

Different diagnostic criteria for periodic leg movements in patients with obstructive sleep apnea after continuous positive airway pressure titration

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Objective: Periodic leg movement in sleep (PLMS) is common among patients with obstructive sleep apnea (OSA). The PLMS frequency changes after continuous positive airway pressure (CPAP) titration. This study investigated the effects of two PLMS diagnostic criteria on PLMS prevalence and the restless leg syndrome (RLS) detection rate in patients with OSA before and after CPAP titration.

Methods: This retrospective study included patients with OSA who received polysomnography (PSG) and successful CPAP titration from December 2012 to December 2014. Their clinical variables and sleep parameters were evaluated using the PLMS diagnostic criteria: PLMS index (PLMI) ≥ 5 and ≥ 15 . PLMS prevalence and the RLS detection rate were analyzed according to the PLMI before and after CPAP.

Results: In patients with OSA with a PLMI of ≥ 5 and ≥ 15 after PSG with CPAP titration, the PLMS prevalence was 20.1% (76/378) and 4.5% (17/378), respectively, which revealed CPAP titration increased PLMI. Moreover, in terms of PLMI ≥ 5 and ≥ 15 , PSG with CPAP titration led to significantly higher PLMS prevalence than PSG alone (20.1% vs 7.1% and 4.5% vs 0.8%, respectively; both $P < 0.001$). PLMI ≥ 5 also demonstrated a higher RLS detection rate than PLMI ≥ 15 did (69.2% vs 15.4%; $P = 0.016$).

Conclusion: In patients with OSA, CPAP titration increases PLMS prevalence and the PLMI regardless of whether PLMI is ≥ 5 or ≥ 15 . The use of the current diagnostic criteria, PLMI ≥ 15 , for PLMS may lead to underestimation of PLMS prevalence and the RLS detection rate in patients with OSA.

Keywords: continuous positive airway pressure, obstructive sleep apnea, periodic leg movements in sleep, polysomnography, restless leg syndrome

Introduction

Periodic leg movement in sleep (PLMS) involves repetitive leg movement at night, which is recorded through polysomnography (PSG). Periodic leg movement (PLM) consists of ≥ 4 consecutive events of 0.5–10-second-long stereotypical leg movements (LMs) occurring at a 5–90-second interval in sleep.¹ Periodic limb movement disorder (PLMD) is characterized by the presence of PLMS accompanied by insomnia. PLMD may also be associated with daytime hypersomnia or unrefreshing sleep after the exclusion of other sleep disorders.² PLMS is frequently present in patients with restless legs syndrome (RLS). A study found that more than 80% of patients with RLS had PLMS.³ The International Restless Legs Syndrome Study Group (IRLSSG) reported that PLMS is a supportive criterion for RLS diagnosis.⁴

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Before 2005, a PLMS index (PLMI) of ≥ 5 was considered clinically significant.⁵ According to this criterion, studies reported that PLMS prevalence was 4–11% in adults⁶ and the PLMS prevalence increased with age.⁷ In 2005, the American Academy of Sleep Medicine (AASM) established the current PLMI cut-off of ≥ 15 as the PLMD criterion.⁸ However, clinically, the differences in the PLMS diagnostic criteria used may influence PLMS prevalence and the RLS detection rate.

In PSG studies, PLMS is usually concurrently noted with obstructive sleep apnea (OSA). Moreover, patients with sleep-disordered breathing may present with RLS. However, very few studies have examined PLMS prevalence and RLS detection rate in patients with OSA. A retrospective study in Canada reported PLMS in 48% of patients with OSA.⁹ Moreover, a small prospective study found that RLS occurred in 8.3% of patients with OSA in the United States.¹⁰ The occurrence and clinical relevance of patients with OSA coexisting with PLMS remain unclear.

Continuous positive airway pressure (CPAP) is the most effective therapy for OSA. Some studies have noted that administering CPAP therapy to patients with OSA may increase PLMS prevalence.¹¹ Studies also indicate that the presence of PLMS represents persistent sleep-disordered breathing.¹² By contrast, another investigation reported a decrease in the PLMI after CPAP therapy.¹³ Recent studies have suggested that OSA masks post-CPAP titration PLMS.^{14,15} Thus, PLMS prevalence and frequency in relation to CPAP titration in patients with OSA remains unclear.

The main purpose of this study was to evaluate two PLMS diagnostic criteria and their effects on PLMS prevalence and the RLS detection rate in patients with OSA before and after CPAP titration.

Methods

Participants

This retrospective study included 443 patients with an apnea–hypopnea index (AHI) of ≥ 5 . The patients underwent both baseline PSG and a second-night PSG for manual CPAP titration between December 2012 and December 2014. The patients were excluded if CPAP titration failed. Patients were also excluded if they used dopaminergic agents or antidepressants, which could affect PLMS before baseline PSG. Before data review, this study was approved by The Institutional Review Board of Chang Gung Memorial Hospital (IRB/CGMH No. 201600860B0) and the informed consent to review

their medical records was not required. Patient confidentiality was maintained as no patients' identifiers were collected and the private will be carefully protected. All research process was in accordance with the Declaration of Helsinki.

The age, gender, body mass index (BMI), neck circumference (NC), and medical history of the patients were recorded. Detailed sleep parameters were measured, including the total sleep time (TST), sleep efficiency, slow wave sleep (SWS) and rapid-eye movement (REM) percentages, mean and minimal oxyhemoglobin saturation, and mean desaturation. The daytime sleepiness severity was measured on the Epworth Sleepiness Scale (ESS).¹⁶ RLS was diagnosed according to the five clinical criteria defined by the IRLSSG in 2014.¹⁷

PSG and CPAP titration

Standard overnight PSG was performed using a computerized PSG system (N7000 Embla, Broomfield, USA). The recorded parameters were as follows: electroencephalograms (EEGs), bilateral electrooculograms (EOGs), submental and bilateral anterior tibialis electromyograms (EMGs), electrocardiograms (ECGs), the nasal and oronasal airflow (by using nasal pressure monitor and thermistor), arterial oxygen saturation (through finger probe pulse oximetry), chest and abdominal movements (through inductance plethysmography), body position, and sound intensity. Sleep stages were scored manually in 30-second epochs by using the AASM scoring criteria.¹⁸ CPAP titration was administered using AutoSet Spirit S8 (ResMed, Sydney, Australia) in the sleep laboratory on a separate night. In the CPAP titration study, manual CPAP titration was performed to determine an optimal CPAP level.¹⁹ The optimal CPAP level was defined as the lowest effective pressure to eliminate most respiratory events, including apnea, hypopnea, and snoring in all body positions and all sleep stages, particularly in the supine position and REM sleep, respectively.

Scoring

Obstructive apnea was defined as the absence of airflow for at least 10 seconds in the presence of respiratory effort, whereas central apnea was defined as the absence of airflow without concurrent respiratory effort. Hypopnea was considered when more than a 50% decrease in airflow occurred for more than 10 seconds, followed by at least 3% oxygen desaturation or EEG arousal.¹⁸ The AHI was defined as the average number of apneas and hypopneas per hour of sleep. LM caused an 8- μ V increase in the EMG voltage of the right and left anterior tibialis above the resting EMG voltage. The increase lasted

0.5–10 seconds. LM with EEG arousal was also calculated during sleep, which allowed a LM arousal index (LMAI) to be generated. LMs occurring in a wide time window from 0.5 seconds before the start of a respiratory event (apnea or hypopnea) until 0.5 seconds after its end were not counted. PLM was defined as a minimum of four consecutive LM events with a 5–90-second interval during sleep. The PLMI was scored as the number of PLM per hour of TST.²⁰ Two PLMS diagnostic criteria with a PLMI of ≥ 5 ^{3,5} and ≥ 15 ² were assessed. The RLS detection rate was defined as the percentage of patients with RLS matching the PLMS diagnostic criteria divided by the total number of patients with RLS who were diagnosed using the clinical criteria.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows (version 19.0; SPSS Inc., Chicago, IL, USA). The patient characteristics after using the PLMS diagnostic criteria (PLMI ≥ 5 and ≥ 15) are presented as a mean \pm standard deviation or number (%). The Wilcoxon signed-rank tests were used to compare the sleep parameters, AHI, and PLMI of the patients at baseline and after CPAP titration. Pearson's correlation coefficient was used to evaluate the relationship between PLMI and AHI before CPAP titration and the relationship between the increase of PLMI and the decrease of AHI after CPAP titration. McNemar's test was used to evaluate the differences in PLMS prevalence and the RLS detection rate after using PLMI ≥ 5 or 15 with PSG alone and PSG with CPAP titration. The variables associated with PLMS were evaluated through multivariate logistic regression by using PLMI ≥ 5 and 15. A *P*-value of <0.05 was considered statistically significant.

Results

Subject description

After the exclusion of 20 patients with failed CPAP titration and 45 patients with dopaminergic agent or antidepressant use, 378 patients with OSA were finally included in this study. The patients that met the PLMS diagnostic criterion of PLMI ≥ 5 or ≥ 15 at both PSG with and without CPAP titration were considered to have PLMS one time. Among the patients with PLMI ≥ 5 , 27 (7.1%) had PLMS after PSG alone and 76 (20.1%) had PLMS after PSG with CPAP titration. Among the patients with PLMI ≥ 15 , three (0.8%) had PLMS after PSG alone and 17 (4.5%) had PLMS after PSG with CPAP titration (Figure 1). The basic patient

characteristics, including the age, gender, BMI, ESS, NC, AHI, RLS, and past history are listed in Table 1. The mean age of the participants was 49.5 years, with a mean BMI of 28.5 kg/m², and 83.1% of the patients were male.

PLMI and sleep parameters after PSG with CPAP titration

In patients with PLMI ≥ 5 , the PLMI increased in 60 (78.9%) patients and decreased in the others (*n*=16, 21.1%) after CPAP titration. In patients with PLMI ≥ 15 , the PLMI increased in 15 (88.2%) patients and decreased in the others (*n*=2, 11.8%) after CPAP titration. The PLMI, AHI, and sleep parameters of the patients with PLMI ≥ 5 and ≥ 15 after PSG with CPAP titration are listed in Table 2. CPAP titration significantly improved nocturnal desaturation and sleep architecture. The TST, SWS, and REM sleep of both the groups increased. Among patients with PLMI ≥ 5 and ≥ 15 , compared with baseline PSG, CPAP titration reduced AHI (5.92 \pm 4.45 vs 55.68 \pm 25.26 and 4.61 \pm 3.00 vs 53.02 \pm 25.42, respectively; both *P*<0.001) and increased PLMI (10.09 \pm 6.98 vs 4.08 \pm 4.91, *P*<0.001 and 19.67 \pm 7.70 vs 5.96 \pm 6.59, *P*=0.002, respectively). PLMI (*r*=-0.611, *P*<0.001) was negatively correlated with AHI before CPAP and the increase of PLMI (*r*=0.426, *P*<0.001) was positively correlated with the decrease of AHI from baseline PSG to CPAP titration among OSA patients coexisting with PLMS.

PLMS prevalence and the RLS detection rate

PLMS prevalence using PLMI ≥ 5 or ≥ 15 after PSG alone and PSG with CPAP titration is listed in Table 3. PLMS prevalence after PSG with CPAP titration was significantly higher than that after PSG alone irrespective of the diagnostic criteria (PLMI ≥ 5 : 20.1% vs 7.1%; PLMI ≥ 15 : 4.5% vs 0.8%; both *P*<0.001). Moreover, different PLMS diagnostic criteria significantly affected PLMS prevalence both after PSG alone and PSG with CPAP titration.

The RLS detection rate was also influenced by the PLMS diagnostic criteria (Table 4). In total, 13 patients were diagnosed as having RLS according to the IRLSSG diagnostic criteria. Of them, seven (53.8%) and two (15.4%) had a PLMI of ≥ 5 and ≥ 15 after PSG alone, respectively; however, the results were not significant. By contrast, nine (69.2%) and two (15.4%) patients had a PLMI of ≥ 5 and ≥ 15 after PSG with CPAP titration, respectively, and the results were significant.

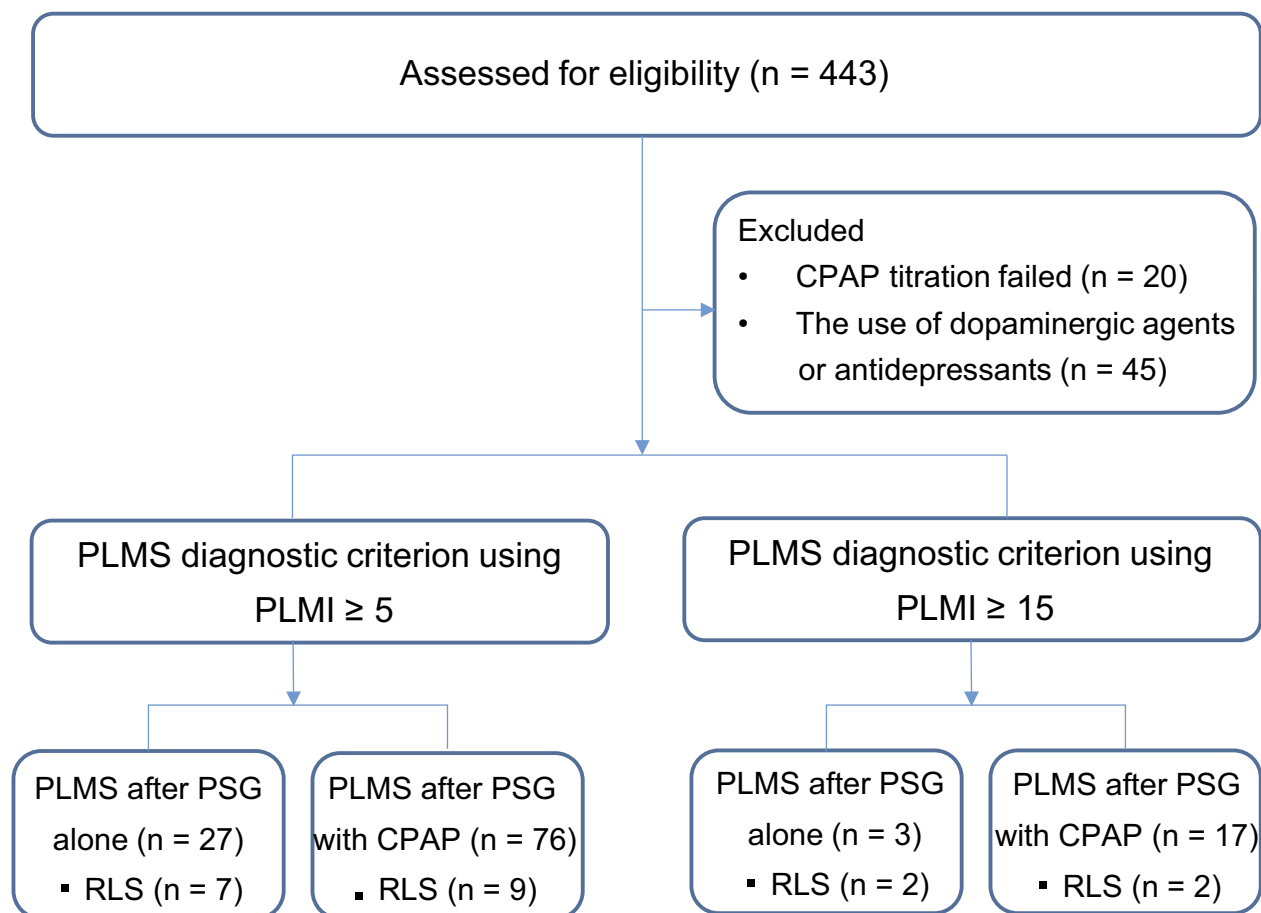


Figure 1 Study flow. In this study, 443 patients with an AHI of ≥ 5 were enrolled. These patients underwent both baseline PSG and a second-night PSG for manual CPAP titration. Among the 443 patients, 20 and 45 were excluded because of CPAP titration failure and dopaminergic agent or antidepressant use, respectively. Finally, 378 patients were included in this study. Patients with a PLMI of ≥ 5 or ≥ 15 after PSG with CPAP titration were considered to have PLMS one time. Among the patients with PLMS, 27 (7.1%) and 76 (20.1%) had a PLMI of ≥ 5 after PSG alone and PSG with CPAP titration, respectively, whereas only three (0.8%) and 17 (4.5%) had a PLMI of ≥ 15 after PSG alone and PSG with CPAP titration, respectively.

Abbreviations: AHI, apnea-hypopnea index; PSG, polysomnography; CPAP, continuous positive airway pressure; PLMI, periodic leg movement in sleep index; PLMS, periodic leg movement in sleep.

Factors associated with PLMS

The results of the multivariate logistic regression of the factors associated with PLMS after using the two diagnostic criteria (PLMI ≥ 5 and ≥ 15) are presented in Table 5. For PLMI ≥ 5 , RLS (OR: 15.101, 95% CI: 3.965–57.515; $P < 0.001$) and chronic kidney disease (OR: 3.633, 95% CI: 1.084–12.172; $P = 0.037$) were independently associated with PLMS; however, no variables were associated with PLMS for PLMI ≥ 15 .

Discussion

In a sample of consecutive patients with OSA, different PLMS diagnostic criteria and CPAP application had a significant influence on PLMS prevalence and the RLS

detection rate. The PLMS prevalence and frequency were higher when PSG was combined with CPAP titration compared with when PSG was used alone. PLMS prevalence and the RLS detection rate were higher when the PLMI was ≥ 5 than when the PLMI was ≥ 15 .

PLMS appears to be more common in patients with OSA than in the general population. PLMS prevalence in OSA patients with a PLMI of ≥ 5 was 48% in Canada⁹ and 33% in the United States.²¹ However, very few studies have examined PLMS prevalence in Asian patients with OSA. In our study, 20.1% of patients with OSA had PLMS with a PLMI of ≥ 5 . These data reveal a lower PLMS prevalence in patients with OSA in Taiwan than in Western countries. By using the PLMS diagnostic criterion of PLMI ≥ 15 , Ren et al reported that PLMS prevalence

Table 1 Patient characteristics stratified according to the PLMS diagnostic criteria (PLMI ≥ 5 and ≥ 15) after PSG with CPAP titration

Characteristics	Total (n=378)	PLMI ≥ 5 (n=76)	PLMI ≥ 15 (n=17)
Age (years)	49.53 \pm 12.57	51.61 \pm 13.20	52.65 \pm 12.05
Male	314 (83.1)	61 (80.3)	11 (64.7)
BMI (kg/m ²)	28.49 \pm 4.75	29.02 \pm 4.83	29.23 \pm 5.12
ESS	10.40 \pm 4.50	10.91 \pm 4.09	9.00 \pm 3.74
NC (cm)	39.74 \pm 3.61	40.16 \pm 4.16	39.71 \pm 4.07
AHI (events/h)	51.95 \pm 22.04	55.68 \pm 25.26	53.02 \pm 25.42
RLS	13 (3.4)	9 (11.8)	2 (11.8)
Past history			
CKD	14 (3.7)	8 (10.1)	3 (17.6)
Hypertension	162 (42.9)	44 (57.9)	11 (64.7)
DM	54 (14.3)	13 (17.1)	5 (29.4)
CVA	12 (3.2)	3 (3.9)	0 (0.0)
Heart failure	10 (2.6)	5 (6.6)	1 (5.9)

Notes: Data are presented as mean \pm SD or number (%).

Abbreviations: PLMS, periodic leg movements in sleep; PLMI, periodic leg movement index; PSG, polysomnography; CPAP, continuous positive airway pressure; BMI, body mass index; ESS, Epworth Sleepiness Scale; NC, neck circumference; AHI, apnea-hypopnea index; RLS, restless leg syndrome; CKD, chronic kidney disease; DM, diabetes mellitus; CVA, cerebrovascular accident.

Table 2 Sleep parameters of patients with a PLMI of ≥ 5 (n=76) and ≥ 15 (n=17) after PSG with CPAP titration

	PLMI ≥ 5			PLMI ≥ 15		
	Baseline PSG	CPAP titration	P	Baseline PSG	CPAP titration	P
TST (minutes)	285.20 \pm 60.38	309.61 \pm 53.94	0.004*	271.79 \pm 64.49	316.79 \pm 56.66	0.033*
SE (% of TST)	74.41 \pm 15.27	81.05 \pm 13.89	0.001*	69.88 \pm 15.99	81.78 \pm 13.66	0.055
Stage SWS (% of TST)	14.92 \pm 11.44	23.75 \pm 12.40	<0.001*	16.92 \pm 13.41	28.65 \pm 13.87	0.003*
Stage REM (% of TST)	13.59 \pm 8.48	19.95 \pm 9.49	<0.001*	10.22 \pm 8.48	18.54 \pm 7.04	0.006*
AHI (events/h)	55.68 \pm 25.26	5.92 \pm 4.45	<0.001*	53.02 \pm 25.42	4.61 \pm 3.00	<0.001*
Mean SaO ₂ (%)	91.68 \pm 3.87	94.21 \pm 1.83	<0.001*	92.56 \pm 2.06	94.31 \pm 1.16	0.001*
Minimal SaO ₂ (%)	72.26 \pm 12.14	84.21 \pm 11.04	<0.001*	71.88 \pm 11.95	85.00 \pm 6.45	0.001*
Mean desaturation (%)	8.46 \pm 4.74	4.28 \pm 1.42	<0.001*	7.54 \pm 3.49	4.08 \pm 1.47	0.001*
PLMI (events/h)	4.08 \pm 4.91	10.09 \pm 6.98	<0.001*	5.96 \pm 6.59	19.67 \pm 7.70	0.002*
LMAI (events/h)	1.18 \pm 1.81	3.64 \pm 4.60	<0.001*	1.21 \pm 2.00	6.27 \pm 7.64	0.006*

Note: Data are presented as mean \pm SD. *Significant at $P < 0.05$.

Abbreviations: PLMI, periodic leg movement index; PSG, polysomnography; CPAP, continuous positive airway pressure; TST, total sleep time; SE, sleep efficiency; SWS, slow wave sleep; REM, rapid eye movement; AHI, apnea-hypopnea index; SaO₂, oxyhemoglobin saturation; LMAI, leg movement arousal index.

Table 3 PLMS prevalence stratified according to the PLMS diagnostic criteria (PLMI ≥ 5 and ≥ 15) after PSG alone and PSG with CPAP titration

Different criteria	PLMI ≥ 5	PLMI ≥ 15	P
PLMS after PSG alone	27 (7.1)	3 (0.8)	<0.001*
PLMS after PSG with CPAP titration	76 (20.1)	17 (4.5)	<0.001*
P	<0.001*	<0.001*	

Note: Data are presented as number (%). *Significant at $P < 0.05$.

Abbreviations: PLMS, periodic leg movements in sleep; PLMI, periodic leg movement index; PSG, polysomnography; CPAP, continuous positive airway pressure.

was 20.1% in a sample of 364 patients with OSA in China.²² In our study, PLMS prevalence in patients with a PLMI of ≥ 15 was 4.5% lower than the values reported by Ren et al. However, we could not clearly elucidate the

reason for this relatively low PLMS prevalence. In a Japanese study, among patients with PLMI ≥ 15 , women had a higher PLMS prevalence than men.²³ Our study had a higher men/women ratio (4.9/1) than did the study of

Table 4 The RLS detection rate stratified according to the PLMS diagnostic criteria (PLMI ≥ 5 and ≥ 15) after PSG alone and PSG with CPAP titration

Different criteria	PLMI ≥ 5	PLMI ≥ 15	P
RLS after PSG alone	7 (53.8)	2 (15.4)	0.063
RLS after PSG with CPAP titration	9 (69.2)	2 (15.4)	0.016*

Note: Data are presented as number (%). *Significant at $P < 0.05$.

Abbreviations: RLS, restless leg syndrome; PLMS, periodic leg movements in sleep; PLMI, periodic leg movement index; PSG, polysomnography; CPAP, continuous positive airway pressure.

Table 5 Multivariate analyses of the PLMS associated characteristics for PLMI ≥ 5 and ≥ 15

Variables	PLMI ≥ 5			PLMI ≥ 15		
	OR	95% CI	P	OR	95% CI	P
Age	1.005	0.981–1.031	0.671	1.004	0.956–1.055	0.866
Male	0.570	0.255–1.276	0.171	0.293	0.079–1.087	0.066
BMI	1.000	0.922–1.085	0.993	1.031	0.897–1.185	0.668
ESS	1.039	0.978–1.103	0.217	0.931	0.829–1.045	0.225
AHI	1.012	0.998–1.025	0.086	1.005	0.980–1.030	0.700
RLS	15.101	3.965–57.515	$<0.001^*$	4.656	0.739–29.337	0.101
CKD	3.633	1.084–12.172	0.037*	4.329	0.905–20.703	0.067
Hypertension	1.749	0.975–3.139	0.061	1.902	0.621–5.823	0.260
Heart failure	2.992	0.742–12.063	0.123	1.182	0.114–12.305	0.889

Note: *Significant at $P < 0.05$.

Abbreviations: PLMS, periodic leg movements in sleep; PLMI, periodic leg movement index; BMI, body mass index; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index; RLS, restless leg syndrome; CKD, chronic kidney disease.

Ren et al (men/women =1/1). Therefore, different gender ratios may have led to the relatively low PLMS prevalence in our study.

A large multinational study that included 15,391 adults from the United States and five European countries reported the RLS prevalence was 7.2% in the general population.²⁴ However, the RLS prevalence in the Taiwanese population (1.57%) has been reported to be much lower than that in Caucasians due to genetic differences.²⁵ Our study revealed a higher RLS prevalence (3.4%) in patients with OSA than in the general population in Taiwan. Moreover, clinicians consider that PLMS occurrence is likely associated with RLS after the exclusion of other precipitating factors because PLMS is noted in most patients with RLS. In our study, we examined the RLS detection rate in PLMS patients by using two criteria and found that only two out of 13 patients with RLS had a PLMI of ≥ 15 , whereas nine out of 13 patients with RLS had a PLMI of ≥ 5 . Moreover, RLS was an independent factor when the PLMS diagnostic criterion of PLMI ≥ 5 was used, whereas no such relationship was seen for PLMI ≥ 15 . Although RLS should be diagnosed with clinical criteria, using the diagnostic criterion of PLMI ≥ 15 in clinical practice can influence the RLS detection rate. Various specialists

arrange PSG for different sleep disorders and they may not routinely evaluate RLS symptoms that would miss RLS diagnosis. In our study, PLMI ≥ 5 demonstrated a higher RLS detection rate than PLMI ≥ 15 (69.2% vs 15.4%). If PLMS is discovered through PSG with CPAP titration, it will remind the clinician to check clinical symptoms and increase the RLS detection rate. Therefore, our study want to illustrate the PLMI ≥ 5 or ≥ 15 , CPAP titration, and routinely evaluate RLS symptoms are important factors to affect the detection rate of PLMS and RLS.

Numerous studies have discussed the etiology of the change in PLMI from baseline PSG to CPAP titration, and various theories have been proposed. A 1989 study indicated that CPAP therapy can worsen PLMS.¹¹ Subsequent studies have found that the influence of CPAP on PLMI may be related to the score unmasking PLMS when respiratory events are adequately controlled by CPAP.^{14,15} By contrast, Yamashiro and Kryger reported that PLMI decreased after CPAP titration.¹³ A recent investigation hypothesized that CPAP therapy improves residual respiratory-effort related arousals, which may lead to decreased PLMI.¹⁴ In our study, only small proportion of patients were decreased PLMI and high proportional patients were increased PLMI

after CPAP titration. It means that the mechanism of the score unmasking PLMS and CPAP therapy improves residual respiratory-effort related arousals are existence in different type of OSA patients. Nevertheless, the PLMI increased from the baseline PSG to CPAP titration with a reduction in AHI in patients with both OSA and PLMS regardless of PLMI ≥ 5 or ≥ 15 . A negative correlation was demonstrated between PLMI and AHI before CPAP titration and a positive correlation was demonstrated between the increase of PLMI and the decrease of AHI after CPAP titration. Those data support that the mechanism of the score unmasking PLMS seems play more important role. These findings are consistent with that of Hedli et al,¹⁵ which indicates that respiratory events may mask PLMS, which appears with CPAP therapy. Furthermore, the current AASM scoring criteria emphasize that PLM should only be counted if the PLM is spontaneous and not caused by respiratory events.²⁰ Thus, LM events occurring within 0.5 seconds of apnea or hypopnea are considered as respiratory-related LMs and deleted during manual scoring. PLMS prevalence in patients with OSA may be underestimated in baseline PSG. The real presentation of PLMS should occur after a treatment for OSA, such as CPAP, is implemented.

The recognition and distribution of true PLMS and respiratory event-associated LMs in patients with OSA have been debated considerably. Recent studies have suggested that the elimination of all LMs associated with respiratory events is possibly an incorrect practice because the distribution of respiratory-related LMs increases mainly over an interval of -2 to 10.25 seconds around the end of respiratory events.^{26,27} Manconi et al reported that respiratory-related LMs were not augmented at the beginning or middle of respiratory events but clustered only around the end of respiratory events.²⁸ These findings suggest that the duration and distribution of respiratory-related LMs are different compared with the AASM criteria for scoring LMs. After the application of the AASM criteria, many cases of PLMS can be eliminated from the counts that have not been eliminated under CPAP therapy because of the disappearance of most respiratory events.

The analysis of hypersomnia symptoms indicated that ESS was not an independent factor associated with PLMS occurrence based on either PLMI ≥ 5 or ≥ 15 as the PLMS diagnostic criterion in patients with OSA. Chervin et al and Haba-Rubio et al have also reported that concurrent OSA and PLMS are not associated with increased hypersomnia.^{29,30} We propose that PLMS is not treated even if the PLMI increases after CPAP therapy without

any clinical symptoms. Further investigation is required for confirming whether concurrent PLMS and OSA results in additive consequences, such as cardiovascular events.

This study has certain limitations. First, we did not investigate PLMD. The diagnosis of PLMD requires the exclusion of other sleep disorders. However, all these sleep disorders cannot be identified through a simple chart review. Thus, we did not include PLMD in this study. Second, this study was a retrospective one and we did not obtain follow-up data after long-term CPAP therapy. Additional prospective studies are required to assess the effect of long-term CPAP on PLMS in patients with OSA. Third, the common medical or behavioral condition (eg, myalgia, venous stasis, leg edema, arthritis, leg cramps, positional discomfort, habitual foot tapping) can be mistaken for RLS. A retrospective study with chart review may not exclude RLS-mimics completely.

Conclusion

CPAP titration increases the prevalence of PLMS, which suggests that OSA masks PLMS. PLMS prevalence and the RLS detection rate were higher when the PLMI was ≥ 5 than when the PLMI was ≥ 15 . Therefore, the current AASM criteria for scoring LMs and the PLMS diagnostic criterion with PLMI ≥ 15 require reconsideration.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Zucconi M, Ferri R, Allen R, et al. The official World Association of Sleep Medicine (WASM) standards for recording and scoring periodic leg movements in sleep (PLMS) and wakefulness (PLMW) developed in collaboration with a task force from the International Restless Legs Syndrome Study Group (IRLSSG). *Sleep Med.* 2006;7(2):175–183. doi:10.1016/j.sleep.2006.01.001
2. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *CHEST.* 2014;146(5):1387–1394. doi:10.1378/chest.14-0970
3. Montplaisir J, Boucher S, Poirier G, Lavigne G, Lapierre O, Lesperance P. Clinical, polysomnographic, and genetic characteristics of restless legs syndrome: a study of 133 patients diagnosed with new standard criteria. *Mov Disord.* 1997;12(1):61–65. doi:10.1002/mds.870120111
4. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisir J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med.* 2003;4(2):101–119.

5. Coleman RM, Pollak CP, Weitzman ED. Periodic movements in sleep (nocturnal myoclonus): relation to sleep disorders. *Ann Neurol*. 1980;8(4):416–421. doi:10.1002/ana.410080413
6. Hornyak M, Feige B, Riemann D, Voderholzer U. Periodic leg movements in sleep and periodic limb movement disorder: prevalence, clinical significance and treatment. *Sleep Med Rev*. 2006;10(3):169–177. doi:10.1016/j.smrv.2005.12.003
7. Ohayon MM, Roth T. Prevalence of restless legs syndrome and periodic limb movement disorder in the general population. *J Psychosom Res*. 2002;53(1):547–554.
8. American Academy of Sleep Medicine. *International Classification of Sleep Disorders. Diagnostic and Coding Manual*. 1st ed. Westchester (IL): American Academy of Sleep Medicine; 2005.
9. Al-Alawi A, Mulgrew A, Tench E, Ryan CF. Prevalence, risk factors and impact on daytime sleepiness and hypertension of periodic leg movements with arousals in patients with obstructive sleep apnea. *J Clin Sleep Med*. 2006;2(3):281–287.
10. Lakshminarayanan S, Paramasivan KD, Walters AS, Wagner ML, Patel S, Passi V. Clinically significant but unsuspected restless legs syndrome in patients with sleep apnea. *Mov Disord*. 2005;20(4):501–503. doi:10.1002/mds.20366
11. Fry JM, DiPhillipo MA, Pressman MR. Periodic leg movements in sleep following treatment of obstructive sleep apnea with nasal continuous positive airway pressure. *CHEST*. 1989;96(1):89–91. doi:10.1378/chest.96.1.89
12. Seo WH, Guilleminault C. Periodic leg movement, nasal CPAP, and expiratory muscles. *CHEST*. 2012;142(1):111–118. doi:10.1378/chest.11-1563
13. Yamashiro Y, Kryger MH. Acute effect of nasal CPAP on periodic limb movements associated with breathing disorders during sleep. *Sleep*. 1994;17(2):172–175. doi:10.1093/sleep/17.2.172
14. Baran AS, Richert AC, Douglass AB, May W, Ansarin K. Change in periodic limb movement index during treatment of obstructive sleep apnea with continuous positive airway pressure. *Sleep*. 2003;26(6):717–720. doi:10.1093/sleep/26.6.717
15. Hedli LC, Christos P, Krieger AC. Unmasking of periodic limb movements with the resolution of obstructive sleep apnea during continuous positive airway pressure application. *J Clin Neurophysiol*. 2012;29(4):339–344. doi:10.1097/WNP.0b013e3182624567
16. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;14(6):540–545. doi:10.1093/sleep/14.6.540
17. Allen RP, Picchetti DL, Garcia-Borreguero D, et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria—history, rationale, description, and significance. *Sleep Med*. 2014;15(8):860–873. doi:10.1016/j.sleep.2014.03.025
18. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2012;8(5):597–619. doi:10.5664/jcsm.2172
19. Kushida CA, Chediak A, Berry RB, et al. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. *J Clin Sleep Med*. 2008;4(2):157–171.
20. American Academy of Sleep Medicine. *American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*. Westchester: American Academy of Sleep Medicine; 2007.
21. Javaheri S, Abraham WT, Brown C, Nishiyama H, Giesting R, Wagoner LE. Prevalence of obstructive sleep apnoea and periodic limb movement in 45 subjects with heart transplantation. *Eur Heart J*. 2004;25(3):260–266. doi:10.1016/j.ehj.2003.10.032
22. Ren R, Huang G, Zhang J, et al. Age and severity matched comparison of gender differences in the prevalence of periodic limb movements during sleep in patients with obstructive sleep apnea. *Sleep Breath*. 2016;20(2):821–827. doi:10.1007/s11325-015-1231-x
23. Aritake-Okada S, Namba K, Hidano N, et al. Change in frequency of periodic limb movements during sleep with usage of continuous positive airway pressure in obstructive sleep apnea syndrome. *J Neurol Sci*. 2012;317(1–2):13–16. doi:10.1016/j.jns.2012.03.013
24. Allen RP, Walters AS, Montplaisir J, et al. Restless legs syndrome prevalence and impact: REST general population study. *Arch Intern Med*. 2005;165(11):1286–1292. doi:10.1001/archinte.165.11.1286
25. Chen NH, Chuang LP, Yang CT, et al. The prevalence of restless legs syndrome in Taiwanese adults. *Psychiatry Clin Neurosci*. 2010;64(2):170–178. doi:10.1111/j.1440-1819.2010.02067.x
26. Fulda S, Heinzer R, Haba-Rubio J. Characteristics and determinants of respiratory event associated leg movements. *Sleep*. 2017.
27. Manconi M, Zavalko I, Bassetti CL, Colamartino E, Pons M, Ferri R. Respiratory-related leg movements and their relationship with periodic leg movements during sleep. *Sleep*. 2014;37(3):497–504. doi:10.5665/sleep.3484
28. Manconi M, Zavalko I, Fanfulla F, Winkelman JW, Fulda S. An evidence-based recommendation for a new definition of respiratory-related leg movements. *Sleep*. 2015;38(2):295–304. doi:10.5665/sleep.4418
29. Chervin RD. Periodic leg movements and sleepiness in patients evaluated for sleep-disordered breathing. *Am J Respir Crit Care Med*. 2001;164(8 Pt 1):1454–1458. doi:10.1164/ajrccm.164.8.2011062
30. Haba-Rubio J, Staner L, Krieger J, Macher JP. Periodic limb movements and sleepiness in obstructive sleep apnea patients. *Sleep Med*. 2005;6(3):225–229. doi:10.1016/j.sleep.2004.08.009

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