

Title: Restless legs syndrome and mortality in hemodialysis patients

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Letter to the Editor

Restless legs syndrome and mortality in hemodialysis patients

To the Editor:

We thank Elias et al. for their concerns regarding our findings [1] of missing association between Restless Legs Syndrome (RLS) and mortality in hemodialysis, contradicting previous survival studies [2,3]. However, there was agreement on RLS prevalence between our study (26.6%) and the studies by La Manna et al. (31%) and Lin et al. (25%) [1–3].

We agree that predictors of RLS in hemodialysis may also influence mortality and might have confounded survival analyses so

far. In our study RLS hemodialysis patients were younger than those without RLS [1]. However, RLS patients had higher diabetes prevalence in the study by Lin et al. [3], while patients had lower frequency of rest-diuresis >500 ml/d in the study La Manna et al. [2]. Age, diabetes, and missing rest-diuresis are all indubitably strong mortality predictors. While of course adjustments for confounders were done, whether in our study or in past studies, confounding bias might not be abolished, even with properly planned multivariate analysis. Serum intact parathormone (iPTH) and phosphorus, predicting uremic RLS in our study, were not associated with mortality in either univariate or multivariate analyses. These negative findings remained, whether iPTH and phosphorus were examined in different multivariate models or in subgroup analyses, ie, subgroups with high (>150 ng/ml) or low iPTH (<150 ng/ml).

Furthermore, investigating prevalent cases [1–3] using a crosssectional design may lead to significant survivor bias. In the only previous survival report [4] that investigated incident hemodialysis patients, RLS screening was not based on the international criteria and might have had limited reliability [5].

The above facts, along with the high probability of publication bias [1] and lack of power in some reports [2], implicate a rigorous need for more prospective investigations of mortality risk in uremic RLS.

Conflict of interest

None.

References

- [1] Stefanidis I, Vainas A, Giannaki CD, et al. Restless legs syndrome does not affect 3-year mortality in hemodialysis patients. *Sleep Med* 2015;16:1131–8.
- [2] La Manna G, Pizza F, Persici E, 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;26:1976–83.
- [3] Lin CH, Sy HN, Chang HW, et al. Restless legs syndrome is associated with cardio/cerebrovascular events and mortality in end-stage renal disease. *Eur J Neurol* 2015;22:142–9.
- [4] Unruh ML, Levey AS, D'Ambrosio C, et al. Restless legs symptoms among incident dialysis patients: association with lower quality of life and shorter survival. *Am J Kidney Dis* 2004;43:900–9.
- [5] Cirignotta F, Mondini S, Santoro A, et al. Reliability of a questionnaire screening restless legs syndrome in patients on chronic dialysis. *Am J Kidney Dis* 2002;40:302–6.

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