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Can periodic limb movement disorder be diagnosed without polysomnography? A case-control study

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Abstract

Objectives: (1) To determine whether clinical information can predict the presence of periodic limb movement disorder (PLMD). (2) To examine whether clinical data correlate with PLMD severity

Methods: Sixty-one adult patients (48 males and 13 females, aged 55.1 ± 14.1 years) with PLMD (without a clinical diagnosis of restless legs syndrome) were compared with 61 control patients without PLMD (43 males and 18 females, aged 49.6 ± 16.1 years) in this case-control study. All patients completed a detailed questionnaire which included (1) demographics, (2) sleep complaints, (3) medical disorders, (4) use of medication, nicotine, and caffeine, and (5) history of nocturnal motor/sensory leg symptoms. All patients underwent standard polysomnography.

Results: The PLMD and control groups were similar in the prevalence of insomnia, hypersomnia, diabetes, peripheral neurologic disorders, anemia, spinal disease, antidepressant medication use, smoking, caffeine intake, and leg pain. Compared with the control group, the PLMD group reported more leg kicks (28% vs. 5%, $P < 0.001$) and more crawling or aching sensations in legs (28% vs. 11%, $P = 0.023$). The logistic regression analysis showed that only age ($P = 0.044$), leg kicks (odds ratio (OR) 12.70, 95% confidence interval (CI) 2.80–57.63, $P = 0.001$), and crawling or aching in legs (OR 5.23, 95% CI 1.16–23.44, $P = 0.029$) were significantly related to the presence of PLMD. The positive predictive value of leg kicks in the diagnosis of PLMD was 85% and the negative predictive value was 57%. Within the PLMD group, only age correlated positively with the PLM-index ($r = 0.47$, $P < 0.001$). Both the PLM-index and the PLM arousal-index were negatively correlated with sleep efficiency on polysomnography ($P = 0.005$ and $P = 0.006$, respectively).

Conclusions: Clinical data are not sufficiently predictive of the presence of PLMD to rule in or rule out the diagnosis. Polysomnography is required for establishing the diagnosis of PLMD in patients with insomnia or hypersomnia.

Keywords: Nocturnal myoclonus syndrome; Periodic limb movement disorder; Sleep-related periodic leg movements; Restless legs syndrome; Sleep disorders

1. Introduction

Periodic limb movement disorder (PLMD) is characterized by periodically recurring limb movements during sleep (PLMS), typically with extension of the great toe, and flexion of the ankles, knees, or hip every 20–40 s, often associated with symptoms of hypersomnia or insomnia [1]. By definition, polysomnography is required for diagnosis, along with clinical correlation [2]. PLMS are common and have been reported in approximately 5% of normal individuals, 17% of sleep clinic patients with insomnia [3], and 45% of the community-dwelling elderly [4,5]. Montplaisir et al. [6] recently reported the prevalence of PLMS of five or more movements per hour of sleep in 55% of controls, 40% of patients with insomnia, 30% of patients with hypersomnia, and over 80% of patients with narcolepsy or restless legs syndrome (RLS), suggesting that PLMS may be a manifestation of abnormalities in the dopaminergic system.

PLMD is distinct from RLS, a separate but related disorder that is defined by clinical criteria and does not require polysomnography for diagnosis [7]. PLMS are seen on polysomnography in the majority of patients with RLS [8], but PLMS are neither necessary nor sufficient to make a diagnosis of RLS [2,8]. PLMS have been described in asymptomatic individuals [8–10], in patients with insomnia [3,8,11] or hypersomnia [3,8,12], as well as in multiple sleep/wake disorders including RLS [3,8], narcolepsy [3,8,13], REM sleep behavior disorder

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[8], obstructive sleep apnea with or without treatment with continuous positive airway pressure [3,13,14], and upper airway resistance syndrome [15]. RLS, PLMD, and/or PLMS have been described in over 30 different clinical conditions [16] although many of these associations are based on case reports and small case series and/or include an overlap of patients. Some of the more consistent associations have been with aging [5,17], uremia [18–21], pregnancy [22–24], anemia [25–27], and neuropathy [28–33] and neurodegenerative diseases [34,35]. However, PLMS or RLS have been described in diabetes [17,36], lumbosacral spinal disease or anesthesia [35,37,38], antidepressant medication use [39,40], caffeine use [41], and smoking [17,42,43].

Symptoms of PLMD include complaints of leg kicks at night [5] or perception of poor sleep/insomnia [5] or hypersomnia. Symptoms may respond to correction of the underlying cause or to treatment with dopaminergic agents, benzodiazepines, or opiates [44,45]. In the absence of concomitant RLS, a diagnosis of PLMD may not be possible without polysomnography [46]. In one study of patients with insomnia, experienced clinicians were able to predict only 56% of PLMS cases later diagnosed on polysomnography [11]. Patient sleep and wake symptoms have a low positive and negative predictive value in PLMD [47], even using a structured interview [48]. A recent Editorial debated the utility of monitoring limb movements as part of routine polysomnography [49,50]. The debate about the definition or mechanism of PLMD notwithstanding, treatment of PLMD may be associated with clinical improvement [44,45,49]. Thus, it is imperative to rule in or rule out PLMD in a symptomatic patient with sleep complaints. We undertook this study to determine whether detailed clinical information including historical features and symptoms would be sufficient to predict the diagnosis or to exclude PLMD in patients without RLS.

2. Materials and methods

2.1. Definitions

PLMS are regular stereotypic limb movements that occur during sleep, which can be identified and recorded electromyographically [51]. PLMS usually last 0.5–5 s and occur every 20–40 s with a minimum train of four throughout sleep. More than five movements per hour has been regarded as abnormal. PLMD is diagnosed when frequent PLMS are associated with and thought to be the cause of a major sleep complaint of insomnia or hypersomnia, although occasionally patients may be asymptomatic [1].

2.2. Study cohort

Patients referred to a university-based sleep center with a variety of sleep complaints who ultimately underwent overnight polysomnography served as the base from which the study population was drawn. Patients were physician-referred and all patients completed a detailed sleep and medical questionnaire prior to polysomnography. The presence of PLMD was defined according to the aforementioned American Sleep Disorders Association (ASDA) criteria [1]. Inclusion criteria for the PLMD group were a PLM-index of $\geq$5 movements/h and symptoms of insomnia and/or hypersomnia on sleep questionnaire, as defined below. Exclusion criteria for the PLMD group were (1) polysomnographic evidence of significant sleep-disordered breathing, (2) narcolepsy, idiopathic hypersomnia, or RLS on the basis of referring physician history and responses to open-ended sections of the sleep questionnaire (in which patients were asked to write out their primary complaints and to indicate their interpretation of symptom etiology), or (3) incomplete data. For example, patients who described leg restlessness in open-ended sections were considered to have probable RLS for the purpose of this study and were excluded. The control group included a random sample of patients with other sleep disorders presenting to the Sleep Center with the absence of any PLMS on polysomnography.

2.3. Sleep questionnaire

The subjects were administered a detailed questionnaire, which included demographics, major sleep complaint, history of medical disorders, medications, and habits, and history of nocturnal motor or sensory leg symptoms. Continuous and ordinal demographics were derived from self-reported age, sex, body weight, and height. All other variables were binary. Insomnia was noted if patients reported difficulty initiating sleep and/or difficulty maintaining sleep. Hypersomnia was noted if the Epworth Sleepiness Score [52] was $\geq$10. Presence of diabetes, spinal disease, peripheral neurologic disorders (including peripheral neuropathy and neurodegenerative diseases), and anemia were abstracted from the medical database part of the questionnaire and referring physician history. Use of antidepressant medications (defined as tricyclic antidepressants, selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors) was abstracted from current self-reported medication lists. Cigarette smoking was noted if the current smoking level was $\geq$20 cigarettes per day. Significant caffeine intake was noted if coffee consumption was $\geq$4 cups of coffee per day. Individual motor/sensory symptoms were noted if patients reported 'always or frequently having' symptoms of 'leg kicks', 'crawling or aching in legs', or 'leg pain'.

2.4. Polysomnography

All subjects underwent full overnight polysomnography with the following variables monitored: electroencephalogram (EEG) (C4/A1, C3/A2, O2/A1, O1/A2), submental electromyogram (EMG), right and left electro-oculogram (ROC, LOC), right and left anterior tibialis EMG by surface electrodes, nasal/oral airflow by thermistors, respiratory effort by piezo-electric bands, arterial oxygen saturation (SaO_2) by pulse oximetry (Biox 3700c; Ohmeda: Louisville,

Table 1
Demographics, major sleep complaint, medical history, medication use, habits, and motor/sensory leg symptoms in the PLMD and control groups[a]

	PLMD ($n = 61$)	Control ($n = 61$)	P value
Demographics			
Age (years)	55.2 ± 14.1	49.6 ± 16.1	0.044*
Males	48 (78)	43 (70)	NS
BMI	30.9 ± 6.0	33.4 ± 7.7	0.044*
Major sleep complaint			
Insomnia	49 (80)	47 (77)	NS
Hypersomnia (ESS ≥10)	34 (57)	33 (54)	NS
ESS	11.1 ± 5.5	11.1 ± 5.8	NS
Medical conditions	19 (31)	13 (21)	NS
Diabetes	8 (13)	7 (11)	NS
Spinal disease	7 (11)	3 (5)	NS
Neuropathy	3 (4)	1 (2)	NS
Anemia	5 (8)	2 (3)	NS
Ingestions/habits			
Antidepressant use	13 (21)	6 (10)	NS
Smoking	7 (11)	4 (7)	NS
Caffeine	16 (26)	8 (13)	NS
Motor/sensory symptoms			
Leg kicks	17 (28)	3 (5)	< 0.001*
Crawling/aching in legs	17 (28)	7 (11)	0.023*
Leg pain	15 (25)	8 (13)	NS

[a] Data are expressed as means ± SD, or total # (%); BMI, body mass index; ESS, Epworth sleepiness scale; *$P < 0.05$; NS, $P > 0.05$.

CO), and electrocardiography (ECG) by single chest lead. All variables were continuously and simultaneously recorded on a Grass 16-channel polygraph (model 8-20E; Astro-Med; West Warwick, RI) or computerized sleep data acquisition system (Healthdyne Technologies, Respironics; Marietta, GA) at paper speed of 10 mm/s. Polysomnograms were scored manually using standard criteria for sleep staging [53] and arousals [54]. Scoring criteria for respiratory events were as follows: (1) obstructive and central apneas were defined by a reduction in airflow to less than 20% of baseline for at least 10 s, with or without effort, respectively; and (2) hypopnea was defined as a reduction in airflow by 50% for at least 10 s accompanied by a 4% oxygen desaturation and/or arousal. The apnea-hypopnea-index (AHI), defined as the sum of apneas plus hypopneas per hour of sleep, was used as the summary statistic for sleep-disordered breathing. PLMS were scored according to ASDA criteria [51] as bursts of muscle activity in the anterior tibialis EMG of 0.5–5 s duration, at least 25% of the amplitude of the calibration level, which were part of a series of four or more movements separated by at least 5 and not more than 90 s. PLMS were scored only during sleep and only if unrelated to respiratory events. Total PLMS and PLMS associated with arousal were recorded and indexed to number per hour of sleep (PLM-index and PLM arousal-index, respectively).

2.5. Statistical analysis

Quantitative data were summarized as means ± standard deviation (SD) and categorical data were summarized as proportions; differences between the groups were analyzed by t-tests for independent samples and Chi-square analysis, respectively. Logistic regression was used to determine the effects of clinical data on the presence of PLMD. PLMD was the dependent variable and the independent variables, selected based on previous literature indicating an association with PLMS, were age, insomnia, hypersomnia, diabetes, spinal disease, peripheral neurologic disorders, anemia, antidepressant medication use, caffeine, smoking, leg kicks, crawling or aching in legs, and leg pain. Because of the possibility that the leg discomfort complaints of crawling or aching in legs and leg pain might indicate RLS, a subgroup analysis was performed in which patients with these complaints were excluded from the PLMD and control groups. Linear regression was used to determine the effects of clinical data on the severity of PLMD (as determined by the PLM-index and PLM arousal-index) and to determine relationships between the severity of PLMD and polysomnographic data. All statistical tests were two-tailed and $P \leq 0.05$ was considered to indicate statistical significance.

3. Results

3.1. Description of study cohort

The PLMD group included 61 patients consisting of 48 males and 13 females with a mean age of 55.2 ± 14.1 years. The mean PLM-index was 41.8 ± 28.4 (range 10–121) movements/h. Twenty-two (36%) patients had a PLM-index of 5–24, 20 (33%) patients had a PLM-index of 25–49, and 19 (31%) patients had a PLM-index of ≥50. The mean PLM arousal-index was 25.9 ± 23.2, with 21 (34%)

patients having a PLM arousal-index of ≥25. The mean AHI for the group was 2.6 ± 2.9 events/h. The control group included 61 patients (43 males and 18 females, mean age 49.6 ± 16.1 years) with a variety of sleep disorders, but the predominant diagnosis was OSA (61% of patients). By definition, the PLM-index was 0 and the mean AHI for the group was 27.2 ± 35.0 (range 0–143).

3.2. Comparison of the PLMD group and control group

As shown in Table 1, the PLMD group was older and had a lower body mass index (BMI) compared with the control group. Gender distribution was similar. There was no difference in the frequency of the presenting complaint, i.e. insomnia or hypersomnia, between the two groups. Thirty-one percent of the PLMD group and 21% of the control group had at least one medical disorder that had been reported to have an association with PLMS, a difference that was not significant. There was no significant difference in the frequency of diabetes, spinal disease, peripheral neurologic disorders, or anemia and none of the patients reported chronic renal failure or pregnancy. Furthermore, there was no significant difference in antidepressant medication use, caffeine consumption, or smoking between the two groups. In terms of specific leg symptoms, there was a five-fold difference (28% vs. 5%, PLMD vs. control) in the frequency of leg kicks in the two groups, a difference that was highly significant ($P < 0.001$). Crawling or aching in legs was also more frequently reported by the PLMD group as compared with the control group (28% vs. 11%, $P = 0.023$). There was no difference in the frequency of leg pain between the two groups.

In the PLMD and control subgroups, in which patients with symptoms of crawling or aching in legs and leg pain were excluded ($n = 40$, aged 54.5 ± 14.7 years and $n = 51$, aged 49.3 ± 15.7 years, respectively), univariate analysis showed no differences in demographics except for BMI (30 vs. 33, $P = 0.007$), no differences in major sleep complaint, no differences in medical conditions, no differences in ingestions/habits except for caffeine (11 (27%) vs. 5 (10%), $P = 0.023$), and a significant difference in leg kicks (11 (27%) vs. 2 (4%), $P = 0.001$).

3.3. Predictors of PLMD

A logistic regression model was created using PLMD as the dependent variable and clinical data as independent variables. As shown in Table 2, age was a significant, although small, predictor of PLMD, with a Wald statistic of 2.01 ($P = 0.044$). Leg kicks, with an odds ratio (OR) of 12.7 (95% confidence interval (CI) 2.80–57.63), and crawling or aching sensation in legs, with an OR of 5.23 (95% CI 1.16–23.44), were significantly related to PLMD. None of the other clinical data were significantly related to PLMD. A review of the partial correlations confirmed that the greatest contribution to the overall model was leg kicks (partial $R = 0.232$), with lesser contribution of crawling or aching in legs (partial $R = 0.128$) and age (partial $R = 0.110$). Analysis of model and residual deviance showed that the percentage of total deviance explained by the model was 21%. The sensitivity of the model in the prediction of PLMD was 67% and the specificity was 82%. Seventy-five percent of the cases were correctly classified. Leg kicks alone had a sensitivity of 28%, a specificity of 95%, a positive predictive value of 85% and a negative predictive value of 57% in the diagnosis of PLMD.

Table 2
Results of multiple logistic regression analysis for the diagnosis of PLMD

Variable	Odds ratio	95% confidence interval	P value[a]
Age	–	–	0.044*
Insomnia	1.20	0.44–3.33	NS
Hypersomnia	0.53	0.21–1.39	NS
Diabetes	1.10	0.31–3.87	NS
Spinal disease	2.25	0.42–11.96	NS
Neuropathy	1.34	0.08–22.66	NS
Anemia	2.73	0.41–18.26	NS
Antidepressant use	3.33	0.95–11.72	NS
Caffeine	2.10	0.68–6.46	NS
Smoking	1.28	0.28–5.84	NS
Leg kicks	12.70	2.80–57.63	0.001*
Crawling in legs	5.23	1.16–23.444	0.029*
Leg pain	0.51	0.11–2.35	NS

[a] *$P < 0.05$; NS, $P > 0.05$.

The logistic regression analysis was repeated using the subgroups of PLMD and control patients without crawling or aching in legs and leg pain. Of all the clinical data, only leg kicks, with an OR of 16.9 (95% CI 2.50–114.48), was related to the presence of PLMD. The sensitivity, specificity, positive predictive value, and negative predictive value of leg kicks in the diagnosis of PLMD were similar to the full data set at 27%, 96%, 85%, and 62%, respectively.

3.4. Predictors of PLMD severity

Within the PLMD group, multiple linear regression was performed using PLM-index as the dependent variable and clinical data as independent variables. Only age ($\beta = 0.354$, $P = 0.009$) was significantly related to PLM-index ($R = 0.60$, adjusted $R^2 = 0.18$). Using simple linear regression, age was positively related to PLM-index ($r = 0.47$, adjusted $r^2 = 0.20$, $P < 0.001$). However, none of the clinical data, including age, were significantly related to PLM-index in the subgroup of PLMD patients that excluded patients with leg discomfort. Multiple linear regression was also performed using PLM arousal-index as the dependent variable, with the same independent variables as above. Only hypersomnia ($\beta = 0.388$, $P = 0.016$) was related (negatively) to PLM arousal-index ($R = 0.58$, adjusted $R^2 = 0.15$). Simple linear regression failed to show a significant relationship between PLM arousal-index and either hypersomnia or Epworth Sleepiness Score.

3.5. PLMD severity and polysomnographic findings

Within the PLMD group, multiple linear regression was performed using sleep efficiency as the dependent variable and age and PLM-index as the independent variables. PLM-index ($\beta = -0.378$, $P = 0.005$), but not age ($\beta = -0.162$, $P = 0.219$) was related (negatively) to sleep efficiency ($R = 0.47$, adjusted $R^2 = 0.19$). Using sleep efficiency as the dependent variable again and PLM arousal-index and age as independent variables, PLM arousal-index and age ($\beta = -0.334$, $P = 0.006$ and $\beta = -0.278$, $P = 0.021$, respectively) were both related (negatively) to sleep efficiency ($R = 0.47$, adjusted $R^2 = 0.19$). Similar analysis was performed using latency to stage 2 sleep as the dependent variable; neither the PLM-index nor the PLM arousal-index was related to the latency to stage 2 sleep.

4. Discussion

Our results indicate that, in patients presenting to sleep centers with a variety of sleep–wake complaints and multiple comorbidities, only age, the presence of leg kicks, and the presence of crawling/aching sensations in legs are to some extent predictive of PLMD. The finding that age is important in PLMD is consistent with other studies [4,5]. The contribution of aging to PLMD in our study was relatively small, but this may be related to the fact that the control group used was not healthy controls, but symptomatic patients with other sleep disorders, primarily sleep-disordered breathing. Previous studies have also noted a positive correlation with aging and PLM-index [12] and between aging and PLM arousal-index [43]. Within our group of patients with PLMD, of all the clinical data analyzed, only age was associated with PLM-index. However, the strength of the association was weak, with age explaining only 20% of the variance. Age was not a significant predictor in the subgroup analysis, in which patients with leg discomfort were excluded. The symptom of always or frequently having leg kicks was associated with a 13-fold increased odds of PLMD. The specificity of this symptom was 95%, suggesting that the presence of leg kicks is helpful in ruling in the diagnosis of PLMD. The symptom of leg kicks noted by patients or their bedpartners has been previously reported in PLMD [19]. However, the majority of patients with PLMD in our study did not report frequent or constant leg kicks, and the sensitivity of leg kicks was only 28%. Therefore, the absence of leg kicks is not helpful in ruling out the diagnosis. The symptom of frequent or constant crawling or aching in legs was associated with a five-fold increased odds of PLMD. Interestingly, crawling or aching sensations occurred in 28% of the PLMD group and 11% of the control group, despite excluding patients with known RLS or clear-cut RLS symptoms on the descriptive portion of the questionnaire. As these symptoms could potentially represent patients with mild RLS (or perhaps indicate nonspecific pain), subgroup analysis was done excluding patients with other leg discomfort. Leg kicks, when present, remained a significant predictor of PLMD in the subgroup.

Specific medical conditions failed to add to the prediction of PLMD. In part, this may indicate that some of the disorders included in our analysis are truly not more prevalent in PLMD than in other sleep disorders. For example, while diabetes has been thought to be associated with PLMS/RLS based on small series [36] and based upon a larger epidemiologic survey [17], a recent study of 58 type 2 diabetics compared with age- and sex-matched non-diabetic controls failed to demonstrate an increased prevalence of RLS in diabetics [55]. Even if there is a relationship between diabetes and RLS or PLMD, it may be obscured in our study by a potential link between diabetes and other sleep disorders such as sleep deprivation [56] or sleep-disordered breathing [57–59]. In this case, the presence of diabetes would not add to the prediction of PLMD in a general sleep medicine population. A potential limitation of this study was that the presence of these conditions was established based upon patient and physician history, not on objective data. For example, clinical anemia may not be as strongly correlated with RLS/PLMS as serum or cerebrospinal fluid ferritin [26]. Neuropathic symptoms and routine neurologic exam may fail to document peripheral axonal neuropathy noted on electromyography, quantitative thermal testing, or nerve biopsy in patients with RLS [29]. However, patients rarely present to sleep centers knowing such data.

We had a symptomatic group of PLMD patients, with 80% reporting insomnia and 57% reporting hypersomnia. However, these major sleep–wake symptoms failed to distinguish patients with PLMD from our controls, perhaps because these are nonspecific symptoms that are common to many sleep disorders. Although the symptom of insomnia was not associated with PLM-index or PLM arousal-index in multivariable analysis of our PLMD group, both PLM-index and PLM arousal-index were associated with reduced sleep efficiency on polysomnography, even controlling for age. PLM-index was not associated with the symptom of hypersomnia. Using PLM arousal-index as the dependent variable in multiple regression, we initially found a negative relationship between PLM arousal-index and hypersomnia. However, this was not supported by further analysis. Similar to our findings, Mendelson [43] previously reported a positive association between PLM arousal-index and age and between PLM arousal-index and wake after sleep onset. He also found no correlation between PLM arousal-index and the sense of awakening refreshed in the morning or hypersomnia as measured by multiple sleep latency testing or by a subjective sleepiness scale. In a previous study of 34 patients with excessive daytime sleepiness and elevated PLM-index, Nicolas et al. [12] found a positive correlation between PLM-index and age, but no association between PLM-index and sleep efficiency on polysomnography or daytime sleepiness as measured by multiple sleep latency testing. The variable correlation in our study and others between quantitative indexes of PLMS and symptoms or polysomnographic findings raises the question of whether

the PLM-index and PLM arousal-index are valid markers of severity in PLMD. The arbitrary definition of PLM-index of $\geq$5 or other cut-offs to define abnormality were not found to predict sleep–wake symptoms in a previous study in older individuals [60]. In part, this may be because PLMS have been shown to vary night to night [61] and vary with sleep stages [62]. Alternatively, PLMS may be a marker for another underlying mechanism that gives rise to symptoms. Given that studies such as these have failed to demonstrate the clinical correlates of PLMS in the absence of RLS, debate about the significance of PLMD continues [3,6,49,50].

Our study has multiple strengths and also some limitations. Compared with other studies, we attempted to avoid any overlap in conditions that would alter our results. We deliberately excluded RLS as well as sleep-disordered breathing and narcolepsy from our control group. We excluded any patients with PLMS from our control group. We used a patient sample of diverse sleep disorders for our control rather than a healthy control group to answer the question of prediction in a clinical setting. We added detailed historical information to sleep symptoms to increase the likelihood of prediction of PLMD. In terms of limitations, much of our data were abstracted from questionnaire data, leading to issues in reliability. However, these are often the only data available on the initial evaluation of the patient. We monitored airflow with thermistors so we cannot exclude the possibility of some patients with UARS or mild OSA in our PLMD group. In some cases, the frequency of medical conditions was low and we could have missed an association.

In summary, we have shown that only age, the presence of crawling or aching sensations in legs, and, in particular, the presence of leg kicks are predictive of PLMD in patients who present to a sleep center with sleep–wake complaints. While frequent leg kicks are the strongest predictor of PLMD, this symptom was usually absent in PLMD patients. Other clinical data were not helpful. We found that, in patients with PLMD, indexes of severity do not correlate with clinical data except for age, but are associated with reduced sleep efficiency, even adjusting for age.

What practical conclusions can be drawn from the findings in our study? If responses to queries regarding leg kicks are negative, as they are in the majority of patients with PLMD, polysomnography is needed to rule out PLMD. If responses regarding leg kicks are positive, this increases the likelihood of PLMD. Options may then include an empiric medication trial, a confirmatory test (polysomnography), or inaction. Medical decision-making for an individual patient, in turn, depends upon the probability or odds of disease and the value or utility of the outcome for the action [63]. The odds of disease in a given patient depend upon, not only the test results, but also the prior probability of disease. Therefore, a positive result on a highly specific test (such as an affirmative response to questioning regarding leg kicks) may be less useful if the prior probability of PLMD is lower, such as in younger patients. As the probability of disease increases (e.g. as patients age), the test becomes more useful. However, older individuals are also at risk for other sleep disorders, such as sleep-disordered breathing, which may be present instead of, or in addition to, PLMD. In one study of 145 elderly individuals who underwent portable sleep recording, 18% met criteria for sleep apnea, 34% met criteria for PLMS, and 10% met criteria for both sleep apnea and PLMS [4]. Older individuals or those with sleep-disordered breathing may be at increased risk of sedative side effects or drug interactions with empiric trials of dopaminergic agents, benzodiazepines, opiates or other medications used for symptomatic patients with PLMD [44,45]. Establishing an accurate diagnosis of PLMD and ruling out other competing diagnoses are therefore warranted in many clinical situations, even at the expense of a diagnostic test. Polysomnography thus remains the gold standard for establishing the diagnosis of PLMD. Further work is needed to define the mechanism of sleep–wake symptoms in patients with PLMS.

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