

Restless Legs Syndrome Among Veterans With Spinal Cord Lesions

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Researchers developed a restless legs syndrome questionnaire using diagnostic criteria to assess its prevalence among veterans with spinal cord injuries and disorders.

Spinal cord injuries (SCI) are common in veteran populations.¹ Veterans with spinal cord injuries and disorders (SCI/D) also may have concurrent sleep disturbances. Spinal cord injury typically causes spasticity.^{2,3} Hypersensitivity of the flexor reflex pathways is believed to cause painful muscle spasms in patients with SCI.⁴ Neuropathic pain at or below the level of the lesion also is common.

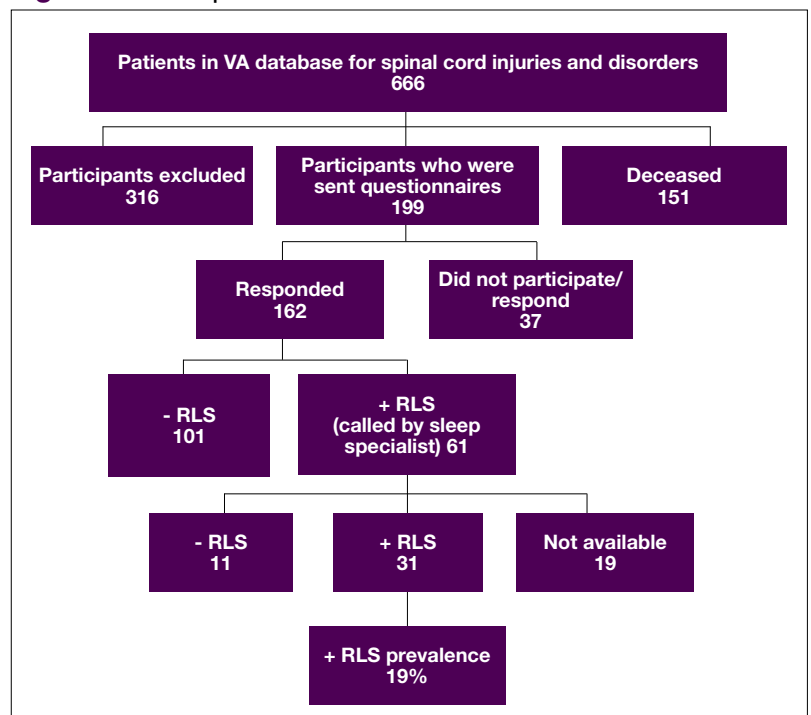
Restless legs syndrome (RLS) is a common sleep disorder that affects sleep quality and can occur concomitantly with spinal cord lesions.⁵ In about 80% of RLS cases, involuntary movements of legs across hip, knee, and ankle joints during sleep, known as periodic limb movement during sleep (PLMS), occurs.⁶ Several studies showed increased prevalence of PLMS in patients with SCI, and some case reports suggest an increased prevalence of RLS in this population.^{7,8} One small study showed that 100% of patients with SCI had symptoms of RLS.⁶ Another study found that SCI could trigger PLMS.⁸

The pathophysiology of RLS and PLMS in patients with SCI is not fully understood, but case reports describing PLM in SCI patients points to a possible role of central pattern generators and the flexor reflex afferents in the pathophysiology of PLMS.^{9,10} Changes of the tissue microstructure in the midbrain and upper cervical

spinal cord have been described in patients with RLS.¹¹

The objective of this study was to assess the prevalence of RLS in a veteran population with SCI/D and to determine possible neuroanatomical patterns involved in RLS and SCI/D.

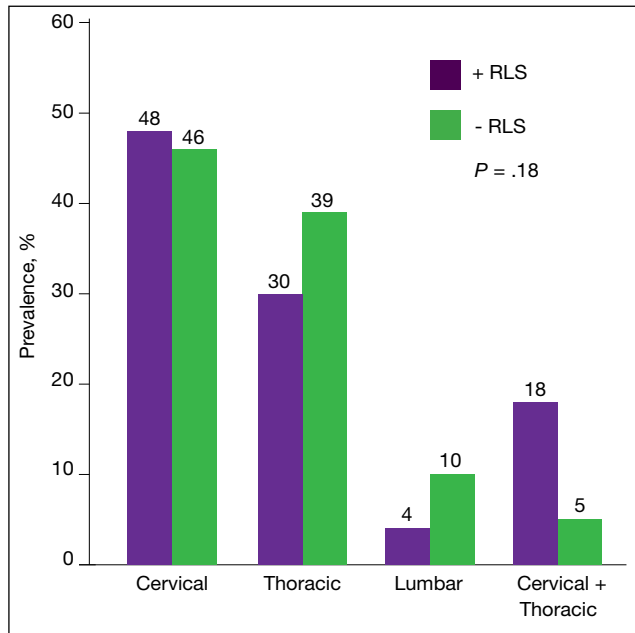
Figure 1. Participant Flowchart



Abbreviation: RLS, restless legs syndrome.

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Figure 2. Restless Legs Syndrome Prevalence for Each Spinal Cord Injury Level^a

Abbreviation: RLS, restless legs syndrome.

^aThe cervical + thoracic subgroup (18% + RLS vs 5% - RLS) showed a significant difference compared with other spinal cord injury levels.

METHODS

The institutional review and ethical approval boards of the Minneapolis VA Health Care System approved the study. Within the VA system, 666 patients with SCI/D were identified using a national database. Of the 666 people, 316 were excluded, 199 were included, and 151 were deceased.

Patients aged between 18 and 65 years were included in the study. Charts of patients who had been discharged with the diagnosis of SCI from 2002 to 2008 were studied. All patients met the inclusion criteria of the International Restless Legs Syndrome Study Group diagnosis.

Exclusion criteria were as follows: Patients with evidence of brain pathology (eg, stroke), concurrent neurologic condition associated with RLS (Parkinson disease, spinocerebellar ataxia, peripheral neuropathy), concurrent psychiatric condition within the setting of treatment with dopamine antagonists, secondary causes of RLS (renal failure/uremia, iron deficiency, rheumatoid arthritis, and pregnancy) and a recent history of alcohol or drug misuse or current evidence of substance use of < 1 year.

A patient list was compiled that included the etiology of the SCI (vascular injury, multiple sclerosis [MS], trauma, unknown, and other), the level(s) and com-

pleteness of the SCI per radiology report, RLS pharmacotherapies, and pertinent medical history.

Axial T2-weighted images on magnetic resonance imaging (MRI) scans were retrospectively reviewed. Sagittal T1/T2-weighted and axial T2-weighted sequences were performed routinely on all patients with spinal cord lesions. The analysis included the extension of the lesion on both sagittal and axial distributions. The anatomic location of the cord lesion was categorized by the following: (1) pure gray matter (central cord); (2) white matter (dorsal [D], dorsolateral [DL], ventral [V], ventrolateral areas [VL]).

A questionnaire using standard diagnostic criteria for RLS was mailed to the 199 patients who met the inclusion criteria (Appendix A). Those screening positive for RLS by questionnaire underwent a structured telephone interview by board-certified sleep specialists who were blinded to the diagnosis of SCI (Appendix B).

All analyses were carried out using StataCorp STATA 13 (College Station, TX). Descriptive statistics were used. The analyses were carried out using chi-square and Fisher exact tests. Differences between the groups were considered statistically significant at *P* < .05. The data were analyzed to obtain point prevalence among patients with SCI, and comparisons were made among the different subgroups.

RESULTS

Of the 162 patients who chose to participate in the study, the sleep specialists confirmed 31 (19%) to have RLS, 112 (69%) were confirmed negative for RLS, and an additional 19 (12%) screened positive for RLS but were not confirmed to have RLS by the sleep specialists (Figure 1).

The etiology of SCI was subdivided into 4 groups: MS, trauma, vascular, and other/unknown. Within each group (- RLS vs + RLS), MS and trauma were the most common etiologies with 55% MS and 36% trauma in the + RLS group.

When comparing RLS among the spinal cord levels (cervical, thoracic, lumbar and cervical + thoracic), only the cervical + thoracic subgroup (18% + RLS vs 5% - RLS) showed a significant difference (Figure 2).

There was no significant difference found with the prevalence of RLS in the axial plane of the spinal cord lesions (ventral/ventro-lateral/central cord vs dorsal/dorsolateral) or by the completeness of spinal cord lesions, *P* = .76. There was a higher prevalence of incomplete cord injury, however, within each subgroup of RLS.

The Mann-Whitney test was used to analyze the burden of disease in both groups (+ RLS vs - RLS). Moderate level of burden was most frequently reported with a

higher prevalence within the + RLS group. Of those receiving treatment for RLS, 71% were + RLS vs 46% – RLS with a *P* value of .01. Symptoms of RLS after cord injury were 89% + RLS vs 55% – RLS with a *P* value of .03.

DISCUSSION

This study represents one of the first studies to determine the prevalence of RLS in veterans with spinal cord disease. Research in this area is important to raise awareness of RLS among the veteran population with and without SCI and disorders. Restless legs syndrome often escapes diagnosis because of difficulty understanding the patient's descriptions of their sensations. In addition, RLS may cause debilitating symptoms of sleep deprivation, daytime sleepiness, discomfort, and fatigue, which often results in decreased quality of life (QOL). Proper screening and treatment may improve QOL.

A study by Kumru and colleagues showed a similar rate of RLS in patients with SCI and RLS symptoms presented in the first year after SCI as did this study (18% vs 19%, respectively).⁴ In that study, RLS was more common in patients with lesions in lumbosacral area. Kumru and colleagues also showed that a dopaminergic medication improved symptoms of RLS in this population, whereas this study did not explore treatment outcomes.⁴

The pathogenesis of RLS is not fully known, but hereditary factors, iron metabolism, and the brain dopaminergic system are thought to be involved.¹¹ It is hypothesized that spinal cord lesions allow the appearance of RLS symptoms and spinal leg movement generator by blocking descending inhibitory spinal pathways.¹² One hypothesis is that damage to A11 nuclei (the main source of dopamine in the spinal cord or its diencephalospinal tract in animals) causes hyperexcitability of the spinal cord and leads to PLM and RLS symptoms.¹³ As the axons of A11 nuclei are present along the whole span of the spinal cord, SCI/D in patients with RLS might interrupt this dopaminergic tract and produce the RLS symptoms.

Limitations

This study included only veterans, so the prevalence may not apply to the nonveteran SCI population. Also, the population mainly was male, and there was no accurate information on race. Ferritin levels of the patients were not checked and is a major factor in RLS. The reported onset of RLS after the SCI could be due to recall bias.

CONCLUSION

The prevalence of RLS in veterans with SCI is above that reported in the general population (19% vs 10%, respec-

Appendix A. Restless Legs Syndrome Questionnaire

Patient ID No. _____		
Please circle only yes, no or unknown for each question.		
1a. Do you have restlessness and the urge to move your legs?	Yes	No Unknown
1b. Is it associated with unpleasant sensations like crawling, pain, or other sensations in the legs?	Yes	No Unknown
Please continue with the survey only if you have answered YES to questions 1a and 1b.		
2a. Do these symptoms occur only at rest?	Yes	No Unknown
2b. Does movement improve or relieve these symptoms?	Yes	No Unknown
3. Are these symptoms worse in the evening or at night compared with the morning?	Yes	No Unknown
4. Do you feel that these symptoms disturb your sleep?	Yes	No Unknown
5. Did these symptoms occur after your spinal cord injury or after your diagnosis of multiple sclerosis?	Yes	No Unknown
6. Do you feel rested during the day?	Yes	No Unknown
7. Have you been told that you have a sleep disorder and if so, which one?	Yes. Sleep disorder: _____ No	
8. Gender:	Male	Female
9. Race:	White	African American Asian
	Hispanic/Latino	Other

tively). Furthermore, those with RLS have symptoms that often started after the SCI (suggesting causality) and required therapy due to their level of RLS symptom burden. A spectrum of severity of symptoms is present among those with RLS, with 83% having moderate-to-severe RLS affecting their QOL.

Although there was not a statistically significant relationship between RLS and spinal cord lesion level, there was a slightly higher prevalence of RLS at the cervical and thoracic levels, which may be relevant for future studies. There was no difference found between the RLS subgroups with respect to the location of the lesion within the spinal cord; however, a larger sample size may be needed to determine whether this would reach statistical significance. Prompt search for symptoms of RLS in veterans with SCI is warranted to provide adequate treatment to improve sleep health and QOL in this population.

Appendix B

Telephone Interview Script

Good afternoon/evening Mr./Mrs. _____, my name is Dr. [fill in name] and I am calling you to follow-up with additional questions for our research study on restless legs syndrome. Do you have a moment?

If no: When would be a good time for me to call back?

If yes: Great. This should only take approximately 10 minutes. I will be asking you some pertinent questions to determine whether you have the diagnosis of restless legs syndrome. If so, this will be followed by a couple of questions related to symptom onset and severity. If I determine that you have restless legs syndrome, I will be sure to provide you with some expert advice and educate you on basic treatment options. At the end of the interview, I would like to give you the opportunity to ask any questions that you may have.

RLS Telephone Interview Questionnaire

1. Does the patient meet the IRLS criteria for diagnosis of RLS?
Yes No
 (Answers 'Yes" to all 3 questions labeled 1a-1c):

- 1a. Do you have unpleasant sensations like crawling, paraesthesias, or pain in the legs combined with a motor restlessness and an urge to move? Yes No
- 1b. Do these symptoms occur only at rest and does moving improve them? Yes No
- 1c. Are these symptoms worse in the evening or at night compared with the morning? Yes No

Did the symptoms of RLS start AFTER the spinal cord disease?

Is there a family history of RLS?
None Mild Moderate Severe

Level of burden from symptoms of RLS?

Checklist of additional topics to cover during the telephone interview completed:

- 1. Inform the participants of their diagnosis.
- 2. Do the participants have any questions?
- 3. If diagnosed with RLS, complete items 3a-3e:
- 3a. Offer expert advice about RLS.
- 3b. Educate with basic treatment approach (medical management).
- 3c. Inform them that an educational pamphlet about RLS will be mailed to them.
- 3d. Inform them that we will be entering the diagnosis of RLS into CPRS (medical charts).
- 3e. Offer follow-up care for the RLS with a Neurologist.

Abbreviation: RLS, restless legs syndrome.

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Author disclosures

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Disclaimer

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