Diabetes and Bone Disease

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KEYWORDS

• Diabetes • Bone • Osteoporosis • Fracture • Bone mineral density
• Dual-energy x-ray absorptiometry

KEY POINTS

- Both TYPES 1 and 2 diabetes are associated with an increased risk of fracture.
- The pathophysiology of the increased fracture risk differs between types 1 and 2 diabetes.
- Several modalities, including bone mineral density, are available to stratify risk, but may not accurately capture the increased risk of fracture.
- First-line management is with bisphosphonates, although their efficacy in diabetes-induced osteoporosis is uncertain.
- Treatment-related suppression in bone turnover has not been shown to influence glucose metabolism or precipitate diabetes.

INTRODUCTION

The World Health Organization estimated that diabetes mellitus occurs in more than 415 million people worldwide, and that this number could double by 2040, because the incidences of both TYPE 1 (T1D) and TYPE 2 (T2D) diabetes are increasing.[1] T1D accounts for less than 10% of all patients with diabetes, and recent studies have shown that the global incidence is increasing by approximately 2% to 3% per year.[2,3] T2D currently affects 25% of older adults in the United States (including diagnosed and undiagnosed cases),[4] with worldwide estimates suggesting that it affects more than 15% of adults greater than age 55 years.[1]

The major complications of diabetes are well-known, namely, microvascular complications such as nephropathy, retinopathy, and neuropathy, as well as the macrovascular complications including cardiovascular disease. More recently, epidemiologic data have shown that other tissues and organs may be adversely impacted by diabetes. The skeletal system seems to be an additional target of

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diabetes-mediated damage, leading to the subsequent development of diabetes-induced osteoporosis. A conceptual framework for this increase in fracture burden is illustrated in Fig. 1.

Osteoporosis and diabetes are increasingly prevalent diseases, in part owing to aging populations worldwide.[1,5] At the age of 50, the lifetime risk of hip fracture is approximately 17.5% for women, and 6% for men in the United States,[6] with an even higher lifetime risk for vertebral fracture.[7] Nine percent of adults aged 50 and over have osteoporosis, as defined by a low bone mineral density (BMD) at either the femoral neck or the lumbar spine.[8] The total number of hip fractures in 1990 was estimated to be 1.26 million, and is projected to double twice, to 2.6 million hip fractures annually by 2025 and 4.5 million by 2050.[9]

EPIDEMIOLOGY

It has long been well-established that T1D is associated with an increased risk of both osteoporosis and osteopenia.[10–14] A metaanalysis demonstrated reduced BMD.[15] In addition, there is an increased risk of fracture in patients with T1D, more so than in those with T2D.[15] In a study of more than 33,000 Swedish adults (ages 25–60 years old), the strongest risk factor for hip fracture in both women and men was diabetes (relative risk [RR], 3.89; 95% confidence interval [CI], 1.69–8.93 [$P = .001$] for women; RR, 6.13; 95% CI 3.19–11.8 [$P = .001$] for men).[16] The increase in fracture risk, which is particularly marked at the hip, is much greater than what would be expected on the basis of the BMD decrement, implying that there are other factors independent of BMD that contribute to this increased fracture risk.[15,17]

Both T2D and low-trauma fracture become more common with advancing age. T2D is associated with both greater weight and higher BMD,[18] which was historically assumed to be protective against fracture. However, a paradoxic increased risk of fracture has been observed in many[19–23] but not all studies.[24,25] A metaanalysis by Janghorbani and colleagues[26] described an increased risk for all nonvertebral fractures (adjusted RR, 1.2; 95% CI, 1.01–1.5). An updated metaanalysis by Dytfeld and

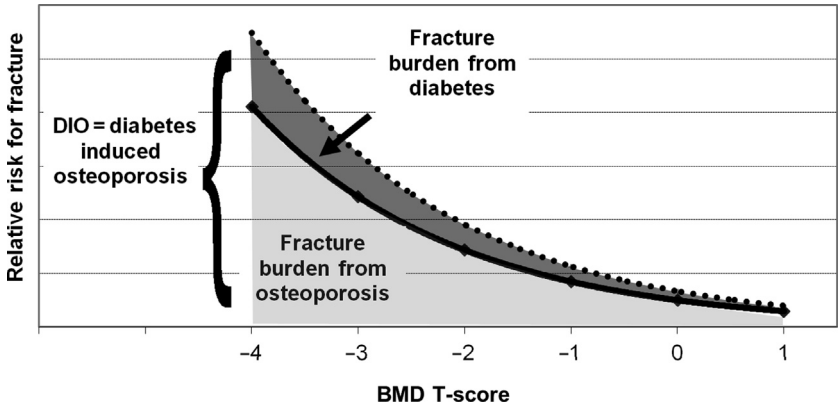

Fig. 1. Conceptual framework for diabetes and fractures. The light gray region below the solid line indicates the fracture burden attributable to osteoporosis; the dark gray region between the dotted and solid lines indicates the additional fracture burden attributable to diabetes. BMD, bone mineral density. (*Reprinted from* Schacter GI, Leslie WD. DXA based measurements in diabetes: can they predict fracture risk? Calcif Tissue Int 2016. [Epub ahead of print]; with permission.)