Rheumatology

Lupus Low-Income SLE Patients at High Risk for Fracture

-Fracture risk was about 2.5-fold higher in this SLE subgroup with nephritis versus non-SLE patients

by Zeena Nackerdien, CME Writer, MedPage Today February 8, 2019

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Target Audience and Goal Statement:

Rheumatologists, orthopedists, nephrologists, and primary care physicians

The goal of the study was to learn more about fracture risks among low-income patients with systemic lupus erythematosus (SLE) and SLE patients with lupus nephritis compared with matched controls without those conditions.

Questions Addressed:

What were the fracture incidence rates within a large cohort of low-income SLE and lupus nephritis patients?

How do relative risks for fracture in SLE patients compare with a matched non-SLE cohort?

What were the clinical outcomes when evaluating subgroups by age and with lupus nephritis?

Action Points

Low-income patients with systemic lupus erythematosus (SLE) had double the risk of fractures compared with matched controls without SLE, according to analysis of Medicaid data.

Note that risks were even higher among SLE patients with nephritis, which underscores the importance of identifying high-risk SLE and lupus nephritis patients for fracture prevention strategies.

Synopsis and Perspective:

Currently, SLE is understood to be a clinically heterogeneous, remitting-relapsing, autoimmune condition inflicted by a disturbed immune system on passive target organs, such as bones and kidneys. Lupus flares often manifest as fatigue, painful or swollen joints, fever, skin rashes, and kidney issues. Women between puberty and menopause are prime candidates for SLE.

SLE-induced bone loss is of particular concern among women (90% of SLE patients) since they are already at increased risk for osteoporosis. Inactivity due to pain and fatigue caused by SLE may trigger bone loss. Glucocorticoids -- medications that are often prescribed to treat SLE -- can also cause significant bone loss. Other risk factors for osteoporosis in SLE include smoking, drinking too much alcohol, not getting enough calcium, and having a family history of the disease.

SLE pathophysiology also involves lupus nephritis in up to 60% of the cases -- a condition that may lead to renal failure. Secondary hyperparathyroidism, increased osteoclastic bone resorption, and reduced levels of 1,25-dihydroxyvitamin D serum levels are features of severe renal failure that may contribute to the onset of osteoporosis.

Few studies have examined the link between impaired renal function and low bone mass, partly because patients that fit those criteria are excluded from many studies. Additionally, few large cohort studies have compared fracture risks among age- and sex-matched SLE patients. There is also a literature gap with respect to fracture risks among racially and ethnically diverse, low-income SLE patients, who are at particularly high risk for SLE complications.

Sara K. Tedeschi, MD, of Brigham and Women's Hospital and Harvard Medical School in Boston, and colleagues employed 2007-2017 Medicaid data to compare 47,709 SLE patients (19.8% with lupus nephritis) to 190,836 non-SLE comparators (92.6% female; mean age 41.4). Median household income was slightly higher than $45,000.

More patients in the SLE group were African American (42.5% vs 22.1%). About 41.2% of SLE patients were prescribed glucocorticoids, while only 5.7% of non-SLE comparators used these drugs. Hydroxychloroquine -- a mainstay of lupus treatment -- was used by less than half of the SLE cohort. Bisphosphonate prescriptions were very rare and were more frequent in SLE (5.8%) than age- and sex-matched non-SLE comparators (0.7%), noted the authors. About 5.4% of patients in the SLE group had end-stage renal disease versus 0.6% in the non-SLE group.

Pelvis, hip, wrist, or humerus fractures served as the primary outcome. The secondary outcome was the first fracture at each site. But spinal fractures were excluded from the study because these breaks are frequently asymptomatic and difficult to detect using claims data.

Demographics, prescriptions, and comorbidities were assessed during a 180-day baseline period. Tedeschi and colleagues calculated fracture incidence rates (IR) in SLE, lupus nephritis, and non-SLE comparator cohorts, and estimated adjusted hazard ratios (HR) for fractures. Subsets of SLE patients with and without lupus nephritis were also evaluated during the study.

The IRs for any fracture were 4.32/1,000 person-years among SLE patients, 4.60/1,000 for SLE patients with nephritis, and 2.40/1,000 among non-SLE controls. The most common type of fracture in the SLE group overall was pelvic, with an IR of 1.72/1,000 person-years. The risks of pelvic fracture were even higher in the nephritis subgroup, at 2.23/1,000. In the control group, wrist fractures were the most frequent (1.04/1,000).

After adjustment for baseline prednisone use, fracture risks relative to non-SLE individuals were as follows:

Overall: hazard ratio 1.78 (95% CI 1.55-2.05)

Hip: HR 3.22 (95% CI 2.33-4.46)

Pelvis: HR 2.63 (95% CI 2.13-3.24)

Humerus: HR 1.82 (95% CI 1.34-2.47)

Wrist: HR 1.57 (95% CI 1.27-1.94)

The subgroup of SLE patients with nephritis not only had an increased risk of any fracture compared with non-SLE controls, but also compared with SLE patients without nephritis (HR 1.58, 95% CI 1.20-2.07).

Among patients ages <50, the HR for fracture was 2.28 (95% CI 1.90-2.74) compared with controls, and for those ages >50, the HR was 1.92 (95% CI 1.61-2.28), with slight attenuation after adjustment for comorbidities and prednisone use.

Study limitations included a lack of information on duration of disease and no adjust for lifetime exposure to glucocorticoids prior to index date (potentially leading to underestimation of relative risk). Additionally, the researchers did not adjust for calcium or vitamin D due to concern for poor ascertainment.

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Study Highlights: Explanation of Findings

Low-income Americans with SLE had double the risk of fractures compared with matched controls without SLE. The HR for any fracture among patients with SLE was 2.09 (95% CI 1.85-2.37), according to Tedeschi and colleagues. And risks were even higher among SLE patients with nephritis (HR 3.06, 95% CI 2.24-4.17), the researchers reported. Fracture risk was about 2.5-fold higher in this high-risk subgroup versus non-SLE patients, even after adjusting for glucocorticoids and comorbidities such as renal disease.

Younger SLE patients had a slightly higher fracture risk (2.3-fold) versus older patients (1.9-old). Glucocorticoids also slightly attenuated fracture risks, in keeping with evidence from the literature about the detrimental effects of glucocorticoids on bone health.

Adjustments for predefined comorbidities using the Charlson-Deyo Comorbidity Index, which includes renal disease, attenuated fracture risks in lupus nephritis reflecting the role that renal disease plays in fracture risk, noted the authors.

Study strengths included the application of established algorithms to identify SLE, lupus nephritis, and fractures at four anatomic sites among a large sample of >47,000 racially/ethnically diverse SLE patients and age- and sex-matched comparators; the reliability of the claims data in identifying fragility fractures; and ability to adjust for both oral and intravenous glucocorticoid use based on filled prescriptions, and other potential confounders.

"Differences in study populations and methodology may explain the slightly higher fracture risks that we observed compared to prior studies. Suboptimal SLE treatment among Medicaid enrollees and poor outcomes in this population, as has been shown in prior work, may have contributed to elevated fracture risks," Tedeschi and colleagues noted.

Glucocorticoid use could account for only some of the increased risk, and suboptimal practice patterns also may have contributed, as evidenced by the low rate of hydroxychloroquine use, Tedeschi's group added.

Based on the 2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis, calcium and vitamin D plus an additional osteoporosis medication (oral bisphosphonate preferred) may be used in adults with moderate-to-high fracture risk who are beginning or continuing long-term (≥3 months) glucocorticoid treatment.

However, renal disease contraindicates preventive treatment with bisphosphonates. Moreover, bisphosphonate use was infrequent among SLE and non-SLE patients and it was unclear if bisphosphonate use would be associated with lower fracture risk due to its biological effect, or higher fracture risk due to confounding by indication (e.g., preferential prescribing to patients perceived to be at highest fracture risk). Therefore, the authors did not use bisphosphonate in any of their analytical models.

"This work underscores the importance of identifying high-risk SLE and lupus nephritis patients for fracture prevention," the authors concluded.

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Secondary Source

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