Brief Report

Prevalence of Restless Legs Syndrome and Its Effects on Sleep and Health-Related Quality of Life in Patients With Heart Failure

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ABSTRACT

Background: Restless legs syndrome (RLS) is a neurological disorder characterized by leg restlessness and dysesthesia. Although the relationship between RLS and heart failure (HF) has been reported, the prevalence and clinical significance of RLS in patients with HF remain to be elucidated.

Methods and Results: We enrolled consecutive patients with HF who were admitted to our institutions. RLS was diagnosed using the International Restless Legs Syndrome Study Group criteria. Subjective sleepiness, sleep quality, and quality of life (QoL) were assessed using the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), and 8-item Short Form (SF-8), respectively. Among the 133 patients, 18 (13.6%) had RLS and were younger than those without RLS (62.4±13.4 vs 70.0±12.2, $P = .017$). The RLS group had significantly disrupted sleep quality and QoL, with greater PSQI score (8.0±3.2 vs 5.9±3.3, $P = .015$) and lower SF-8 physical component summary (PCS) score (35.6±6.5 vs 40.7±9.5, $P = .031$), despite similar ESS and SF-8 mental component summary scores. In the multivariable regression analysis, RLS was associated with greater PSQI (β=0.211; $P = .014$) and lower PCS score (β=−0.177; $P = .045$).

Conclusion: In the patients with HF, RLS was prevalent, and sleep quality and QoL may be disrupted by RLS. (*J Cardiac Fail 2019;25:837−842*)

Key Words: Restless legs syndrome, heart failure, sleep quality, quality of life, sleep.

Although treatments and care systems for heart failure (HF) have recently advanced, the quality of life (QoL) of patients with HF remains poor, and some reports suggest that poor health-related QoL in patients with HF was associated with poor clinical outcomes.[1] Although health-related QoL is an important target in treatment of patients with HF, effective treatments to improve health-related QoL have not been established. Patients with HF have various symptoms such as sleeplessness and difficulty falling asleep, and these may be major contributors of poor health-related QoL.[2] Thus, patients with HF must identify conditions that can affect their sleep and health-related QoL. One such condition may be restless legs syndrome (RLS).

RLS is a neurological disorder characterized by symptoms of unpleasant leg sensations and the urge to move the legs. As the symptoms usually appear at night, they may disrupt sleep and QoL.[3] The prevalence of RLS in the general population was reported to be ∼2%−5% in Japan[4] and

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5%−10% in Western countries.[3] RLS has also been suggested as a risk factor of HF, possibly through the disruption of patient sleep, sympathetic nerve overactivity, and enhanced vascular resistance.[5] However, little is known regarding the prevalence and clinical impact of RLS in patients with HF. Thus, we conducted an exploratory study to evaluate the prevalence and effects of RLS on sleep and health-related QoL in patients with HF.

Methods

Study Participants

This study was a prospective multicenter study conducted at the Juntendo University Hospital and Juntendo Tokyo Koto Geriatric Medical Center. We enrolled consecutive patients with HF from June 2015 to December 2016. The inclusion criteria were patients with HF aged ≥20 years, who had stable clinical status evidenced by the absence of acute exacerbations of dyspnea and could communicate verbally and complete questionnaires by themselves. The exclusion criteria were psychiatric and neurodegenerative diseases, treatment for sleep-disordered breathing (SDB), and dialysis. The study protocol was approved by the review board of the hospitals. Written informed consent was obtained from all the patients.

All the participants were interviewed face-to-face by trained physicians blinded to the results of other assessments. RLS was diagnosed based on the 2012 International RLS Study Group (IRLSSG) criteria and a positive answer to all 5 interview questions.[6] The patients were divided into 2 groups according to the presence or absence of RLS.

Data Collection

The Epworth Sleepiness Scale (ESS) is used for evaluating subjective sleepiness, and higher ESS scores indicate greater sleepiness.[7] The Pittsburgh Sleep Quality Index (PSQI) is used for assessing subjective sleep quality, and a higher global PSQI score indicates worse sleep quality.[8] The 8-item Short Form Health Survey (SF-8) is used for evaluating health-related QoL. Two aggregate scores, the physical component summary score (PCS) and mental component summary score (MCS), were derived from 8 subscales, and higher scores represent better health.[9]

Blood pressure (BP) and heart rate measurements and blood sampling were performed in the morning on the day of RLS assessments. Echocardiography was performed in accordance with the guidelines.[10] Nocturnal pulse oximetry was performed a night before RLS assessment to examine the number of desaturations of ≥3%/h (ie, 3% oxygen desaturation index [ODI]).

Statistical Analyses

Continuous variables were presented as mean ± standard deviation or median (interquartile range), and were compared using the Student t test or Mann−Whitney U test. Effect sizes were assessed using Cohen's d. Categorical data are shown as numbers and percentages, and were compared using the χ^2 or Fisher exact test. Simple and multiple linear regression analyses were performed to identify factors associated with ESS, PSQI scores, and component summary scores, including age; sex; body mass index; implantable cardioverter-defibrillator use; cardiac resynchronization therapy; diabetes; current smokers; previous history of hospitalization for acute decompensated HF (ADHF); atrial fibrillation; systolic BP; heart rate; left ventricular ejection fraction; E/e'; levels of hemoglobin, iron, ferritin, albumin, sodium, potassium, high- and low-density lipoprotein cholesterol, triglycerides, C-reactive protein (CRP), B-type natriuretic peptide (BNP), and estimated glomerular filtration rate; use of a beta-blocker, angiotensin-converting enzyme inhibitor and/or angiotensin II receptor blocker, aldosterone blocker, loop diuretics, or oral inotropes; and 3%ODI as independent variables. Variables with P values $< .10$ in the simple linear regression analyses were entered into a mixed stepwise multiple linear regression analysis ($P < .10$ for inclusion and $P < .05$ for exclusion). The natural log-transformed values were used for iron, ferritin, CRP, and BNP levels, and 3%ODI because they were skewed. All P values were two-tailed and considered significant if $<.05$. Statistical analyses were performed using JMP v12.0 (SAS Institute, Cary, NC).

Results

Among the 133 eligible patients, 18 had RLS (13.6%; 95% confidence interval, 8.7−20.4). The characteristics of the patients with and without RLS are shown in Table 1.

No significant difference in ESS score was found between the patients with and without RLS (5.7±5.0 and 6.6±3.9, $P = .480$, d=0.18; Fig. 1A), and RLS was not associated with ESS scores (β=−0.061, $P = .480$). PSQI scores were significantly higher in the patients with RLS than in those without RLS (8.0±3.2 and 5.9±3.3, $P = .015$, d=0.64; Fig. 1B). In the stepwise multiple linear regression analysis, RLS and previous history of hospitalization for ADHF positively correlated with the PSQI scores (Table 2). In terms of health-related QoL, general health, physical function scores were significantly lower in the patients with RLS than in those without RLS (Fig. 1C). The PCS was significantly lower in the patients with RLS than in those without (35.6±6.5 and 40.7±9.5, $P = .031$, d=0.56). However, no significant difference in MCS was observed between the 2 groups (44.8±11.3 and 47.0±8.3, $P = .329$, d=0.25). In the stepwise multiple linear regression analysis, previous history of

Table 1. Baseline Characteristics of the Patients

	No RLS (n=115)	RLS (n=18)	*P*
Age, y	70.0±12.2	62.4±13.4	.017
Males, n (%)	82 (71.3)	14 (77.8)	.569
BMI, kg/m^2	23.2±4.5	23.4±5.1	.915
ICD, n (%)	3 (2.63)	0 (0)	.345
CRT, n (%)	8 (7.0)	0 (0)	.119
Diabetes, n (%)	38 (33.6)	5 (27.8)	.619
Current smoker, n (%)	13 (11.6)	1 (5.6)	.407
Previous history of ADHF hospitalization, n (%)	77 (67.0)	12 (66.7)	.981
Atrial fibrillation, n (%)	37 (32.5)	6 (33.3)	.941
Systolic BP, mmHg	125.2±23.4	132.8±36.5	.245
Diastolic BP, mmHg	71.4±18.0	76.5±21.2	.277
Heart rate, per min	69.9±18.2	66.9±11.4	.395
Ejection fraction, %	48.6±18.0	52.1±18.0	.441
E/*e*′	17.0±10.4	14.2±6.1	.283
Hemoglobin, g/dL	12.5±2.4	12.3±2.5	.693
Fe, μg/dL	71.0 [47.5]	79.5 [53.0]	.386
Ferritin, ng/mL	126 [208.9]	83 [114.5]	.185
Albumin, g/dL	3.61±0.6	3.61±0.6	.991
Sodium, mmol/L	140.0±3.3	140.2±2.7	.815
Potassium, mmol/L	4.20±0.5	4.21±0.6	.229
eGFR, mL/min/1.73 m^2	56.2±23.6	65.2±30.3	.152
Triglycerides, mg/dL	101.1±47.9	97.4±52.5	.769
HDL-cholesterol, mg/dL	44.0±15.7	45.0±19.3	.810
LDL-cholesterol, mg/dL	94.7±28.9	93.7±34.7	.900
BNP, pg/dL	306.4 [519.4]	126.6 [383.9]	.203
CRP, mg/dL	0.29 [0.6]	0.20 [0.33]	.315
ACE-I/ARB, %	80 (70.2)	11 (61.1)	.448
β-blocker, %	84 (74.3)	15 (83.3)	.392
Loop diuretics, %	87 (75.7)	14 (77.8)	.843
Aldosterone blocker, %	56 (48.7)	9 (50.0)	.918
Oral inotropes, %	9 (7.8)	1 (5.6)	.724
3%ODI, per hour	17.4 [31.9]	18.8 [38]	.491

Data are expressed as mean±SD or median (interquartile range) for continuous variables and numbers (%) for nominal variables.

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; CRT, cardiac resynchronized therapy; *E*/*e*′, early diastolic peak LV pulse Doppler inflow velocities (*E*)/peak early diastolic mitral septum and lateral annular tissue Doppler velocities (*e*′); eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; ICD, implantable cardioverter-defibrillator; LDL, low-density lipoprotein.

hospitalization for ADHF, *E*/*e*′, and RLS were negatively and age was positively associated with the PCS scores (Table 2). In addition, no significant association was observed between RLS and MCS (Table 2).

Discussion

The prevalence of RLS in the adult general population was reported to be 2%−5% in Asian populations.[4] In our previous study, we reported that the prevalence of RLS in patients with coronary artery disease (CAD) was 8.0%.[11] Although the prevalence of RLS seems to be greater in patients with CAD than in general Asian populations, the prevalence of RLS was greater than that in our study (13.5% vs 8.0%).[11] One study in which the 2012 IRLSSG criteria were not used to identify RLS reported that only 4% of patients have a symptom suggesting RLS.[12] In another study, RLS was found in 39.5% of HF patients. However, all the patients enrolled in that study had HF with anemia and chronic renal failure,[13] both of which are common risk factors of RLS.[14] Thus, the 2 previous studies may not reflect the real prevalence of RLS in patients with HF.

The reasons for the high prevalence of RLS in patients with HF remain uncertain. RLS can be a risk factor of HF possibly through the disruption of patient sleep, sympathetic nerve overactivity, and enhanced vascular resistance[5]; thus, the prevalence of RLS is high in HF patients. Comorbidities of HF such as renal failure and anemia even at a subclinical level can also contribute to the high prevalence of RLS in patients with HF.[14] However, neither renal function nor anemic status differed between the patients with and without RLS in this study. Increased sympathetic activity was also suggested to downregulate the dopamine receptors and contribute to RLS.[11,14] Furthermore, as previously reported, severe periodic leg movement (PLM) was highly prevalent in patients with ADHF (ie, 22%) and RLS and PLM often coexist.[15] Although we did not have data regarding PLM in the present study, coexisting PLM may play some role. Further study is needed to clarify this possible relationship.

RLS can impair sleep quality and health-related QoL.[3] Although the previous studies were not conducted in HF-specific patient populations, their results are consistent with ours. Such disruptions of sleep and health-related QoL in association with RLS are important in patients with HF because several studies suggested that patients with HF are likely to have poor sleep quality and health-related QoL, and because both are associated with worse clinical outcomes in patients with HF.[1,2]

Several limitations should be recognized when assessing the findings of the present study. The major limitation of this study is the lack of overnight polysomnography, the gold standard assessment tool for SDB and PLM. Second, the sample size of this study is relatively small. Third, although we considered confounding factors, we cannot exclude the possibility that unmeasured factors may explain some of our findings. Finally, although we elucidated that RLS was independently associated with poor sleep quality and the physical component of QoL, whether RLS is a factor associated with impaired outcome and a therapeutic target for improving sleep quality and QoL in patients with HF remains to be elucidated.

Conclusion

RLS is prevalent in patients with HF and should be recognized as an important clinical issue because it disrupts sleep, which consequently impairs QoL in patients with HF.

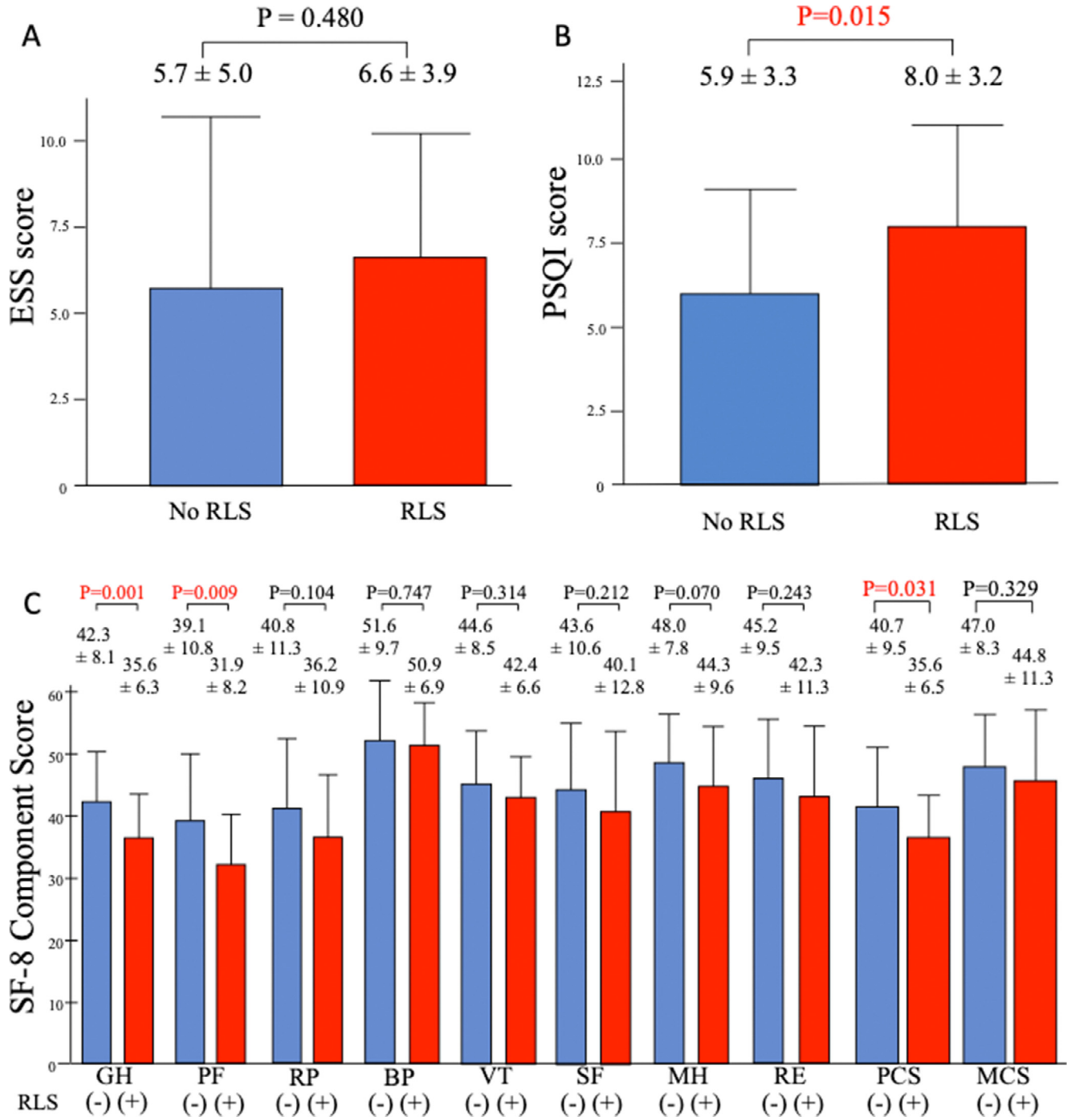

Figure 1. (**A**) Comparisons of ESS scores between patients with and without RLS. ESS scores were not significantly different between the patients with and without RLS ($P = .480$). Values are mean±SD. (**B**) Comparisons of PSQI scores between the patients with and without RLS. PSQI scores were significantly higher in the patients with RLS than in those without RLS ($P = .015$). Values are mean±SD. (**C**) Comparisons of SF-8 subscale and component summary scores between the patients with and without RLS. GH and PF were significantly lower in the patients with RLS than in those without RLS ($P = .001$ and $P = .009$, respectively). Although MCS was not significantly different between the 2 groups ($P = .329$), PCS was significantly lower in the patients with RLS ($P = .031$). Values are mean and ±SD. ESS, Epworth Sleepiness Scale; GH, general health perception; PF, physical functioning; RP, role-physical; BP, bodily pain; VT, vitality; SF, social functioning; MH, mental health; RE, role-emotional.

Table 2. Simple and Stepwise Multiple Linear Regression Analyses of PSQI, PCS, and MCS

	PSQI				PCS				MCS			
	Simple		Multiple		Simple		Multiple		Simple		Multiple	
	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*
Age	—	—	—	—	0.219	.014	0.224	0.012	—	—	—	—
BMI	—	—	—	—	—	—	—	—	0.195	0.027	0.198	.021
Diabetes; yes	—	—	—	—	−0.142	.074	—	—	—	—	—	—
Previous history of hospitalization for ADHF; yes	0.170	0.029	0.192	0.024	−0.222	.005	−0.184	0.040	—	—	—	—
Atrial fibrillation; yes	—	—	—	—	—	—	—	—	−0.150	0.059	—	—
Systolic BP	—	—	—	—	—	—	—	—	0.188	0.034	—	—
Heart rate	—	—	—	—	—	—	—	—	−0.174	0.050	−0.255	.003
E/*e*′	—	—	—	—	−0.205	.026	−0.201	0.026	—	—	—	—
Sodium	—	—	—	—	—	—	—	—	0.288	0.001	0.287	<.001
Triglycerides	—	—	—	—	—	—	—	—	0.178	0.045	—	—
HDL cholesterol	−0.145	0.098	—	—	—	—	—	—	0.149	0.095	—	—
ACE-I/ARB; yes	0.159	0.055	—	—	—	—	—	—	—	—	—	—
β-blocker; yes	0.159	0.055	—	—	—	—	—	—	—	—	—	—
Loop diuretics; yes	—	—	—	—	—	—	—	—	−0.158	0.060	—	—
Aldosterone blockers; yes	—	—	—	—	—	—	—	—	−0.162	0.030	—	—
RLS; yes	0.230	0.018	0.211	0.014	−0.215	.028	−0.177	0.045	—	—	—	—

In the simple linear regression analysis, only variables with $P < .10$ are shown. In the stepwise multiple linear regression analysis, only variables in the final models are shown.

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; BMI, body mass index; *E*/*e*′, early diastolic peak LV pulse Doppler inflow velocities (*E*)/peak early diastolic mitral septum and lateral annular tissue Doppler velocities (*e*′); HDL, high-density lipoprotein.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2019.08.022.

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