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Paroxysmal atrial fibrillation is associated with poor sleep quality: Tamagawa cross-sectional study on the relationship between lifestyle and atrial fibrillation (TAMAGAWA-AF study)

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Abstract

Background: Quality of life (QOL) is reduced in patients with atrial fibrillation (AF). However, data regarding the association between sleep quality, one of the major components of QOL, and AF are insufficient. This cross-sectional study aimed to elucidate whether sleep quality is reduced in patients with AF.

Methods: We recruited 2054 consecutive outpatients (64 ± 10 years, 1089 men) who had regularly presented to 26 clinics affiliated with the Tamagawa Medical Association, Tokyo, Japan. The patients were divided into paroxysmal AF (PaAF), persistent or permanent AF (PeAF), and non-AF groups. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI). The global PSQI score was calculated according to the answer to each question, and poor sleep quality was defined as a global PSQI score ≥6 points. Logistic regression analysis was used to obtain odds ratio for poor sleep quality in the PaAF and PeAF groups, relative to the non-AF group.

Results: The PaAF group showed significantly increased odds ratio for poor sleep quality (1.49, 95% confidence interval 1.02–2.17), after adjusting for multiple potential confounders. In contrast, no significant odds ratio for poor sleep quality was observed in the PeAF group (1.09, 95% confidence interval 0.70–1.71). Among the PSQI components, poor subjective sleep quality and sleep disturbances were the main determinants of poor sleep quality in the PaAF group.

Conclusion: Sleep quality was found to be reduced in patients with PaAF, and this may be attributed to poor subjective sleep quality and sleep disturbances.

KEYWORDS
atrial fibrillation, community clinics, cross-sectional study, Pittsburgh sleep quality index, sleep disturbances

Toshiaki Otsuka and Haruhiko Ikegami were authors contributed equally to this work.

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

[Correction added on 11 December 2024, after first online publication: The fifth author's name has been corrected from Kouichi Hatano to Hirokazu Hatano in this version.]

1 | INTRODUCTION

Atrial fibrillation (AF) is the most prevalent tachyarrhythmia in daily clinical practice,[1] and is known to significantly impact cardiovascular prognoses. AF also adversely influences quality of life (QOL) as a result of several pathophysiological mechanisms such as activation of sympathetic tone, increase in symptomatic palpitation, and impairment of exercise tolerance.[2]

Poor sleep quality is a major determinant of QOL. Poor sleep quality elevates blood pressure,[3] impairs glucose tolerance,[4] and increases the risk of developing metabolic syndrome,[5] resulting in the progression of atherosclerosis. Insomnia is also well known to be associated with depression, a potential psychosocial risk factor for cardiovascular disease (CVD).[6] Therefore, it is important to accumulate evidence regarding the relationship between sleep quality and the presence of AF, not only to improve QOL in patients with AF but also to further reduce their CVD risk.

Several studies have reported reduced sleep quality in patients with AF.[7–9] However, these studies did not include Japanese patients or have an adequate sample size. A previous meta-analysis suggested that insomnia and/or frequent night awakening increased the risk of AF[10]; however, a comprehensive assessment of sleep quality was not performed in the analyses. In the present study, we sought to examine the cross-sectional relationship between sleep quality, evaluated using a comprehensive assessment tool, and AF in a multicenter study that included more than 2000 patients with and without AF who visited community clinics in Japan.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

The Tamagawa Cross-Sectional Study on the Relationship between Lifestyle and AF (the TAMAGAWA-AF Study) is a community clinic-based, cross-sectional study. This study aimed to investigate the relationships between lifestyle and prevalence of AF. Patients aged 40–79 years who suffered from chronic disease and regularly visited one of 26 clinics affiliated with the Tamagawa Medical Association, located in southern district of Setagaya ward, Tokyo, Japan, were enrolled in this study between August 22 and October 31, 2016. Patients who first visited the clinic during the participation period, those who were not physically or mentally stable 1 week prior to their last clinic visit, those without sufficient cognitive function, or those who were judged inappropriate for participation by the attending physicians were excluded from this study. A total of 2295 patients were enrolled in this study. Of these, 241 patients did not provide sufficient answers to questionnaires regarding sleep conditions, and hence, were further excluded. Finally, 2054 patients were included in the analysis. The TAMAGAWA-AF study was approved by the ethics committee of Nippon Medical School (approval No. 28-06) and conducted in accordance with the Declaration of Helsinki. All patients provided informed consent to participate in the TAMAGAWA-AF study.

2.2 | Collection of clinical information

All anthropometric and clinical information, including patient comorbidities, were obtained from medical records. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2). Obesity was defined as a BMI ≥25 kg/m^2. Hypertension, impaired glucose tolerance/diabetes, dyslipidemia, and hyperuricemia were diagnosed by the attending physicians, in accordance with the current guidelines.

2.3 | Assessment of sleep quality and other lifestyles

Sleep quality over the previous month was evaluated using the Pittsburgh Sleep Quality Index (PSQI).[11] This self-reported questionnaire consists of 19 questions that assess the following seven components: subjective sleep quality (C1), sleep latency (C2), sleep duration (C3), sleep efficacy (C4), sleep disturbances (C5), use of sleep medications (C6), and daytime dysfunction (C7). Each component is scored from 0 to 3, yielding a global PSQI score between 0 and 21 points. Higher scores indicated lower sleep quality. Poor sleep quality was defined as a global PSQI score ≥6 points.[11] In addition, the presence of C1 to C7 were defined as a score ≥2 points for C1 and C3, and a score ≥1 point for other components.

Information on other lifestyle factors, such as smoking status and alcohol intake were obtained using a self-reported questionnaire. Smoking status was classified as current or non-smoking. Alcohol intake was asked as frequency of alcohol intake per week and classified as follows: no intake, ≤ 4 days/week, or ≥5 days/week.

2.4 | Diagnosis of AF

AF was diagnosed by attending physicians based on current or previous documentation of AF on a 12-lead electrocardiogram (ECG), Holter monitoring, or ambulatory ECG at the time of study enrollment. Therefore, even if the patient did not have AF at the time of study enrollment, they were diagnosed with AF if it was recorded in the past. In the present study, atrial flutter was included in AF. Patients with AF were categorized into two groups according to the clinical types, paroxysmal AF (PaAF) and persistent or permanent AF (PeAF), based on the physician's perception of AF. PaAF was defined as AF that lasted ≤7 days. PeAF was defined as AF lasting >7 days. These definitions do not consider whether pharmacological or electrical cardioversion was performed. In cases where the attending physicians had not obtained any documentation of AF at the time of study enrollment, patients were categorized into the non-AF group.

2.5 | Statistical analysis

All statistical analyses were performed using Stata software (version 18.0, StataCorp, College Station, Texas, USA). Continuous

variables with and without skewed distribution are presented as median (interquartile range) and mean ± standard deviation, respectively. Categorical data are shown as the numbers (percentages). Continuous and categorical variables among the groups were compared using analysis of variance and the chi-square test, respectively. Age- and sex-adjusted and multi-adjusted logistic regression analyses were performed to obtain odds ratios (OR) and 95% confidence intervals (CI) for poor sleep quality in the PaAF and PeAF groups, relative to the non-AF group. In the multi-adjusted model, the OR was adjusted for the following potential confounders: age, sex, BMI, frequency of alcohol intake, heart failure, chronic obstructive pulmonary disease, sleep apnea syndrome, diuretic use, and benign prostate hyperplasia/overactive bladder. All statistical tests were two-sided, and a p-value <.05 was considered to be statistically significant.

3 | RESULTS

The baseline characteristics of the study participants are shown in Table 1. The mean age of the participants was 64.0 ± 9.9 years and 53% were men. The number of patients classified into non-AF, PaAF, and PeAF groups were 1814, 130, and 110, respectively. When comparing the non-AF, PaAF, and PeAF groups, age, prevalence in male sex, impaired glucose tolerance/diabetes, hyperuricemia, history or presence of heart failure, use of diuretics, and chronic obstructive pulmonary disease were the highest in the PeAF group, whereas the prevalence of benign prostate hyperplasia/overactive bladder was highest in the PaAF group. The frequency of alcohol intake also differed significantly among the three groups.

The global PSQI and component scores in the three groups are presented in Table 2. Overall, the global PSQI score was 5.26 ± 2.89 points and 807 patients (39.3%) had poor sleep quality (global PSQI score ≥6 points). There was no significant difference in the global PSQI score or the percentage of patients with poor sleep quality among the three groups. However, the component score for sleep disturbance (C5) was significantly different among the three groups, with the highest score in the PaAF group. The component score for subjective sleep quality (C1) appeared to differ among the groups but the difference did not reach statistical significance.

Table 3 shows the results of the logistic regression analysis of the association between AF status and poor sleep quality. In the multi-adjusted model, the PaAF group showed significantly increased OR (1.49, 95% CI 1.02–2.17) for poor sleep quality compared with the non-AF group. However, any significant OR for poor sleep quality was not observed in the PeAF group. Female sex, benign prostate

TABLE 1 Baseline characteristics of study patients.

Characteristics	Overall $n = 2054$	Non-AF $n = 1814$	PaAF $n = 130$	PeAF $n = 110$	p-value
Age, years	64.0 ± 9.9	63.4 ± 10.0	67.8 ± 9.0	69.6 ± 7.2	<.001
Male sex, *n* (%)	1089 (53.0)	914 (50.4)	94 (72.3)	81 (73.6)	<.001
BMI, kg/m^2	23.6 ± 3.8	23.5 ± 3.8	23.5 ± 3.4	24.1 ± 4.0	.28
Obesity, *n* (%)	635 (30.9)	551 (30.4)	41 (31.5)	43 (39.1)	.16
Current smoking, *n* (%)	247 (12.0)	219 (12.1)	15 (11.5)	13 (11.8)	.98
Frequency of alcohol intake ($n = 2053$)					<.001
No dinking, *n* (%)	821 (40.0)	738 (40.7)	53 (40.8)	30 (27.5)	
≤ 4 days/week, *n* (%)	632 (30.8)	564 (31.1)	43 (33.1)	25 (22.9)	
≥ 5 days/week, *n* (%)	600 (29.2)	512 (28.2)	34 (26.2)	54 (49.5)	
Hypertension ($n = 2053$), n (%)	1346 (65.5)	1182 (65.2)	89 (69.0)	75 (68.2)	.57
Dyslipidemia, *n* (%)	1184 (57.6)	1050 (57.9)	75 (57.7)	59 (53.6)	.68
Impaired glucose tolerance/diabetes, *n* (%)	428 (20.8)	367 (20.2)	23 (17.7)	38 (34.5)	.001
Hyperuricemia, *n* (%)	345 (16.8)	273 (15.0)	32 (24.6)	40 (36.4)	<.001
History/presence of heart failure, *n* (%)	74 (3.6)	30 (1.7)	11 (8.5)	33 (30.0)	<.001
Use of diuretics, *n* (%)	102 (5.0)	67 (3.7)	7 (5.4)	28 (25.5)	<.001
Chronic obstructive pulmonary disease, *n* (%)	36 (1.8)	26 (1.4)	5 (3.8)	5 (4.5)	.009
BPH/OAB ($n = 1967$), *n* (%)	129 (6.6)	101 (5.8)	16 (12.6)	12 (11.2)	.002
Sleep apnea syndrome ($n = 2040$)					.40
No, *n* (%)	1816 (89.0)	1607 (89.2)	110 (85.3)	99 (90.8)	
Yes (with CPAP treatment), *n* (%)	186 (9.1)	162 (9.0)	17 (13.2)	7 (6.4)	
Yes (without CPAP treatment), *n* (%)	38 (1.9)	33 (1.8)	2 (1.6)	3 (2.8)	

Abbreviations: AF, atrial fibrillation; BMI, body mass index; BPH, benign prostate hyperplasia; OBA, overactive bladder; PaAF, paroxysmal atrial fibrillation; PeAF, persistent or permanent atrial fibrillation.

TABLE 2 Comparison of the PSQI among non-AF, PaAF, and PeAF groups.

	Overall	Non-AF	PaAF	PeAF	
	n = 2054	*n* = 1814	*n* = 130	*n* = 110	*p*-value*
Global PSQI score	5.26 ± 2.89	5.24 ± 2.88	5.57 ± 3.05	5.24 ± 2.93	.46
Global PSQI score ≥6, *n* (%)	807 (39.3)	706 (38.9)	58 (44.6)	43 (39.1)	.44
Component score					
Subjective sleep quality (C1)	1.09 ± 0.64	1.08 ± 0.64	1.21 ± 0.71	1.05 ± 0.65	.08
Sleep latency (C2)	0.70 ± 0.83	0.71 ± 0.83	0.60 ± 0.81	0.65 ± 0.82	.27
Sleep duration (C3)	1.40 ± 0.80	1.41 ± 0.80	1.42 ± 0.77	1.31 ± 0.84	.44
Habitual sleep efficiency (C4)	0.32 ± 0.70	0.32 ± 0.7	0.27 ± 0.62	0.35 ± 0.68	.64
Sleep disturbances (C5)	0.71 ± 0.52	0.70 ± 0.52	0.88 ± 0.48	0.66 ± 0.49	<.001
Use of sleeping medication (C6)	0.51 ± 1.07	0.50 ± 1.05	0.62 ± 1.16	0.66 ± 1.21	.15
Daytime dysfunction (C7)	0.53 ± 0.65	0.52 ± 0.65	0.57 ± 0.66	0.55 ± 0.72	.69

Abbreviations: AF, atrial fibrillation; PaAF, paroxysmal atrial fibrillation; PeAF, persistent or permanent atrial fibrillation; PSQI, Pittsburgh Sleep Quality Index.

*Chi-square test for Global PSQI score ≥6 and analysis of variance for other variables among the three groups.

TABLE 3 Odds ratio for poor sleep quality in patients with PaAF or those with PeAF.

	No. of cases (poor sleep quality)/ at risk	Odds ratio (95% confidence interval)	
		Age- and sex-adjusted model	Multi-adjusted model[a]
non-AF	706 / 1814	1.00 (reference)	1.00 (reference)
PaAF	58 / 130	1.42 (0.99–2.06)	1.49 (1.02–2.17)
PeAF	43 / 110	1.14 (0.76–1.71)	1.09 (0.70–1.71)

Abbreviations: AF, atrial fibrillation; PaAF, paroxysmal atrial fibrillation; PeAF, persistent or permanent atrial fibrillation.

[a]Adjusted for age, sex, body mass index, frequency of alcohol intake, heart failure, chronic obstructive pulmonary disease, sleep apnea syndrome, use of diuretics, and benign prostate hyperplasia/overactive bladder. Poor sleep quality is defined as the global Pittsburgh Sleep Quality Index score ≥6.

hyperplasia/overactive bladder, and sleep apnea syndrome were other factors that showed significantly increased OR for poor sleep quality in the multi-adjusted model (data not shown).

The ORs for the presence of each PSQI component in the multi-adjusted model are shown in Table 4. The PaAF group showed a significantly increased OR for the presence of subjective sleep quality (C1; OR 2.04, 95% CI 1.35–3.08) and sleep disturbances (C5; OR 2.24, 95% CI 1.39–3.62); however, there were no significant association with any PSQI components in the PeAF group.

The results of subgroup analyses by age (< 65 years and ≥ 65 years), sex, obesity, or sleep apnea syndrome are shown in Figure 1. Increased OR for poor sleep quality in the PaAF group was observed in patients aged <65 years (OR 1.93, 95% CI 1.08–3.43), those without obesity (OR 1.86, 95% CI 1.18–2.95), and those without sleep apnea syndrome (OR 1.55, 95% CI 1.03–2.34) (Figure 1A). In contrast, there was no significant OR for poor sleep quality in the PeAF group in any of the subgroup analyses (Figure 1B). In these subgroup analyses, no significant interaction between the presence of PaAF and any subgroups was observed for poor sleep quality.

4 | DISCUSSION

In the present study, a significant increase in poor sleep quality, defined as a global PSQI score ≥6 points, was found in the PaAF group. Among the seven PSQI component scores, impaired subjective sleep quality and sleep disturbances were significantly associated with PaAF. Considering these results, the present study suggests that

TABLE 4 Logistic regression analysis for the association between AF status and the presence of each component of PSQI.

	Multi-adjusted odds ratio[a] (95% confidence interval)						
	Subjective sleep quality (C1)	Sleep latency (C2)	Sleep duration (C3)	Habitual sleep efficiency (C4)	Sleep disturbances (C5)	Use of sleeping medication (C6)	Daytime dysfunction (C7)
Non-AF	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
PaAF	2.04 (1.35–3.08)	0.79 (0.54–1.15)	1.15 (0.78–1.68)	0.91 (0.57–1.43)	2.24 (1.39–3.62)	1.16 (0.75–1.80)	1.20 (0.83–1.75)
PeAF	1.08 (0.63–1.87)	0.77 (0.50–1.20)	1.11 (0.71–1.73)	1.18 (0.71–1.95)	0.92 (0.58–1.46)	1.11 (0.66–1.86)	1.16 (0.75–1.80)

Abbreviations: AF, atrial fibrillation; PaAF, paroxysmal atrial fibrillation; PeAF, persistent or permanent atrial fibrillation; PSQI, Pittsburgh Sleep Quality Index.

[a]Adjusted for age, sex, body mass index, frequency of alcohol intake, heart failure, chronic obstructive pulmonary disease, sleep apnea syndrome, use of diuretics, and benign prostate hyperplasia/overactive bladder. The presence of C1 to C7 were defined as a score ≥2 points for C1 and C3, and a score ≥1 point for other components.

PaAF is significantly associated with poor sleep quality, and both the presence of impaired subjective sleep quality and sleep disturbances appear to be the main contributing factors to this relationship. From a pathophysiological viewpoint, our present findings suggest that the coexistence of poor sleep quality is a potential mechanism for increased CVD risk in patients with AF, particularly in those with PaAF. Of note, increased odds of having sleep disturbances in the PaAF group were independent of the presence of sleep apnea syndrome in the multivariate analysis. This highlights the importance of treating sleep disturbances and their causes in patients with PaAF, regardless of whether they have sleep apnea syndrome.

According to the Global Burden of Disease 2019 study, more than 59 million people were estimated to have AF around the world in 2019.[12] In Japan, approximately 0.71–1.75 million people (0.6%–1.4% of Japanese population) are estimated to suffer from AF.[13–15] The incidence rate of newly documented AF has also been reported to be 2.5–9.3/1000 person-years in a population-based survey in Japan.[15,16] These data suggest that AF is the most commonly encountered arrhythmia in Japan as well. Therefore, our results may be applicable to a large number of patients with PaAF, including Japanese patients, in order to reduce the risk of CVD by improving sleep quality.

Several previous studies have reported sleep quality status in patients with AF.[7–9] Szymanski et al. reported that the prevalence of poor sleep quality, as evaluated by the PSQI, gradually increased with an increase in the severity of AF symptoms.[9] Kayrak et al. demonstrated that AF was an independent predictor of poor sleep quality, and interestingly, the PSQI score improved significantly in patients successfully maintained in sinus rhythm 6 months after cardioversion.[7] Kwon et al. reported that AF was more prevalent in individuals with poor sleep quality, as measured by reduced slow-wave sleep time, in a multi-ethnic population.[8] Although our present findings are almost in line with those previous observations, the patients who participated in those previous studies were not Japanese and their number was somewhat lower compared with that of the participating patients in our study. In this regard, our present findings may contribute to the accumulation of evidence detailing a possible association between AF and sleep quality, particularly in Japanese patients with PaAF.

In the present study, an increased OR for poor sleep quality was demonstrated in the PaAF group but not in the PeAF group. One potential explanation for this is the difference in the prevalence of AF-related symptoms between the PaAF and PeAF groups. In the Fushimi AF registry, approximately 62% of patients with PaAF and 33% of patients with PeAF were reported to have symptoms related to AF.[17] Although we did not collect detailed data on AF-related symptoms, the higher percentage of symptomatic patients in the PaAF group than in the PeAF group may explain the increased OR for poor sleep quality in the PaAF group in the present study.

Subgroup analyses revealed increased odds of poor sleep quality in patients aged <65 years, those without obesity, and those without sleep apnea syndrome in the PaAF group. In contrast, no significant odds of poor sleep quality were noted in PaAF patients aged

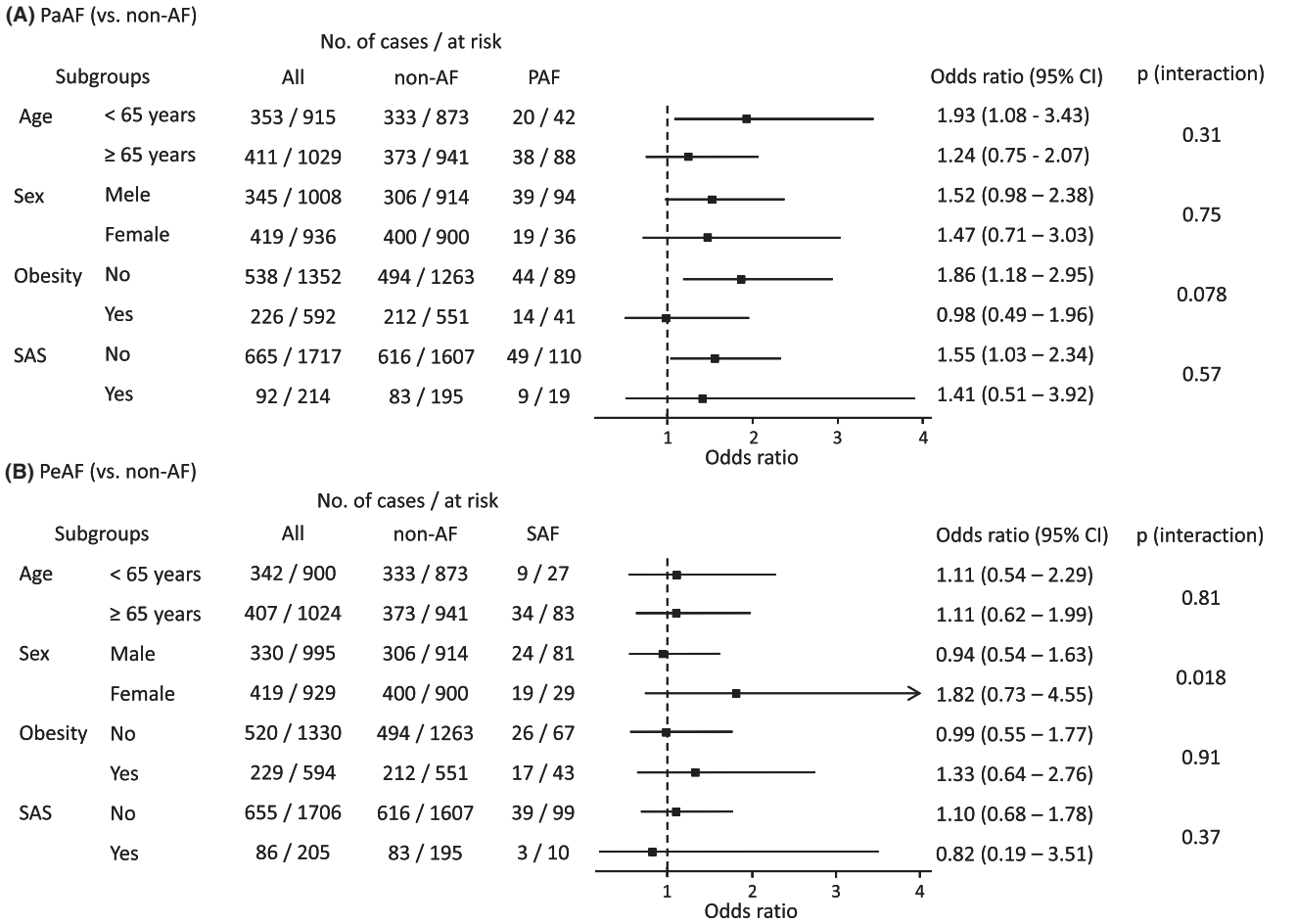

FIGURE 1 Forrest plot subgroup analyses of the odds ratio for poor sleep quality in the presence of (A) PaAF and (B) PeAF, relative to non-AF. AF; atrial fibrillation, PaAF; paroxysmal atrial fibrillation, PeAF; persistent or permanent atrial fibrillation, SAS; sleep apnea syndrome.

≥65 years, those with obesity, or those with sleep apnea syndrome. Older patients,[18] those with obesity[19] and/or those with sleep apnea syndrome[20] have been reported to have an increased likelihood of having poor sleep quality, irrespective of whether they suffer from PaAF. Therefore, the adverse effects of the PaAF on sleep quality may attenuate in these subgroups. However, interactions between the presence of PaAF and any subgroups did not reach statistical significance. These points are expected to be clarified in future studies.

The present study has some potential limitations. First, the design of the present study was cross-sectional, and the causal relationship between sleep quality and the presence of AF could not be elucidated. Indeed, the presence of AF is thought to reduce sleep quality, and previous studies have suggested an increased risk of future occurrence of AF in persons who have sleep problems.[10] Further longitudinal studies are needed to clarify the causal relationship between sleep quality and AF. Second, detailed clinical information on patients with AF, such as echocardiographic findings, was not available, because various examinations were not necessarily conducted in all participating clinics. Finally, the study population consisted of patients who suffered from any chronic disease and regularly visited community clinics located in the Tokyo metropolitan area. Therefore, it is unknown whether our results can be extrapolated to populations in other areas or to those without chronic diseases.

5 | CONCLUSIONS

Our findings demonstrate that sleep quality, as evaluated with the PSQI, is reduced in patients with PaAF, which may result from decreased subjective sleep quality and sleep disturbances. We anticipate that our results will contribute to the accumulation of evidence for reducing the risk of CVD by improving sleep quality in patients with PaAF.

FUNDING INFORMATION

No funding was received for this study.

CONFLICT OF INTEREST STATEMENT

Authors declare no conflict of interests for this article.

DATA AVAILABILITY STATEMENT

The study participants did not provide written consent for their data to be shared publicly. Therefore, supporting data are unavailable because of the sensitive nature of the research.

ETHICS STATEMENT

The present study complies with your ethics and integrity policies. This study was approved by the ethics committee of Nippon Medical School (Approval No. 28-06).

CONSENT

All patients provided informed consent.

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