COMMENTARY
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Can Early Onset of Disease Be One of the Risk Factors for Low Bone Mineral Density in Patients with Inflammatory Bowel Disease?

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See "The Early Onset of Disease May Be a Risk Factor for Decreased Bone Mineral Density in Patients with Inflammatory Bowel Disease" by Hwa Jong Kim, Su Jin Hong, Young Woo Jeon, et al., on page 71-76

The incidence of fractures among patients with inflammatory bowel disease (IBD) is reported to be approximately 40% higher than in the general population.[1] Osteoporosis and osteopenia, characterized by low bone mineral density (BMD), are increasingly recognized as common extraintestinal manifestations of IBD that increase the risk of fracture. However, only 13% of the patients with IBD who had already sustained a fracture were on any form of antifracture treatment.[2] Therefore, in terms of low BMD, many patients with IBD are being neglected. For physicians managing IBD patients, the importance of increasing awareness of low BMD should be emphasized. Low BMD in IBD is complex and considered to have multifactorial pathogenesis. Factors that contribute to osteoporosis in the general population may be important in patients with IBD as well. Potential risk factors for development of low BMD include age, gender, smoking, underweight, reduced food intake, malabsorption, cumulative corticosteroid therapy, small bowel resection, vitamin D (25-hydroxyvitamin D) deficiency, hypogonadism, disease duration, proinflammatory cytokines (tumor necrosis factor-α, interleukin-6, etc.), and genetic factors.

To recognize the increased risk for fractures in patients with low BMD, the American College of Gastroenterology (ACG) and the American Gastroenterology Association (AGA) guidelines recommended screening IBD patients with dual energy X-ray absorptiometry (DXA) if they have one or more of the following risk factors: postmenopausal state, ongoing corticosteroid treatment, cumulative prior use of corticosteroids exceeding three months, history of low trauma fractures, or age over 60.[3] According to Etzel et al.,[4] the presence of any of the four criteria had a sensitivity of 84%, specificity of 23%, positive predictive value of 27%, and negative predictive value of 81% for detection of osteoporosis in the DXA tested population. They insisted that use of DXA to screen for low BMD in patients with IBD is underutilized. In addition, Atreja et al.[3] suggested that because the ACG and AGA guidelines may miss many patients at risk, adherence to the ACG and AGA guidelines alone will not be sufficient in decreasing fracture risk in the IBD population. They insisted that efforts should be made not only in better adoption of guidelines but also in revising the current guidelines to include nonconventional risk factors, such as body mass index (BMI), in the assessment of fracture risk. In addition, some researchers insist that BMD should be examined in all IBD patients.

According to several studies, low BMI, glucocorticoid exposure, and increased age are the variables most frequently associated with low BMD.[3-8]

A low BMI is known to be one of the strongest independent risk factors associated with low BMD in IBD patients. However, Kim et al.[9] failed to confirm a significant difference in BMI between IBD patients with a normal BMD and those with a low BMD (21.8±3.1 vs. 21.8±4.8, p=0.97) even as a known a risk factor for low BMD. This result coincides with that of the study reported by Park et al.[10]

Corticosteroids, which are most often used during periods of active inflammation, have several adverse effects on bone metabolism and cause osteoporosis and fractures in a high percentage of IBD patients. Treatment with corticosteroids has been reported to result in bone loss, especially at trabecular bone sites such as the lumbar spine. The main mechanism by

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which corticosteroids cause bone loss is the impairment of osteoblast function, inducing osteoblast apoptosis, reducing intestinal calcium absorption, and increasing renal excretion of calcium.[4] Although corticosteroid use is clearly an important variable, investigators define and quantify the use in widely differing ways. In the article by Kim et al.,[9] the cumulative steroid dose was higher in the reduced BMD group than in the normal BMD group among IBD patients, but the difference was not significant (5,120.8±4,402.1 mg vs. 3,350.5±3,269.8 mg, p=0.17).

Although numerous cross-sectional studies have evaluated BMD and assessed risk factors for low BMD, there is a paucity of data on early onset of disease among patients with IBD. Several studies have identified that older IBD patients are at higher risk for low BMD.[3-6] In addition, population-based studies have confirmed an association of IBD with only a small increase in fracture risk and that the greatest risk is in elderly persons with IBD.[11,12] However, the peak age of incidence of IBD is the second and third decades of life. This is also an important time during which peak bone mass is established. It is possible that the age of onset of IBD might be critical in determining the final peak BMD attained.[13] Accordingly, some studies have described younger age at diagnosis of disease as a predictor of low BMD.[7,14,15] Sylvester et al.[14] observed that a reduced BMD can be detected at the time of diagnosis in children with IBD, suggesting that disease factors affect skeletal health before a treatment is started. Younger patients with IBD had a mildly elevated risk of osteoporosis, compared with older patients. This could be due to a more active disease in young patients, leading to osteoporosis via circulating cytokines which affect osteoclast and osteoblast function.[7] Kim et al.[9] attempted to analyze the impact of early onset of disease before attainment of a peak bone mass in patients with IBD. They reported that bone mass reduction was more severe in patients who were diagnosed with IBD before the age of 30 than in those diagnosed after the age of 30; however, the differences did not reach statistical significance probably due to the small number of patients (odds ratio, 3.96; 95% confidence interval, 0.89 to 17.62; p=0.06).

The article by Kim et al.[9] has several limitations. First, the author conducted a case-control study for comparison of BMD; however, there is no detailed description for the selected control group, such as inclusion and exclusion criteria from the healthy population. Second, in the multivariate logistic regression analysis, the author analyzed risk factors for reduced BMD, including age at diagnosis, inflammation (C-reactive protein), dose of steroids, and calcium and vitamin D intake. However, there are no explanations for why these risk factors were selected and how the confounding variables were adjust. Third, as the author stated, the sample size of the patients does not exclude a type II error. Nevertheless, They suggest the new possibility that early onset (younger than 30 years old) of disease can be considered one of the risk factors for low BMD in patients with IBD, although statistically not significant at this time.

Conflicts of Interest

The authors have no financial conflicts of interest.

REFERENCES

1. Bernstein CN, Blanchard JF, Leslie W, Wajda A, Yu BN. The incidence of fracture among patients with inflammatory bowel disease. A population-based cohort study. Ann Intern Med 2000;133:795-799.
2. van Staa TP, Cooper C, Brusse LS, Leufkens H, Javaid MK, Arden NK. Inflammatory bowel disease and the risk of fracture. Gastroenterology 2003;125:1591-1597.
3. Atreja A, Aggarwal A, Licata AA, Lashner BA. Low body mass index can identify majority of osteoporotic inflammatory bowel disease patients missed by current guidelines. ScientificWorldJournal 2012;2012:807438.
4. Etzel JP, Larson MF, Anawalt BD, Collins J, Dominitz JA. Assessment and management of low bone density in inflammatory bowel disease and performance of professional society guidelines. Inflamm Bowel Dis 2011;17:2122-2129.
5. Targownik LE, Leslie WD, Carr R, et al. Longitudinal change in bone mineral density in a population-based cohort of patients with inflammatory bowel disease. Calcif Tissue Int 2012;91:356-363.
6. Van Schaik FD, Verhagen MA, Siersema PD, Oldenburg B. High prevalence of low bone mineral density in patients with Inflammatory Bowel Disease in the setting of a peripheral Dutch hospital. J Crohns Colitis 2008;2:208-213.
7. Frei P, Fried M, Hungerbuhler V, Rammert C, Rousson V, Kullak-Ublick GA. Analysis of risk factors for low bone mineral density in inflammatory bowel disease. Digestion 2006;73:40-46.
8. Ezzat Y, Hamdy K. The frequency of low bone mineral density and its associated risk factors in patients with inflammatory bowel diseases. Int J Rheum Dis 2010;13:259-265.
9. Kim HJ, Hong SJ, Han JP, et al. The early onset of disease may be a risk factor for decreased bone mineral density in patients with inflammatory bowel disease. Clin Endosc 2013;46:71-76.
10. Park JJ, Jung SA, Noh YW, et al. Analysis of risk factors for low bone mineral density in patients with inflammatory bowel disease. Korean J Gastroenterol 2010;55:237-244.
11. Vestergaard P, Mosekilde L. Fracture risk in patients with celiac disease, Crohn's disease, and ulcerative colitis: a nationwide follow-up study of 16,416 patients in Denmark. Am J Epidemiol 2002;156:1-10.
12. Loftus EV Jr, Crowson CS, Sandborn WJ, Tremaine WJ, O'Fallon WM, Melton LJ 3rd. Long-term fracture risk in patients with Crohn's disease: a population-based study in Olmsted County, Minnesota. Gastroenterology 2002;123:468-475.
13. Bernstein CN, Leslie WD, Taback SP. Bone density in a population-based cohort of premenopausal adult women with early onset inflammatory bowel disease. Am J Gastroenterol 2003;98:1094-1100.
14. Sylvester FA, Wyzga N, Hyams JS, et al. Natural history of bone metabolism and bone mineral density in children with inflammatory bowel disease. Inflamm Bowel Dis 2007;13:42-50.
15. Abitbol V, Roux C, Chaussade S, et al. Metabolic bone assessment in patients with inflammatory bowel disease. Gastroenterology 1995;108:417-422.