Strong bones and restless legs
New data about bone remodeling in women with RLS

Disorders of bone metabolism are a common concern for older women, since there are known associations among bone loss, sex, and age. Women with restless legs syndrome (RLS) who have not yet been treated with medication have signs of increased sympathetic nervous system activity. The autonomic nervous system appears to be a major regulator of bone mineral density (BMD) through signals sent to osteoblasts, and increased sympathetic activity is associated with more osteoporosis in older women because of decreased osteoblast proliferation. These observations created a plausible hypothesis that there would be a higher incidence of osteopenia or osteoporosis in drug-naïve women with RLS. In a new study reported in this issue of Neurology®, Cikrikcioglu et al. examined this relationship and found no evidence to support this hypothesis. In fact, they discovered the opposite result in their case-control study: an increase in lumbar BMD in 78 women with RLS, compared to 78 age-matched and body mass index (BMI)-matched controls. There was a positive bivariate correlation between duration of RLS and lumbar BMD. They also studied 2 markers of bone resorption, c-telopeptide of type 1 collagen (CTX) and sclerostin, and found lower levels in women with RLS. There were negative bivariate correlations between the severity of RLS and bone resorption markers.

There are several strengths of this study. It was a prospective, cross-sectional examination of drug-naïve women with RLS. Those who had mood disorders, neurodegenerative diseases, or medications to treat those disorders were excluded. Therefore, the patients with RLS who were studied had primary, not secondary, disease. Those who had thyroid problems, collagen diseases, chronic kidney disease, chronic lung disease, fractures, and bone prostheses were also excluded. Patients with RLS were matched with controls with respect to BMI. This is important, since body mass has a protective effect on osteoporosis and osteopenia. Process variables (CTX, sclerostin, and vitamin D3) were assessed in addition to the primary endpoint of BMD.

Cikrikcioglu et al. also found vitamin D3 deficiency in slightly more of their patients with RLS compared to age-matched controls, which is consistent with the observations of other recent studies. For example, Wali et al. have shown that vitamin D3 levels were low in 12 adults with RLS and that vitamin supplementation improved the median RLS severity score from 26 at baseline to 10 after the correction of vitamin D levels. Jimenez-Jimenez et al. analyzed a possible relationship between 2 vitamin D receptor polymorphisms and the risk for RLS. They discovered that patients with RLS carrying the rs731236G allele had an earlier age at onset of RLS and those with the rs731236GG allele had higher severity scores for RLS. Kim et al. recently recognized genetic variations in the vitamin D receptor in association with osteoporosis among patients with chronic lung disease.

Since osteopenia and osteoporosis are conditions usually seen later in life, and fracture risk is age-dependent, the inclusion of younger women in this study might complicate the analysis of the results (the age range was from 21 to 75 years). Another weakness of the study was the cross-sectional design, since this limits the possibility of making statements about causality. Nevertheless, this study is an important first step in the direction of our understanding the role of bone remodeling in women with RLS.

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REFERENCES
1. Freitas PM, Garcia Rosa ML, Gomes AM, et al. Central and peripheral body fat mass have a protective effect on osteopenia or osteoporosis in adults and elderly. Osteoporos Int Epiph 2015 Dec 9.


