

Editorial



Is Trabecular Bone Score a More Sensitive Marker for Osteoporosis in Asthmatics?

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► See the article “Trabecular Bone Score Is More Sensitive to Asthma Severity and Glucocorticoid Treatment Than Bone Mineral Density in Asthmatics” in volume 11 on page 343.

Asthma is a chronic inflammatory disorder of the airway and requires long-term treatment with inhaled corticosteroids (ICS) and oral corticosteroids (OCS) as controller and/or rescue medications. The cumulative lifetime corticosteroid exposure may be very high due to the chronicity of asthma. In particular, severe asthma, which accounts for 5%–10% of asthma, is difficult to control and requires high doses of ICS therapy and intermittent OCS therapy. Therefore, patients with severe asthma are at greater risk of the adverse effects of corticosteroids.¹

Osteoporosis is a disease characterized by low bone mass and altered bone microarchitecture, which can lead to decreased bone strength with increased fracture risk.² The diagnosis of osteoporosis is currently based on the results of bone mineral density (BMD) assessed by dual-energy X-ray absorptiometry (DXA) image. Corticosteroid-induced osteoporosis is the most common secondary cause of osteoporosis. Bone loss is directly related to the dose and duration of corticosteroid use and begins as early as 3 to 6 months after the initiation of OCS therapy. Patients with OCS have increased fracture risk than control subjects with similar BMD values.³ Approximately 10%–20% of the inhaled dose of ICS reaches the lungs, where it is absorbed into systemic circulation. Several pharmacokinetic studies on ICS have shown measurable serum concentrations of corticosteroids. Therefore, ICS could lead to potentially similar side effects to OCS.³

The skeletal effects of ICS are poorly understood, and the results of studies comparing BMD values of adult patients with asthma using ICS with those of untreated controls are conflicting. Although the results for BMD or fracture risk are different, a dose-dependent harmful effect has been reported in patients with high daily doses and larger cumulative dose of ICS.³ The amount of ICS and treatment duration needed to cause adverse skeletal effect are still unknown; however, deleterious effects were noted even in subjects receiving a median daily dose of 500 µg of fluticasone.^{4–6} Studies on the BMD changes during ICS treatment have also shown different results.^{4,5} In a recent study for the effects of different asthma regimens on BMD, there were no significant decrease in BMD for over 1 year in subjects treated with mometasone, fluticasone, or montelukast.⁷ Recently, Chen *et al.*⁸ reported the results of a registry-based cohort study, wherein cross-sectional and longitudinal analyses were performed to assess the association between long-term ICS use and BMD among 6,561 older women with asthma or chronic obstructive pulmonary disease (COPD). They

confirmed statistically significant but relatively weak change in BMD, which would take approximately 50 years of continuous ICS use to produce 1 standard deviation reduction in BMD. Thus, although statistically significant, no clinically important change in BMD due to long-term ICS use in older women with asthma or COPD was observed.⁸ However, despite no difference in BMD, ICS can change the different properties of the bone. Liu *et al.*⁶ compared BMD, microarchitecture and bone stiffness between postmenopausal (PM) women using ICS and control women. Based on their study, ICS users had greater trabecular separation and lower cortical thickness, trabecular number, and bone stiffness at the radius, suggesting major unrecognized skeletal deficits in PM women using ICS. These results suggest that the metabolically active trabecular bone is more susceptible to the effects of long-term corticosteroid exposure and indicate that BMD alone may not sufficiently identify bone changes caused by corticosteroids.⁶ In fact, BMD accounts for only 60%–70% of the variation in bone strength, and many patients with fragility fractures have BMD values within the normal range.^{2,9,10} Thus, BMD is not always an accurate predictor of fracture risk. These inconsistencies may be attributed to qualitative changes in bones caused by ICS use, which cannot be ascertained by BMD.⁶ BMD measures only bone density and fails to assess bone microarchitecture, which is a key determinant of bone strength and an important component of osteoporosis. Therefore, new measures are needed to identify qualitative changes in bones, and the trabecular bone score (TBS) is one such surrogate marker.

TBS is a texture parameter that can be extracted from the DXA image. Although not directly measured, TBS is closely related to bone microarchitecture. A high TBS value correlates with better skeletal microstructure and a low TBS correlates with weaker microstructure.^{2,11} Many studies have shown that TBS predicts the fracture risk in PM women. The largest published study assessing TBS was conducted in Canada, and it comprised 29,407 PM women. BMD and TBS predicted fractures equally well, and the combination of BMD and TBS significantly improved fracture prediction compared with BMD or TBS alone.¹² TBS is superior in identifying osteoporosis or fracture risk, especially in case of corticosteroid use where BMD does not accurately reflect bone changes. Leib and Winzenrieth¹³ showed that TBS was more sensitive to bone deterioration than BMD in patients treated with OCS. Moreover, Paggioli *et al.*¹⁴ showed that women treated with OCS had significantly decreased TBS than control women. However, no significant difference in BMD was noted.

In the current issue of *Allergy, Asthma and Immunology Research*, Choi *et al.*¹⁵ revealed that patients with severe asthma exhibited lower TBS values than those with either patients with non-severe or non-active asthma or non-asthmatic subjects. However, no significant difference was observed in BMD among the study groups. Older patients with asthma, patients with severe asthma and high systemic corticosteroid (SCS) exposure during the past year were identified as independent predictors of lower TBS. In addition, TBS was also significantly correlated with airway obstruction and hyper-reactivity and ICS doses used over the previous year, which were not correlated with BMD. To the best of our knowledge, this is the first study to evaluate the usefulness of TBS among patients with asthma. Despite the limitations of this retrospective cross-sectional study conducted without distinguishing the age or sex of the study population that could affect BMD or TBS values, this study highlights that TBS is a potentially good predictive marker to reduce corticosteroid-induced fractures in patients with severe asthma.

The prevalence of asthma is consistently increasing in the elderly and female population who are prone to osteoporosis.¹⁶ In severe asthma, the mean ICS and total SCS in the previous year

was 1,102 µg/d of budesonide and 802.7 mg of prednisolone respectively, which are enough to cause bone changes. Nevertheless, data on osteoporosis in severe asthma are lacking.¹⁷ There is a dose-response relationship between ICS use and fracture risk in asthmatics.³ These results suggest that there are many patients with asthma with a high risk of osteoporosis or fracture, and that the number may continue to increase. However, there are no guidelines for the diagnosis and management of corticosteroid-induced osteoporosis in high-risk patients with asthma. Under these circumstances, TBS may have the potential to act as a key biomarker in screening high-risk patients and determining whether medical treatment should be initiated. Further large-scale prospective studies are needed.

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