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Fracture risk in type 1 diabetes: Think beyond bone mineral density

Type 1 diabetes (T1D) is caused by insulin deficiency resulting from immune mediated destructions of pancreatic beta cells. Though it is believed that T1D is common in children, nearly 50% of cases of T1D are diagnosed in adults.[1] With availability of newer insulin and diabetes technologies such as insulin pumps and continuous glucose monitors, there has been a remarkable improvement in diabetes care and a reduction in long-term diabetes complications. As a result, people with T1D are living longer. There has been a shift in research focus to understand the effect of long standing diabetes on age-related diseases such as osteoporosis and cognitive impairment.

A number of studies including population-based,[2] clinic registry-based,[3] and meta-analyses[4] have shown three-to-six-fold higher fracture risk in people with T1D compared to people without diabetes. Fracture risk is also higher in T1D compared to people with T2D[5] suggesting some differences in the pathophysiology of bone involvement in T1D such as age of onset of diabetes, duration of diabetes, body weight and insulin resistance compared to T2D. Despite the high fracture risk in this population, fracture is an under recognized complication of T1D.

Fracture is a mechanical event where force exceeds the strength of the bone. Therefore, both bone mineral density (BMD) and bone quality (such as microarchitecture and tissue material quality) are important to understand mechanisms of fractures in T1D.[6] Bone density estimation by dual x-ray absorptiometry (DXA) is considered the gold standard clinical tool to evaluate fracture risk in general population. DXA is a relatively simple, non-invasive and inexpensive tool to evaluate bone density at axial (lumbar spine or hip) and peripheral bones (distal radius) to calculate fracture risk and make appropriate treatment decisions to improve bone health. However, DXA-based BMD is 2-dimentional and due to limited resolution, cannot be used to study bone microarchitecture. Studies in children and adolescents with T1D showed lower or similar BMD compared to controls without diabetes.[7] A meta-analysis in adults with T1D showed modestly lower BMD at femoral neck and hip but no difference in spine BMD compared to adults without diabetes.[8] However, BMD is not well studied in people with long-standing diabetes (diabetes duration >50) years. In a study of 985 subjects having T1D for >50 years at Joslin Diabetes Center reported normal *Z*-score at spine and modestly lower BMD at femoral neck.[9] However, lack of control group for comparison was one of the major limitations of that study. To provide more evidences to existing limited literature, in this issue, Alhuzaim and colleagues have reported DXA-measured BMD at spine and hip in 75 older adults with long standing diabetes from Canadian study of Longevity in Type 1 Diabetes compared to 75 age and sex frequency matched older adults without diabetes.[10]

The mean age of older adults with T1D was 66 years with 54 years of diabetes duration. Most patients were diagnosed with T1D at young age and >90% of them have some form of microvascular complications. Self-reported fractures were higher in females with T1D (66% vs 42%) compared to females without diabetes. Despite higher self-reported fractures, lumbar spine T-score was higher and there was a modest reduction in femoral neck BMD in females with T1D compared to controls. Though the study is well executed, the results should be interpreted with caution due to the cross-sectional study design, aspects of the study population that may not be representative of the underlying population with T1D, such as age at onset, diabetes duration and prevalence of complications, and potential confounders. For example, degenerative spine diseases are common among people with long duration of diabetes, which may result in higher BMD at the spine.

The results of this study have important clinical and research implications. These data were consistent with earlier studies in young adults with T1D suggesting that DXA-measured BMD does not provide true estimation of facture risk in people with T1D. Therefore, diabetes related factors in addition to DXA-measured BMD should be taken in account when making osteoporosis treatment decisions in this population.[11] A recent review suggested using a lower T-score or use of FRAX score adjusted for diabetes (by adding rheumatoid arthritis and TBS for FRAX calculations) for fracture risk evaluation and treatment decisions in people with diabetes.[11] This study also highlights the importance of bone quality for fracture risk in this population. Studies in both animal models and humans suggest that collagen quality is impaired in diabetes and may explain the higher fracture risk in this population despite normal or modestly lower BMD at spine and hip.[12,13] Bone biopsy to study collagen quality and tissue material properties is invasive, costly and not feasible clinically for fracture risk evaluation. Therefore, research is needed to evaluate simple non-invasive techniques such as non-invasive AGE readers and osteoprobe (in vivo bone material strength index) and the impact of these techniques on fracture risk and fracture treatment.

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Declaration of competing interest

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