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Restless legs syndrome, insomnia, and quality of life after renal transplantation

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Abstract

Objective: Restless legs syndrome (RLS) is associated with insomnia and impaired quality of life (QoL) in patients on maintenance dialysis; however, no information has been published on the association of RLS and QoL in kidney-transplanted patients. In a cross-sectional study, we analyzed the complex relationship between RLS, insomnia, and health-related QoL in kidney-transplanted patients. **Methods:** In a cross-sectional survey at a single transplant center, 1067 patients were invited to participate. Complete data set was available from 785 kidney-transplanted patients. The RLS Questionnaire and the Athens Insomnia Scale were used to assess the prevalence of RLS and insomnia, respectively. QoL was measured using the Kidney Disease QoL-SF Questionnaire. **Results:** Patients with RLS were three times more likely to have insomnia than patients without RLS (29% vs. 9%, P=.001), and the presence of RLS was a significant and independent predictor of insomnia in multivariate analysis. The presence of RLS was independently associated with impaired health-related QoL along several QoL domains after statistical adjustment for clinical and sociodemographic covariables. Importantly, this association remained significant even after adjusting for insomnia for some QoL domains. **Conclusion:** RLS is associated with poor sleep, increased odds for insomnia, and impaired QoL in kidney-transplanted patients. Our results suggest that both sleep-related and sleep-independent factors may contribute to the association of RLS and QoL.

Keywords: Chronic insomnia; Renal transplantation; Restless legs syndrome; Quality of life

Introduction

Restless legs syndrome (RLS) is characterized by an urge to move the legs, which is usually but not always associated with disagreeable leg sensations. The symptoms usually occur during inactivity and may interfere with sleep [1]. RLS can occur in an idiopathic form or secondary to other conditions such as end-stage renal failure. Recently, it has been suggested that RLS is associated with increased mortality and impaired health-related quality of life (QoL) in patients on maintenance dialysis [2,3]. An important factor that may mediate the effect of RLS on QoL is the impact of RLS on sleep. However, only a few papers, using

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mainly nonvalidated instruments, assessed the relationship between RLS and sleep complaints or insomnia in the dialysis population [4–8]. Employing validated instruments, we recently showed that RLS was associated with poor sleep, increased risk of insomnia, and impaired QoL in patients on maintenance dialysis [9]. We are not aware of any published data on RLS, sleep, and QoL in kidney-transplanted patients.

Clinical diagnostic criteria for RLS have been established by the International RLS Study Group (IRLSSG) and have recently been modified [1]. Four minimal criteria are required to diagnose the disorder: (a) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs; (b) the urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity; (c) the urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues; (d) the urge to move or unpleasant sensations are worse in the evening or night than during the day. Based on the IRLSSG criteria, a diagnostic questionnaire [RLS Questionnaire (RLSQ)] has been developed and validated by Allen and Early [10,11]. The instrument provides a relatively simple tool to detect RLS in a uniform and comparable manner.

A prevalence of 5–15% and 10–25% has been reported for RLS in the general population [10] and in the dialysis population [2,7,8,12], respectively, using the IRLSSG diagnostic criteria. Only a few studies reported on RLS in kidney-transplanted patients [13,14]. Recently, we reported a prevalence of almost 5% RLS in a large sample of kidney-transplanted patients, using the RLSQ [14].

In this study, we utilized the RLSQ to assess the association of RLS with insomnia and QoL in a large sample of kidney-transplanted patients. A simple, easy-to-administer questionnaire, the Athens Insomnia Scale (AIS), which is based on the International Classification of Diseases-10 criteria [15], was used to assess insomnia and specific insomnia symptoms. Health-related QoL was measured using the Kidney Disease QoL-SF (KDQoL-SF) questionnaire.

Methods

Sample of patients and data collection

All patients 18 years or older (N=1067) who were regularly followed up at a single outpatient transplant center at the Department of Transplantation and Surgery at the Semmelweis University Budapest have been approached to participate in a cross-sectional study aiming to study sleep and mood disorders and health-related QoL in renal transplant recipients (TransQoL-HU Study). All patients had received cadaveric renal transplant between 1977 and 2002.

Demographic information and details of medical history were collected at enrollment when information about age, gender, level of education, etiology of chronic kidney disease (CKD), and the presence or absence of diabetes and other comorbidities were obtained. The patients completed a battery of validated questionnaires, including the AIS, the KDQoL-SF questionnaire, the RLSQ, and the Center for Epidemiologic Studies Depression Scale (CES-D), while waiting for their regular follow-up visit at the transplant center.

Laboratory data were extracted from the patients' charts. The following laboratory parameters were tabulated: serum hemoglobin, iron studies [serum iron, serum transferrin, transferrin saturation (TSAT)], serum creatinine, blood urea nitrogen, and serum albumin. Glomerular filtration rate (eGFR) was calculated using the abbreviated Modification of Diet in Renal Disease study formula [16]:

$$\mathrm{GFR}\left(\mathrm{ml/min\ per\ 1.73\ m^2}\right) = 186 \times (S_{\mathrm{Cr}})^{-1.154} \times (\mathrm{Age})^{-0.203} (\times 0.742 \text{ if female}).$$

Data extracted from the medical records included the following information: time of transplantation; "transplant vintage," that is, time elapsed since the transplant; medications (including current immunosuppressive medications); and time spent on dialysis prior to transplantation ("dialysis vintage").

The study has been approved by the Ethics Committee of the Semmelweis University. Before enrollment, patients received detailed written and verbal information regarding the aims and protocol of the study and signed informed consent.

Assessment of RLS

Symptoms of RLS were identified by using the RLSQ. This scale has been validated as a screening instrument for RLS in the sleep disorders clinic [11] and was used in a recent epidemiologic survey [10] and in our earlier work [9,14]. RLS was identified only if the patient met all the diagnostic criteria. If the questionnaire was not filled completely or if the patient did not follow the instructions, the scale was not scored and the information was considered missing.

Assessment of insomnia

The AIS was used to assess sleep complaints and identify insomnia [15,17]. The AIS consists of eight items (score range=0–24, with higher scores indicating worse sleep). The first five items cover nighttime symptoms of insomnia (difficulty initiating sleep, difficulty maintaining sleep, and early morning awakening), and three items probe daytime consequences of disturbed sleep (well-being, functioning capacity, and daytime sleepiness). Subjects are asked to grade the severity of these complaints (absent, mild, severe, or very severe) only if the particular complaint occurred at least three times per week during the last month. To identify cases of potentially significant insomnia, we used a cutoff