Uremic Restless Legs Syndrome Pleads “Not Guilty”

Giorgos K. Sakkas^{a, b}

^aFaculty of Health, Plymouth Marjon University, Plymouth, UK; ^bSchool of PE and Sport Sciences, University of Thessaly, Trikala, Greece

Disorders of the brain are becoming more prevalent and are both threatening quality of life as well as creating major challenges for the national health systems. Restless legs syndrome (RLS; or Willis/Ekbom disease) is one of the most common neurological disorders associated with significant personal, social and economic burden. With an adult prevalence of approximately 2.7% in the general population, RLS is underdiagnosed [1]. It is estimated to affect 20 million European citizens and many more around the world. Recent data from the “value of treatment for brain disorders” research project, conducted by the European Brain Council [2], demonstrated that RLS is the fifth most expensive neurological disorder after mood disorders and dementia.

Notably, RLS prevalence in hemodialysis (HD) patients is much higher than in the general population reaching approximately 30% [3, 4]. Uremic RLS is frequently associated with increased morbidity and enhanced mortality in HD patients, linked to cardiovascular diseases [5]. A recent 3-year mortality study was the first to show that the diagnosis of RLS, according to the essential criteria of the International RLS Study Group, does not affect mortality in HD patients [6]. The mortality rate was 15.6% (5.2%/year) in RLS-HD patients and 22.3% (7.4%/year) in non-RLS HD patients. Moreover,

there was no significant association between RLS and 3-year mortality, either with age and gender as covariates [6].

In the current issue of the *American Journal of Nephrology*, an unprecedented 15-year follow-up of RLS survivorship is presented by Baiardi et al. [7]. These investigators demonstrate that RLS-HD patients had a lower mortality rate compared to those HD patients without the syndrome (63.8% [4.3%/year] RLS-HD vs. 87.6% [5.8%/year] non-RLS HD, $p = 0.04$). Similarly, the mortality rate was not influenced by gender ($p = 0.15$) and even more importantly by RLS severity ($p = 0.11$). In addition, the study by Baiardi et al. [7] revealed no difference among the causes of death between the 2 groups; this is in contrast to previous studies linking RLS to cardiovascular diseases [5]. The studies by Stefanidis et al. [6] and Baiardi et al. [7] clearly suggest that mortality in HD patients is not influenced by the presence of RLS/WED, as they provide no clinical evidence linking uremic RLS/WED to cardiovascular mortality.

Considering the discordant literature on the mortality risk in uremic RLS patients and the fact that cardiovascular disease is the number one cause of death in HD patients, the recent evidence by Baiardi et al. [7] provides important data that will inform the design of the next prospective

studies addressing non-traditional uremia-related variables and cardiovascular risk. In this way, perhaps new approaches for reducing cardiovascular mortality and to improve patients' survival and quality of life will evolve.

RLS symptoms during HD sessions and during rest hours continue to be one of the most disturbing disease factors seen in HD patients. RLS impacts on affecting patients' quality of life and their overall health mainly by increasing depressive symptoms. Unfortunately, due to the limited knowledge of the disease and possible treatment, patients often go through long periods of suffering until the correct diagnosis is made and proper treatment is started. This leads to an unnecessary burden on health

care budgets and severe deterioration of patients' mood status. Extensive education of both patients and nephrologists is needed to improve this situation. Since at the moment there is no cure and the existing available treatments are far from optimal, more research into the pathophysiology of uremic RLS and its disease mechanism is needed to provide specific symptomatic and future curative treatments.

Disclosure Statement

The authors have no conflicts of interest to declare.

References

- 1 Allen RP, et al: Restless legs syndrome prevalence and impact: REST general population study. *Arch Intern Med* 2005;165:1286–1292.
- 2 www.braincouncil.eu/activities/news/press-release-value-of-treatment-for-brain-disorders-in-europe/.
- 3 Sakkas GK, et al: The effect of cold dialysis in motor and sensory symptoms of RLS/WED occurring during hemodialysis: a double-blind study. *ASAIO J* 2017, Epub ahead of print.
- 4 Stefanidis I, et al: Restless legs syndrome in hemodialysis patients: an epidemiologic survey in Greece. *Sleep Med* 2013;14:1381–1386.
- 5 La Manna G, et al: Restless legs syndrome enhances cardiovascular risk and mortality in patients with end-stage kidney disease undergoing long-term haemodialysis treatment. *Nephrol Dial Transplant* 2011;26:1976–1983.
- 6 Stefanidis I, et al: Restless legs syndrome does not affect 3-year mortality in hemodialysis patients. *Sleep Med* 2015;16:1131–1138.
- 7 Baiardi S, Mondini S, Baldi Antognini A, Santoro A, Cirignotta F: Survival of dialysis patients with restless legs syndrome: a 15-year follow-up study. *Am J Nephrol* 2017;46:224–230.