnosis of ESRD, or December 31, 2013, whichever came first. A flow chart showing the study patient selection process is presented in Fig 1.
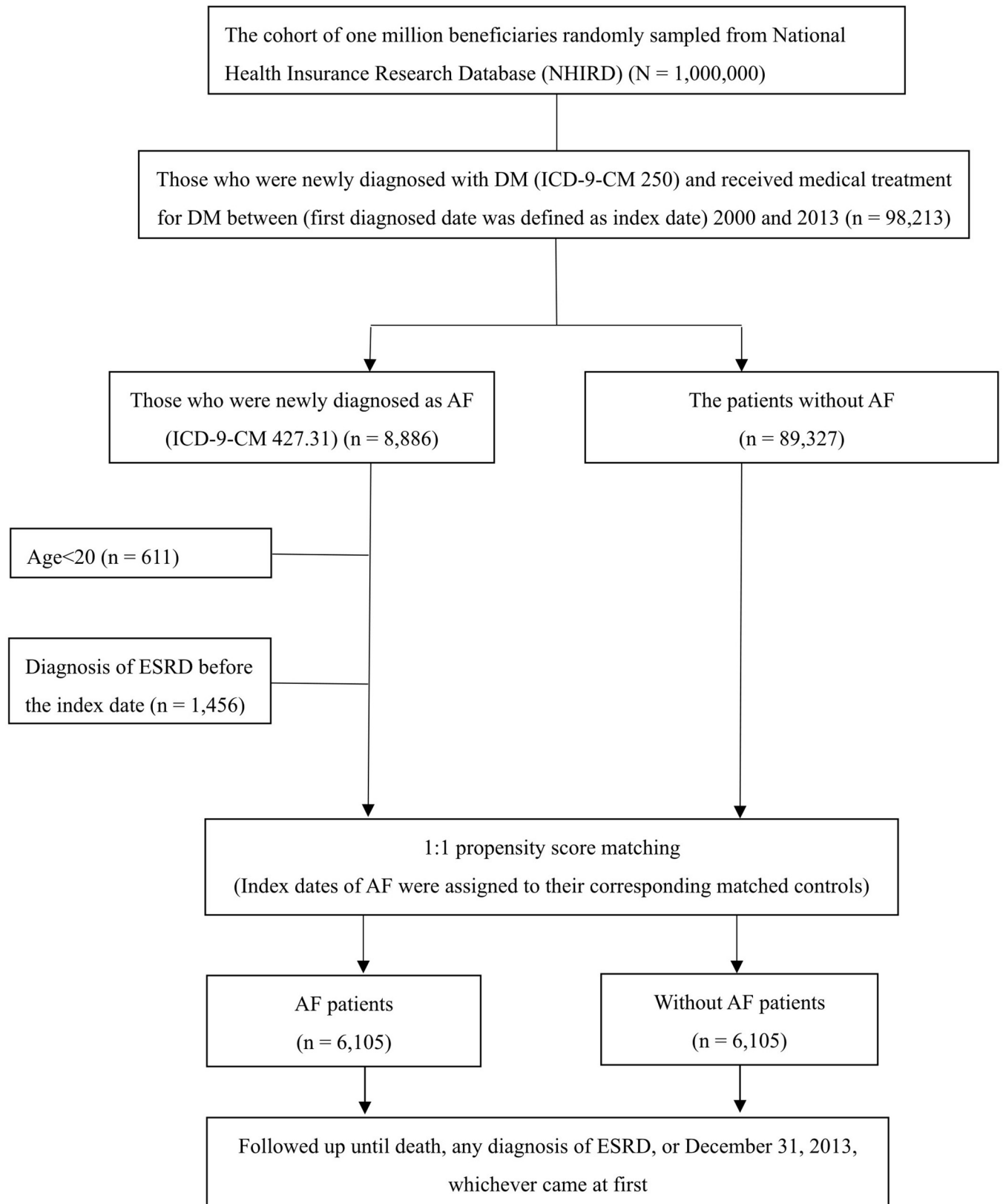
Definition of research variables

The main outcome of this study was ESRD occurrence, defined as having received dialysis treatment between 2000 and 2013. The main comorbidities that were controlled for in this study were hypertension (ICD-9-CM code 401), heart failure (ICD-9-CM code 428), hyperlipidemia (ICD-9-CM code 272), cardiovascular disease (ICD-9-CM codes 390–459), COPD (ICD-9-CM code 490–496), stroke (ICD-9-CM code 430–438), cancer (ICD-9-CM code 140–208), and chronic kidney disease (CKD; ICD-9-CM code 585). Study patients were considered to have one of these comorbidities if they underwent at least two ambulatory visits and one hospitalization associated with the respective diagnosis.

Statistical analysis

The selection of patients without AF was performed using a 1:1 propensity score matching method [22], and matching was performed based on the nearest neighbor algorithm with a perfect proportion of 0.995 to 1.0 [23]. Propensity scores for all study patients were calculated using multivariable logistic regression adjusted for age, sex, geographic region, and Charlson Comorbidity Index (CCI) score [24].

The baseline data for patients with and without AF are presented as the frequency and percentage for categorical variables and as the mean and standard deviation for continuous variables. T-tests and χ^2 tests were used to describe differences between groups with and without AF for categorical and continuous variables, respectively. The ESRD incidence rate was defined as the number of events divided by follow-up person-years, which were calculated as the time from the index date to the first received dialysis treatment, death, or December 31, 2013, whichever occurred first. We used Cox proportional hazards regression to determine adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for ESRD comparing between groups with and without AF. By conducting the Schoenfeld residual test [25], we confirmed that the proportional hazards assumption was not violated. In multivariable analyses, we adjusted for all covariates shown in Table 2. In order to consider the competing risks of ESRD and death before ESRD, we used the cause-specific hazard model to account for the distribution hazard for competing risks [26]. The Kaplan–Meier model was used to compare ESRD risk between groups with and without AF and between groups stratified according to CKD status (Fig 2). We further performed subgroup analyses to assess differences in AF risk among individual subgroups stratified by sex, age, hypertension, heart failure, dyslipidemia, CAD, COPD, stroke, cancer, CKD, and CCI score. Aside from the stratified variable being examined, all aHRs were adjusted for all other covariates (Fig 3). All p-values were two-sided, and any p-value <0.05 was considered significant. All analyses were computed using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina).

The cohort of one million beneficiaries randomly sampled from National

Health Insurance Research Database (NHIRD) (N = 1,000,000)

Those who were newly diagnosed with DM (ICD-9-CM 250) and received medical treatment

for DM between (first diagnosed date was defined as index date) 2000 and 2013 (n = 98,213)

Those who were newly diagnosed as AF

(ICD-9-CM 427.31) (n = 8,886)

The patients without AF

(n = 89,327)

Age<20 (n = 611)

Diagnosis of ESRD before

the index date (n = 1,456)

1:1 propensity score matching

(Index dates of AF were assigned to their corresponding matched controls)

AF patients

(n = 6,105)

Without AF patients

(n = 6,105)

Followed up until death, any diagnosis of ESRD, or December 31, 2013,

whichever came at first

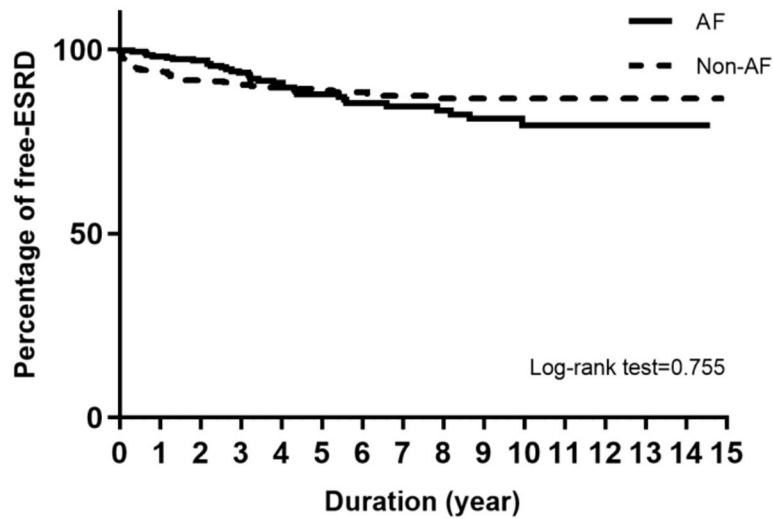**Fig 1. A flow chart of the patient selection process for this study.**

(a) CKD patients

The comparison of free-ESRD curve between AF and non-AF with CKD

(b)Non-CKD patients

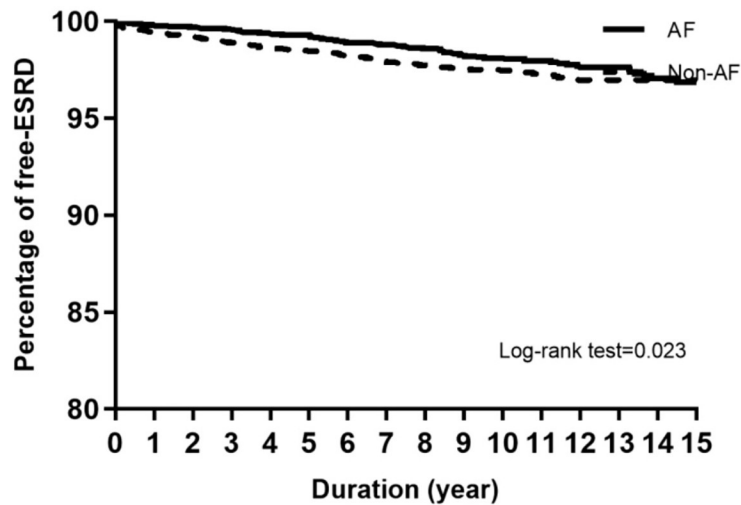The comparison of free-ESRD curve between AF and non-AF without CKD

Fig 2. Comparison of the end-stage renal disease curve between patients with diabetes with and without AF.

https://doi.org/10.1371/journal.pone.0273646.g002

Subgroup analysis

	Adjusted HR (95%CI)	p value
Sex		
Male	1.12(0.76-1.64)	0.574
Female	1.15(0.83-1.59)	0.399
Age		
<60	1.22(0.77-1.96)	0.398
60-69	1.26(0.83-1.90)	0.227
70-79	1.20(0.73-1.92)	0.485
80+	0.36(0.13-1.03)	0.053
Hypertension		
Yes	1.22(0.88-1.70)	0.236
No	1.04(0.71-1.52)	0.850
Heart failure		
Yes	3.23(1.01-10.74)	0.048
No	1.04(0.80-1.35)	0.766
Dyslipidemia		
Yes	1.67(1.04-2.68)	0.035
No	1.05(0.80-1.37)	0.710
CAD		
Yes	2.74(0.90-8.36)	0.077
No	1.06(0.82-1.37)	0.688
COPD		
Yes	1.36(0.63-2.92)	0.430
No	1.11(0.85-1.44)	0.444
Stroke		
Yes	0.87(0.45-1.66)	0.687
No	1.32(1.01-1.65)	0.043
Cancer		
Yes	3.98(0.90-17.63)	0.103
No	1.09(0.85-1.40)	0.489
CKD		
Yes	0.92(0.57-1.47)	0.721
No	1.31(1.01-1.72)	0.037
CCI		
<5	0.28(0.03-2.31)	0.220
5-9	1.34(0.92-1.94)	0.128
10+	1.00(0.75-1.48)	0.784

Hazard Ratio and 95%CI

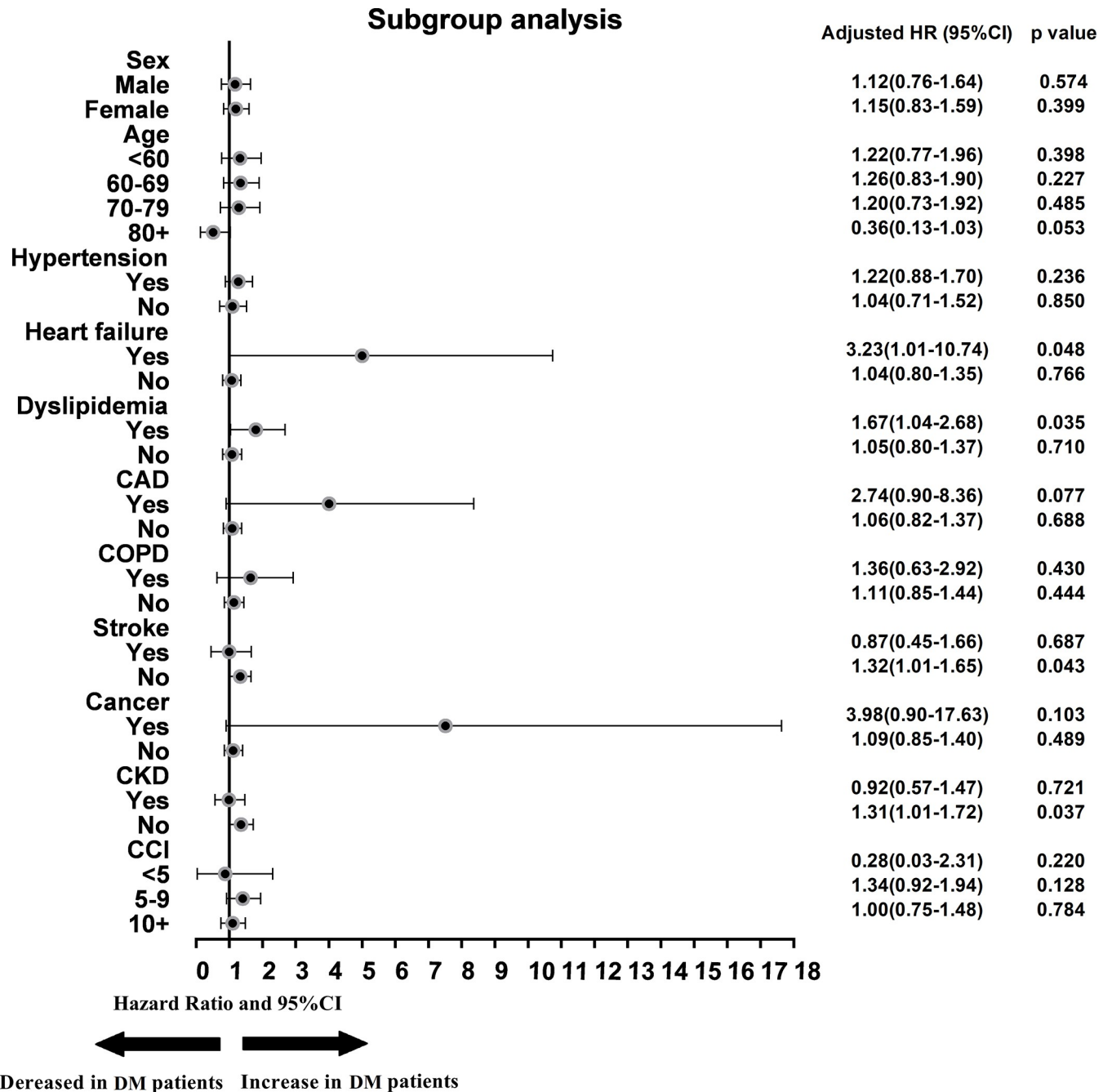Dereased in DM patients   Increase in DM patients

Fig 3. Risks of developing end-stage renal disease among patients with diabetes with and without atrial fibrillation, stratified according to demographic characteristics and comorbidities.

Results

Basic characteristics of study patients

The baseline characteristics of the patients and their matched controls are shown in Table 1. The average age was 68.7 years, and 51% of patients were men. Compared with DM patients without AF, those with AF were more likely to have hypertension, heart failure, dyslipidemia,

Table 1. Distribution of demographic characteristics and comorbidities among DM patients with and without AF.

	AF	Without AF	
	n (%)	**n (%)**	**_P_-value**
Sex	n = 6,105	n = 6,105	
Male	3,126 (51.2)	3,138 (51.4)	0.828
Female	2,979 (48.8)	2,967 (48.6)	
Age, years			
<60	1,344 (22)	1,263 (20.7)	0.169
60–69	1,780 (29.2)	1,861 (30.5)	
70–79	2,087 (34.2)	2,117 (34.7)	
≥80	894 (14.6)	864 (14.2)	
Hypertension			
Yes	3,145 (51.5)	2,075 (34)	<0.001
No	2,960 (48.5)	4,030 (66)	
Heart failure			
Yes	1,197 (19.6)	279 (4.6)	<0.001
No	4,908 (80.4)	5,826 (95.4)	
Dyslipidemia			
Yes	1,499 (24.6)	1,229 (20.1)	<0.001
No	4,606 (75.5)	4,876 (79.9)	
CAD			
Yes	573 (9.4)	281 (4.6)	<0.001
No	5,532 (90.6)	5,824 (95.4)	
PAOD			
Yes	7 (0.1)	5 (0.1)	0.564
No	6,098 (99.9)	6,100 (99.9)	
COPD			
Yes	1,171 (19.2)	637 (10.4)	<0.001
No	4,934 (80.8)	5,468 (89.6)	
Stroke			
Yes	1,278 (20.9)	761 (12.5)	<0.001
No	4,827 (79.1)	5,344 (87.5)	
Cancer			
Yes	334 (5.5)	439 (7.2)	<0.001
No	5,771 (94.5)	5,666 (92.8)	
CKD			
Yes	433 (7.1)	321 (5.3)	<0.001
No	5,672 (92.9)	5,784 (94.7)	
CCI score, mean ± SD	9.2 ± 3.5	9.2 ± 4.0	0.692
<5	800 (13.1)	1,114 (18.3)	<0.001
5–9	3,335 (54.6)	2,943 (48.2)	
≥10	1,970 (32.3)	2,048 (33.6)	
DM duration, mean ± SD	5.7 ± 4.7	5.6 ± 4.8	0.056
Duration period, mean ± SD	7.6 ± 4.6	7.5 ± 4.9	0.092

Abbreviations: AF, atrial fibrillation; CAD, cardiac artery disease; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disorder; DM, diabetes mellitus; PAOD, peripheral arterial occlusive disease.

CAD, COPD, stroke, and CKD; have lower percentages of cancer; and have CCI scores <5. As expected, DM patients with AF had higher prevalences of common comorbidities than those without AF. No significant difference was observed in the duration between the index date and new-onset ESRD between the case (7.6 years) and control groups (7.5 years).

Hazard ratio estimation for new-onset ESRD

As shown in Table 2, male sex was associated with a lower risk of developing ESRD than female sex (aHR = 0.68, 95% CI = 0.53–0.86, p = 0.015). The risk of developing ESRD decreased (aHR = 0.67, 95% CI = 0.50–0.89, p = 0.007 for 60–69 years; aHR = 0.33, 95% CI = 0.20–0.54, p < 0.001 for ≥80 years) with increasing age compared with patients <60 years. AF, hypertension, CKD, and CCI score were strong predictors of ESRD in patients with DM. Compared with DM patients without AF, the those with AF had an increased risk of developing ESRD (aHR = 1.18, 95% CI = 1.01–1.46, p = 0.043). Patients with DM with hypertension had a higher risk of developing ESRD than those with DM without hypertension (aHR = 1.89, 95% CI = 1.46–2.42, p < 0.001). Furthermore, the risk of developing ESRD was higher for patients with DM with CKD (aHR = 6.35, 95% CI = 4.80–8.41, p < 0.001) than for those with DM without CKD. The risk of developing ESRD increased with increasing CCI scores (aHR = 7.53, 95% CI = 3.07–18.45, p < 0.001 for CCI 5–9; aHR = 13.25, 95% CI = 5.39–32.58, p < 0.001 for CCI ≥ 10) compared with CCI ≤ 5. Conversely, patients with DM with stroke and cancer were associated with decreased risks of developing ESRD than patients with DM without stroke and cancer. Furthermore, the cause-specific hazard ratio of death before ESRD due to a competing was 1.57 (95% CI, 1.21–3.81).

Subgroup analyses

The influence of AF status on ESRD among patients with DM was examined by subgroup analyses stratified according to sex (male or female), age (<60, 60–69, 70–79, or ≥80 years), and potential comorbidities (Fig 3). The presence of certain comorbidities significantly increased the risk of developing ESRD among DM patients with AF. Among subgroups of patients with DM with comorbidities, heart failure (aHR = 3.23, 95% CI = 1.02–10.54, p = 0.048) and dyslipidemia (aHR = 1.67, 95% CI = 1.04–2.68, p = 0.035) significantly elevated the risks of developing ESRD compared with those without these comorbidities. However, a distinct difference was observed between DM patients with and without hypertension. Among patients with DM without CKD, those with AF had a higher risk of developing ESRD than those without AF (aHR = 1.31, 95% CI = 1.01–1.72, p = 0.037). When patients with DM were stratified into two groups based on CKD prevalence (Fig 2), the cumulative incidence curve analyzed by the log-rank test showed that among patients with DM without CKD, AF increased the risk of developing ESRD compared with those without AF (p = 0.023), but AF incidence did not appear to have a significant effect on ESRD risk in patients with DM with CKD.

Discussion

The present population-based study investigated the relationship between atrial fibrillation and ESRD among patients with DM using data from the Taiwan NHIRD and found that AF was associated with a higher risk of subsequent ESRD in patients with DM, and this association was significantly stronger among DM patients without CKD. To the best of the authors' knowledge, this is the first study to investigate the relationship between AF and ESRD among patients with DM in Taiwan.

Table 2. Association of DM progression to ESRD with AF, sociodemographic characteristics, and comorbidities.

	Crude HR (95% CI)	*P*-value	Adjusted HR (95% CI)	*P*-value
DM				
Without AF	Ref.		Ref.	
AF	1.36 (1.08–1.83)	0.011	1.18 (1.01–1.46)	0.043
Sex				
Female	Ref.		Ref.	
Male	0.67 (0.53–0.84)	0.001	0.68 (0.53–0.86)	0.015
Age, years				
<60	Ref.		Ref.	
60–69	0.81 (0.61–1.08)	0.809	0.67 (0.50–0.89)	0.013
70–79	0.46 (0.34–0.63)	0.462	0.40 (0.29–0.55)	<0.001
≥80	0.32 (0.20–0.51)	0.320	0.33 (0.20–0.54)	<0.001
DM duration	1.02 (0.98–1.05)	0.267	0.99 (0.94–1.03)	0.117
Hypertension				
No	Ref.		Ref.	
Yes	2.32 (1.82–2.95)	<0.001	1.89 (1.46–2.42)	<0.001
Heart failure				
No	Ref.		Ref.	
Yes	1.52 (1.11–2.09)	0.009	1.15 (0.83–1.60)	0.415
Dyslipidemia				
No	Ref.		Ref.	
Yes	2.07 (1.61–2.67)	<0.001	1.17 (0.89–1.52)	0.262
CAD				
No	Ref.		Ref.	
Yes	1.28 (0.84–1.97)	0.253	0.91 (0.59–1.41)	0.677
COPD				
No	Ref.		Ref.	
Yes	0.76 (0.53–1.10)	0.146	0.67 (0.44–1.02)	0.068
Stroke				
No	Ref.		Ref.	
Yes	0.89 (0.64–1.25)	0.892	0.62 (0.44–0.90)	0.029
Cancer				
No	Ref.		Ref.	
Yes	0.64 (0.34–1.20)	0.637	0.46 (0.25–0.88)	0.046
CKD				
No	Ref.		Ref.	
Yes	8.51 (6.54–11.06)	<0.001	6.35 (4.80–8.41)	<0.001
CCI score				
<5	Ref.		Ref.	
5–9	7.65 (3.13–18.69)	<0.001	7.53 (3.07–18.45)	<0.001
≥10	12.74 (5.22–31.07)	<0.001	13.25 (5.39–32.58)	<0.001

Abbreviations: AF, atrial fibrillation; CAD, cardiac artery disease; CCI, Charlson Comorbidity Index; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disorder; DM, diabetes mellitus; ESRD, end-stage renal disease; HR, hazard ratio; Ref., reference.

The primary new finding of this study is that AF is an important predictor of ESRD in patients with DM. Previous studies have reported that DM is an independent risk factor for AF [27–29], and metabolic syndrome is hypothesized to increase epicardial adipose tissue

thickness, leading to the release of pro-inflammatory substances that contribute the endothelial dysfunction and fibrosis and influence structural and electrical atrial remodeling [30, 31]. However, no previously published studies have evaluated the impacts of incident AF on the progression from DM to adverse renal events. Our study of a large community-based cohort of patients with DM found that incident AF was associated with a higher rate of ESRD, suggesting that incident AF contributes to progression from DM to ESRD.

Multiple biological mechanisms may underlie the accelerated progression to ESRD from DM in patients with AF. First, AF triggers systemic inflammation [32]. A cohort study showed that ESRD risk in patients with DM was strongly associated with elevated concentrations of circulating pro-inflammatory cytokines, which might be responsible for kidney dysfunction [33]. Second, increasing evidence supports an association between inflammation and AF [34–36]. Additionally, various inflammatory biomarkers have been associated with AF, suggesting an important role for inflammation in AF [34], resulting in a prothrombotic state that induces renal micro-infarcts, decreased renal function, and rapid progression from DM to ESRD. Third, AF reduces left ventricular systolic and diastolic function, which may accelerate ESRD progression and impair kidney function through altered hemodynamics, reduced renal perfusion, and renin-angiotensin-aldosterone system activation [37, 38]. Fourth, some medications used to treat AF are nephrotoxic and can result in renal impairment.

We found that the association of incident AF with ESRD risk was stronger among DM patients without CKD. This finding is particularly interesting because CKD is generally accepted to increase the risk of developing AF [39–41]. The reasons for this finding are unclear; however, AF may result in stronger impacts among patients with DM without CKD because these patients are less likely to have other concomitant comorbidities that contribute to ESRD risk. Further studies are warranted to clarify this finding.

Patients with DM with AF were significantly more likely to have comorbid conditions compared with the patients without AF, including hypertension, heart failure, dyslipidemia, CAD, COPD, stroke, and CKD (Table 1). Remarkably, elevated blood pressure has been known to increase the risks of ESRD occurrence [42, 43]. As shown in univariate analyses (Table 2), hypertension plays a significant role in ESRD occurrence. However, in subgroup analyses according to the presence of hypertension, incident AF was not significantly associated with ESRD among DM patients with hypertension. The reasons for this are complex. For example, the role of hypertension as a risk factor may be masked by successful strategies designed to control blood pressure. However, data regarding the use of blood pressure medications were not available in the Taiwan NHIRD.

The present study has some limitations. First, individual behaviors associated with ESRD development were not able to be evaluated, and not all clinical data were fully available in the Taiwan NHIRD. Thus, we were not able to adjust for other potential confounding factors, such as relevant medications, blood pressure, residual renal function, and hemoglobin level. Second, all diagnoses were based on ICD-9-CM diagnosis codes, which do not differentiate among AF types and pose a risk for coding bias. Lastly, the results generated from our study may not be applicable to other countries as the study was conducted in only one country.

Conclusions

In conclusion, incident AF is associated with a relative increase in the risk of ESRD development among patients with DM. Further research remains necessary to delineate contributing factors that lead to AF development in the setting of DM and elucidate potential modifiable pathways through which AF contributes to the progression to ESRD.

Supporting information

S1 Checklist. STROBE statement.
(DOC)

Author Contributions

Conceptualization: Yu-Kang Chang, Hueng-Chuen Fan, Wan-Ni Tsai, Paik-Seong Lim.

Data curation: Yu-Kang Chang, Wan-Ni Tsai, Paik-Seong Lim.

Formal analysis: Yu-Kang Chang.

Investigation: Yu-Kang Chang, Wan-Ni Tsai, Paik-Seong Lim.

Methodology: Yu-Kang Chang, Yuan-Hung Wang, Paik-Seong Lim.

Project administration: Wan-Ni Tsai.

Supervision: Paik-Seong Lim.

Validation: Hueng-Chuen Fan, Paik-Seong Lim.

Visualization: Hueng-Chuen Fan.

Writing – original draft: Yu-Kang Chang, Chi-Chien Lin, Yuan-Hung Wang, Wan-Ni Tsai, Paik-Seong Lim.

Writing – review & editing: Chi-Chien Lin, Yuan-Hung Wang, Wan-Ni Tsai, Paik-Seong Lim.

References

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. Diabetes Res Clin Pract. 2019; 157:107843. Epub 2019/09/14. https://doi.org/10.1016/j.diabres.2019.107843 PMID: 31518657.

2. Martin-Timon I, Sevillano-Collantes C, Segura-Galindo A, Del Canizo-Gomez FJ. Type 2 diabetes and cardiovascular disease: Have all risk factors the same strength? World J Diabetes. 2014; 5(4):444–70. Epub 2014/08/16. https://doi.org/10.4239/wjd.v5.i4.444 PMID: 25126392; PubMed Central PMCID: PMC4127581.

3. Collins AJ, Foley RN, Chavers B, Gilbertson D, Herzog C, Johansen K, et al. 'United States Renal Data System 2011 Annual Data Report: Atlas of chronic kidney disease & end-stage renal disease in the United States. Am J Kidney Dis. 2012; 59(1 Suppl 1):A7, e1–420. Epub 2011/12/30. https://doi.org/10.1053/j.ajkd.2011.11.015 PMID: 22177944.

4. Saran R, Li Y, Robinson B, Abbott KC, Agodoa LY, Ayanian J, et al. US Renal Data System 2015 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2016;67(3 Suppl 1):Svii, S1-305. Epub 2016/03/02. https://doi.org/10.1053/j.ajkd.2015.12.014 PMID: 26925525; PubMed Central PMCID: PMC6643990.

5. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis. 1998;32(5 Suppl 3):S112-9. Epub 1998/11/20. https://doi.org/10.1053/ajkd.1998.v32.pm9820470 PMID: 9820470.

6. 2018 USRDS annual data report: Epidemiology of kidney disease in the United States. System USRD, editor2018 2018.

7. Odutayo A, Wong CX, Hsiao AJ, Hopewell S, Altman DG, Emdin CA. Atrial fibrillation and risks of cardiovascular disease, renal disease, and death: systematic review and meta-analysis. BMJ. 2016; 354: i4482. Epub 2016/09/08. https://doi.org/10.1136/bmj.i4482 PMID: 27599725.

8. McManus DD, Saczynski JS, Ward JA, Jaggi K, Bourrell P, Darling C, et al. The Relationship Between Atrial Fibrillation and Chronic Kidney Disease: Epidemiologic and Pathophysiologic Considerations for a Dual Epidemic. J Atr Fibrillation. 2012; 5(1):442. Epub 2012/06/15. https://doi.org/10.4022/jafib.442 PMID: 28496745; PubMed Central PMCID: PMC5153080.

9. Reinecke H, Brand E, Mesters R, Schabitz WR, Fisher M, Pavenstadt H, et al. Dilemmas in the management of atrial fibrillation in chronic kidney disease. J Am Soc Nephrol. 2009; 20(4):705–11. Epub 2008/12/19. https://doi.org/10.1681/ASN.2007111207 PMID: 19092127.

10. Genovesi S, Pogliani D, Faini A, Valsecchi MG, Riva A, Stefani F, et al. Prevalence of atrial fibrillation and associated factors in a population of long-term hemodialysis patients. Am J Kidney Dis. 2005; 46 (5):897–902. Epub 2005/10/29. https://doi.org/10.1053/j.ajkd.2005.07.044 PMID: 16253730.

11. Konigsbrugge O, Posch F, Antlanger M, Kovarik J, Klauser-Braun R, Kletzmayr J, et al. Prevalence of Atrial Fibrillation and Antithrombotic Therapy in Hemodialysis Patients: Cross-Sectional Results of the Vienna InVestigation of AtriaL Fibrillation and Thromboembolism in Patients on HemoDIalysis (VIVALDI). PLoS One. 2017; 12(1):e0169400. Epub 2017/01/05. https://doi.org/10.1371/journal.pone.0169400 PMID: 28052124; PubMed Central PMCID: PMC5213813.

12. Zimmerman D, Sood MM, Rigatto C, Holden RM, Hiremath S, Clase CM. Systematic review and meta-analysis of incidence, prevalence and outcomes of atrial fibrillation in patients on dialysis. Nephrol Dial Transplant. 2012; 27(10):3816–22. Epub 2012/11/02. https://doi.org/10.1093/ndt/gfs416 PMID: 23114904.

13. Vazquez E, Sanchez-Perales C, Garcia-Garcia F, Castellano P, Garcia-Cortes MJ, Liebana A, et al. Atrial fibrillation in incident dialysis patients. Kidney Int. 2009; 76(3):324–30. Epub 2009/06/06. https://doi.org/10.1038/ki.2009.185 PMID: 19494800.

14. Liao JN, Chao TF, Liu CJ, Wang KL, Chen SJ, Lin YJ, et al. Incidence and risk factors for new-onset atrial fibrillation among patients with end-stage renal disease undergoing renal replacement therapy. Kidney Int. 2015; 87(6):1209–15. Epub 2015/01/15. https://doi.org/10.1038/ki.2014.393 PMID: 25587708.

15. Winkelmayer WC, Patrick AR, Liu J, Brookhart MA, Setoguchi S. The increasing prevalence of atrial fibrillation among hemodialysis patients. J Am Soc Nephrol. 2011; 22(2):349–57. Epub 2011/01/15. https://doi.org/10.1681/ASN.2010050459 PMID: 21233416; PubMed Central PMCID: PMC3029907.

16. Genovesi S, Vincenti A, Rossi E, Pogliani D, Acquistapace I, Stella A, et al. Atrial fibrillation and morbidity and mortality in a cohort of long-term hemodialysis patients. Am J Kidney Dis. 2008; 51(2):255–62. Epub 2008/01/25. https://doi.org/10.1053/j.ajkd.2007.10.034 PMID: 18215703.

17. Lau DH, Nattel S, Kalman JM, Sanders P. Modifiable Risk Factors and Atrial Fibrillation. Circulation. 2017; 136(6):583–96. Epub 2017/08/09. https://doi.org/10.1161/CIRCULATIONAHA.116.023163 PMID: 28784826.

18. Klem I, Wehinger C, Schneider B, Hartl E, Finsterer J, Stollberger C. Diabetic atrial fibrillation patients: mortality and risk for stroke or embolism during a 10-year follow-up. Diabetes Metab Res Rev. 2003; 19 (4):320–8. Epub 2003/07/25. https://doi.org/10.1002/dmrr.386 PMID: 12879410.

19. Karayiannides S, Lundman P, Friberg L, Norhammar A. High overall cardiovascular risk and mortality in patients with atrial fibrillation and diabetes: A nationwide report. Diab Vasc Dis Res. 2018; 15(1):31–8. Epub 2017/10/21. https://doi.org/10.1177/1479164117735013 PMID: 29052435.

20. Cheng TM. Taiwan's new national health insurance program: genesis and experience so far. Health Aff (Millwood). 2003; 22(3):61–76. Epub 2003/05/22. https://doi.org/10.1377/hlthaff.22.3.61 PMID: 12757273.

21. Wen YH, Wu SS, Lin CH, Tsai JH, Yang P, Chang YP, et al. A Bayesian Approach to Identifying New Risk Factors for Dementia: A Nationwide Population-Based Study. Medicine (Baltimore). 2016; 95(21): e3658. https://doi.org/10.1097/MD.0000000000003658 PMID: 27227925; PubMed Central PMCID: PMC4902349.

22. D'Agostino RB Jr., Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. Stat Med. 1998; 17(19):2265–81. https://doi.org/10.1002/(sici)1097-0258(19981015)17:19<2265::aid-sim918>3.0.co;2-b PMID: 9802183.

23. Martinez EA, Donelan K, Henneman JP, Berenholtz SM, Miralles PD, Krug AE, et al. Identifying meaningful outcome measures for the intensive care unit. Am J Med Qual. 2014; 29(2):144–52. https://doi.org/10.1177/1062860613491823 PMID: 23892372.

24. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol. 1992; 45(6):613–9. https://doi.org/10.1016/0895-4356(92)90133-8 PMID: 1607900.

25. Ng'andu NH. An empirical comparison of statistical tests for assessing the proportional hazards assumption of Cox's model. Stat Med. 1997; 16(6):611–26. https://doi.org/10.1002/(sici)1097-0258(19970330)16:6<611::aid-sim437>3.0.co;2-t PMID: 9131751.

26. Lau B, Cole SR, Gange SJ. Competing risk regression models for epidemiologic data. Am J Epidemiol. 2009; 170(2):244–56. Epub 2009/06/06. https://doi.org/10.1093/aje/kwp107 PMID: 19494242; PubMed Central PMCID: PMC2732996.

27. Aune D, Schlesinger S, Neuenschwander M, Feng T, Janszky I, Norat T, et al. Diabetes mellitus, blood glucose and the risk of heart failure: A systematic review and meta-analysis of prospective studies. Nutr Metab Cardiovasc Dis. 2018; 28(11):1081–91. Epub 2018/10/16. https://doi.org/10.1016/j.numecd.2018.07.005 PMID: 30318112.

28. Seyed Ahmadi S, Svensson AM, Pivodic A, Rosengren A, Lind M. Risk of atrial fibrillation in persons with type 2 diabetes and the excess risk in relation to glycaemic control and renal function: a Swedish cohort study. Cardiovasc Diabetol. 2020; 19(1):9. Epub 2020/01/20. https://doi.org/10.1186/s12933-019-0983-1 PMID: 31954408; PubMed Central PMCID: PMC6969407.

29. Huxley RR, Filion KB, Konety S, Alonso A. Meta-analysis of cohort and case-control studies of type 2 diabetes mellitus and risk of atrial fibrillation. Am J Cardiol. 2011; 108(1):56–62. Epub 2011/05/03. https://doi.org/10.1016/j.amjcard.2011.03.004 PMID: 21529739; PubMed Central PMCID: PMC3181495.

30. Tadic M, Cuspidi C. Type 2 diabetes mellitus and atrial fibrillation: From mechanisms to clinical practice. Arch Cardiovasc Dis. 2015; 108(4):269–76. Epub 2015/04/11. https://doi.org/10.1016/j.acvd.2015.01.009 PMID: 25858534.

31. Packer M. Disease-treatment interactions in the management of patients with obesity and diabetes who have atrial fibrillation: the potential mediating influence of epicardial adipose tissue. Cardiovasc Diabetol. 2019; 18(1):121. Epub 2019/09/26. https://doi.org/10.1186/s12933-019-0927-9 PMID: 31551089; PubMed Central PMCID: PMC6760044.

32. Friedrichs K, Klinke A, Baldus S. Inflammatory pathways underlying atrial fibrillation. Trends Mol Med. 2011; 17(10):556–63. Epub 2011/07/19. https://doi.org/10.1016/j.molmed.2011.05.007 PMID: 21763201.

33. Niewczas MA, Gohda T, Skupien J, Smiles AM, Walker WH, Rosetti F, et al. Circulating TNF receptors 1 and 2 predict ESRD in type 2 diabetes. J Am Soc Nephrol. 2012; 23(3):507–15. Epub 2012/01/24. https://doi.org/10.1681/ASN.2011060627 PMID: 22266663; PubMed Central PMCID: PMC3294310.

34. Boos CJ, Anderson RA, Lip GY. Is atrial fibrillation an inflammatory disorder? Eur Heart J. 2006; 27 (2):136–49. Epub 2005/11/10. https://doi.org/10.1093/eurheartj/ehi645 PMID: 16278230.

35. Hernandez Madrid A, Moro C. Atrial fibrillation and C-reactive protein: searching for local inflammation. J Am Coll Cardiol. 2007; 49(15):1649–50. Epub 2007/04/17. https://doi.org/10.1016/j.jacc.2007.02.009 PMID: 17433957.

36. Anderson JL, Allen Maycock CA, Lappe DL, Crandall BG, Horne BD, Bair TL, et al. Frequency of elevation of C-reactive protein in atrial fibrillation. Am J Cardiol. 2004; 94(10):1255–9. Epub 2004/11/16. https://doi.org/10.1016/j.amjcard.2004.07.108 PMID: 15541240.

37. Iravanian S, Dudley SC Jr., The renin-angiotensin-aldosterone system (RAAS) and cardiac arrhythmias. Heart Rhythm. 2008; 5(6 Suppl):S12–7. Epub 2009/02/10. https://doi.org/10.1016/j.hrthm.2008.02.025 PMID: 18456194; PubMed Central PMCID: PMC2600881.

38. Khatib R, Joseph P, Briel M, Yusuf S, Healey J. Blockade of the renin-angiotensin-aldosterone system (RAAS) for primary prevention of non-valvular atrial fibrillation: a systematic review and meta analysis of randomized controlled trials. Int J Cardiol. 2013; 165(1):17–24. Epub 2012/03/17. https://doi.org/10.1016/j.ijcard.2012.02.009 PMID: 22421406.

39. Alonso A, Lopez FL, Matsushita K, Loehr LR, Agarwal SK, Chen LY, et al. Chronic kidney disease is associated with the incidence of atrial fibrillation: the Atherosclerosis Risk in Communities (ARIC) study. Circulation. 2011; 123(25):2946–53. Epub 2011/06/08. https://doi.org/10.1161/CIRCULATIONAHA.111.020982 PMID: 21646496; PubMed Central PMCID: PMC3139978.

40. Baber U, Howard VJ, Halperin JL, Soliman EZ, Zhang X, McClellan W, et al. Association of chronic kidney disease with atrial fibrillation among adults in the United States: REasons for Geographic and Racial Differences in Stroke (REGARDS) Study. Circ Arrhythm Electrophysiol. 2011; 4(1):26–32. Epub 2010/11/16. https://doi.org/10.1161/CIRCEP.110.957100 PMID: 21076159; PubMed Central PMCID: PMC3049935.

41. Soliman EZ, Prineas RJ, Go AS, Xie D, Lash JP, Rahman M, et al. Chronic kidney disease and prevalent atrial fibrillation: the Chronic Renal Insufficiency Cohort (CRIC). Am Heart J. 2010; 159(6):1102–7. Epub 2010/06/24. https://doi.org/10.1016/j.ahj.2010.03.027 PMID: 20569726; PubMed Central PMCID: PMC2891979.

42. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet. 2000; 355(9200):253–9. Epub 2000/02/16. PMID: 10675071.

43. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, et al. Blood pressure and end-stage renal disease in men. N Engl J Med. 1996; 334(1):13–8. Epub 1996/01/04. https://doi.org/10.1056/NEJM199601043340103 PMID: 7494564.