The risks for falls and fractures in multiple sclerosis

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Fractures, particularly hip fractures, are a major public health issue, being associated with high morbidity and mortality.[1] Less than half of all hip fracture patients will ever fully recover ability to perform basic activities of daily living.[1]

A number of the risk factors for falls and fractures are of particular relevance in multiple sclerosis (MS), including reduced mobility, altered gait, concomitant medications, reduced bone density, osteoporosis, comorbidities, altered diet, and lower serum levels of vitamin D.[2] However, few studies have evaluated fracture risk in MS.

In this issue of *Neurology*®, Bazelier et al.[3] access health administrative data in the Netherlands to examine the risk of fracture in patients with MS compared to population controls. Over 5 years of follow-up in this relatively young cohort (mean age of cases and controls was 43 years), fractures occurred in 2.4% of patients with MS compared to 1.8% of controls. In analyses stratified by sex, fracture risk was increased only in women (adjusted hazard ratio = 1.67; 95% confidence interval [CI] 1.17–2.38). The greatest magnitude of effect was for hip fracture (adjusted hazard ratio [HR] = 4.08; 95% CI 2.21–7.56) and sustaining a fracture after a fall was more common in the MS group (HR = 2.06; 95% CI 1.40–3.02).[3]

By linking with pharmacy prescription data, the authors showed that prior exposure of patients with MS to hypnotics or antidepressants was associated with a 3-fold increased risk of osteoporotic fracture compared to controls.[3] Notably, the increase in risk persisted when the comparison control group were those prescribed antidepressants (or hypnotics), rather than all controls,[3] i.e., the adverse effects of these drugs on fracture risk was greater in those who also had MS. Both depression and antidepressant use are known risk factors for falls and fractures,[4] while hypnotics, usually prescribed to assist sleeping, impair balance,[5] possibly posing a particular problem for the patient with MS making frequent nighttime trips to the bathroom. Although no association was found between oral corticosteroid use and fractures,[3] the authors did not examine the dose or duration of steroid exposure and were unable to access information on perhaps the most commonly used steroid in MS: IV methylprednisolone. Nevertheless, evidence to date indicates that short courses of corticosteroids are not detrimental to bone health.[2]

Longer disease duration was associated with a modestly elevated fracture risk (adjusted for age and concomitant medications),[3] while previous studies have shown a strong relationship between higher Expanded Disability Status Scales scores and lower bone mineral density.[2] Limitations of available data meant that Bazelier et al.[3] could not examine disability, and they also had to use a proxy for disease onset (and thus disease duration), being the first recorded International Classification of Diseases (ICD) code for MS (ICD-9-CM = 340) requiring hospitalization. This may have resulted in a biased selection of more severely affected patients with MS, compared to the general population controls, who could be selected based on having a prescription dispensed at a community pharmacy only.

The authors were unable to consider other known risk factors for fractures including body mass index, smoking, alcohol intake, postmenopausal status, use of over-the-counter medications such as calcium and vitamin D supplements, or other important MS-related factors that could also influence risk such as cognition and mobility. Neither was the MS disease course available (primary progressive vs relapsing onset) nor was the use of MS disease-modifying therapies reported. The reported data were for fractures leading to a hospital admission only. While this might overestimate risk if a patient with MS with a fracture was more likely to be hospitalized than a control, the major findings were unlikely affected as osteoporotic and hip fractures will invariably require hospitalization, regardless of the patient's comorbidities.

The authors were able to corroborate, to a considerable extent, their findings using other population-

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based databases in different geographic areas, all recently accepted for publication.[6,7] Their UK study verified the increased risk of hip and osteoporotic fractures,[7] and their large Danish data linkage study indicated an increased risk of tibia, hip, and femur fractures in MS.[6] Several cross-sectional studies or case reports show that patients with MS have higher rates or risk profile for fracture,[2] including in the newly diagnosed.[8]

Strengths of their current study included the reasonable follow-up time in a broadly population-based Dutch PHARMO record linkage system, which covers almost all community-based dispensed pharmacy prescriptions and hospital admissions for some 3 million residents of the Netherlands.[3]

More could be done to identify, treat, or even prevent comorbidities in chronic diseases such as MS. Preventing falls and fractures in people with MS could represent a major step forward in maintaining their (safe) mobility. The elevated risk associated with specific concomitant medications serves as a reminder to prescribe wisely and monitor carefully those already at risk of falls or fractures. Adequate vitamin D in conjunction with calcium may also be a simple intervention to help preserve bone health, further reducing fracture risk.[9] Vitamin D has already generated much interest in MS, with lower serum levels being associated with both a higher risk of developing MS as well as higher disease activity. However, whether vitamin D supplementation will have effects on prevention or disease progression in MS is unknown and the optimal doses or long-term safety have not been established. For optimum bone health, vitamin D alone appears insufficient, and an annual megadose (500,000 IU) has been associated with increased falls and fractures in older community-dwelling women.[10] The current recommended daily intake for bone health in a typical North American adult has been increased recently to 600 IU/day, in combination with 1,000 mg of elemental calcium. However, whether this intervention alone would actually reduce falls and fractures in MS is unknown. Perhaps a more comprehensive multifaceted approach, including a medication screen, lifestyle choice modifications (related to diet, exercise, smoking, and alcohol), as well as appropriate mobility aids and home adaption to minimize falls would be of value.

DISCLOSURE

The authors report no disclosures relevant to the manuscript. **Go to Neurology.org for full disclosures.**

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