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Prevalence, Risk Factors and Impact on Daytime Sleepiness and Hypertension of Periodic Leg Movements With Arousals in Patients With Obstructive Sleep Apnea

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Study Objective: To determine the prevalence, risk factors, and impact on daytime sleepiness and hypertension of periodic leg movements of sleep (PLMS) with associated arousals in patients with obstructive sleep apnea (OSA).

Methods: A single-center retrospective case series of 798 consecutive patients who underwent diagnostic overnight polysomnography for suspected OSA. We performed discriminant function analysis using clinical and polysomnographic variables to examine the relationship between PLMS (periodic leg movement arousal index ≥ 5 per hour) and potential risk factors, including OSA.

Results: Mean ± SD age was 50 ± 12 years, body mass index 32 ± 8 kg/m^2, Epworth Sleepiness Scale (ESS) score 11 ± 5, and apnea-hypopnea index 31 ± 26 per hour. Sixty-eight percent were men, 30% had systemic hypertension, and 19% were smokers. Ninety-two percent had OSA (apnea-hypopnea index ≥ 5); 47% had PLMS; 44% had both OSA and PLMS; and among patients with OSA, 48% had PLMS. Significant predictors of PLMS, in order of importance, were number of predisposing medical conditions, age, number of predisposing medications, obesity, and OSA. Medical conditions that significantly predicted PLMS were depression, fibromyalgia, and diabetes mellitus. The ESS score and hypertension status were no different between those with both OSA and PLMS and those with OSA alone.

Conclusions: One in 2 patients investigated for OSA has PLMS. Risk factors for PLMS include preexisting medical conditions—particularly depression, fibromyalgia, and diabetes mellitus—increasing age, predisposing medications, obesity, and OSA. The combination of OSA and PLMS results in no greater subjective daytime sleepiness or prevalence of hypertension than OSA alone.

Keywords: Periodic leg movements, obstructive sleep apnea, daytime sleepiness, hypertension

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Periodic limb movements of sleep (PLMS) are characterized by repetitive highly stereotyped limb-muscle movements, which, in the legs, comprise dorsiflexion of the great toe in combination with partial flexion of the ankle, the knee, and sometimes the hip.[1] These limb movements may be associated with arousals.[2] Periodic limb movement disorder (PLMD) is arbitrarily defined as 5 or more periodic limb movement-related arousals per hour of total sleep time based on strict scoring criteria,[3] usually associated with a complaint of insomnia or excessive sleepiness and in the absence of any other disorder to account for the patient's primary complaint[1]. Restless legs syndrome is characterized by unpleasant sensations in the legs during wakefulness, usually prior to sleep onset, that cause an almost irresistible urge to move the legs.[4] Although the 2 syndromes are distinct, approximately 80% of individuals with restless legs have evidence of PLMD on polysomnography.[5] Restless legs syndrome and PLMD accounted for 12% of cases of insomnia evaluated at a sleep disorders center in 1 national cooperative study.[6] Periodic limb movements resulting in arousal from sleep are present in up to 6% of the general population[7]; however, the combination of nocturnal limb movements and a syndrome of sleep disturbance (i.e., PLMD) is less common at 3.9%.[8] The prevalence of periodic limb movements increases with age; 45% of 427 patients aged 65 and older were found to have polysomnographic evidence of myoclonic activity during sleep.[9] Evidence also supports an increased prevalence in obesity.[8] Various medical conditions have been associated with PLMS and/or restless leg syndrome, including uremia, diabetes mellitus, iron deficiency, chronic lung disease, congestive heart failure, rheumatoid arthritis, spinal cord lesions, post-poliomyelitis, peripheral neuropathy, and a variety of other neurologic disorders.[8,10-16] Certain medications have been associated with PLMS, including tricyclic antidepressants, selective serotonin reuptake inhibitors[8,17,18] and dopamine antagonists. There may be an association between PLMS and systemic hypertension,[19,20] suggesting that arousals caused by PLMS may be a risk factor for cardiovascular disease. The association with arousals and sleep fragmentation notwithstanding, PLMS has not been shown to cause subjective or objective daytime sleepiness when found incidentally on polysomnography.[21]

Periodic limb movements are frequently identified on poly-

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somnography performed in patients with suspected sleep-disordered breathing, raising the possibility that these 2 conditions are associated. Strollo[22] et al found PLMS in 14% of 51 consecutive patients with obstructive sleep apnea (OSA), and Ancoli-Israel[9] demonstrated PLMS and OSA in 145 elderly volunteers. In a large clinical series of 1124 patients with suspected or confirmed sleep-disordered breathing, Chervin[21] found that 84% had an apnea-hypopnea index (AHI) > 5 per hour and 24% had a periodic limb movement index > 5 per hour. The prevalence of PLMS (periodic limb movements with arousals) among patients with OSA was not reported in that study. Mendelson found a prevalence of PLMS (periodic limb movement arousal index > 5 per hour) of 10% among 518 patients with OSA.[23] In a recent study of the prevalence of concomitant sleep disorders in 643 patients with OSA, 8.1% had a periodic limb movement arousal index of > 5 per hour.[24] An association has been suggested between PLMS and upper airway resistance syndrome.[25] Treatment of sleep-disordered breathing with nasal continuous positive airway pressure has been shown to lead to the emergence of PLMS.[26]

The diagnosis of PLMD combines the observation of periodic limb movements and associated arousals with an otherwise unexplained syndrome of sleep disturbance. The significance of periodic limb movements with arousals (PLMS) is much less clear in patients who do not complain of any sleep disorder or who have a primary complaint of another sleep disorder (e.g., OSA). The primary purpose of this study was to measure the prevalence of PLMS among patients with OSA who underwent diagnostic polysomnography at a university-based sleep disorders clinic. We also wished to identify potential risk factors for PLMS in patients with suspected OSA, to determine whether there was an association between PLMS and OSA, and to assess whether the combination of PLMS and OSA was associated with a greater degree of daytime sleepiness than OSA alone. Finally we wished to determine whether PLMS was a risk factor for systemic hypertension.

METHODS

We examined the data of all patients with suspected OSA who underwent a diagnostic full overnight polysomnogram at the UBC Hospital Sleep Laboratory between January 1, 2001, and December 31, 2001. Data were systematically extracted by a single investigator (AA) from the patients' charts and polysomnogram reports and entered into a software database for later analysis. The study protocol was approved by our institutional ethics review board.

Chart Review

Data on age, sex, smoking status, established diagnosis of systemic hypertension, predisposing medical conditions, predisposing medications, protective medications, Epworth Sleepiness Scale (ESS) score, and body mass index were obtained from the referral correspondence and consultation notes composed at the time of the patient's initial assessment, as well as from any follow-up correspondence. The presence or absence of the following medical conditions was recorded—chronic cardiac, pulmonary or renal disease, diabetes mellitus, anemia, depression, and fibromyalgia. Any neurologic or generalized musculoskeletal disorder was considered to be a predisposing medical condition. Examples included epilepsy, traumatic quadriparesis, poliomyelitis, narcolepsy, multiple sclerosis, parkinsonism, Friedrich's ataxia, Arnold-Chiari malformation with hydrocephalus, diabetes mellitus, and uremia. Tricyclic antidepressants and selective serotonin reuptake inhibitors were considered to be predisposing medications. Iron, folate, vitamin B_{12}, dopamine agonists, gabapentin, codeine, trazodone, and hemodialysis were considered to be protective. Since patients were referred primarily for suspected OSA, information about some symptoms such as insomnia and restless legs were not consistently recorded and were therefore not included in the analysis.

Polysomnography

Full overnight polysomnography was performed using conventional instrumentation and analysis according to the recommendations on syndrome definition and measurement techniques published by the American Academy of Sleep Medicine.[27] Sleep and its various stages were documented by standard electroencephalographic, electrooculographic, and electromyographic criteria. Apneas and hypopneas were recorded by oronasal flow cannulae attached to a pneumotachograph. Chest wall and abdominal movement were recorded using inductive plethysmography to document respiratory effort. Oxygen saturation was measured by pulse oximetry using a finger probe. Periodic leg movements were recorded from 2 surface electromyographic electrodes positioned 2 to 4 cm apart over the belly of the tibialis anterior muscle of each lower limb. Leg movements were recorded on a separate channel for each leg using an amplifier at a frequency of 128 Hz and band-pass filter settings of 10 to 50 Hz. The complete record was scored manually for sleep stage, arousals, apneas, hypopneas, total periodic leg movements, and periodic leg movements associated with arousals.

Definitions

Arousal: A clearly visible episode of alpha rhythm lasting 3 seconds or longer but not necessarily associated with stage or state change.
Periodic leg movements: Bursts of muscle contraction of 0.5 to 5.0 seconds in duration and an amplitude of at least 25% of bursts recorded during calibration occurring with a periodicity of 5 to 120 seconds between each movement, without the requirement for a sequence of 3 or more leg movements. Leg movements associated with respiratory events and phasic activity in rapid eye movement sleep were not scored.
Period leg movement index–total: Number of periodic leg movements per hour of total sleep time.
Periodic leg movement arousal index: Number of periodic leg movements with associated arousals per hour of total sleep time.
PLMS: Five or more periodic leg movements with arousal per hour of total sleep time.
Apnea: A cessation of airflow at the nose and mouth lasting at least 10 seconds.
Hypopnea: A 50% decrease from baseline in the amplitude of oronasal flow, or, if less, a clear reduction in oronasal flow in association with either an arousal or a 3% oxygen desaturation.
OSA: Five or more obstructive apneas or hypopneas per hour of total sleep time.
Excessive daytime sleepiness: A score of 10 or greater on the ESS.
Obesity: A body mass index ≥ 27 kg/m^2.

Statistical Analysis

SPSS Version 10.0.7 (SPSS, Inc., Chicago, IL) was used for all analyses. All preliminary and multivariate analyses conformed to reference guidelines.[28-30] The statistical strategy was to determine which clinical variables could be broadly applied to predict which patients were more likely to have PLMS. Preliminary analyses indicated that the data set was suitable for multivariate analysis. Missing data that were randomly distributed among variables were substituted using the overall group mean. The majority of variables were missing less than 2% of the values. Three multivariate outliers were deleted, reducing the original data set to 795 patients.

Discriminant-function analyses were performed to examine the relationships between PLMS, OSA, and 3 sets of potential risk factors: (1) OSA, age, sex, obesity, hypertension, predisposing medications, protective medications, and number of predisposing medical conditions; (2) specific predisposing medical conditions; and (3) ESS score and hypertension. Due to the small number of individuals taking any 1 class of medication, predisposing and protective medications were collapsed into 2 groups: (1) fewer than 1 medication was coded as '0', and (2) 1 or more medications was coded as '1.' The total number of predisposing medical conditions was counted and ranged from values of 0 to 3. Obesity was coded as '1' for nonobese and '2' for obese. For OSA, '1' indicated absence of (AHI < 5 per hour) and '2' indicated presence of OSA (AHI ≥ 5 per hour). Correlations of > 0.30 in the discriminant analysis were considered significant. Finally, a stepwise discriminant-function analysis was performed to determine if age, body mass index, number of predisposing medical conditions, AHI, and periodic leg movement arousal index were related to the presence or absence of hypertension. Summary data are presented as mean ± SD.

RESULTS

As a group, these patients were middle-aged, were moderately obese, and had moderate OSA. Obesity was present in 73% of patients, and 19% were current smokers. The male/female ratio was 2:1, and 107 patients (14%) were over 65 years of age. Twenty-seven percent of patients had 1 or more predisposing medical conditions; 10% were taking 1 or more predisposing medications; and 4% were taking 1 or more protective medications. The ESS score was greater than 10 out of 24 in 61% of patients. Of the 795 patients whose data were analyzed, 729 (92%) had OSA, 377 (47%) had PLMS, 351 (44%) had both OSA and PLMS, and 26 (3%) had PLMS without OSA The prevalence of PLMS among patients with OSA was 48%. Summary data for the demographic, polysomnographic, and clinical variables are provided in Table 1.

Table 1—Summary of the Demographic, Polysomnographic, and Clinical Variables in 795 Patients Presenting for Investigation of Sleep-Disordered Breathing

Variable	Results
Age, y	50 ± 12
Ratio of Men/Women	2/1
ESS, score	11 ± 5
BMI, kg/m^2	32 ± 8
AHI, no./h	31 ± 26
Total PLM Index, no./h	20 ± 26
PLM Arousal Index, no./h	9 ± 11
Predisposing Medical Conditions, no.[a]	0.38 ± 0.64
Number of Predisposing Medications, no.[b]	0.10 ± 0.32
Number of Protective Medications, no.[c]	0.04 ± 0.23

Data are presented as mean ± SD unless otherwise indicated.
[a]Chronic cardiac, pulmonary or renal disease, diabetes mellitus, anemia, depression, fibromyalgia, or any neurologic or generalized musculoskeletal disorder.
[b]Tricyclic antidepressants, selective serotonin reuptake inhibitors.
[c]Vitamin B_{12}, trazodone, folate, codeine, iron, gabapentin, dopamine agonists, dialysis.
ESS refers to Epworth Sleepiness Scale; BMI, body mass index; AHI, apnea-hypopnea index; PLM, periodic leg movements.

PLMS and Demographic Variables

Discriminant-function analysis confirmed that the clinical variables of interest could be used to discriminate between those with and without PLMS. Results of the first discriminant function, c^2 (8) = 16.58, $p < .05$, are presented in Table 2. The size of each correlation or function (F) describes the strength of the relationship between the predictor variable and PLMS. Patients with PLMS, in order of importance, had a higher number of predisposing medical conditions, were older, were taking more predisposing medications, were more obese, and were more likely to have OSA. Information on smoking status was available in only 613 patients. When analyzed separately, these data revealed no relationship between smoking status and PLMS.

PLMS and Predisposing Medical Conditions

In the second analysis, we examined the relationship between PLMS and specific predisposing medical conditions. The second discriminant function, c^2 (2) = 24.12, $p < .05$, is shown in Table 3. Patients with PLMS were more likely to suffer from depression, fibromyalgia, and diabetes mellitus than those without PLMS.

PLMS, OSA, Sleepiness, and Hypertension

In the third analysis, we examined whether ESS score and hypertension status could be used to discriminate between patients with OSA alone and those with both OSA and PLMS. The third discriminant function, c^2 (2) = 0.48, $p > .05$, indicated that patients with both OSA and PLMS could not be differentiated from patients with OSA alone by ESS score or the presence or absence of systemic hypertension.

Table 2—First Discriminant-Function Analysis for the Prediction of PLMS[a]

Variable	Function[b]
Number of predisposing medical conditions	0.65[c]
Age	0.59[c]
Number of predisposing medications	0.45[c]
Obesity	0.36[c]
Obstructive sleep apnea	0.36[c]
Hypertension	0.16
Number of protective medications	0.11
Sex	0.09

[a]Periodic leg movement arousal index ≥ 5/h of total sleep time in 778 patients; 372 with PLMS; 406 without PLMS
[b]The size of each correlation (function) reveals the strength of the relationship between the variable and PLMS.
[c]Significant correlation.

PLMS as a Potential Risk Factor for Hypertension

The results of the stepwise discriminant function analysis are shown in Table 4. The minimum F value required for retention at each step was 3.84. Periodic leg movement arousal index had an F value of 3.33, indicating that it did not contribute to the prediction of hypertension.

DISCUSSION

In this retrospective case series, we found a higher prevalence of periodic leg movements with arousals in patients with OSA than has been reported previously. During a calendar year in which 798 patients underwent polysomnography for suspected OSA at our institution, 92% of the 795 patients whose data were submitted for analysis had OSA as defined by an AHI ≥ 5 per hour. Of these, 48% also had PLMS as defined by a periodic leg movement arousal index of ≥ 5 per hour. The major risk factors for PLMS were more frequent predisposing medical conditions, increasing age, higher number of predisposing medications, obesity, and OSA. However, OSA was less strongly related to PLMS. Patients with both OSA and PLMS were not sleepier than those with OSA alone.

The prevalence of PLMS in the general population is reported to be between 5% and 15%.[8,31] Some studies have shown higher prevalences in older patients. Newer techniques indicate that periodic limb movements may be even more common than previously thought; actigraphy performed in a community sample indicated a prevalence of 37%.[32] Periodic leg movements appear to be more common in patients with sleep-disordered breathing. Chervin[19] recently reported another large series of patients with suspected or confirmed OSA. Of 1124 patients studied, 84% had OSA (AHI ≥ 5 per hour) and 266 (24%) had a periodic limb movement index ≥ 5 per hour. In his paper, Chervin did not report the prevalence of periodic limb movements with arousals in patients with OSA, but, based on his published data, it was not greater than 28%. Mendelson found a prevalence of PLMS (periodic limb movement arousal index > 5 per hour) of 10% among 518 patients with OSA.[23] Scharf[24] et al, in a more recent retrospective case series, found a periodic limb movement arousal index > 5 per hour in 8.1% of 643 patients with a primary diagnosis of OSA . In a much smaller prospective study, Iriarte[33] et al found a prevalence of PLMS of 24% in patients with OSA. Our study shows that periodic leg movements associated with arousals are extremely common among patients being investigated for possible OSA; 47% of men and 48% of women in the total sample had a periodic leg movement arousal index of ≥ 5. The higher prevalence of PLMS in our study may be related to our method of scoring PLMS, in that we did not specify the requirement for a sequence of 3 or more periodic limb movements. We decided to score all periodic leg movements with arousals because we were primarily interested in whether these arousals could contribute to daytime sleepiness in patients with OSA, rather than in making a diagnosis of PLMD. Since our data were derived from a retrospective case series, we cannot say that the prevalence of PLMS in patients with OSA is greater than in patients of comparable age in the general population. Our study revealed a weak association between PLMS and OSA. In Chervin's[21] study, the overall interaction between periodic limb movements and OSA was not significant, although the periodic limb movement index did show an interaction with severe OSA and minimum SaO_2. The association between PLMS and OSA could be partly explained by sleep fragmentation caused by OSA that leads to an increased proportion of non-rapid eye movement sleep, the sleep stage in which the vast majority of periodic limb movements occur.[34]

A higher number of predisposing medical conditions was the strongest predictor of PLMS in our study. Medical comorbidity is often associated with limb movements during sleep. In our sample, 36% of patients with PLMS had at least 1 predisposing medical condition. Among the various medical conditions of interest, depression, fibromyalgia, and diabetes mellitus were significant predictors of PLMS. In the case of depression, this may be partly related to antidepressant medications, although we did not specifically look for this interaction. Restless legs syndrome has previously been reported to occur in about 30% of patients with fibromyalgia,[35] although the pathophysiologic basis for this association is unclear. The association between diabetes mellitus and PLMS is not well characterized. There is some evidence that peripheral neuropathy is associated with PLM, and we speculate that diabetic neuropathy may be a potential link between these 2 conditions. Among our patients taking 1 or more medications considered to be predisposing, 57% had PLMS. Antidepressants medications appear to predispose to PLMS, and selective serotonin reuptake inhibitors and tricyclic antidepressants were significant in our model. The link between PLMS and antidepressants has been characterized mostly through

Table 3—Second Discriminant Function Analysis for the Relationship Between Specific Predisposing Medical Conditions and PLMS[a]

Variable	Function[b]
Depression	0.61[c]
Fibromyalgia	0.48[c]
Diabetes	0.45[c]
Renal	0.22
Lung	-0.22
Other	-0.22
Cardiac	0.16
Anemia	-0.11

[a]Periodic leg movement arousal index ≥ 5/h of total sleep time in 778 patients; 372 with PLMS; 406 without PLMS.
[b]The size of each correlation (function) reveals the strength of the relationship between the variable and PLMS.
[c]Significant correlation.

Table 4—Stepwise Discriminant Function Analysis for the Predictors of Hypertension in 795 Patients Presenting for Investigation of Sleep-Disordered Breathing

Variable	Function[a]
Age	45.83[b]
BMI	18.26[b]
Number of predisposing medical conditions	10.76[b]
AHI	18.96[b]
PLM arousal index	3.33

[a]The size of each correlation (function) reveals the strength of the relationship between the variable and the presence of hypertension.
[b]Significant correlation.
BMI refers to body mass index; AHI, apnea-hypopnea index; PLM, periodic leg movements.

case reports or case series.[36] It appears that tricyclic antidepressants decrease rapid eye movement sleep[37] whereas selective serotonin reuptake inhibitors appear to be associated with increased muscle tone during rapid eye movement sleep.[38] The use of selective serotonin reuptake inhibitors has been associated with restless leg symptoms in a very large European telephone survey.[8] The use of selective serotonin reuptake inhibitors may contribute to the increased prevalence of periodic limb movements in both depressed patients and in patients with fibromyalgia. A range of medications was considered to exert a protective effect but was not helpful in discriminating between patients with and without PLMS.

We have confirmed the previous finding that the prevalence of PLMS increases with age[39]; 56% of patients aged 65 and older had evidence of periodic leg movements with arousal. The increase in periodic limb movements associated with ageing has been explained as an epiphenomenon of loss of dopaminergic function.[40] Other authors have argued that the age-related decline in renal function may explain the increasing prevalence of periodic limb movements in the elderly.[41] What remains unclear is whether the objective increase in arousals seen in the sleep studies of elderly patients has any significance in terms of subjective symptoms of sleepiness.[42] Indeed the extent of periodic limb movements has also been poorly correlated with daytime symptoms in this group of patients.[43] Our results confirm the previously reported association between PLMS and obesity.[8] Other obesity-related factors—lower income, lack of exercise, diabetes, and of course OSA—may all contribute to the risk of PLMS in this group.[44]

Whether periodic limb movements contribute to excessive daytime sleepiness in patients with sleep-disordered breathing has been an ongoing source of controversy in the sleep literature. The association between limb movements and electroencephalographic arousal on polysomnography has led to the somewhat intuitive conclusion that the limb movements must cause sleepiness.[45,46] Because our interest lay mainly in sleepiness, we therefore focused primarily on the periodic leg movement arousal index. The presence of 5 or more arousals per hour associated with leg movements might be expected to increase daytime sleepiness; however, several clinical series have failed to show any predictable correlation between periodic limb movements and subjective sleepiness or sleep propensity as measured by the Multiple Sleep Latency Test.[9,21,47] Interestingly, some authors have noted the opposite effect, with increased periodic limb movement arousals being associated with less-severe Multiple Sleep Latency Test-defined sleepiness.[21,23] The coexistence of OSA and PLMS in our study did not increase the degree of subjective daytime sleepiness as determined by the ESS. The level of sleepiness did not discriminate between patients with OSA alone and those with both OSA and PLMS. The vast majority of our patients with PLMS also had OSA. Patients with a combination of OSA and PLMS were equally represented in sleepy and nonsleepy groups of patients. Chervin[21] found that, among patients suspected or confirmed to have OSA, increased numbers of periodic limb movements were not associated with increased sleepiness, as measured by the Multiple Sleep Latency Test, regardless of whether they were associated with arousals. Haba-Rubio et al,[48] in a recent retrospective case series of 57 consecutive patients diagnosed with OSA, found no difference in the degree of sleepiness on Multiple Sleep Latency Test or ESS between patients with or without coexisting periodic limb movements, either before or after 1 year of treatment with nasal continuous positive airway pressure. Arousals associated with periodic limb movements were not scored in that study. Other studies[23,45] have also failed to show a relationship between PLMS and sleepiness. Our data lend further credence to the argument that PLMS in patients with OSA are a common polysomnographic phenomenon of dubious clinical significance. This raises the question whether there is any clinical utility in scoring PLM in these patients.

It is uncontested that periodic limb movements are frequently associated with electroencephalographic arousal—our own data confirm the high prevalence of this phenomenon—however, it appears likely that periodic limb movements simply represent a manifestation of the physiologic arousal process. As many as 50% of periodic limb movements occur before an arousal, while the remainder occur simultaneously with or after an arousal.[49] Over 90% of periodic limb movements occur during recognizable periods of cyclic alternating pattern on electroencephalography, which is felt by most observers to represent normal arousal instability during non-rapid eye movement sleep.[34]

OSA is a recognized risk factor for systemic hypertension.[50] There may also be an association between PLMD and systemic hypertension.[19,20] Periodic limb movements are frequently associated with other physiologic changes (e.g., variation in heart rate), which may be pertinent to sleep fragmentation, even in the absence of electroencephalographic arousal. Indeed, autonomic markers of arousal are as well correlated with symptoms of sleepiness in OSA patients as is the AHI.[51] Thus, the combination of OSA and PLMS might be expected to increase the risk of hypertension. In our study, however, we found that hypertension status did not help differentiate between patients with OSA alone and those with both OSA and PLMS. Furthermore, the periodic leg movement arousal index did not contribute to the prediction of hypertension in the stepwise discriminant analysis. In a posthoc analysis using linear regression (details not included), we found no significant relationship between periodic leg movement index-total and hypertension ($r = 0.06$; $p > .05$).

There are some limitations to the interpretation of our results. Our study was performed on patients who were referred for the evaluation of possible sleep-disordered breathing, and our findings should not be extrapolated beyond this group. Findings may differ in patients referred specifically for the evaluation of restless leg syndrome or for the investigation of disorders of initiating and maintaining sleep. Based on the supposition that it is the arousals that cause sleepiness, we did not include data on periodic leg movements occurring without electroencephalographic arousal in our discriminant analyses. Current techniques may be inadequate to detect differences in the magnitude of arousals associated with different events, and this may explain some of the poor correlations between conventional measures of sleep-apnea severity and daytime sleepiness.[52] However, in the posthoc linear regression analysis, we found no relationship between the periodic leg movement index- total and the ESS score.

Our results raise a significant practical question. Since periodic limb movements appear not to be associated with increased sleepiness or cardiovascular risk, should they continue to be routinely recorded and scored in patients undergoing polysomnography for suspected OSA? Currently it is standard practice in many sleep laboratories to score limb movements meticulously in all patients undergoing polysomnography. In patients who are being investigated for suspected OSA, this process consumes valuable re-

sources and may provide little useful clinical information. On the contrary, the potential exists for up to 50% of these patients to be mislabeled as having an additional sleep disorder of dubious clinical significance, for which they may be prescribed unnecessary and potentially harmful treatment. In the absence of symptoms of restless legs syndrome or a disorder of initiating and maintaining sleep, we suggest that, in patients undergoing polysomnography for the evaluation of OSA, the routine practice of scoring leg movements may be safely abandoned.

REFERENCES

1. International Classification of Sleep Disorders, revised: Diagnostic and Coding Manual. Rochester: American Sleep Disorders Association; 1997.
2. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. Sleep 1992;15:173-84.
3. Recording and scoring leg movements. The Atlas Task Force. Sleep 1993;16:748-59.
4. Toward a better definition of the restless legs syndrome. Mov Disord 1997;12:61-65.
5. 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;12:61-5.
6. Coleman RM, Miles LE, Guilleminault CC, Zarcone VP, Jr., van den Hoed J, Dement WC. Sleep-wake disorders in the elderly: polysomnographic analysis. J Am Geriatr Soc 1981;29:289-96.
7. Bixler EO, Kales A, Vela-Bueno A, Jacoby JA, Scarone S, Soldatos CR. Nocturnal myoclonus and nocturnal myoclonic activity in the normal population. Res Commun Chem Pathol Pharmacol 1982;36:129-40.
8. Ohayon MM, Roth T. Prevalence of restless legs syndrome and periodic limb movement disorder in the general population. J Psychosom Res 2002;53:547-54.
9. Ancoli-Israel S, Kripke DF, Klauber MR, Mason WJ, Fell R, Kaplan O. Periodic limb movements in sleep in community-dwelling elderly. Sleep 1991;14:496-500.
10. Wetter TC, Stiasny K, Kohnen R, Oertel WH, Trenkwalder C. Polysomnographic sleep measures in patients with uremic and idiopathic restless legs syndrome. Mov Disord 1998;13:820-4.
11. Reynolds G, Blake DR, Pall HS, Williams A. Restless leg syndrome and rheumatoid arthritis. Br Med J (Clin Res Ed) 1986;292:659-60.
12. Hanly PJ, Zuberi-Khokhar N. Periodic limb movements during sleep in patients with congestive heart failure. Chest 1996;109:1497-502.
13. Matthews WB. Letter: Iron deficiency and restless legs. Br Med J 1976;1(6014):898.
14. Schiavi RC, Stimmel BB, Mandeli J, Rayfield EJ. Diabetes, sleep disorders, and male sexual function. Biol Psychiatry 1993;34:171-7.
15. Spillane JD. Restless legs syndrome in chronic pulmonary disease. Br Med J 1970;4:796-8.
16. Lee MS, Choi YC, Lee SH, Lee SB. Sleep-related periodic leg movements associated with spinal cord lesions. Mov Disord 1996;11:719-22.
17. Wetter TC, Pollmacher T. Restless legs and periodic leg movements in sleep syndromes. J Neurol 1997;244(4 Suppl 1):S37-45.
18. Wetter TC, Brunner J, Bronisch T. Restless legs syndrome probably induced by risperidone treatment. Pharmacopsychiatry 2002;35:109-11.
19. Espinar-Sierra J, Vela-Bueno A, Luque-Otero M. Periodic leg movements in sleep in essential hypertension. Psychiatry Clin Neurosci 1997;51:103-7.
20. Ali NJ, Davies RJ, Fleetham JA, Stradling JR. Periodic movements of the legs during sleep associated with rises in systemic blood pressure. Sleep 1991;14:163-5.
21. Chervin RD. Periodic leg movements and sleepiness in patients evaluated for sleep-disordered breathing. Am J Respir Crit Care Med 2001;164:1454-8.
22. Strollo PJ, Jr., Sanders MH, Atwood CW. Positive pressure therapy. Clin Chest Med 1998;19:55-68.
23. Mendelson WB. Are periodic leg movements associated with clinical sleep disturbance? Sleep 1996;19:219-23.
24. Scharf SM, Tubman A, Smale P. Prevalence of concomitant sleep disorders in patients with obstructive sleep apnea. Sleep Breath 2005;9:50-6.
25. Exar EN, Collop NA. The association of upper airway resistance with periodic limb movements. Sleep 2001;24:188-92.
26. 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;96:89-91.
27. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999;22:667-89.
28. Pedhazur E. Multiple Regression in Behavioural Research, Explanation and Prediction, 2nd ed. New York: Holt, Rinehart & Winston; 1982.
29. Tabachnik BS. Using Multivariate Statistics. Boston: Allyn & Bacon; 2001.
30. Tabachnik BS. Using Multivariate Statistics. 3rd ed. New York: Harper Collins; 1996.
31. Wichniak A, Wierzbicka A, Jernajczyk W. Restless legs syndrome and periodic limb movements in sleep: clinical features, epidemiology, diagnosis. Neurol Neurochir Pol 2002;36:1173-84.
32. Morrish E, King MA, Pilsworth SN, Shneerson JM, Smith IE. Periodic limb movement in a community population detected by a new actigraphy technique. Sleep Med 2002;3:489-95.
33. Iriarte J, de Castro P. Periodic movements of legs and sleep stages. Neurologia 1998;13:40.
34. Parrino L, Boselli M, Buccino GP, Spaggiari MC, Di Giovanni G, Terzano MG. The cyclic alternating pattern plays a gate-control on periodic limb movements during non-rapid eye movement sleep. J Clin Neurophysiol 1996;13:314-23.
35. Yunus MB, Aldag JC. Restless legs syndrome and leg cramps in fibromyalgia syndrome: a controlled study. BMJ 1996;312:1339.
36. Sanz-Fuentenebro FJ, Huidobro A, Tejadas-Rivas A. Restless legs syndrome and paroxetine. Acta Psychiatr Scand 1996;94:482-4.
37. Sharpley AL, Cowen PJ. Effect of pharmacologic treatments on the sleep of depressed patients. Biol Psychiatry 1995;37:85-98.
38. Winkelman JW, James L. Serotonergic antidepressants are associated with REM sleep without atonia. Sleep 2004;27:317-21.
39. Youngstedt SD, Kripke DF, Klauber MR, Sepulveda RS, Mason WJ. Periodic leg movements during sleep and sleep disturbances in elders. J Gerontol A Biol Sci Med Sci 1998;53:M391-4.
40. Silber MH. Commentary on controversies in sleep medicine. Montplaisir et al.: Periodic leg movements are not more prevalent in insomnia or hypersomnia but are specifically associated with sleep disorders involving a dopaminergic mechanism. Sleep Med 2001;2:367-369.
41. Bliwise D, Petta D, Seidel W, Dement W. Periodic leg movements during sleep in the elderly. Arch Gerontol Geriatr 1985;4:273-81.
42. Mosko SS, Dickel MJ, Paul T, et al. Sleep apnea and sleep-related periodic leg movements in community resident seniors. J Am Geriatr Soc 1988;36:502-8.
43. Dickel MJ, Mosko SS. Morbidity cut-offs for sleep apnea and periodic leg movements in predicting subjective complaints in seniors. Sleep 1990;13:155-66.
44. Phillips B, Young T, Finn L, Asher K, Hening WA, Purvis C. Epidemiology of restless legs symptoms in adults. Arch Intern Med 2000;160):2137-41.
45. Coleman RM, Bliwise DL, Sajben N, Boomkamp A, de Bruyn

LM, Dement WC. Daytime sleepiness in patients with periodic movements in sleep. Sleep 1982;5 Suppl 2:S191-202.
46. Ancoli-Israel S, Seifert AR, Lemon M. Thermal biofeedback and periodic movements in sleep: patients' subjective reports and a case study. Biofeedback Self Regul 1986;11:177-88.
47. Bastuji H, Garcia-Larrea L. Sleep/wake abnormalities in patients with periodic leg movements during sleep: factor analysis on data from 24-h ambulatory polygraphy. J Sleep Res 1999;8:217-23.
48. Haba-Rubio J, Staner L, Krieger J, Macher JP. What is the clinical significance of periodic limb movements during sleep? Neurophysiol Clin 2004;34:293-300.
49. Karadeniz D, Ondze B, Besset A, Billiard M. EEG arousals and awakenings in relation with periodic leg movements during sleep. J Sleep Res 2000;9:273-7.
50. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378-84.
51. Pitson DJ, Stradling JR. Autonomic markers of arousal during sleep in patients undergoing investigation for obstructive sleep apnoea, their relationship to EEG arousals, respiratory events and subjective sleepiness. J Sleep Res 1998;7:53-9.
52. Stradling JR, Pitson DJ, Bennett L, Barbour C, Davies RJ. Variation in the arousal pattern after obstructive events in obstructive sleep apnea. Am J Respir Crit Care Med 1999;159:130-6.