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Association between atrial fibrillation burden and cognitive function in patients with atrial fibrillation☆

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ABSTRACT

Background: Accumulating evidence has demonstrated an association between clinical atrial fibrillation (AF) and cognitive impairment. This study aimed to further clarify the impact of AF burden on cognitive function based on detailed electrophysiological recordings and standardized assessments of cognitive function.

Methods: This prospective cohort study, conducted at the Cardiac Electrophysiology Clinic of a tertiary center, included patients with non-valvular AF. AF burden was evaluated using 14-day patch-based electrocardiography. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA).

Results: Enrolled patients ($n = 253$) were grouped according to the median AF burden (13.52%). Patients with higher AF burden were significantly older and had larger left atrium size, a worse ejection fraction, and a lower MoCA score than those with lower AF burden. Predictors of MoCA score included age, CHA_2DS_2-VASc score, AF burden, and Center for Epidemiologic Studies Depression Scale scores. The association between MoCA scores and AF burden remained significant after adjustment for demographic characteristics, underlying diseases, and echocardiographic parameters (standardized beta coefficient: −0.159, 95% confidence interval: −0.020 to −0.004, $p = 0.004$).

Conclusion: AF burden is associated with cognitive function in patients with AF. Further studies are required to determine whether reducing AF burden can preserve cognitive function in these patients.

1. Introduction

Maintaining good cognitive function is crucial for living independently and having a satisfactory quality of life. Accumulating evidence has demonstrated an association between clinical atrial fibrillation (AF) and cognitive impairment [1–3], which may be mediated by various factors such as thromboembolic risk [4–6]. However, in 2018, the American Heart Association stated that AF should not be evaluated dichotomously (i.e., present/absent or non-paroxysmal/paroxysmal). Rather, AF burden should be quantified in detail using new monitoring technologies. Applying these techniques in conjunction with standardized cognitive assessments may aid in investigating the relationships between AF burden and cardiovascular/neurological outcomes, in validating the definitions and measures of AF burden, in identifying the optimal cut-off value for AF burden indicating increased risk, and in determining the mechanisms underlying the weak temporal correlation between AF and stroke [7,8]. To achieve these goals, we prospectively enrolled patients with AF based on assessments performed using the longest electrocardiographic recording patch available on the market to define AF burden. In this study, we aimed to clarify the impact of low and high AF burden on cognitive function as well as risk factors influencing cognitive impairment in patients with AF, based on assessments performed using the standardized Montreal Cognitive Assessment (MoCA) questionnaire.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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2. Methods

The current study was approved by the institutional review board of National Taiwan University Hospital (202003090RINA). The study has been reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [9]. All participants provided written informed consent.

3. Patient enrolment

From May 2020 to May 2022, we prospectively enrolled all patients referred to the Cardiac Electrophysiology Clinic of a tertiary center for AF management. Patients with a documented diagnosis of AF based on the results of a 12-lead electrocardiogram (ECG) or single-lead strip reviewed by an electrophysiologist were enrolled. All patients underwent preliminary testing, including blood sampling and echocardiography, prior to enrolment. Patients with a history of abnormal thyroid function or primary valvular heart disease were excluded. The patients were informed of the study design and content, and those who could not comply with all examinations or could not provide informed consent were excluded. Furthermore, patients with a history of stroke, previous diagnosis of vascular dementia, disabilities precluding cognitive testing (e.g., aphasia, hemiparesis resulting in difficulty writing), or significant functional disability (modified Rankin Scale score ≥ 2) were excluded.

In addition to baseline characteristics, we collected data related to underlying diseases, echocardiographic findings, and medications. Participants also underwent assessments of depression, daytime sleepiness, and quality of life using the Center for Epidemiologic Studies Depression Scale (CES—D), the Epworth Sleepiness Scale (ESS), and the 36-item Short Form Health Survey (SF-36), respectively. The CES-D is a 20-item questionnaire with scores ranging from 0 to 60. Higher CES-D scores indicate a higher risk of depression. Patients with scores 16 and above were considered to have depression and were referred to a psychiatrist for further evaluation. The ESS is an 8-item questionnaire scored from 0 to 24, with higher scores indicating more severe daytime sleepiness. ESS scores of 11 and above are considered indicative of excessive daytime sleepiness. The SF-36 is widely utilised to assess quality of life in clinical settings. Scores on the SF-36 range from 0 to 100, with higher scores indicating better health-related quality of life. For this study, scores for individual items were transformed into Physical and Mental Component Summary scores.

4. Evaluation of AF burden

To evaluate AF burden, all patients underwent a 14-day ambulatory ECG (EZYPRO, Sigknow Biomedical Co., Ltd., Taipei, Taiwan) with a single lead placed over the left upper chest. The patients were encouraged to perform their daily activities as usual, including working and exercising. Bathing was permitted because the ECG patch was waterproof and was firmly attached to the chest. Patients could record episodes of subjective symptoms by pushing a button in the middle of the recorder. The patch was removed after 14 days by the patient or the research assistant. The recorder was first sent to technicians for preliminary analysis and then to an electrophysiologist for signal interpretation. The recorded signals were automatically and manually analysed by experienced technicians with no knowledge of the patients' clinical conditions. AF burden was defined as the percentage of time spent in AF.

5. Evaluation of cognitive function

On the day of ECG patch placement, a well-trained technician administered the the standardized Montreal Cognitive Assessment questionnaire (MoCA) to evaluate cognitive function in each patient. The MoCA is a single-page scale used to assess a patient's capacity in several cognitive domains, including executive function, visuospatial abilities, naming, short-term memory, attention, working memory, language, concentration, verbal abstraction, and orientation. Administration of the MoCA takes up to 10 min, with a maximum score of 30, indicating that no errors were made. All participants were of Chinese ethnicity and spoke Mandarin as their primary language. Therefore, the Mandarin version of the MoCA was used. For individuals with $\leq$12 years of education, one point was added for correction. Previous studies have verified that the cut-off value of 24 is a good indicator of cognitive impairment [10].

6. Statistical analyses

Study data were collected and managed using REDCap electronic data capture tools hosted at National Taiwan University Hospital [11]. Continuous variables are presented as means $\pm$ standard deviations, and categorical variables are presented as counts and percentages. Continuous variables were assessed for conformance to a normal distribution using the Kolmogorov–Smirnov test, and Levene's test was used to check the homogeneity of variances between groups. Independent Student's *t*-tests were used to compare continuous variables, while chi-square tests were used to compare categorical variables. If the number in any cell was less than five, Fisher's exact test was used to compare categorical variables.

Linear regression analyses were used to determine the effects of demographic characteristics, underlying diseases, echocardiographic parameters, and clinically related questionnaire scores on cognitive function. These effects are reported as standardized beta coefficients and 95% CIs. For multivariate analysis, two models were created. Model 1 included variables with p-values <0.10 in the univariate analysis as inputs. Model 2 included all variables considered related to cognitive function, including baseline demographics, underlying diseases, echocardiographic parameters, and questionnaire scores. A forward stepwise approach was used for regression, and a two-sided p-value <0.05 was considered statistically significant. A ROC curve was generated to identify the cut-off value that yielded the greatest sensitivity and specificity for predicting cognitive impairment. A two-sided p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS Statistics version 21 (IBM Corp., Armonk, NY, USA).

7. Results

7.1. Patient characteristics

Overall, 253 patients with AF were prospectively enrolled in this study. The patients' demographic characteristics, underlying diseases, medications, echocardiographic parameters, and questionnaire scores are shown in Table 1. The median AF burden of was 13.53%, which was used to divide participants into two groups.

Patients with a high AF burden were slightly older and had more congestive heart failure (CHF) than those with a low AF burden. The percentages of male and diabetes mellitus (DM) were slightly higher in the high AF burden group, but the difference was insignificant. Other than that, there were no significant differences in the presence of underlying diseases between the groups. Patients with high AF burden had a significantly larger left atrium and significantly lower left ventricular ejection fraction (LVEF) than those with low AF burden, but both groups had a mean LVEF within the normal range. Propafenone and dronedarone tended to be less frequently prescribed in patients with high AF burden than in those with low AF burden, while oral anticoagulant agents were more frequently prescribed. The 14-day ECG results indicated that patients with high AF burden had lower values for minimum heart rate (HR) and higher values for maximum and average HR than those with low AF burden. There were no differences in CES—D, ESS, or SF-36 scores between the high and low AF burden groups. However, MoCA scores were significantly lower in patients with high AF burden

Table 1
Participant characteristics stratified by AF burden.

	Burden below median (≤13.53%)	Burden above median (>13.53%)	*P* value
Number (%)	127	126	
Age (years)	61.0 ± 10.0	64.1 ± 10.7	0.016
Sex, male (%)	85 (66.9)	98 (77.8)	0.054
Body mass index (kg/m^2)	25.5 ± 3.9	25.9 ± 3.7	0.335
Smoking status			0.850‡
Never smoked	106 (83.5)	103 (81.7)	
Former smoker	15 (11.9)	15 (11.9)	
Current smoker	6 (4.7)	8 (6.3)	
Alcohol status			0.002‡
Never consumed	117 (92.1)	115 (91.3)	
Past consumption	8 (6.3)	1 (0.8)	
Current consumption	2 (1.6)	10 (7.9)	
Diabetes mellitus	14 (11.0)	25 (19.8)	0.052
Hypertension	50 (39.4)	46 (36.5)	0.639
Hyperlipidaemia	34 (26.8)	32 (25.4)	0.803
Coronary artery disease	15 (11.8)	19 (15.1)	0.446
Congestive heart failure	5 (3.9)	14 (11.1)	0.030
PAOD	0 (0.0)	1 (0.8)	0.498†
COPD	1 (0.8)	4 (3.2)	0.213†
Liver cirrhosis	2 (1.7)	2 (3.8)	0.586†
CKD	8 (6.3)	5 (4.0)	0.393
ESRD	1 (0.8)	0 (0.0)	1.000†
SSS	7 (5.5)	4 (3.2)	0.362
CHA_2DS_2-VASc	1.62 ± 1.31	2.39 ± 1.55	0.403‡
0	24 (18.9)	27 (21.4)	
1	41 (32.3)	32 (25.4)	
2	34 (26.8)	25 (19.8)	
3	18 (14.2)	25 (19.8)	
4	6 (4.7)	12 (9.5)	
5	3 (2.4)	3 (2.4)	
6	1 (0.8)	2 (1.6)	
USG			
LA diameter (cm)	3.9 ± 0.5	4.4 ± 0.7	<0.001
LVEDD (cm)	4.8 ± 0.4	4.8 ± 0.5	0.826
LVEF (%)	71.7 ± 7.6	67.5 ± 9.2	<0.001
Medications			
Flecainide	27 (21.3)	15 (11.9)	0.046
Propafenone	66 (52.0)	31 (24.6)	<0.001
Beta-blocker	75 (59.1)	71 (56.3)	0.663
Amiodarone	30 (23.6)	29 (23.0)	0.909
Dronedarone	8 (6.3)	1 (0.8)	0.036†
OAC	60 (47.2)	85 (67.5)	0.001
Warfarin	4 (3.1)	8 (6.3)	0.231
NOAC	56 (44.1)	78 (61.9)	0.005
Anti-platelet agent	17 (13.4)	7 (5.6)	0.034
Statins use	34 (26.8)	42 (33.3)	0.255
Fourteen-day ECG			
Analysis time (days)	11.7 ± 2.9	11.2 ± 3.4	0.243
Minimum HR (bpm)	44.8 ± 8.4	42.4 ± 8.9	0.024
Average HR (bpm)	68 ± 7.9	78 ± 12.0	<0.001
Maximum HR (bpm)	155 ± 44.5	176 ± 30.0	<0.001
AF burden (%)	2.2 ± 3.4	76.6 ± 32.3	<0.001
Questionnaire			
CES-D score	12.5 ± 8.2	11.2 ± 7.8	0.173
ESS score	7.2 ± 4.0	7.3 ± 4.0	0.831
SF-36 PCS	54.5 ± 8.1	53.8 ± 9.4	0.557
SF-36 MCS	58.2 ± 15.4	59.1 ± 15.1	0.632
MoCA	26.7 ± 2.5	25.4 ± 3.7	0.001
MoCA <24	13 (10.2)	30 (23.8)	0.004
Education below 12 years	43 (33.9)	42 (33.3)	0.930

AF, atrial fibrillation; bpm, beats per minute; CES—D: Center for Epidemiologic Studies Depression Scale; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥ 75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65–74 years, female; CKD, chronic kidney disease; cm, centimetre; COPD, chronic obstructive pulmonary disease; ECG, electrocardiography; ESRD, end-stage renal disease; HR, heart rate; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MCS, mental component summary; MoCA, Montreal Cognitive Assessment; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulant; PAOD, peripheral arterial occlusive disease; PCS, physical component summary; SSS, sick sinus syndrome; USG, ultrasonography.
† Fisher's exact test.
‡ Likelihood ratio.

than in those with low AF burden, and the frequency of cognitive impairment was significantly higher in the high AF burden group when the cut-off point was set at 24.

7.2. Predictors of cognitive function in patients with AF

In the univariate linear regression analysis, the factors significantly associated with MoCA score were age, DM, coronary artery disease (CAD), CHF, CHA_2DS_2-VASc score, left atrium (LA) and left ventricle (LV) diameter, LVEF, and AF burden. When these factors were incorporated into Model 1 of the multivariate analysis, significant associations were observed for age, CHA_2DS_2-VASc score, AF burden, and depression scores (Table 2). Model 2 included all variables exhibiting significant associations in the univariate analysis as well as all other factors known to be associated with cognitive function. The results were consistent with those of Model 1, except that a significant association with hypertension emerged in Model 2.

Fig. 1 shows MoCA scores for the included patients stratified based on age and CHA_2DS_2-VASc score. The effects of AF burden on cognitive function were more evident in patients with higher CHA_2DS_2-VASc scores (CHA_2DS_2-VASc score ≥ 2, standardized beta coefficient − 0.242, 95% confidence interval (CI): −2.987 to −0.516, $p = 0.006$) than in patients with lower CHA_2DS_2-VASc scores (CHA_2DS_2-VASc score < 2, standardized beta coefficient − 0.160, 95% CI: −1.571–0.078, $p = 0.075$).

7.3. Predictors of cognitive impairment (MoCA score < 24) in patients with AF

As mentioned in the Methods section, cognitive impairment was defined as a MoCA score below 24. The odds ratio (OR) of AF burden (per 1% of AF burden increase) was 1.010 (95% CI: 1.001–1.019, $p = 0.033$) (Table 3). Accordingly, for every 10% or 50% increase in AF burden, the ORs increased to 1.105 and 1.645, respectively. When data were analysed for patients with paroxysmal AF only, the OR of AF burden increased to 1.031 (95% CI: 1.009–1.053, $p = 0.005$). The OR for every 10% or 50% increase in AF burden increased to 1.357 and 4.602. Receiver operating characterstics (ROC) analysis performed to identify the cut-off value of AF burden for predicting cognitive impairment revealed an area under the curve of 0.618 (95% CI: 0.521–0.716, $p = 0.014$). When the cut-off value of AF burden was set at 54.4%, the sensitivity and specificity were 58.1% and 70.0%, respectively (Supplementary Fig. 1).

8. Discussion

To the best of our knowledge, this is the first prospective study to clearly demonstrate the association between cognitive function and AF burden, evaluated by well standardized cognitive function test and mid-term continuous ECG recording system that balance research objectivity and patient acceptability. Reducing AF burden can be an alternative treatment target, if cannot be eliminated, in terms of preserving cognitive function and potentially improving outcome.

8.1. Cognitive function and AF burden

Previous studies have demonstrated that the presence of permanent

Table 2
Univariate and multivariate analyses of the associations with cognitive function.

MoCA												
Variables	Univariate analysis				Multivariate				Multivariate			
					Model 1				Model 2			
	Standardized beta coefficient	95% CI lower limit	95% CI upper limit	*P* value	Standardized beta coefficient	95% CI lower limit	95% CI upper limit	*P* value	Standardized beta coefficient	95% CI lower limit	95% CI upper limit	*P* value
Age (years)	−0.471	−0.176	−0.110	<0.001	−0.035	−0.146	−0.060	<0.001	−0.281	−0.130	−0.042	<0.001
Sex, male	0.072	−0.358	1.364	0.251								
Body mass index	0.045	−0.065	0.140	0.475								
Smoking	0.027	−0.570	0.887	0.668								
Alcohol	−0.074	−1.377	0.338	0.234								
Diabetes mellitus	−0.162	−2.477	−0.357	0.009								
Hypertension	0.002	−0.787	0.811	0.976					0.171	0.276	1.980	0.010
Hyperlipidaemia	0.003	−0.862	0.903	0.964								
Statins use	−0.141	−1.814	−0.132	0.024								
Coronary artery disease	−0.213	−3.078	−0.858	0.001								
Congestive heart failure	−0.128	−3.033	−0.079	0.039								
CHA_2DS_2-VASc	−0.403	−1.197	−0.675	<0.001	−0.181	−0.750	−0.102	0.010	−0.302	−1.096	−0.324	<0.001
USG												
LA diameter	−0.170	−1.305	−0.217	0.006								
LVEDD	0.172	0.316	1.829	0.006								
LVEF	0.158	0.013	0.100	0.011								
Fourteen-day ECG												
AF burden	−0.233	−0.026	−0.008	<0.001	−0.165	−0.020	−0.004	0.004	−0.159	−0.020	−0.004	0.004
Questionnaire												
CES-D score	−0.107	−0.093	0.007	0.092	−0.146	−0.103	−0.015	0.009	−0.135	−0.097	−0.011	0.014
ESS score	0.069	−0.046	0.156	0.281								
SF-36 pcs	0.117	−0.307	8.850	0.067								
SF-36 mcs	0.117	−0.173	5.094	0.067								

Model 1 included the following variables: age, DM, CAD, CHF, CHA_2DS_2-VASc, LA diameter, LVEDD, LVEF, AF burden, CES-D score, and SF-36 PCS and MCS scores. Model 2 included all variables listed in the table.

AF, atrial fibrillation; CES—D: Center for Epidemiologic Studies Depression Scale; CHA_2DS_2-VASc: congestive heart failure, hypertension, age ≥ 75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65–74 years, female; CI: confidence interval; ECG: electrocardiography; HR: heart rate; LA: left atrium; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; MoCA: Montreal Cognitive Assessment; NOAC: non-vitamin K antagonist oral anticoagulant; OAC: oral anticoagulant; OR: odds ratio; USG: ultrasonography.

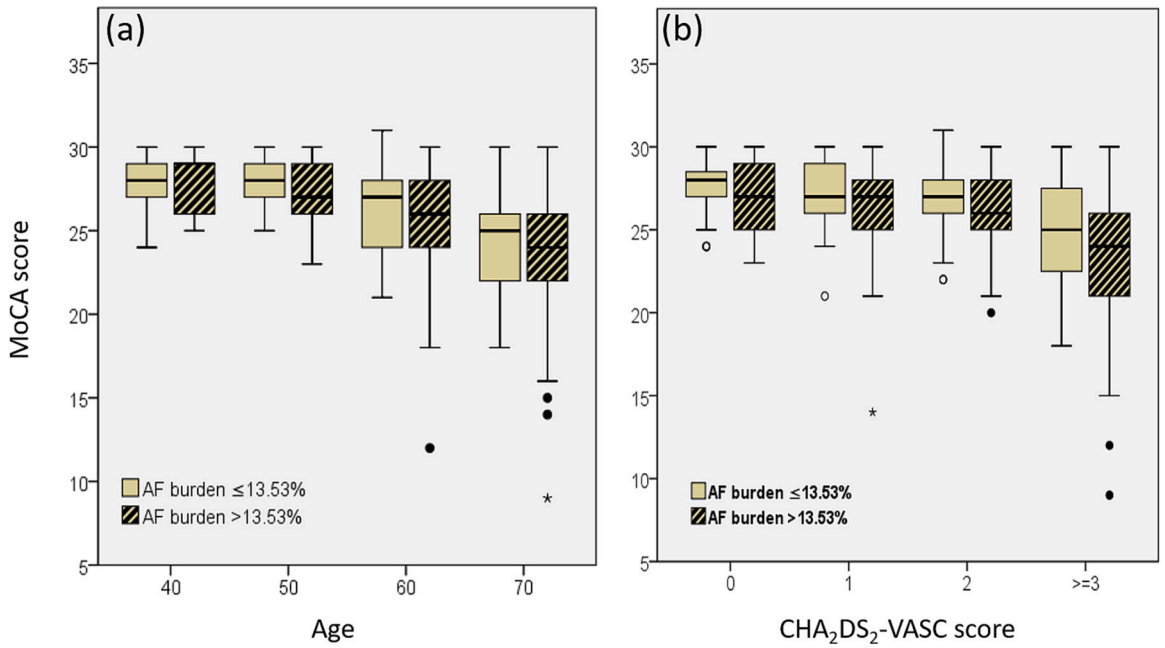

Fig. 1. MoCA Scores of Patients with AF stratified by AF burden and age (a) or CHA_2DS_2-VASc score (b).
AF, atrial fibrillation; MoCA, Montreal Cognitive Assessment.

Table 3
Multivariate analysis of associations with cognitive impairment (MoCA <24).

	Odds Ratio	95% CI Lower limit	95% CI Upper limit	*P* value
Age (years)	1.108	1.039	1.182	0.002
CHA_2DS_2-VASc	1.501	1.073	2.100	0.018
AF burden (%)	1.010	1.001	1.019	0.033
CES-D score	1.017	0.968	1.068	0.503
Paroxysmal AF				
Age (years)	1.145	1.039	1.263	0.006
CHA_2DS_2-VASc	1.614	1.004	2.595	0.048
AF burden (%)	1.031	1.009	1.053	0.005
CES-D score	0.993	0.929	1.061	0.829

AF, atrial fibrillation; CES—D: CES—D: Center for Epidemiologic Studies Depression Scale; CHA_2DS_2-VASc: congestive heart failure, hypertension, age ≥ 75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65–74 years, female; CI: confidence interval.

AF is associated with cognitive impairment regardless of stroke history [2,12]. Even in patients with no history of stroke, brain magnetic resonance imaging studies have revealed that AF is associated with reduced grey and white matter volumes in the frontal lobe and cerebellum [6,13]. Other functional studies using transcranial Doppler imaging or near-infrared spectroscopy to assess cerebral microcirculation reported that impaired neurovascular coupling and autoregulation occurred in patients with a higher burden of extreme single-beat hemodynamic events [3,4]. Silent brain infarction, cerebral hypoperfusion due to widely fluctuating ventricular rates, altered haemostatic function, and systemic inflammation may exacerbate cognitive impairment in patients with AF. In our study, the obseration of the dose-response relationship between AF burden and cognitive function supports the findings in those basic studies.

In addition to all the risk factors related to cognitive function, such as systemic hypertension, sleep apnea, possibly hyperlipidemia and other cardiovascular comorbidities, our study adds AF burden to the list as a new treatment target. Even when it cannot be eliminated, reducing AF burden by either medication or ablation may help to preserve cognitive function when treating patients with AF.

8.2. Measures of AF burden

In previous studies, detailed information related to AF burden was only available for patients with cardiac implantable electronic devices (CIEDs). In the CASTLE-AF study, a prospective randomised clinical trial, 363 patients with coexisting heart failure (HF) and AF who had implantable cardioverter defibrillation (ICD) or cardiac resynchronisation therapy-defibrillation (CRT—D) devices were randomised to either catheter ablation or pharmacological therapy. A high AF burden, defined as ≥50% of the cumulative duration of all atrial arrhythmia episodes 6 months after randomisation, predicted mortality and HF [14]. Another retrospective cohort study found that both the percentage of time spent in AF and the duration of the longest AF episode were associated with the incidence of stroke and transient ischemic attack [15]. A nationwide cohort study from the USA that used data from a remote monitoring database of CIEDs and Medicare claims found that AF burden predicted new-onset HF, hospitalisation due to HF, and all-cause mortality in patients with non-permanent AF [16]. However, these findings could not be generalized to the general population given that the need for CIEDs implies a more severe underlying cardiac pathology. In our cohort, only five patients had undergone CIED implantation (four in the low-burden group and one in the high-burden group), and the prevalence of underlying comorbidities was low, implying that they have similar characteristics to real-world patients with AF.

With recent advances in ECG recording technology, long-term cardiac monitoring has become available at a reasonable cost. We adopted a 14-day ambulatory ECG patch to evaluate AF burden in the current study. Although differences in AF burden may exist for longer recording durations, the use of a non-invasive patch-based ECG is more rational and practical for use in daily clinical practice. Cell phone or watch-based technology can also be used for convenient recording. However, such recordings are patient-triggered events, and values for AF burden measured using these methods may be unreliable given that AF can be minimally symptomatic and that AF during sleep cannot be recorded.

Furthermore, in this study, we observed that the longest AF duration (standardized beta coefficient − 0.099, 95% CI: −0.010–0.001, p = 0.116) and the number of AF events (standardized b coefficient − 0.084, 95% CI -0.000053–0.000010, p = 0.181) were not associated with cognitive impairment. Therefore, defining AF burden as the percentage of time spent in AF (rather than the longest AF duration or number of AF events) may represent a better and easier method for evaluating the severity of AF.

8.3. Interplay between AF burden and CHA_2DS_2-VASc score in predicting cognitive function

Current guidelines for AF management recommend the use of CHA_2DS_2-VASc scores to predict the risk of stroke, irrespective of AF burden [17,18]. However, recent studies have reported increased stroke risk in patients with higher AF burden, comparing either non-paroxysmal to paroxysmal clinical AF or higher to lower atrial high-rate episodes based on CIED registry data [19]. Tiver et al. further combined AF burden with CHA_2DS_2-VASc score to refine and individualise predictions of stroke risk in patients with AF, especially those with borderline risk based on CHA_2DS_2-VASc scores of 1 [20]. In this study, the effects of AF burden on cognitive function became more evident as the CHA_2DS_2-VASc score increased. It is possible that patients with higher CHA_2DS_2-VASc scores had more severe underlying vascular conditions and were more vulnerable to unstable beat-to-beat hemodynamic. However, as this was an observational study, we could not clarify whether the effects of AF on cognitive function are reversible. Further longitudinal studies involving follow-up assessments of cognitive function are required to address this issue.

8.4. Limitations

This study had some limitations, including the use of 14-day ambulatory ECG to determine AF burden, which may have differed if recordings had been performed for a longer duration using an implantable loop recorder or CIED. However, methods involving an implantable loop recorder or CIEDs are invasive, and 14-day patch-based ECG represents the longest available recording duration to precisely and non-invasively evaluate AF burden. Therefore, this recording method is practical for use in clinical settings. In addition, information concerning the history of thromboembolic stroke was acquired via interviews and clinic-based neurological examinations. No brain imaging studies were performed to identify silent strokes and small vessel disease. Therefore, the contribution of stroke or small vessel disease to cognitive impairment may have been underestimated. This was a study conducted in a society with Chinese origin, limiting the generalization of the study finding. Furthermore, as this was a cross-sectional study, we were unable to conclude whether there is a temporal link between the occurrence of cognitive impairment and exposure to a certain AF burden. Lastly, the sample size of this study was relatively small, limiting the statistical power of our findings. Nevertheless, our finding of a significant association between AF burden and cognitive function implies an important connection between these variables. Further large-scale investigations or intervention studies are warranted.

9. Conclusion

Cognitive function in patients with AF is associated with AF burden, especially in patients with higher CHA_2DS_2-VASc scores (≥2). Future

prospective trials should aim to determine whether interventions designed to reduce AF burden can preserve cognitive function in patients with AF.

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Author statement

SCT, YBL, LYL, LPL, WJC, YLH, and CCT designed and conceptualized the study. YBL, LYL, HCH, LTH, and CCY are responsible for the clinical data collection and validation. SCT, YBL, and CCY are responsible for the manuscript draft. SCT is responsible for the neurological aspects, and YBL and CCT are responsible for the cardiology aspects. SCT and YBL contributed equally to this study. CCY is in charge of the funding obtaining. All authors read and approved the final manuscript.

Disclosures

There are no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2023.01.007.

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