

A Prevalent Sleep Disorder in Older Adults: Restless Legs Syndrome (Is There Any Association with Other Geriatric Syndromes?)

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Abstract

Objective: Restless legs syndrome (RLS) is a common sleep disorder which affects quality of life in older individuals. We aimed to find out the geriatric syndromes and other factors significantly associated with RLS in an older study population.

Materials and Methods: This was a retrospective, cross-sectional study conducted with the participants ≥ 60 years old who admitted to the geriatric outpatient clinic of a tertiary hospital. The essential clinical features of RLS had to be present for diagnosis of RLS. We assessed geriatric syndromes like sleep disturbance, falls, polypharmacy (≥ 5 medications/day), constipation, chronic pain, cognitive impairment, depression, dysphagia, urinary and fecal incontinence, malnutrition, sarcopenia, frailty, dependency in basic and instrumental activities of daily living and reduced quality of life.

Results: There was a female predominance (67.7%) in the overall study group ($n=492$). Median age was 73 (69-78). RLS was seen in 28.5% and it was significantly higher in female participants ($p=0.03$). Sleep disturbance, depressive mood, fear of falling, reduced quality of life, frailty and polypharmacy were significantly more prevalent in the RLS group ($p<0.001$, 0.001, 0.04, 0.004, 0.01 and 0.02, respectively). Multivariate analysis revealed that the only factor independently associated with RLS was age [odds ratio (95% confidence interval) =0.9 (0.87-0.96); $p<0.001$].

Conclusion: Although depression, fear of falling, frailty, polypharmacy, sleep disturbance and reduced quality of life were more prevalent in the RLS group, none of them were independently associated with RLS. Advanced age in the older population might be protective for RLS.

Keywords: Aging, geriatric assessment, geriatric syndromes, restless legs syndrome, sleep disorders

Introduction

Restless legs syndrome (RLS), also known as Willis-Ekbom disease, is a neurological movement disorder characterised by an uncontrollable urge to move (mainly the legs), exclusively during times of inactivity/rest (1). It was introduced by Sir Thomas Willis as a clinical condition in 1685 and the term RLS was coined and clinical features described by Karl-Axel-Ekbom in 1944 (2). It was suggested that RLS was associated with low intracerebral iron stores and downregulation of striatal dopamine receptors. Therefore, dopaminergic medications have been the basis of RLS treatment for years (3).

The prevalence of RLS was reported to be 5-15% and women are affected as twice as men (4). The prevalence increases with age, as it has been reported up to 35% in older adult population (4,5). Besides from well-known risk factors like iron deficiency and uremia, several other medical conditions including arthritis, sensory neuropathy and neurodegenerative diseases are associated with RLS and are also more prevalent in older adults (3). As a frequent but mostly undiagnosed sleep disorder, RLS was reported to have significant relationship with negative outcomes like decrease in quality of life, impaired daytime functioning, falls and impaired cognitive performance in older adults (6-8). Although these findings might be in line

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with expectations, the results are not always consistent in the literature (9,10). Apart from dependency in activities of daily living, falls, or impaired cognitive functioning, there are also other common clinical conditions in older adults, called geriatric syndromes, whose relationship with RLS needs to be clarified. In fact, there is a lack of studies in the literature regarding relationship between RLS and geriatric syndromes, identified by a comprehensive geriatric assessment (CGA).

Therefore, this study aims to detect RLS prevalence, and find out the RLS associated geriatric syndromes and other clinical conditions in community dwelling older adults.

Materials and Methods

Population and setting

This study is a retrospective, cross-sectional study conducted in a tertiary health clinic. We included the patients aged ≥ 60 years who admitted to the geriatric outpatient clinic between November 2012–December 2019. The exclusion criteria were: i. Being younger than 60 years, ii. Refusal to participate, iii. Moderate to severe dementia or getting ≤ 20 points from mini-mental state examination, iv. Communicative problems (like severe hearing loss), severe form of depression or psychosis that would prevent establishing healthy communication and getting reliable information. We obtained informed consent from all of the participants. The İstanbul University Local Ethics Committee approved the study (reference: 905400/2022).

RLS diagnosis and CGA

We obtained demographic (age, gender, education level and marital status) and clinical (chronic diseases, number of medications, tobacco use and alcohol intake) characteristics of the study population. We assessed for RLS based on the International Restless Legs Syndrome Study Group (IRLSSG) diagnostic criteria (11). We performed CGA to all of the participants. We asked for sleep disorders, by asking whether they had trouble falling asleep, staying asleep, or if they thought they were having insufficient sleep or excessive sleepiness. We assessed falls during previous year (if yes, how many times), and fear of falling. We asked for chronic constipation using the Rome IV criteria for the definition (12). We evaluated whether they had urinary and/or fecal incontinence affecting daily life. Also, we asked whether they suffer chronic pain that last for at least three months. We checked all of the prescribed medications, over-the-counter drugs and supplements and considered taking ≥ 5 medications/day as polypharmacy. We assessed dysphagia by simply asking whether subjects had difficulty in swallowing food and/or drink.

We assessed basic Activities of Daily Living (ADL) via Katz ADL index and Instrumental ADL by Lawton IADL scale (13,14). Katz ADL is six-itemed and Lawton IADL is 8-itemed scales with a

score of zero means complete dependency and full points mean complete independency, for both tests. We checked for frailty via FRAIL (Fatigue, Resistance, Ambulation, Illnesses, Loss of weight) scale. FRAIL scale is a five-itemed questionnaire with a scoring system of: 0 point means robustness, 1–2 points pre-frailty and 3 or more points frailty (15). We assessed nutritional status via Mini-Nutritional Assessment–Short Form (MNA-SF). An MNA-SF score of < 8 was interpreted as malnutrition, and 8–11 was interpreted as malnutrition risk (16). We evaluated cognitive status via Mini-Mental State Examination (MMSE), with a threshold of ≤ 24 points regarded as cognitive impairment (17). We determined the degree of cognitive impairment according to MMSE scores as follows: 21–24 points meant mild, 10–20 points moderate, and < 10 points severe dementia. We used Geriatric Depression Scale to screen depressive mood and a threshold of ≥ 10 points was regarded as positive for depressive mood (18). We also evaluated quality of life via EuroQol-5 Dimension-3 Levels questionnaire (EQ-5D-3L) descriptive system. It consists of five domains (i.e., mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with three levels of functioning (i.e., no problems, some problems or severe problems). Higher scores reflect a reduced quality of life (19).

Measurements

We measured height and weight using a standardized stadiometer with participants wearing light clothing and no shoes. We measured body weight and height to the nearest 0.1 kg and 0.1 cm. We calculated body mass index (BMI) as weight (kilograms) divided by height² (meters). We evaluated sarcopenia in line with the European Working Group on Sarcopenia in Older People (EWGSOP2) guideline (20). Accordingly, we measured handgrip strength via Jamar hydraulic hand dynamometer in the sitting position, elbows in 90° flexion and wrist in neutral position. We asked the participants to apply maximum grip strength for three times with both hands. We considered maximal grip strength as the grip strength value (21,22). We used the cut-offs recommended by the EWGSOP2 for low muscle strength (< 27 kg and 16 kg for males and females, respectively) and defined having low muscle strength as “probable sarcopenia” (20). We measured muscle mass via Tanita BC-532 bioimpedance analyzer (BIA). BIA provided fat-free mass (FFM) and we calculated total skeletal muscle mass (SMM) by the following equation: $SMM (kg) = FFM \times 0.566$ (23). We adjusted SMM for BMI to identify decreased muscle mass. Although EWGSOP2 recommends the use of standard cut-off values for appendicular SMMI, use of national total SMMI thresholds, if available, is suggested for total SMM evaluation (24). The Turkish older population SMMI thresholds was reported as 1.049/0.823 kg/BMI, for males and females, respectively (25). The presence of both low muscle strength and low muscle mass was defined as “confirmed sarcopenia”. We excluded the patients having certain conditions that might prevent reliable assessment of handgrip

strength (hand osteoarthritis, peripheral artery disease, stroke, etc.) or FFM (metal implants, cardiac pacemakers, etc) from the measurements stated. The geriatricians performed all of the questionnaires and assessments on geriatric syndromes and a qualified physiotherapist performed all of the measurements.

Statistics

We investigated whether the numerical variables distributed normally or skew using visual (histograms and probability plots) and analytical methods. We presented parametrical variables as mean \pm standard deviation and non-parametrical variables as median and interquartile range. We presented categorical variables as numbers and percentages. We used the chi-square test with Yates correction and Fisher's Exact test as appropriate for categorical variables. We used independent samples t-test or Mann-Whitney U test in order to compare differences between two independent groups. We performed logistic regression analyses to identify factors independently associated with RLS. Before running regression analyses, we performed Pearson, Spearman or Kendall's tau-b correlation analyses to check for multicollinearity between independent variables expected to have a close relationship with each other. We accepted a cut-off p-value of <0.05 for statistical significance. We used the Statistical Package for Social Sciences (SPSS) for Windows 21.0 program for statistical analysis.

Results

We included 492 older adults with 333 (67.7%) being female. Median age was 73 (69-78). One-hundred forty patients (28.5%) had RLS diagnosis. Demographic and clinical characteristics of the study group can be found in Table 1.

Subjects with RLS were younger; had higher percentage of female gender, higher number of chronic illnesses and regular drugs, and higher BMI (p-values were 0.007, 0.03, 0.02, 0.03, and 0.03, respectively). According to the CGA findings, RLS group had significantly higher prevalence of depressive mood, fear of falling, frailty, reduced quality of life, polypharmacy and sleep disturbance (p-values were 0.001, 0.04, 0.01, 0.004, 0.02 and <0.001; respectively). CGA findings can be found in Table 2.

We ran a multivariate analysis, defining the factors associated with RLS (according to the univariate analyses) as independent variables and found out that "age" was the only factor independently associated with RLS [Odds Ratio (95% Confidence Interval) =0.9 (0.87-0.96); p<0.001]. Logistic regression analysis findings are presented in Table 3.

Discussion

In this study, we found out that RLS patients had significantly higher prevalence of geriatric syndromes like depression, fear of falling, frailty, polypharmacy and sleep disturbance; and their

Table 1. Demographic and clinical characteristics of the study population (n=492)

Age (years) (med; IQR)	73 (69-78)
Gender (female) (n, %)	333 (67.7%)
Education level (n, %)	
Illiterate	133 (27.2%)
Primary school	197 (40.3%)
Secondary school	37 (7.6%)
High school	51 (10.4%)
University	71 (14.5%)
Marital status	
Single	6 (1.3%)
Married	279 (58.4%)
Divorced	10 (2.1%)
Widow	183 (38.3%)
Tobacco use (n, %)	43 (9.1%)
Alcohol use (n, %)	18 (4.7%)
Number of chronic illnesses (med; IQR)	4 (2-5)
Number of regular drugs (med; IQR)	6 (4-8)
BMI (kg/m²) (mean \pm standard deviation)	30.4 \pm 5.9
BMI: Body mass index, med: Median, IQR: Interquartile range	

quality of life significantly reduced compared to the subjects without RLS. According to the logistic regression analysis, age was the only independent factor associated with RLS, and it seemed that individuals with very advanced age might be suffering less from RLS in the older adult community.

RLS prevalence in our study was in line with the literature. There are a few studies on RLS from Turkey reported a prevalence range of 15-28% (7,26,27) in older population. The prevalence and severity of RLS has known to be increased with increasing age, as certain conditions that accompany RLS are seen more frequent in advanced age; like chronic kidney disease, chronic neurological disorders and use of medications that are considered to exacerbate RLS. Likewise, "age" was the only factor independently associated with RLS in our study, but in an unexpected manner: Older age seemed protective for RLS. In fact, there are a plenty of studies reporting increasing prevalence by age (28,29), however this does not seem to be the case in older adult population. Some studies reported an increase up to 70 years and then a decrease in RLS prevalence in older subjects (30-32). Also, certain studies conducted on specifically older populations did not report an increase in RLS prevalence with increasing age as well (33). Advanced age being a favorable trait for RLS may be explained by "survival effect". It is well-known that certain comorbidities like chronic kidney disease or diabetes mellitus are companions of RLS, especially when RLS is a late onset. Patients with these comorbidities would have ended up with early mortality and the rest of the long living seniors are probably more healthy and have less

Table 2. Comprehensive geriatric assessment findings of the study population

Geriatric syndrome	Total	RLS (-)	RLS (+)	p-value
Sleep disturbance	195 (39.6%)	117 (33.2%)	78 (55.7%)	<0.001
Falls in the previous year	198 (40.4%)	139 (39.6%)	59 (42.4%)	0.6
Fear of falling	219 (44.7%)	146 (41.7%)	73 (52.1%)	0.04
Malnutrition	125 (25.4%)	86 (24.4%)	39 (27.9%)	0.4
Frailty	99 (20.7%)	61 (17.8%)	38 (27.9%)	0.01
Sarcopenia (probable)	60 (12.5%)	17 (12.6%)	43 (12.4%)	0.9
Sarcopenia (confirmed)	31 (6.5%)	22 (6.4%)	9 (6.7%)	0.9
Dependency in ADL	139 (28.3%)	95 (27.0%)	44 (31.4%)	0.3
Dependency in IADL	154 (31.3%)	114 (32.4%)	40 (28.6%)	0.4
Dysphagia	40 (10.1%)	25 (8.9%)	15 (13.0%)	0.2
Urinary incontinence	200 (40.7%)	140 (39.8%)	60 (42.9%)	0.5
Fecal incontinence	22 (4.5%)	16 (4.5%)	6 (4.3%)	0.9
Constipation	129 (26.4%)	85 (24.4%)	44 (31.4%)	0.1
Cognitive impairment	44 (8.9%)	34 (9.7%)	10 (7.1%)	0.4
Depression	154 (48.3%)	94 (42.3%)	60 (61.9%)	0.001
Polypharmacy	309 (65.1%)	211 (61.9%)	98 (73.1%)	0.02
Chronic pain	287 (58.6%)	196 (56%)	91 (65%)	0.07
Reduced QoL	359 (80.0%)	244 (76.5%)	115 (88.5%)	0.004

ADL: Activities of daily living, IADL: Instrumental activities of daily living, QoL: Quality of life

Table 3. Multivariate analysis regarding factors independently associated with RLS

Variables	OR (95% CI)	p-value
Age	0.9 (0.87-0.96)	<0.001
BMI	1.01 (0.9-1.1)	0.8
Depression	1.4 (0.8-2.5)	0.3
Decreased QoL	1.8 (0.8-4.3)	0.2
Fear of falling	0.9 (0.6-1.8)	0.9
Female gender	0.6 (0.31-1.14)	0.12
Frailty	1.7 (0.9-3.5)	0.1
Number of chronic diseases	1.02 (0.9-1.2)	0.8
Polypharmacy	1.7 (0.9-3.1)	0.1
Sleep disturbance	1.6 (0.9-2.8)	0.1

BMI: Body mass index, CI: Confidence interval, OR: Odds ratio, QoL: Quality of life, RLS: Restless leg syndrome, p-value of less than 0.05 was accepted as statistically significant

comorbidity burden in their ageing period. In addition, the older adults who applied to our outpatient clinic were mostly those under the long-term follow-up of our clinic and whose treatments for secondary causes of RLS are optimally arranged. Apart from all these, some older adults in very old age might have neglected their symptoms, or showed a stoic approach that those sensations were a natural part of normal ageing process, like chronic pain. Therefore, symptoms might be underreported by older subjects.

Female predominance in RLS diagnosis in our study was also consistent with the previous studies (28,30). Estrogens,

dopamine and RLS have a close relationship with each other; as the prevalence of RLS significantly increases with pregnancy as estrogen levels are rising (34). Estrogen acting as a dopamine antagonist has been hypothesized as its role in RLS. However, it was also suggested that fluctuations rather than absolute level (as in pregnancy or perimenopausal period) might be the main reason behind RLS tendency in female individuals (35). In fact, there are surveys manifesting that nulliparous women were at the same risk of RLS as same aged men, while the risk was increased in direct proportion as the number of pregnancies increased (36,37). There are other RLS studies reporting male predominance as well (38). Although female subjects had significantly higher numbers of RLS diagnosis, "female gender" was not a risk factor for RLS, according to our regression analysis.

The secondary outcome of our study was to investigate the relationship between RLS and geriatric syndromes and we found out that older adults suffering RLS had higher prevalence of sleep disturbance, depression, fear of falling, frailty, polypharmacy and reduced QoL. RLS and mental health are considered to have a "chicken and egg" relationship: People with RLS often have depression, anxiety, and other mental health issues. And, people with depression or anxiety often have restless legs (39). Clinical and epidemiological studies have reported data supportive of this hypothesis (40). Increase in depressive mood has been attributed to the RLS related sleep impairment and its sequelae; as impaired sleep can create a loss of energy and decreased daytime functionality, which are the somatic symptoms of depression. Dopamine was also implicated in the

causation of depression and treatment of RLS is thought to improve depression in RLS (41). Several antidepressants that are frequently used in treatment of depression, like selective serotonin re-uptake inhibitors or atypical antidepressants like mirtazapine, were also reported to aggravate RLS symptoms (42). In our study, although there were significant relationships between depressive mood and RLS, depression was not an independent factor related to RLS.

Fear of falling has a significant importance in geriatric health. It may develop after falls or without any falling experience and may bring out significant negative outcomes like deconditioning, decreased muscle strength and mass, increased risk of future falls and mood disorders like depression and anxiety (43). Although we did not find any relationship between RLS and falls during past year, fear of falling was significantly more prevalent in patient suffering RLS. This might be attributed to the certain factors strongly associated with RLS that might also be facilitators of previous falling episodes, like neuropathies or Parkinson's disease. Again, the significant relationship between fear of falling and RLS was disappeared after regression analysis.

Apart from depression and anxiety (fear of falling); RLS was also significantly associated with reduced QoL, which is an expected finding and consistent with the previous studies (6). EQ-5D-3L has parameters assessing mobility, self-care, day-time functionality, pain/discomfort and anxiety/depression, and most of them were already demonstrated to have a close relationship with RLS (8).

According to our findings, older patients with RLS were more frail than subjects without RLS. To the best of our knowledge, there is no study in the literature investigating the relationship between these two common conditions in older adult population. We screened frailty via FRAIL scale; which comprises five items questioning fatigue, resistance, ambulation, diseases and weight loss. Patients with RLS have sleep disturbance, decreased sleep quality, daytime sleepiness, fatigue and tiredness (8). Fatigue and tiredness might affect daytime functioning and cause difficulty and trouble in ambulation and climbing stairs. Furthermore, we found out that RLS patients had higher number of chronic comorbidities; therefore certain ones that are known to be associated with RLS might have caused fourth item of FRAIL to be positive. Finally, although there was no significant difference between RLS and non-RLS groups in terms of MNA-SF results, patients who had weight losses, but not malnourished according to MNA-SF, might have iron, vitamin B12 or folate deficiencies, which are known to be associated with RLS symptoms as well (1). Indirect relationships stated above might have caused the significant association found in univariate analysis; as the relationship disappeared after adjustments in regression analysis.

Our analysis showed that the RLS group had a higher number of medications and polypharmacy prevalence. Polypharmacy has a strong relationship with adverse outcomes like decreased physical performance, falls, fractures, disabilities, increased hospitalizations and even mortalities in older adult population (44,45). Several medications commonly used in the older adult population are known to aggravate RLS. According to a literature review including 32 articles related to RLS, the strongest evidence available for drug induced RLS are for the following drugs: Escitalopram, fluoxetine, L-dopa/carbidopa, pergolide, L-thyroxine, mianserin, mirtazapine, olanzapine and tramadol (46). Commonly used medications in geriatric practice (like metformin or proton-pump inhibitors) can cause decreased appetite and oral intake or iron and vitamin B12 malabsorption, hence develop RLS symptoms (47). Evaluating "the use of drugs that might predispose to RLS" or "inappropriate medication use", rather than "polypharmacy" might reveal a significant relationship with RLS, as the regression analysis revealed that polypharmacy was not an independently associated factor with RLS.

We found no relationship between RLS and urinary/fecal incontinence, constipation and dysphagia. Similar to our results, a retrospective analysis of a data derived from older adults have reported that although autonomic complaints were significantly increased in RLS patients, there were no differences between RLS and control groups in terms of urinary/fecal incontinence, constipation and dysphagia (48). Finally, we found out that RLS did not demonstrate an association with sarcopenia, whether it was probable or confirmed. There are very limited studies regarding sarcopenia and RLS relationship in the literature. Giannaki et al. (49) conducted a study on uremic RLS patients and assessed total muscle mass via dual energy X-ray absorptiometry and regional (thigh) muscle mass via computerized tomography. They found out that total body composition assessment did not show any differences between the RLS and non-RLS groups; but thigh muscle total area, muscle cross sectional area (CSA) and the level of muscle fat infiltration were significantly reduced in the RLS group. There were no differences in terms of physical performance (evaluated via walking test and sit-to-stand tests) (49). According to a Japanese study conducted on 1592 older adults, sarcopenia (evaluated via Asian Working Group for Sarcopenia definitions) was significantly associated with difficulty initiating and/or maintaining sleep; but there was no subgroup analysis for RLS patients (50). In fact, the relationship between RLS and incontinence, constipation, dysphagia and sarcopenia might seem a little bit forced. However, as previously mentioned, there are studies reporting autonomic dysfunction in RLS patients and this might end up with dysphagia, incontinence or constipation (48). In addition, several conditions like neurodegenerative disorders (like Parkinson's disease) or neuropathies might also

be underlying causes for sarcopenia. Therefore, we wanted to include these geriatric syndromes in the CGA and search whether they have an independent association with RLS. As such, further studies are needed to clarify the exact relationship between RLS and stated geriatric syndromes.

Although there is no study that comprehensively examines the relationship between RLS and geriatric syndromes like our study, some of them studied RLS and certain geriatric syndromes relationship in older adults. In a Turkish study; depressive mood, sleep quality, sleep duration, and difficulty in falling asleep were all significantly associated with RLS; but the relationship did not persist in regression analysis, except for sleeping less than 6 hours/day (26). An American study including 1008 older adults reported that patients with RLS demonstrated increased risk of chronic pain, three or more chronic medications, frequent falls, sleep disturbances and decreased functionality (51). According to a French study comprising of 318 older subjects, participants with RLS had significantly higher anxiety and depression scores, lower cognitive performances and greater hypnotic and antidepressant medications (4). A cross-sectional case-control study from China reported similar results, as RLS patients had higher prevalence of anxiety and depression and to some extent, cognitive impairment (8). In fact, there was no significant difference between MMSE scores of the RLS and control groups; however Montreal Cognitive Assessment (MoCA) performance was poorer in subjects with RLS. Authors discussed this finding as MoCA had a greater sensitivity in identifying mild cognitive impairment compared to MMSE, and it may have detected some of the subjects with mild cognitive impairment in this group (8). In fact, the relationship between RLS and cognitive function is controversial in the literature. Some studies have reported that cognitive decline caused by RLS was related to sleep disturbance or depression, while others have shown that there is no clear relationship between them and that the exact mechanism is unknown (52). In our study, there was no significant relationship between RLS and MMSE performance. Hence, more studies are needed to identify whether RLS has an effect on cognitive functions.

Study Limitations

This study has some limitations. Firstly, because of its cross-sectional design, a causal-effect relationship cannot be claimed. The study population consisted of the older adults admitted to an outpatient clinic of a tertiary hospital, and most of them were under long-term follow-up. Therefore, the findings of this study cannot be generalized to the whole older adult community. Furthermore, due to the subjective evaluation of RLS, "recall bias" might have affected the results. In order to minimize it, we used the most commonly used diagnostic criteria for RLS diagnosis, and excluded individuals getting MMSE scores lower than 21. To the best of our knowledge, this is the first study

assessing the relationship between RLS and a list of geriatric syndromes as a whole, in an older adult population.

Conclusion

RLS is a prevalent, but mostly unquestioned and underdiagnosed sleep disorder in older adults. According to our analyses, RLS had a significant relationship with certain geriatric syndromes like depression, fear of falling, frailty, polypharmacy and sleep disturbance and it was closely related to reduced QoL. Although RLS prevalence is known to be increasing by age, this may not apply to very old ages and advanced age in this particular population may be somewhat protective for suffering RLS. Further comprehensive studies with larger older adult populations are warranted in order to identify exact relationships and underlying mechanisms.

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Ethics

Ethics Committee Approval: The İstanbul University Local Ethics Committee approved the study (reference: 905400/2022).

Informed Consent: We obtained informed consent from all of the participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.Ö., Design: S.Ö., C.K., M.A.K., Data Collection or Processing: S.Ö., Ç.Ö.A., D.E.S., N.M.Ç., T.E., Analysis or Interpretation: S.Ö., M.A.K., Literature Search: S.Ö., Editing: G.B., Writing: S.Ö., M.A.K.

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References

1. Klingelhofer L, Bhattacharya K, Reichmann H. Restless legs syndrome. *Clin Med (Lond)* 2016;16:379-382.
2. Coccagna G, Vetrugno R, Lombardi C, Provini F. Restless legs syndrome: an historical note. *Sleep Med* 2004;5:279-283.
3. During EH, Winkelman JW. Drug Treatment of Restless Legs Syndrome in Older Adults. *Drugs Aging* 2019;36:939-946.
4. Celle S, Roche F, Kerleroux J, Thomas-Anterion C, Laurent B, Rouch I, Pichot V, Barthélémy JC, Sforza E. Prevalence and Clinical Correlates of Restless Legs Syndrome in an Elderly French Population: The Synapse Study. *J Gerontol A Biol Sci Med Sci* 2010;65:167-173.
5. Association ASD. International classification of sleep disorders. Revised: diagnostic and coding manual. Available from: <http://www.absm.org/PDF/ICSD.pdf> 1997.

6. Cuellar NG, Strumpf NE, Ratcliffe SJ. Symptoms of restless legs syndrome in older adults: outcomes on sleep quality, sleepiness, fatigue, depression, and quality of life. *J Am Geriatr Soc* 2007;55:1387-1392.
7. Silay K, Özkaya H, Yalçın A, Akıncı S, Ulaş A, Öztürk E, Canbaz M, Yalçın B. Assessment of Falls In Older People: Is There Any Association Between Restless Leg Syndrome and Falls? *Ankara Med J* 2016;16:13-19.
8. Xu Y, Wen H, Li J, Yang J, Luo K, Chang L. The relationship between sleep disorders, anxiety, depression, and cognitive function with restless legs syndrome (RLS) in the elderly. *Sleep Breath* 2022;26:1309-1318.
9. Trenkwalder C, Tinelli M, Sakkas G, Dauvilliers Y, Ferri R, Rijsman R, Oertel W, Jaarsma J. Socioeconomic impact of restless legs syndrome and inadequate restless legs syndrome management across European settings. *Eur J Neurol* 2021;28:691-706.
10. Lee HB, Ramsey CM, Spira AP, Vachon J, Allen R, Munro CA. Comparison of cognitive functioning among individuals with treated restless legs syndrome (RLS), untreated RLS, and no RLS. *J Neuropsychiatry Clin Neurosci* 2014;26:87-91.
11. 2012 Revised IRLSSG Diagnostic Criteria for RLS: International Restless Legs Syndrome Study Group; [cited 2022 April, 4]. Available from: <http://irlssg.org/diagnostic-criteria>
12. Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel Disorders. *Gastroenterology* 2016;S0016-5085(16)00222-5.
13. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc* 1983;31:721-727.
14. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969;9:179-186.
15. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging* 2012;16:601-608.
16. Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci* 2001;56:M366-372.
17. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. [Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population]. *Turk Psikiyatri Derg* 2002;13:273-281.
18. Yesavage JA. Geriatric Depression Scale. *Psychopharmacol Bull* 1988;24:709-711.
19. Brooks R. EuroQol: the current state of play. *Health Policy* 1996;37:53-72.
20. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;48:16-31.
21. Massy-Westropp NM, Gill TK, Taylor AW, Bohannon RW, Hill CL. Hand Grip Strength: age and gender stratified normative data in a population-based study. *BMC Res Notes* 2011;4:127.
22. Fess EE. Grip strength. In: Casanova JS, editor. *Clinical assessment recommendations*. 2nd ed. Chicago: American Society of Hand Therapists; 1992. p. 41-5.
23. Deurenberg P, Pietrobelli A, Wang Z, Heymsfield S. Prediction of total body skeletal muscle mass from fat-free mass or intra-cellular water. *IJBCR* 2004;2:107-114.
24. Bahat G, Cruz-Jentoft A. Putting Sarcopenia at the Forefront of Clinical Practice. *Eur J Geriatr Gerontol* 2019;1:43-45.
25. Bahat G, Tufan A, Kilic C, Aydın T, Akpınar TS, Kose M, Erten N, Karan MA, Cruz-Jentoft AJ. Cut-off points for height, weight and body mass index adjusted bioimpedance analysis measurements of muscle mass with use of different threshold definitions. *Aging Male* 2020;23:382-387.
26. Safak ED, Gocer S, Mucuk S, Ozturk A, Akin S, Arguvanli S, Mazicioglu MM. The prevalence and related factors of restless leg syndrome in the community dwelling elderly; in Kayseri, Turkey: A cross-sectional study. *Arch Gerontol Geriatr* 2016;65:29-35.
27. Türkmen BÖ. Evaluation of Self-reported Insomnia and Its Association with Some Geriatric Syndromes in Older Adults. *Eur J Geriatr Gerontol* 2019;1:11-16.
28. Fereshtehnejad S-M, Rahmani A, Shafieesabet M, Soori M, Delbari A, Motamed MR, Lökk J. Prevalence and associated comorbidities of restless legs syndrome (RLS): Data from a large population-based door-to-door survey on 19176 adults in Tehran, Iran. *PLoS One* 2017;12:e0172593.
29. Lajous M, Kurth T, Catzin-Kuhlmann A, Romieu I, Lopez-Ridaura R. [Prevalence of restless legs syndrome in 69,830 Mexican women]. *Rev Invest Clin* 2014;66:303-306.
30. Allen RP, Bharmal M, Calloway M. Prevalence and disease burden of primary restless legs syndrome: Results of a general population survey in the United States. *Mov Disord* 2011;26:114-120.
31. Kim TJ, Yoon JE, Park JA, Lee SK, Chu MK, Yang KI, Kim WJ, Park SH, Thomas RJ, Shin C, Yun CH. Prevalence and Characteristics of Restless Legs Syndrome in Korean Adults: A Study in Two Independent Samples of the General Population. *Neuroepidemiology* 2019;52:193-204.
32. Allen RP, Walters AS, Montplaisir J, Hening W, Myers A, Bell TJ, Ferini-Strambi L. Restless Legs Syndrome Prevalence and Impact: REST General Population Study. *Arch Intern Med* 2005;165:1286-1292.
33. Kim KW, Yoon IY, Chung S, Shin YK, Lee SB, Choi EA, Park JH, Kim JM. Prevalence, comorbidities and risk factors of restless legs syndrome in the Korean elderly population - results from the Korean Longitudinal Study on Health and Aging. *J Sleep Res* 2010;19:87-92.
34. Seeman MV. Why Are Women Prone to Restless Legs Syndrome? *Int J Environ Res Public Health* 2020;17:368.
35. Baker JM, Hung AY. Movement Disorders in Women. *Semin Neurol* 2017;37:653-660.
36. Pantaleo NP, Hening WA, Allen RP, Earley CJ. Pregnancy accounts for most of the gender difference in prevalence of familial RLS. *Sleep Meds* 2010;11:310-313.
37. Berger K, Luedemann J, Trenkwalder C, John U, Kessler C. Sex and the risk of restless legs syndrome in the general population. *Arch Intern Med* 2004;164:196-202.
38. Kageyama T, Kabuto M, Nitta H, Kurokawa Y, Taira K, Suzuki S, Takemoto T. Prevalences of periodic limb movement-like and restless legs-like symptoms among Japanese adults. *Psychiatry Clin Neurosci* 2000;54:296-298.
39. Team E. Restless Legs Syndrome and Mental Health 2020 [cited 2022 April, 20]. Available from: <https://restlesslegssyndrome.sleep-disorders.net/coping-mental-health>
40. Kallweit U, Werth E, Seiz A, Sefidan S, Dahmen N, Manconi M, Ehlert U, Bassetti CLA. Psychiatric Comorbidities in Restless Legs Syndrome. *J Neuropsychiatry Clin Neurosci* 2016;28:239-242.
41. Benes H, Mattern W, Peglau I, Dreykluft T, Bergmann L, Hansen C, Kohnen R, Banik N, Schoen SW, Hornyak M. Ropinirole improves depressive symptoms and restless legs syndrome severity in RLS patients: a multicentre, randomized, placebo-controlled study. *J Neurol* 2011;258:1046-1054.
42. Kolla BP, Mansukhani MP, Bostwick JM. The influence of antidepressants on restless legs syndrome and periodic limb movements: A systematic review. *Sleep Med Rev* 2018;38:131-140.
43. Auais M, French S, Alvarado B, Pirkle C, Belanger E, Guralnik J. Fear of Falling Predicts Incidence of Functional Disability 2 Years Later: A Perspective From an International Cohort Study. *J Gerontol A Biol Sci Med Sci* 2018;73:1212-1215.

44. Ozkok S, Aydin CO, Sacar DE, Catikkas NM, Erdogan T, Kilic C, Karan MA, Bahat G. Associations between polypharmacy and physical performance measures in older adults. *Arch Gerontol Geriatr* 2022;98:104553.
45. Chang TI, Park H, Kim DW, Jeon EK, Rhee CM, Kalantar-Zadeh K, Kang EW, Kang SW, Han SH. Polypharmacy, hospitalization, and mortality risk: a nationwide cohort study. *Sci Rep* 2020;10:18964.
46. Hoque R, Chesson AL Jr. Pharmacologically induced/exacerbated restless legs syndrome, periodic limb movements of sleep, and REM behavior disorder/REM sleep without atonia: literature review, qualitative scoring, and comparative analysis. *J Clin Sleep Med* 2010;6:79-83.
47. Bahat G, Ilhan B, Erdogan T, Halil M, Savas S, Ulger Z, Akyuz F, Bilge AK, Cakir S, Demirkan K, Erelel M, Guler K, Hanagasi H, Izgi B, Kadioglu A, Karan A, Kulaksizoglu IB, Mert A, Ozturk S, Satman I, Sever MS, Tukek T, Uresin Y, Yalcin O, Yesilot N, Oren MM, Karan MA. Turkish inappropriate medication use in the elderly (TIME) criteria to improve prescribing in older adults: TIME-to-STOP/TIME-to-START. *Eur Geriatr Med* 2020;11:491-498.
48. Shneyder N, Adler CH, Hentz JG, Shill H, Caviness JN, Sabbagh MN, Beach TG, Driver-Dunckley E. Autonomic complaints in patients with restless legs syndrome. *Sleep Med* 2013;14:1413-1416.
49. Giannaki CD, Sakkas GK, Karatzaferi C, Hadjigeorgiou GM, Lavdas E, Liakopoulos V, Tsianias N, Koukoulis GN, Koutedakis Y, Stefanidis I. Evidence of increased muscle atrophy and impaired quality of life parameters in patients with uremic restless legs syndrome. *PLoS One* 2011;6:e25180.
50. Nagaura Y, Kondo H, Nagayoshi M, Maeda T. Sarcopenia is associated with insomnia in Japanese older adults: a cross-sectional study of data from the Nagasaki Islands study. *BMC Geriatrics* 2020;20:256.
51. Cirillo DJ, Wallace RB. Restless legs syndrome and functional limitations among American elders in the Health and Retirement Study. *BMC Geriatr* 2012;12:39.
52. Jung KY. Cognition in Restless Legs Syndrome. *J Sleep Med* 2015;12:1-6.