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Frequent Periodic Leg Movement During Sleep Is Associated With Left Ventricular Hypertrophy and Adverse Cardiovascular Outcomes

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Abstract

Background—Sleep disturbance caused by obstructive sleep apnea is recognized as a contributing factor to adverse cardiovascular outcomes. However, the effect of restless legs syndrome (RLS), another common cause of fragmented sleep, on cardiac structure, function and long-term outcomes is not known. We assessed the effect of frequent leg movement during sleep on cardiac structure and outcomes in patients with RLS.

Methods—In our retrospective study, RLS patients referred for polysomnography were divided into those with frequent (periodic movement index >35/hour) and infrequent (<35/hour) leg movement during sleep. Long-term outcomes were determined using Kaplan-Meier and logistic regression models.

Results—Of 584 patients, 47% had periodic movement index >35/hour. Despite similarly preserved left ventricular ejection fraction, the group with periodic movement index >35/hour had significantly higher left ventricular mass and mass index reflective of left ventricular hypertrophy (LVH). There were no significant baseline differences in the proportion of patients with hypertension, diabetes, hyperlipidemia, prior myocardial infarction, stroke or heart failure or use of antihypertensive medications between the groups. Patients with frequent periodic movement index were older, predominantly male and had more prevalent coronary artery disease and atrial fibrillation. However, on multivariate analysis, periodic movement index >35/hour remained the strongest predictor for LVH (odds ratio 2.45, 95% confidence interval 1.67–3.59, $P<0.001$).

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Advanced age, female sex and apnea-hypopnea index were other predictors for LVH. Patients with periodic movement index >35/hour had significantly higher heart failure and mortality rates over 33-month median follow-up.

Conclusions—Frequent periodic leg movement during sleep is an independent predictor of severe LVH and associated with increased cardiovascular morbidity and mortality.

Keywords

Left ventricular hypertrophy; Periodic limb movement disorder; Restless legs syndrome; Sleep; Sleep apnea

INTRODUCTION

Sleep disturbance is increasingly recognized as a predisposing factor for cardiovascular dysfunction contributing to increased morbidity and mortality, particularly in the elderly.^{1,2} The relationship between obstructive sleep apnea and cardiovascular disease has been well recognized.^{1,3} However, the effect of restless legs syndrome (RLS),⁴ another common cause of fragmented sleep⁵ that affects more than 12 million Americans,⁶ on cardiac structure and function is not known. More than 80% of patients with RLS have periodic leg movement,⁷ particularly during sleep (PLMS).⁸ This movement sometimes occurs throughout the night, resulting in repeated arousals, sleep fragmentation, and increased sympathetic activity contributing to mental and physical exhaustion with adverse effects on body functions.^{5,9} Fluctuations in blood pressure, heart rate, and heart rate variability have been well described as occurring in association with PLMS.^{9–11} Although higher prevalences of coronary artery disease, heart failure, and stroke were reported in RLS patients with severe symptoms determined by a self-administered questionnaire,⁹ the effect of severity of PLMS on cardiac performance and long-term outcome has not been systematically assessed. The objective of this study was to define the impact of high PLMS frequency – quantified as periodic movement index during polysomnography – on cardiac structure and function and its ability to independently predict adverse cardiovascular outcomes.

METHODS

Patient Population

All patients with an indication for polysomnography due to sleep disorder and a clinical suspicion of RLS^{4,7} as assessed from their medical records (ICD-9 code 333.94) between January 2000 and August 2007 were included in the study. Since clinical diagnosis of RLS requires strict criteria and cannot be assessed from a retrospective review of medical records, the study focused on objective documentation of the severity of periodic leg movements during sleep on overnight polysomnography. Those with a baseline echocardiogram performed at Mayo Clinic, Rochester, MN, within six months prior to polysomnography were included in the study. Both polysomnographic and echocardiographic studies were performed at the state-of-the-art laboratories at Mayo Clinic Rochester, and the data was interpreted by physicians with expertise in sleep medicine and cardiac echocardiography. Patients with end-stage renal disease, severe neuropathy, Parkinson's disease, and Class III or IV heart failure were excluded. Particular attention was

paid to confirm diagnosis of hypertension because of its impact on cardiac structure and function. Individual blood pressure recording documenting hypertension could not be obtained on every patient; however, all patient records were manually reviewed and the diagnosis of hypertension was accepted when confirmed by the primary care physician or cardiologist's note at three separate occasions and established by the use of medications primarily directed at blood pressure control. The study was approved by the Mayo Clinic Institutional Review Board.

Polysomnography

All participants underwent sleep study at the sleep laboratory using a computerized polysomnographic device with simultaneous noninvasive acquisition of electrocardiogram, electroencephalogram, electrooculogram, submental and leg electromyogram, nasal and oral airflow, chest and abdominal respiratory movement, snoring microphone, and body position. Presence of PLMS was defined according to the American Sleep Disorders Association criteria as leg movement that is otherwise not explained by insomnia or hypersomnia and after excluding other causes of sleep disturbances, including breathing-related sleep disturbance.¹² PLMS were scored as bursts of muscle activity on the anterior tibialis electromyogram of 0.5–5.0 seconds duration, >25% of the amplitude of a voluntary movement, and as part of a series of 4 movements separated by 5–90 seconds, only if unrelated to voluntary or breathing-related disturbance.¹² PLMS frequency per hour of total sleep time were quantified as periodic movement index.¹² PLMS were classified as frequent if periodic movement index was >35 movements/hour, a value we obtained from a receiver operating characteristic curve plotting periodic movement index against the echocardiographic finding of LVH (area under the curve: 0.703, 95% confidence interval [CI] 0.664–0.740; $P < 0.001$). PLMS followed by an arousal from sleep were considered relevant in the generation of sleep disturbances and classified as movement-related arousal index, calculated as the number of PLMS-related arousals/hour of total sleep time. Obstructive and central apneas were defined by a reduction in airflow to <20% of baseline lasting for 10 seconds, with or without respiratory effort, respectively, and hypopnea as a reduction in airflow by 50% for 10 seconds accompanied by 4% oxygen desaturation or arousal or both.¹ Apnea-hypopnea index was defined as the sum of apneas and hypopneas per hour of total sleep time.¹³ Arousals due to a breathing-related incident were quantified per hour of total sleep time as breathing-related arousal index. The overall arousal index per hour of total sleep time was calculated as the sum of movement-related arousal index and breathing-related arousal index.

Echocardiography

M-mode and two-dimensional echocardiographic studies were performed from standard transthoracic windows using Acuson Sequoia™ (Siemens Medical Solutions, Malvern, PA) and Vivid 7 (GE Healthcare, Waukesha, WI) equipment, according to the recommendations of the American Society of Echocardiography (ASE).^{14,15} Echocardiographic studies were performed by experienced sonographers and interpreted by cardiologists with expertise in echocardiography at Mayo Clinic Rochester. LV dimensions, including diameters and end-diastolic thickness of the interventricular septum and posterior wall, were measured from M-mode images in the standard parasternal long-axis view. LV mass was calculated from LV

linear dimensions using the Devereux formula and indexed for body surface area.^{14,16} Relative wall thickness was obtained using the formula ($2 \times$ posterior wall thickness in diastole)/LV diastolic dimensions. Relative wall thickness was categorized as concentric if >0.42 or eccentric if ≤ 0.42 .¹⁴ LVH was defined according to criteria outlined by the ASE,¹⁴ with left ventricular [LV] mass index (i.e. LV mass adjusted for body surface area) >88 g/m² for women and >102 g/m² for men by two-dimensional method, and LV mass >150 g for women and >200 g for men. Moderate-to-severe LVH was determined in a sex-specific manner as per ASE guidelines (LV mass index females >100 g/m² and males >116 g/m²).¹⁴ Left ventricular ejection fraction (LVEF) was calculated using Simpson's rule,¹⁴ and LV diastolic function was evaluated using early (E-wave) and late (A-wave) diastolic transmitral velocities, the E/A ratio, and the E-deceleration time obtained from the spectral pulsed-wave Doppler recordings at the tip of mitral valve leaflets in the apical four-chamber view.¹⁷ Apical four-chamber and two-chamber views were used to determine left atrial area and length. Left atrial volume was calculated as per ASE criteria using the algorithm ($0.85 \times$ four-chamber left atrial area $\times$ two-chamber or apical long-axis left atrial area)/average of the two lengths obtained from orthogonal views. Volume was then indexed to body surface area.¹⁴

Follow-up

Patients were divided into two groups based on the frequency of PLMS: periodic movement index >35 /hour were classified as frequent and periodic movement index ≤ 35 /hour as infrequent. Follow-up information was obtained from a comprehensive medical record system. Baseline clinical, echocardiographic and polysomnographic parameters were compared between the two groups to correlate the severity of PLMS to cardiac structural and functional alterations. Differences in cardiovascular endpoints, including incident heart failure, recurrent (≥ 2) cardiac hospitalization and death, were compared between the two PLMS groups. Cardiac hospitalization was defined as hospital admission due to any of the following primary diagnoses: heart failure, dysrhythmia and myocardial ischemia or infarction. Predictors of LVH and long-term outcomes were also determined.

Statistical Analysis

The differences between patient groups were tested using Wilcoxon rank-sum test for continuous variables and chi-square test or Fisher's exact test for categorical variables. Continuous variables were summarized as median $\pm$ interquartile range; discrete variables were described as number and percentage. Predictors for outcomes were identified using logistic regression analysis to calculate odds ratio with 95% CI and to examine the effect of each variable on adverse cardiovascular events. All values were two-tailed, and a P-value <0.05 was considered statistically significant. Survival of patients free of heart failure, death and rehospitalization was estimated by the Kaplan-Meier method and differences in survival compared by log-rank test. All statistical analyses were performed with SAS version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

Patient Population

Of 584 RLS patients referred for polysomnography who also had a baseline echocardiogram, 274 (47%) had a periodic movement index >35 /hour. Table 1 summarizes baseline characteristics of the study population. No significant differences were present between the groups in the proportion of patients with prior diagnoses of hypertension, use of antihypertensives, diabetes mellitus, hyperlipidemia, prior myocardial infarction, heart failure, stroke or abnormal LVEF at the time of polysomnography. Patients with higher periodic movement index were older ($P<0.001$), predominantly male ($P<0.001$) with a lower body mass index ($P=0.02$) and had higher prevalences of coronary artery disease ($P<0.01$) and atrial fibrillation ($P<0.01$).

Differences in Polysomnographic Variables

Results of the overnight polysomnographic parameters are summarized in Table 1. A higher proportion of patients with frequent PLMS had shorter sleep time (<4 hours) compared to those with infrequent PLMS ($P=0.001$), with a marked increase in the number of arousals related to movement ($P=0.001$). Mean apnea-hypopnea index was also higher in the periodic movement index >35 /hour, however, breathing-related arousals were more common in the infrequent periodic movement index group ($P=0.001$).

Cardiac Structural and Functional Differences

The effect of frequent PLMS on cardiac structure and function was determined by echocardiography. Despite a similarly preserved LVEF between those with frequent and infrequent PLMS ($P=0.12$), significant differences existed in LV mass ($P<0.001$) and LV mass index ($P<0.001$) as well as interventricular septal wall and posterior wall thickness ($P<0.001$), as summarized in Table 2. The proportion of patients with LVH and moderate-to-severe LVH was significantly higher in those with frequent PLMS ($P<0.001$). Internal LV end-diastolic and end-systolic dimensions were within the normal range of the population¹⁴ but significantly higher in the periodic movement index >35 /hour group ($P<0.001$). The overall pattern of ventricular geometry in patients with hypertrophy indicated a greater percentage of eccentric LVH in the periodic movement index >35 /hr group ($P<0.001$), whereas the periodic movement index ≤ 35 /hour group had a predominantly concentric form of hypertrophy ($P<0.001$) (Fig. 1). A trend towards a higher prevalence of patients with concentric remodeling also was observed in the periodic movement index ≤ 35 /hour group (27% vs. 20% in the frequent movement group, $P=0.08$). In patients with frequent PLMS, the relative wall thickness was 0.43 ± 0.08 compared with 0.44 ± 0.09 in patients with infrequent PLMS. Both groups had increased left atrial volume index, but the magnitude of atrial enlargement was significantly higher in the frequent periodic movement index group ($P<0.001$), which also had a higher prevalence of atrial fibrillation (Table 1). There were no significant differences between both groups in patients with permanent atrial fibrillation (5 in frequent vs. 4 in infrequent periodic movement index group) at the time of the echocardiogram.

Predictors of Left Ventricular Hypertrophy

Univariate and multivariate predictors for moderate-to-severe LVH in RLS patients as well as odds ratios, 95% CI and P-values are summarized in Table 3. Significant predictors of moderate-to-severe LVH on univariate analysis were periodic movement index >35/hour, total sleep time <4 hours, atrial fibrillation, age, and apnea-hypopnea index. After correction for age, sex, and other risk factors for hypertrophy by logistic regression, periodic movement index >35/hour remained the strongest independent predictor of LVH severity, with odds ratio of 2.45 (95% CI 1.67–3.58, $P<0.001$). Age, female sex, and apnea-hypopnea index were also independently predictive of severe LVH.

Clinical Outcomes

To determine the prognostic significance of frequent PLMS as a risk factor for adverse cardiovascular outcomes, incident HF, rehospitalization, and mortality were determined over a median 33-month (interquartile range 16–50) follow-up. There was a significantly higher risk of heart failure [102 (37%) vs. 83 (27%), $P=0.02$] and mortality [53 (19%) vs. 37 (12%), $P=0.04$] in patients with periodic movement index >35/hour compared to those with periodic movement index ≤35/hour (Fig. 2). There was no difference in the outcome of recurrent cardiac hospitalization between both groups [72 (26%) vs. 70 (23%), $P=0.29$]. On logistic regression analysis, the risk of incident heart failure was 1.6-fold [odds ratio 1.62, 95% CI 1.14–2.30; $P=0.007$] and mortality 1.8-fold [odds ratio 1.77, 95% CI 1.12–2.79; $P=0.014$] higher in the periodic movement index >35/hour group.

DISCUSSION

The main finding of our study is the recognition that frequent PLMS in patients with RLS referred for overnight polysomnography is an independent risk factor for the presence and severity of LVH and is associated with increased incidence of heart failure and mortality independent of other risk factors for cardiovascular disease.

RLS is one of the most common neurological conditions⁵ that increases with advancing age and is diagnosed clinically based on four essential criteria as outlined by the International Restless Legs Syndrome Study Group: a desire to move the limbs, often associated with paresthesias or dysesthesias; symptoms that are worse or present only during rest and are partially or temporarily relieved by activity; motor restlessness; and worsening of symptoms at rest or nocturnally.⁷ Despite a prevalence of 5–18% in the adult population,^{7,8} RLS is considered “the most common disorder you never heard of”^{6,18} and continues to be ignored by healthcare providers, mainly due to the lack of objective evidence regarding its prognostic value in determining clinical outcomes. Disrupted sleep is the most frequent reason RLS patients seek medical assistance, with 82–89% of patients exhibiting PLMS that results in repeated awakenings.^{19,20} Although an association between RLS and cardiovascular disease has been previously described,⁹ with a higher prevalence of coronary artery disease, heart failure, and stroke in those with greater frequency of RLS symptoms as determined by a self-administered questionnaire, no quantitative assessment of the severity of PLMS on cardiac structure and function or cardiovascular events has been reported. Additionally, the accuracy of a questionnaire defining severity of RLS is arguable and, in

this regard, our use of PLMS, which has been described as an endophenotype for RLS²¹ that can be objectively quantitated, provides a more accurate reflection of RLS severity. In this report, we provide evidence for a strong association between periodic movement index – a tangible measure of PLMS severity – and cardiac hypertrophy by echocardiogram, with a greater than twofold increased risk for LVH, and identify periodic movement index >35/hour as a novel marker for risk stratification of RLS patients.

LVH is a known risk factor for adverse cardiovascular outcomes.^{22–26} A twofold higher risk for the development of heart failure has been reported in patients with LVH compared to nonhypertrophic patients in the Framingham Heart Study population.²⁴ An association between increased LV mass and cardiovascular mortality has been repeatedly demonstrated.^{23–25} Since LVH can be regressed with appropriate therapy, the rate of adverse cardiovascular events and mortality can be reduced by controlling factors promoting hypertrophy.²⁷ Frequent PLMS and fragmented sleep, as demonstrated in our study, may serve as an early risk predictor of cardiovascular events and allow identification of high-risk individuals who may benefit from closer monitoring and aggressive management to avert adverse cardiovascular outcomes.

The mechanism for the development of LVH and how it relates to RLS or other sleep-related disorders is not fully understood.¹ The focus of our study was to assess the relationship between frequent PLMS and adverse cardiac outcomes; mechanistic bases for such an association are outside the scope of this retrospective study. Hypertrophic remodeling is a complex process that involves activation of several signaling pathways triggered by enhanced cardiac metabolic demand due to a variety of stimuli, such as myocardial wall stress caused by pressure or volume overload, neurohumoral activation, oxidative stress, or altered calcium homeostasis.²² Disrupted sleep associated with sleep-disordered breathing, particularly obstructive sleep apnea, leads to increased sympathetic activity and has been recognized as a risk factor for hypertension^{13,28,29} and LVH,³⁰ which predispose to cardiac electrical and mechanical dysfunction.³¹ Frequent arousals from sleep due to respiratory events results in elevated catecholamines, a known modulatory factor contributing to LVH.^{30,32–34} Similar autonomic imbalances with oscillations in sympathetic activity and vagal tone has been described with PLMS and, over the long term, could result in cardiac structural and functional alterations. Enhanced sympathetic activation during sleep is reported to be intrinsically related to the pathophysiology of the PLMS and not merely secondary to leg movement, as the magnitude of the sympathetic activation in these patients far exceeds that observed with isolated leg movement or respiratory-related leg movement during sleep and correlates with electromyographic activity.³⁵ This is also suggested by the observation that age-related dysfunction of the descending dopaminergic pathways can contribute to PLMS through an increase in sympathetic drive.³⁶ In patients with RLS, oscillations in sympathetic activity are important determinants of blood pressure and chronotropic responses during leg movements in sleep,^{10,37} leading to nocturnal hypertension¹¹ and cardiac acceleration,^{38,39} factors that can contribute to LVH by their effect on increasing cardiac metabolic demand or through a growth-promoting effect on cardiomyocytes.^{40,41} Since a circadian pattern of symptoms that peak nocturnally is common for patients with RLS,⁵ an altered neurohumoral milieu with heightened sympathetic tone due to frequent sleep arousals⁹ could contribute to severe LVH and

adverse cardiovascular events,^{22–26,42} particularly in the elderly, females, and those with concomitant sleep apnea, other independent predictors of LVH identified in our study. Overall, a chronic state of heightened sympathetic activity or absence of normal nocturnal dip in such activity in susceptible patients with frequent PLMS or obstructive sleep apnea may increase predisposition to adverse cardiac remodeling and cardiovascular events. This is supported by our findings that both periodic movement index >35/hour and apnea-hypopnea index were independently associated with LVH. While apnea-hypopnea index independently predicted LVH (odds ratio 1.01; 95% CI 1.01–1.02, $p=0.004$), periodic movement index remained the strongest independent predictor (odds ratio 2.45; 95% CI 1.67–3.59, $p<0.001$) in our multivariate logistic regression model, even after controlling for apnea-hypopnea index and hypertension in the model. Patients with periodic movement index >35/hour had a predominantly eccentric form of LVH.¹⁴ This is suggestive of mixed volume-induced and pressure overload-induced ventricular remodeling, which is different from the pressure-overload pattern of ventricular remodeling observed in patients with obstructive sleep apnea, obesity, hypertension and advanced age that predominantly results in a concentric form of LVH and suggests a different remodeling mechanism than in those with obstructive sleep apnea or in hypertension alone.^{43–46} Patients with frequent PLMS appear to have an enhanced sympathetic tone that may cause dynamic changes in loading conditions and cardiac workload with the absence of nocturnal dip in blood pressure and transient increases in heart rate and blood pressure as well as stroke volume and cardiac output, a condition mimicking that observed during endurance training exercise, with the heart adapting to volume and pressure overload by increasing LV internal dimensions and LV wall thickness typical of eccentric hypertrophy.⁴⁷ The exact pathophysiological mechanism underlying such changes in cardiac geometry in patients with frequent PLMS needs to be further investigated prospectively.

Our findings should be interpreted within the limitations imposed by the retrospective study design. To our knowledge, however, this is the first study demonstrating an independent effect of PLMS severity – defined objectively by polysomnography – on ventricular remodeling, which was not only statistically significant with a high odds ratio for LVH but also identified those at higher risk for incident heart failure and mortality, indicating its prognostic significance. The patient groups were well matched for the presence of factors promoting LVH, such as hypertension, use of antihypertensive medications, diabetes mellitus, prior myocardial infarction or heart failure. Individual blood pressure recording documenting hypertension could not be obtained on every patient and is a significant limitation of this retrospective study. However, the diagnosis of hypertension was ascertained from the physician's final diagnosis at three separate occasions and use of medications primarily directed at blood pressure control.

In summary, frequent PLMS in patients with RLS referred for overnight polysomnography identifies those at risk for LVH, and recognizing that periodic movement index >35/hour provides incremental prognostic information to established risk factors makes it a promising risk marker for cardiovascular events in patients with RLS. Since RLS is a common clinical disorder that affects millions of Americans, insights into clinical factors and mechanisms that promote the substrates (such as LVH)^{22–26} that increase predisposition to cardiovascular events is critical for developing strategies to reduce adverse outcomes in this population.

These findings need to be prospectively replicated in larger cohorts, and further research is warranted to establish whether control of frequent PLMS by medication decreases predisposition to LVH, thereby reducing the morbidity, death, and cost associated with this condition.^{48,49}

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Abbreviations

ASE	American Society of Echocardiography
CI	confidence interval
LV	left ventricular
LVEF	left ventricular ejection fraction
LVH	left ventricular hypertrophy
PLMS	periodic leg movement during sleep
RLS	restless legs syndrome

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Figure 1. Juxtaposition of periodic movement index frequency and percentage of patients with concentric or eccentric left ventricular hypertrophy (LVH).

Figure 2.

Kaplan-Meier curves for survival free of heart failure (*Panel A*) and death (*Panel B*) in patients with frequent versus infrequent periodic leg movement during sleep quantified as periodic movement index ≤ 35 /hour and >35 /hour. Odds ratios (OR), 95% confidence intervals (CI) and P-values for heart failure and death are shown in *Panel C*. *Denotes periodic movement index.

Table 1

Baseline clinical and polysomnography characteristics

Characteristic	Overall	Periodic Movement Index ≤ 35	Periodic Movement Index >35	P- value
No. (%)	584	310 (53.1%)	274 (46.9%)	
Age, years	65 (55–72)	61 (52–70)	68 (61–75)	<0.001
Female	298 (49.0%)	183 (59.0%)	103 (37.6%)	<0.001
Body mass index	33.8 $\pm$ 7.9	34.5 $\pm$ 8.2	33 $\pm$ 7.4	0.02
Body surface area	2.07 $\pm$ 0.25	2.06 $\pm$ 0.26	2.07 $\pm$ 0.24	0.65
Hypertension	399 (68.3%)	209 (67.4%)	190 (69.3%)	0.62
Diabetes	222 (38.0%)	114 (36.8%)	108 (39.4%)	0.51
Hyperlipidemia	343 (58.7%)	175 (56.5%)	168 (61.3%)	0.23
Coronary artery disease	216 (37.0%)	98 (31.6%)	118 (43.1%)	<0.01
Myocardial infarction	125 (21.4%)	68 (21.9%)	57 (20.8%)	0.74
Heart failure	93 (15.9%)	46 (14.8%)	47 (17.2%)	0.45
Atrial fibrillation	143 (24.5%)	61 (19.7%)	82 (29.9%)	<0.01
Aspirin	276 (47%)	138 (44%)	138 (51%)	0.12
ACE inhibitor/ARB	212 (36%)	104 (33%)	108 (40%)	0.27
Beta blocker	297 (51%)	149 (58%)	148 (54%)	0.11
Calcium channel blocker	134 (23%)	71 (23%)	63 (23%)	0.91
Diuretics	239 (41%)	124 (40%)	115 (42%)	0.54
Nitrates	68 (12%)	35 (11%)	33 (12%)	0.73
Periodic movement index, #/hr	32 (3–72)	3 (0–14)	76 (52–107)	<0.001
Total sleep time <240 min	419 (71.8%)	205 (66.1%)	214 (78.1%)	<0.01
Arousal index, #/hr	32 (21–51)	28 (17–46)	38 (25–56)	<0.001
Movement-related, %	14 (0–37)	2 (0–14)	32 (17–51)	<0.001
Breathing-related, %	54 (27–78)	57 (29–84)	51 (23–70)	<0.001
Apnea-hypopnea index, #/hr	9 (3–25)	6 (2–19)	12 (5–29)	<0.001

Data are expressed as median (interquartile range).

ACE, Angiotensin-converting enzyme; *ARB*, angiotensin receptor blocker.

Table 2

Echocardiographic characteristics of the PMI 35 and >35 groups

Characteristic	Overall	Periodic Movement Index 35	Periodic Movement Index >35	P-value
No. (%)	584	310 (53.1%)	274 (46.9%)	
LV ejection fraction (%)	63 (58–67)	64 (58–67)	62 (56–66)	0.12
LV mass, g	194 (163–241)	185 (153–219)	213 (174–278)	<0.001
LV mass index, g/m ²	94 (79–117)	89 (76–105)	104 (86–131)	<0.001
Septal thickness, mm	11 (10–12)	10 (10–12)	11 (10–12)	<0.001
Posterior wall thickness, mm	10 (9–12)	10 (9–11)	11 (10–12)	<0.001
LV diastolic dimension, mm	49 (46–54)	49 (45–53)	50 (47–55)	<0.001
LV systolic dimension, mm	31 (28–36)	30 (27–34)	32 (29–38)	<0.001
Left atrial volume index, cc/m ²	32 (28–39)	32 (27–36)	34 (29–44)	<0.001
LVH (gender-specific)	292 (50)	127 (41)	165 (60)	<0.001
Moderate-to-severe LVH (gender-specific)	198 (33.9%)	74 (23.9%)	124 (45.3%)	<0.001

Data are expressed as median (interquartile range). Gender-specific LVH was defined as LV mass index >88 g/m² in females and >102 g/m² in males. Moderate-to-severe LVH was defined as >100 g/m² in females and >116 g/m² in males.

LV, left ventricular; LVH, left ventricular hypertrophy.

Table 3

Predictors for moderate-severe left ventricular hypertrophy

Characteristic	Univariate			Multivariate		
	OR	95% CI	P-value	OR	95% CI	P-value
Age, years	1.04	1.02–1.06	<0.001	1.03	1.01–1.04	0.003
Female	1.06	0.76–1.50	0.722	1.64	1.11–2.43	0.013
Hypertension	1.37	0.94–2.00	0.102	1.11	0.73–1.69	0.605
Diabetes	0.99	0.70–1.41	0.991	0.98	0.67–1.45	0.937
Myocardial infarction	1.08	0.71–1.63	0.730	1.12	0.72–1.75	0.617
Atrial fibrillation	1.53	1.03–2.25	0.033	1.38	0.89–2.15	0.149
Total sleep time <240 min	1.60	1.07–2.38	0.021	1.03	0.66–1.61	0.896
Periodic movement index >35/hr	2.64	1.85–3.75	<0.001	2.45	1.67–3.59	<0.001
Apnea-hypopnea index, #/hr	1.01	1.01–1.02	<0.001	1.01	1.01–1.02	0.004

CI, confidence interval; *OR*, odds ratio.