Osteoporosis-associated Fracture and Diabetes

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KEYWORDS

• Bone • Osteoporosis • Diabetes • Diabetes complications • Fracture
• Skeletal disorder

KEY POINTS

- Because osteoporosis and diabetes mellitus are chronic diseases that are increasing in prevalence, understanding their complex interaction is integral to providing optimal care for patients.
- Osteoporosis-associated fracture is an important complication of diabetes to consider when evaluating patients with diabetes.
- Given the different causes of type 1 and type 2 diabetes, they have a unique relationship with bone but also have similar effects on bone when not treated adequately.
- Osteoporosis treatment options for diabetic patients are the same as for nondiabetic patients, including ensuring normal renal function before starting a bisphosphonate.

INTRODUCTION

Osteoporosis and diabetes mellitus (DM) are chronic diseases with increasing prevalence. Both have significant associated morbidity and mortality and may lead to severe debilitation if not treated adequately. Osteoporosis is a skeletal disorder characterized by reduced bone quantity and quality, which predisposes to fracture.[1,2] Fragility fractures, or low-trauma fractures, are common, affecting almost 1 in 2 older women and 1 in 3 older men.[3] The global burden of osteoporosis is significant, with approximately 9 million new osteoporotic fractures worldwide in the year 2000.[4] Diabetes is also increasing in prevalence. Prevalence of diabetes for all age groups is estimated to be 4.4% of the worldwide population by the year 2030.[5]

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Recent evidence shows that both type 1 and type 2 DM are associated with an increased fracture risk.[6] Although microvascular and macrovascular complications are the complications most commonly associated with diabetes, osteoporosis and risk of fracture must also be considered when treating patients with diabetes. Type 1 diabetes (T1D) is defined as a state of insulin deficiency, whereas type 2 diabetes (T2D) is characterized by insulin resistance with increased insulin levels. Given the different causes of T1D and T2D, they have unique interactions with bone. Skeletal disorders often associated with diabetes include osteoporosis-associated fracture, Charcot arthropathy, and renal osteodystrophy secondary to end-stage renal disease as a complication of diabetes.[7,8] Like others in the past,[9,10] this article focuses on osteoporosis-associated fracture as a metabolic complication of diabetes.

In recent years, osteoporosis-associated fracture has come to the forefront of complications associated with diabetes. Controversy exists over the exact mechanisms of bone loss in the setting of diabetes, but there is significant evidence to support that diabetes affects bone health. The meta-analysis by Vestergaard[11] showed that adults with T1D have a 6.9 relative risk of hip fracture and adults with T2D have a 1.3 relative risk of hip fracture. In addition, a meta-analysis by Janghorbani and colleagues[12] showed similar results with a 6.3 relative risk of hip fracture in adults with T1D and a 2.8 relative risk of hip fracture in adults with T2D. In the Vestergaard[11] study, patients with T1D had decreased bone mineral density (BMD) and increased fracture risk, but although the study noted a 6.9 relative risk of hip fracture, the BMD expected relative risk was only 1.4, suggesting that there are additional factors contributing to fracture risk. Another finding of the Vestergaard[11] study was that, despite an increased fracture risk, patients with T2D had higher than expected BMD. With data from the Health, Aging, and Body Composition (Health ABC) Study, Schwartz and colleagues[13] showed increased incidence of vertebral fracture in T2D despite increased BMD. The interaction between diabetes and bone health is complex and requires further exploration.

T1D VERSUS T2D AND BONE: SIMILARITIES

Despite their different underlying causes, without proper treatment or compliance with treatment both T1D and T2D can be complicated by hyperglycemia. Hyperglycemia in turn can be detrimental to bone; it has been shown that glucose can be toxic to osteoblasts, the cells associated with bone formation. High glucose concentrations impair the ability of osteoblastic cells to synthesize osteocalcin, which is a protein integral to bone formation.[14] Also serum osteocalcin levels seem to be suppressed by hyperglycemia in diabetic patients.[15] Bone biopsies done on individuals with diabetes have shown low bone formation on histomorphometry.[16] For a given BMD, diabetic bone seems to be less strong and therefore more likely to fracture.[17,18]

Chronic hyperglycemia also promotes advanced glycation and accumulation of advanced glycation end products (AGEs), which contribute to diabetes complications. Impaired renal function is also thought to lead to accumulation of AGEs. They are formed through a nonenzymatic reaction between reducing sugars and amine residues. AGEs act directly to induce cross-linking of long-lived proteins, resulting in alteration of vascular structure and function.[19] Accumulation of AGEs in bone collagen likely contributes to the reduction in bone strength for a given BMD.[20] The prime targets of AGE accumulation are the structural components of the connective tissue matrix. This accumulation can alter collagen function and thereby alter the function of bone.