Physician-diagnosed restless legs syndrome in a large sample of primary medical care patients in western Europe: Prevalence and characteristics

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ABSTRACT

Background: Restless legs syndrome (RLS) is a medical condition with established neuropathology and genetic associations. Significant questions have, however, recently been raised about its true prevalence, medical significance and the degree to which it is under or over-diagnosed. This study therefore aimed to determine its prevalence, morbidity and adequacy of diagnosis based on physician evaluations of their own patients in primary care practice.

Methods: Screening questionnaires were completed by adult patients attending 62 primary care practices across six western European countries within a one-week period. Patients screening positive for significant RLS symptoms were clinically evaluated for RLS by their physician. Physicians also classified the degree RLS affected the patient’s health and well-being. Patients independently completed the SF-36 Quality of Life and Medical Outcomes Study (MOS) sleep questionnaires.

Results: Ten thousand five hundred and sixty-four patients completed the screening questionnaire; 804 responded positively to RLS symptoms and 630 of these were subsequently evaluated by their physician. The physicians diagnosed RLS in 365 patients. Ninety-one percent of these had not been previously diagnosed with RLS. In this cohort of adult primary care patients (without or with prorating for missed interviews) the estimated prevalence for diagnosed RLS was 3.5% or 4.4% and for medically-significant RLS 2.1% or 2.7%. A moderate to high degree of RLS negative impact on health related strongly to a lower vitality subscale on the SF-36 and short sleep times (5.2–5.4 h) with more sleep disturbance on the MOS sleep scale.

Conclusion: RLS in these western European countries is a common, clinically-significant medical condition that, despite all the publicity, remains largely undiagnosed. RLS evaluation is particularly recommended for patients complaining of insomnia.
the individuals identified with RLS symptoms probably did not actually have RLS. Assuming no systematic bias contributed to the false-positive identifications, the data from these questionnaire studies provided a reasonable first look at medical significance of RLS. But they most likely generally over estimated the prevalence of RLS. Moreover, other medical conditions affecting the legs (e.g., claudication, vascular disease, arthritis, neuropathy) may have contributed to those individuals falsely identified as having RLS [14], thereby artificially inflating assessment of clinical significance and the need for treatment.

This study, therefore, sought to determine a conservative estimate of the prevalence and morbidity of physician-diagnosed RLS in a convenience sample of primary-care doctors. The methods minimise false-positive diagnoses by using appropriately trained primary-care physicians to diagnose and evaluate their own patients. The study focused on five epidemiological issues for the selected cohort of primary-care doctors: (1) prevalence of physician-diagnosed RLS among those self-identified as having frequent and at least moderately distressing RLS symptoms; (2) prevalence and degree of medically-significant RLS in this population based on physician-judged health impact of RLS, ranging from none to severe; (3) patients' reported quality of life and sleep in relation to physician-judged RLS impact on health; (4) poor sleep (insomnia) complaint for the overall population compared to those diagnosed as RLS patients; and (5) the rate of prior correct diagnosis of RLS (the degree of under-diagnosis).

2. Methods

A screening questionnaire for RLS was developed from one used in previous studies [1]. It included questions regarding poor sleep, the four essential RLS diagnostic criteria, and the frequency and degree of distress for RLS symptoms (see table submitted on-line). Primary care physicians (PCPs) from 62 practices in six western European countries agreed to participate in the study. They were selected to represent (as much as possible) areas of each country, but this selection was limited to those willing to participate. Each PCP was trained in the diagnosis and evaluation of RLS by a local expert in RLS. This training emphasised both correct identification of RLS symptoms and also differential diagnoses, particularly in relation to other sources of leg pains or discomfort that produce symptoms that mimic those of RLS [14,15]. A poster board was placed in each of their surgeries asking patients to complete a questionnaire on their health. Patients received no other advanced information of their surgeries asking patients to complete a questionnaire. The frequency and degree of medically-significant RLS in this population based on physician-judged health impact of RLS, ranging from none to severe; (3) patients' reported quality of life and sleep in relation to physician-judged RLS impact on health; (4) poor sleep (insomnia) complaint for the overall population compared to those diagnosed as RLS patients; and (5) the rate of prior correct diagnosis of RLS (the degree of under-diagnosis).

3. Results

3.1. Prevalence of physician-diagnosed RLS

Eight hundred four (7.6%) of the 10,564 original patients responding to the screening questionnaire reported clinically significant symptoms of RLS. Six hundred and thirty (78.4%) of these 804 patients completed the diagnostic interview with the PCP. The remaining 174 dropped out before the diagnostic interview. The exact reasons for dropping out were not established but many patients were not available for interview within the set timelines. The PCPs confirmed a diagnosis of RLS in 365 (57.9%) of the 630 patients interviewed, giving a prevalence of 3.5% for the total cohort sample (365/10,564). The average age of the patients diagnosed with RLS was 55.6 years (SD ± 14.5), and 75.6% (F:M 276:89) were female. If we assume that the 174 patients who dropped out suffered from RLS in the same percentage as those who were interviewed, the prevalence would be prorated to 4.4% for diagnosed RLS in this primary care cohort.

These prevalence figures varied across these European countries, ranging from 2.1% to 5.0% (unadjusted) and from 2.4% to 6.0% (prorated for missing interviews) (Table 1).

3.2. Prevalence and degree of medically-significant RLS based on physician-judged health impact of RLS

The negative health impact of RLS symptoms was judged by the PCPs to be none for 4.7% (17/365), little for 21.6% (79/365), some (moderate) for 43.3% (158/365), and high for 17.3% (63/365) of the patients diagnosed with RLS. The physicians failed to make any comment on the health impact of RLS for 13.2% (48/365) of the patients with RLS (Fig. 1). The very small numbers in the “no impact” group were combined with the “little impact” group for most subsequent analyses. The overall prev-
lence of RLS among all 10,564 patients completing the screening survey with varying degrees of PCP-judged negative health impact was “little or no” impact, 0.9% or 1.2% (not prorated or prorated for missed interviews, respectively); “some/moderate” impact, 1.5% or 1.9%; and “high” impact, 0.6% or 0.8%. This gives a prevalence in this cohort of 2.1% or 2.7% for medically-significant RLS, defined as RLS that had some/moderate or high health impact.

3.3. Patients reported quality of life and sleep relationship to physician-judged RLS impact on health

The SF-36 scores were analysed according to the three categories of health impact independently assessed by the patients’ PCP. As shown in Fig. 2, the average SF-36 domain scores for each of the dimensions decreased (became worse) with the increasing degree of health impact. Differences between the health-impact categories were significant \( (p < 0.05) \) based on one-way analysis of variance (ANOVA) tests for all SF-36 domains except Role Emotional and Mental Health.

The pair-wise comparisons between each of the three health-impact categories were analysed for each SF-36 dimension with an overall significance for health impact factor on the ANOVA. Pair-wise differences were significant \( (p < 0.05) \) Fisher protected least significant difference, FPLSD) for the extremes of “high” impact compared with “little/no” impact on Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality and Social Functioning dimensions. Social Functioning also showed a significant pair-wise difference between the “high” and “some (moderate)” negative impact groups. Vitality was the only dimension that showed significant pair-wise differences between all levels of impact groups including the “some (moderate)” versus “little/no” groups (Fig. 2).

The MOS sleep scale [16] was completed by each of the 365 individuals diagnosed with RLS by their PCP. Fig. 3 shows the MOS scores across each of the seven domains separately for each level of RLS health impact. The normative data provided here as a comparison comes from a general adult population in the USA [17]. No European norms are available.

Statistical analyses for the difference in frequency of sleep problems between the three levels of RLS health impact showed overall significant differences \( (p < 0.05) \) for the MOS scales of Sleep Quantity, Sleep Disturbance, Sleep Adequacy and the Sleep Problems Index. The FPLSD pair-wise comparison showed these differences were significant between each of the three health-impact levels for all of the aforementioned scales except Sleep Quantity. Sleep Quantity had an overall difference between groups that showed significantly lower values for both “high” (mean ± SD, 5.2 ± 2.2 h) and “moderate” (5.4 ± 2.2 h) health compared with “little/no” health impact (6.4 ± 1.8 h) \( (p < 0.01) \), but not for “high” compared with “some (moderate)” health impact \( (p > 0.05) \). The subscale for Shortness of Breath showed an overall effect and a significant difference \( (p < 0.001) \) only between the levels of “high” and “little/no” impact. No significant differences for the MOS scales for Snoring or Daytime Somnolence were reported in relation to health status.

3.4. Poor sleep (insomnia) complaint for the overall population and the diagnosed RLS patients

In the screening questionnaire, all 10,564 patients sampled were asked in the screener questionnaire “How often do you experience poor sleep?” Poor sleep was reported by 10.8% (1145/10,564) every night, 17.5% (1852/10,564) at least 4 nights a week and 30.1% (3175/10,564) at least 2 nights a week. Of the 3175 individuals with poor sleep, at least 2 nights a week (the frequency criteria for RLS symptoms) 9.7% (307/3175) were subsequently diagnosed with RLS by the PCPs.

The frequency of sleep disturbance related to the degree of health impact of RLS (Fig. 4). Those judged to experience a “high”
Some negative impact had significantly greater frequency of sleep disturbance (58.1% at least 4 nights a week) than those with “some (moderate)” (46.5% at least 4 nights a week) or “little/no” negative impact (35.1% at least 4 nights a week) \( (p < 0.001) \).
3.5. Rates of prior correct diagnosis of RLS (degree of under-diagnosis)

Of all patients with RLS, 40% reported having previously consulted their physician with regard to their RLS symptoms. This percentage was greater for those where RLS was judged to have a greater health impact; 46.0% (29/63) with “high” impact, 39.2% (62/158) with “some (moderate)” impact, and 26.0% (25/96) with “little/no” impact. Overall, 28.4% of the 40% who consulted about their symptoms had been given a prior diagnosis of RLS, and this rate was similarly greater for those whose RLS was judged to have greater health impact: 41.4% (12/29) with “high” impact, 27.4% (17/62) with “some (moderate)” impact, and 16.0% (4/25) with “little/no” impact. Overall, 9% of all the diagnosed RLS patients had been previously diagnosed with RLS: 19% of those with “high” impact, 10.8% with “some (moderate)” impact, and 4.2% with “little/no” impact.

3.6. Prior healthcare utilisation by RLS patients

The PCPs’ reports indicated that the patients diagnosed with RLS had consulted with their PCP, on average, 10 times over the past 12 months. These consultations were for any reason and were not limited to RLS symptoms.

4. Discussion

This study provides the first large international assessment of prevalence and medical significance of physician-diagnosed RLS. It was obtained from a cohort of primary-care physicians in 6 western European countries. There are two significant limitations to the study. First, the PCPs were selected from those willing to participate in the study. These PCPs likely had more interest in RLS than most. While this assured care in making a correct diagnosis, it may have also meant that these doctors were aware that their practice included an unusual amount of RLS. But this seems unlikely since only 9% of the RLS patients had been previously diagnosed with RLS. What it does mean is that this cohort cannot be considered to represent the population of all PCPs; rather, this is a convenience sample. The selection, however, seems unlikely to have produced any systematic bias and (to the extent that is the case) can be considered to represent the primary care population in the countries surveyed. Second, the patients were first screened to identify only those self-reporting significantly frequent and distressing RLS symptoms. This likely excluded some with RLS and certain exceedingly less frequent RLS that may have deserved medical attention. The screening was needed in order to make this a manageable project. It was, however, our intention to provide a very conservative evaluation of RLS and thus the very practical limitation to evaluate only those screening positive for RLS. It deserves to be noted that this screening criteria generally worked in that only 5% of the diagnosed cases were considered to have no significant medical or health problems with their RLS. Thus the screening criteria for medical significance, if diagnosed, can be considered to be about 95% specific; the degree of sensitivity was, however, not evaluated in this study.

The estimated prevalence for diagnosed RLS is 3.5–4.4% of adult patients treated by this cohort of primary care doctors in these six western European countries. More significantly the physicians judged that RLS had a moderate-to-high impact on the health and well being for 2.1–2.7% of their patients. It is important to note that the physician was assessing the degree to which the RLS itself adversely affected their patients and thus these figures of 2.1–2.7% provide reasonable conservative estimates of the population expected to benefit from effective treatment. Even in this sample of western European PCPs chosen because of their willingness to learn about RLS, the prevalence of RLS as a medically significant disorder to be diagnosed and treated is about 2–3% and not 10–15%, as suggested by quoted data from prior studies. But this still makes it one of the more common medically significant neurological disorders. Even more important, however, is the considerable number (0.6–0.8% of all adult patients in this study) for whom RLS is judged to have a high negative impact on health, clearly indicating the importance of providing diagnosis, particularly given the availability of reasonably effective treatments [18].

Given all the efforts that have been spent on medical education about RLS, the limited prior diagnosis of this condition in this cohort of western European primary care patients is rather astonishing. Only 9% of all those diagnosed with RLS had been previously diagnosed. While, as expected, the rate of prior RLS diagnosis...
was higher when the medical impact of RLS was greater; nonetheless it remained remarkably low.

This sample of clearly diagnosed RLS patients from this large international primary care population provides evaluation of RLS morbidity without concern about a high level of false RLS identification distorting the results. The MOS sleep scale has been validated for use with RLS patients [16] and its results here indicate that greater clinical significance of RLS, as judged by a PCP, occurs with poorer sleep. A reduced sleep quality is particularly apparent on the MOS domains of Sleep Disturbance, Sleep Adequacy, Sleep Quantity and the Sleep Problems Index II. The average total sleep time of those with high and moderate health impact was less than 5.4 h, with the “high” health impact group reporting on average only 5.2 h of sleep. In contrast, those with little or no health impact from RLS reported on average 6.4 h of sleep approximating, as would be expected, the normative average of 6.8 h for a US general population [17]. These subjective reports of chronic short sleep times for medically significant RLS are consistent with the objective sleep times reported in most polysomnographic recordings of moderate-to-severe untreated RLS patients [19,20]. The very short and disturbed sleep observed in the most severe RLS patients seems likely to be a prime factor driving the adverse health impact of RLS [21]. The MOS scale related to sleep disordered breathing, however, shows significant differences only between the little/no and high health impact groups (see Fig. 3). It is only in this group of high health impact that we see a preponderance of profound sleep loss likely to produce the expected effects of chronic severe sleep loss including increased risk of obesity and consequent sleep apnea [22–24]. It is striking that despite the significant sleep loss, particularly for more severe RLS, there was no significant relation between RLS health effects and increased daytime sleepiness. Another study similarly reported that, despite significant sleep loss, untreated RLS patients showed no significant daytime sleepiness on objective measures [25]. It appears that RLS includes some sort of arousal that compensates for the profound persistent sleep loss. Future evaluations of RLS morbidity should include a focus on putative effects of more severe sleep loss associated with a more severe disorder.

In relation to Quality of Life (QoL), the profound negative effects of RLS reported in questionnaire-based epidemiological studies were confirmed in this study [1,26]. Only the SF-36 domains of Role Emotional and Mental Health show little or no evidence of becoming worse for those judged by the PCP to experience a high compared to little negative impact from their RLS. In contrast, the domain of Vitality was particularly closely related to the judged degree of RLS impact with statistically significant (p < 0.05) differences between each level of clinical impact. This is also consistent with the expected effects of chronic sleep loss in this population. It is noteworthy even though RLS has been associated with mental health problems and an increased risk of depression and panic disorder [27,28]. These data indicate that the primary health impact of the disease involves more physical than mental health issues. It appears that when RLS severely affects health-related QoL it is associated most with physical complaints and limitations (e.g., increased bodily pain).

It might seem surprising that the mainly nocturnal RLS symptoms should relate so much to physical rather than mental health QoL domains, but recent experimental and epidemiological studies of chronic sleep loss have indicated large effects on physical functioning, including increased pain sensitivity [29,30], abnormal hormonal regulation [31], increased insulin resistance and risk of being over weight [32], and of course increased fatigue and decreased “vitality.” Thus, the physical effects on QoL for severe RLS could be expected given the severe chronic sleep loss, and, as noted above, they relate to the degree of sleep loss.

Overall this study demonstrated that medically significant RLS, diagnosed by physicians, is a common disorder affecting 2–3% of adults in this particular primary care population and that 0.6–0.8% of this population suffer from RLS which has a highly significant effect on health and well being. The failure to diagnose and treat 8 out of 10 patients who have this treatable medical disorder with a high impact on their health indicates that for RLS we have, at least for these six western European countries, a significant unmet medical need. These data also suggest that one approach to this problem would be to emphasize RLS in the diagnostic assessment of an insomnia complaint. RLS then becomes an important part of doctors’ education about sleep medicine and another major reason that routine medical evaluation should always include a sleep assessment.

Conflict of interest

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References


