

Management of Restless Legs Syndrome/Willis-Ekbom Disease in Hospitalized and Perioperative Patients



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KEYWORDS

• Restless legs syndrome • Surgery • Perioperative • Hospitalized

KEY POINTS

- Restless legs syndrome (RLS) is chronic and associated with multiple comorbidities; therefore, it may be encountered in the inpatient or perioperative setting.
- Characteristics of the hospitalized or surgical context can exacerbate or unmask RLS and include the following: immobility, sleep deprivation and circadian disruption, blood loss and subsequent iron deficiency, withdrawal from RLS therapy, and adverse effects of medications.
- RLS and the associated discomfort and insomnia can prolong hospital stay and negatively impact outcomes.
- RLS medications should be continued during the hospital admission if possible.
- When surgery or health status precludes orally administered medications, parenteral opioids or transdermal rotigotine should be considered.
- Avoidance of excessive phlebotomy and medications known to trigger RLS may be beneficial.
- Patients should increase activity when acceptable; however other nonpharmacological interventions require further study.

INTRODUCTION

Clinical Manifestations and Epidemiology

Restless legs syndrome (RLS) is a sensorimotor neurologic disorder that also goes by the eponym Willis-Ekbom disease (WED) after the physicians who initially described the condition.¹⁻³ The disorder is defined by its diagnostic criteria, which include

An urge to move the legs that is usually associated with or felt to be precipitated by discomfort in the legs

The motor urgency and discomfort occur during or are worsened by rest or inactivity

The symptoms are partially or completely relieved by movement

The symptoms develop or worsen in the evening or nighttime¹

The combination of the aforementioned symptoms is consistent with a diagnosis of RLS only when not a consequence of another medical or behavioral condition.¹ The prevalence of clinically significant RLS is 2% to 3%,⁴⁻⁶ and the disorder negatively impacts sleep, daytime function, quality of life, and mood.^{4,7-10} Periodic limb movements of sleep (PLMS) are involuntary, stereotyped movements of the legs seen in more than 80% of patients with RLS.⁷

Patients typically present with RLS in the third or fourth decade of life, and the condition is chronic.¹¹ Additionally, RLS is associated with multiple comorbidities¹²; therefore, it is not surprising that this condition is encountered in a perioperative or inpatient setting. In fact, during the 5-year open-label extension of rotigotine for

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moderate-to-severe RLS, nearly 20% of patients underwent a surgical intervention.¹³ When hospitalized or undergoing surgery, RLS symptoms can be exacerbated in individuals with known RLS or become evident in individuals without diagnosed RLS.¹⁴

Pathogenesis of Restless Legs Syndrome in Hospitalized or Perioperative Patients

Multiple factors may precipitate RLS symptoms in hospitalized patients and those undergoing surgical or diagnostic procedures (**Table 1**).

Immobility

RLS is characterized by an urge to move the legs at rest. Immobility is likely the most important factor in RLS exacerbation, as both hospital admissions and surgical procedures are marked by extensive periods of immobility. Up to 83% of the hospitalization may be spent lying in bed based on accelerometer recordings.¹⁵ This degree of immobility was seen despite the ability and willingness of the patient to ambulate.¹⁵ Immobility worsens both sensory and motor symptoms of RLS. Individuals with RLS have marked increases in leg discomfort and periodic limb movements starting after only 10 minutes of immobility during the suggested immobility test (SIT).¹⁶

Sleep deprivation and circadian disruption

Sleep deprivation worsens RLS symptoms¹⁷ and is common in hospitalized individuals. Both intensive care unit (ICU) and general ward patients display short sleep duration (4–6 hours on average), poor sleep efficiency, and frequent arousals.¹⁸ Sleep is also reduced in postsurgical patients.¹⁹ Noise, light, patient care interactions, mechanical ventilation, pain,²⁰ general anesthesia,²¹ medication, and sequelae of the specific illness or procedure can contribute to disturbed sleep in hospitalized or perioperative patients.¹⁸

Table 1

Factors that contribute to restless legs syndrome symptoms in the perioperative or hospitalized setting

Immobility	Adverse effect of medications:
Sleep deprivation	Dopamine antagonist
Blood loss	antiemetics
Cessation of RLS medications	Antipsychotics
	Antihistamines
	Serotonergic antidepressants

Adapted from Raux M, Karroum EG, Arnulf I. Case scenario: anesthetic implications of restless legs syndrome. Anesthesiology 2010;112(6):1511–7.

The circadian rhythm is the approximately 24-hour cycle of sleep and wake,²² as well as multiple other physiologic processes.²³ Melatonin (in the serum, saliva, or urine)²⁴ and core body temperature²⁵ are used to measure circadian phase apart from sleep. The nighttime rise in melatonin parallels the drop in core body temperature, and melatonin secretion peaks just before the core body temperature reaches its nadir 2 to 3 hours prior to habitual wake time. RLS symptoms demonstrate a circadian rhythm with maximal severity between midnight and 4 AM coinciding with the falling portion of the core body temperature rhythm.^{17,26,27} RLS symptoms reach a trough between 9 AM and 1 PM. Hospitalized patients have increased sleep during the daytime and reduced sleep during the night¹⁸; therefore, their sleep-wake behavior may be misaligned with their endogenous circadian phase, unmasking RLS symptoms (**Fig. 1**).

Alternatively, the circadian rhythm may be disturbed in critically ill and postoperative patients. The urinary metabolite of melatonin (6-sulfatoxymelatonin, aMT6s) was measured in ICU patients.²⁸ Nocturnal excretion of aMT6s was reduced in all ICU patients.²⁸ All but 2 ICU patients demonstrated a loss of the normal nocturnal peak of aMT6s.²⁸ Melatonin measured by both serum and urine assays demonstrated a delay of the circadian rhythm in patients after surgery.²⁹ Abnormal light exposure likely explains the disruption in circadian rhythms seen in hospitalized or perioperative patients.³⁰ Bright light is the strongest time giver that entrains the endogenous circadian rhythm to the external environment. Bright light directly suppresses melatonin and can alter circadian rhythms depending on the exposure time (a delay in circadian phase when bright light exposure occurs during the beginning of the biological night and an advance in circadian phase when the exposure occurs in the morning).³¹ Individuals working nontraditional shifts are exposed to abnormal light-dark cycles and have higher prevalence of RLS compared with day shift workers.³² Therefore, circadian disruption may have the potential to exacerbate RLS symptoms in the critically ill or postoperative patient; however, because of the confounding factors of sleep deprivation, comorbid illnesses, and smoking in shift workers, more work is needed to determine the effects of circadian disruption on RLS symptoms.³²

Anemia

The prevalence of anemia in hospitalized patients is 30% to 40% and in most patients, iron deficiency is a significant contributor to anemia.³³

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