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Review article

Type 2 diabetes mellitus and bone fragility: Special focus on bone imaging

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Abstract

Fragility fracture rate is increased in type 2 diabetes patients despite of higher bone mineral density than non-diabetes control subjects. Vertebral fractures are usually asymptomatic; therefore, morphometric radiologic evaluation should be considered especially for diabetes patients.

Bone quality may more contribute to the increased risk of osteoporotic fractures in patients with type 2 diabetes than bone mass. Hip geometry, cortical porosity, and trabecular bone score have been studied as bone quality parameters by imaging in type 2 diabetes mellitus.

Keywords: Cortical porosity; Hip geometry; Trabecular bone score; Vertebral fracture assessment

1. Introduction

Prevalence of fragility fracture has increased in type 2 diabetes patients although bone mass (bone mineral density or bone mineral content) is higher than that in non-diabetic control subjects. When adjusted with body weight (or body mass index), bone mass is lower in diabetes than in controls. Type 2 diabetes is characterized by high serum insulin levels and tissue insulin resistance. Traditionally, insulin has been considered as an anabolic factor, but recent studies revealed that a higher insulin level with insulin resistance was correlated with low bone mass and deteriorated bone strength [1–3].

In the Rotterdam study, the non-vertebral fracture rate was increased in postmenopausal diabetes Caucasian women [4]. The risk of all clinical fractures in diabetes men and women was increased regardless of ethnicity in the US Health ABC Study [5]. A systematic analysis showed that the hip fracture rate was increased in type 2 diabetes patients in the US and Europe [6]. Type 2 diabetes mellitus (DM) patients showed increased hip fracture rates compared to non-diabetic controls in the Chinese population [7]. Type 2 DM adult female patients were also expected to have greater risk of non-vertebral fractures than hypertensive control subjects in the Korean population [8].

Diabetes men and women aged 50 years and older had a significantly higher actual fracture rate in the hip and major osteoporotic areas than the expected Fracture Risk Assessment Tool (FRAX) probability compared with non-diabetic controls in Canada [9]. The calculated FRAX score itself did not show significant difference between type 2 diabetes and control subjects among postmenopausal Korean women [10].

In this paper, we attempted to focus to review on bone imaging studies in diabetes as compared with normal subjects. Firstly, vertebral fracture assessment by radiography. Secondly, hip geometry with dual energy X-ray absorptiometry (DXA) software. Thirdly, cortical porosity by high resolution peripheral quantitative computed tomography (HR-pQCT). Fourthly, trabecular bone score (TBS) using gray scale software. The following three factors: deteriorated hip geometry, increased cortical porosity, and decreased TBS may contribute to poor bone quality and increased fracture rate in patients with type 2 diabetes (Fig. 1).

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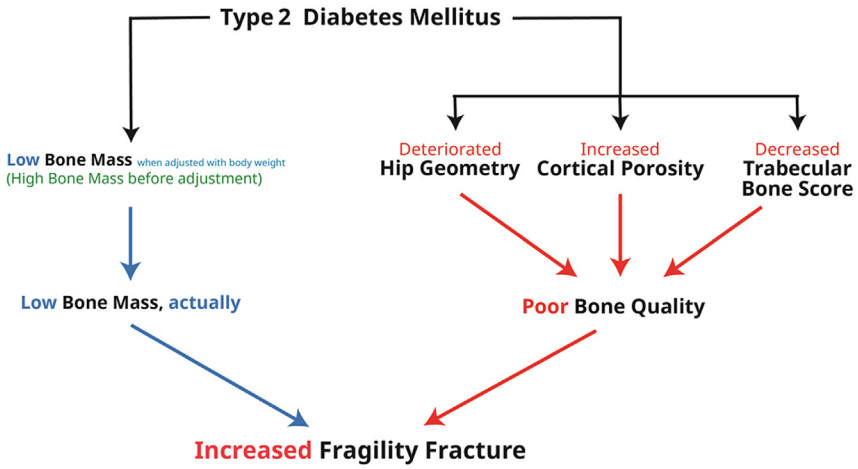

Fig. 1. Type 2 diabetes mellitus with low bone quality resulted in increased risk of fragility fractures, special focus on bone imaging.

2. Vertebral fracture assessment

Spine fractures are usually asymptomatic; therefore, radiologic evaluation should be considered in high-risk subjects. Traditionally, plain X-ray of the lateral spine has been used for the assessment. Nowadays, DXA provides software for lateral spine evaluation. Other modalities including computed tomography scan scout film can be used for evaluation [11,12]. With respect to analysis of spine fractures, classical visual assessment can be performed by a radiologist according to the semi-quantitative Genant's method. Quantitative morphometry can be performed by clinicians with the automatic method on the vertebrae (Fig. 2).

The vertebral compression fracture rate is high in type 2 DM patients. The spinal compression fracture prevalence rate was 46% in Korean diabetes postmenopausal women, including grade 1 mild fracture. Among all fractured vertebral bodies, 37% were grade 2 (moderate) or 3 (severe) [13].

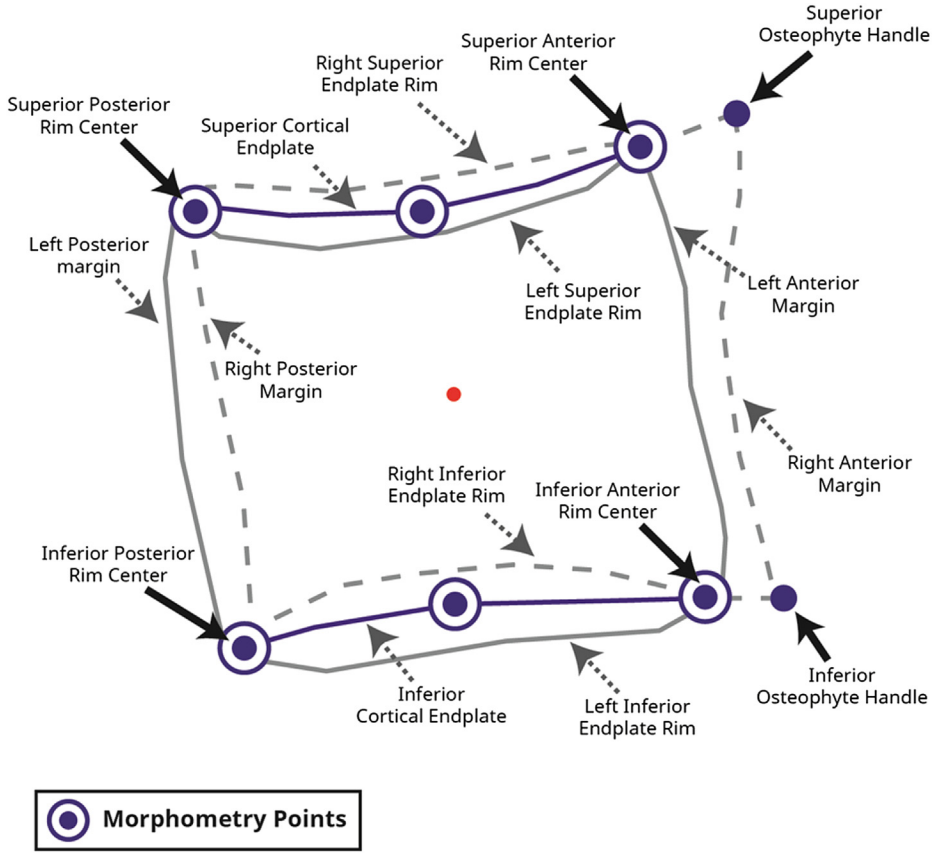

Fig. 2. Quantitative morphometric vertebral fracture assessment method.

3. Hip geometry

DXA allows the measurement of geometric contributions to bone strength in the proximal femur with hip structural (or strength) analysis software (Fig. 3). In the Baltimore Longitudinal Study, diabetes patients showed worse hip geometry including cross sectional area (CSA) and section modulus (Z) than controls [14]. The Canadian Multicentre Osteoporosis Study showed higher stress at the infero-medial margin of the femoral neck in a one-legged stance in diabetes patients than in controls, despite higher femoral neck bone mineral density (BMD) [15]. In the US Women's Health Initiative Observational Study, CSA and Z at the narrow neck of the femur were worse in diabetes patients than in controls [16]. In Asians including Koreans, higher cortical thickness and lower buckling ratio than those in Caucasians might explain the lower proximal hip fracture rate [17].

4. Cortical porosity

Cortical porosity can be assessed by HR-pQCT. Cortical porosity is an important parameter especially in long bones rather than in flat bones (for example, vertebrae). In diabetes Caucasian patients, there is a higher incidence of lower extremity fractures compared to controls. Cortical porosity is increased in some medical conditions including hyperparathyroidism. Recently, diabetes patients were found to have significantly higher cortical porosity than normal controls. Even in the presence of DM, patients in the fracture group had significantly higher cortical porosity than those in the non-fracture group [18]. Chinese women had increased cortical porosity according to aging, and it increased rapidly in the distal tibia and radius after menopause [19].

5. Trabecular bone score

TBS is a grey-level textural index of bone microarchitecture derived from lumbar spine DXA images (Fig. 4). TBS theoretically reflects the microarchitecture of the trabecular bone, which basically declines with age similar but different from BMD [20–22]. TBS has a complementary role in osteoporosis evaluation [23].

The use of TBS may not be recommended in premenopausal women or men aged below 50 years. Also, the use of TBS may not appropriate in patients with body mass index less than 15 or more than 37. Although TBS has potential to predict osteoporotic fractures, it should not be used alone to make a treatment decision but it should be used in association with FRAX and BMD. TBS has a reasonable precision of 1.1–2.1% compared to precision of BMD of 0.9–1.9% [24].

Recently, the ISCD official position recommends TBS as a reliable bone quality parameter [24]. Supporting evidences were obtained from cross-sectional studies and longitudinal studies [24,25]. More evidence was obtained in postmenopausal women compared to premenopausal women or men. TBS showed better response with anabolic agents than anti-resorptives [21]. TBS also showed better response in perimenopausal patients compared to old-aged patients. TBS has a greater impact in association with lower BMD compared to higher BMD [25].

The Manitoba cohort analysis revealed that diabetes women 50 years and older had lower TBS and increased major

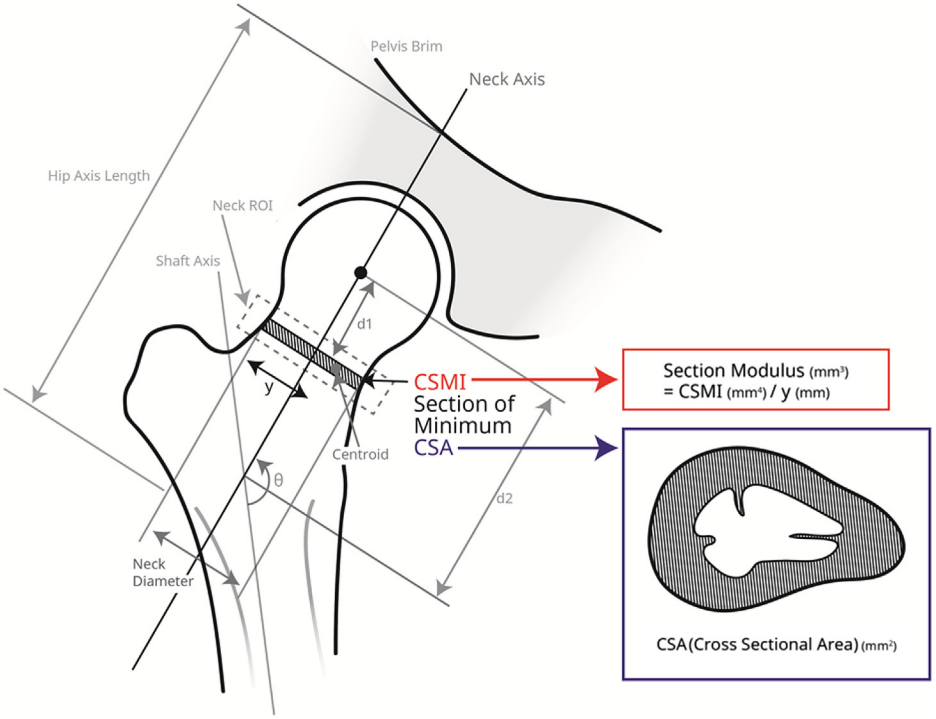

Fig. 3. Hip geometry parameters including cross sectional area and section modulus.

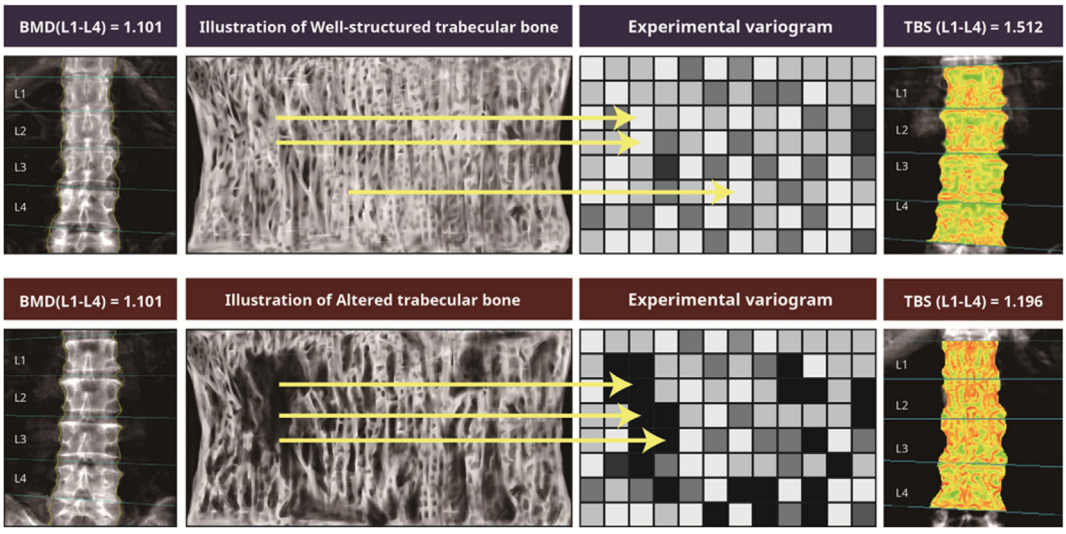

Fig. 4. Trabecular bone score assessed with software in lumbar spine.

osteoporotic fracture risk. TBS was an independent risk factor for fractures even in non-diabetic subjects [26]. Recent studies revealed that TBS was decreased in Caucasian and Asian type 2 DM patients [2,27,28]. TBS was also associated with vertebral fracture risk (higher odds ratio) than BMD in type 2 DM postmenopausal women [7]. TBS adjusted FRAX had better prediction (higher odds ratio) than original non-adjusted FRAX. Recently, FRAX adapted TBS as a reliable risk factor for predicting the 10-year probability of fragility fracture [25]. In a meta-analysis of 14 multinational, prospective, population-based cohort studies, TBS was found to be a significant independent risk factor for fragility fractures [29].

The Korean Cohort study (the retrospective analysis) revealed that TBS could be a significant risk factor in diabetes men and women. The study showed that higher fasting glucose and HbA1c levels are associated with lower TBS. Fasting serum insulin level and calculated homeostatic model assessment of insulin resistance were negatively correlated with TBS. Finally, inflammatory markers such as C-reactive protein showed a negative correlation with TBS. In summary, glucose control, insulin resistance, and inflammation were significantly correlated with TBS [2]. The Japanese Cohort study revealed that TBS is an independent risk factor for future fractures, especially in postmenopausal women [22].

Meta-analysis of 14 multinational, prospective, population-based cohort studies showed that TBS is a significant independent risk factor for fractures of the femur and major osteoporotic areas (vertebrae, radius, humerus). Major osteoporotic fractures depend more on TBS compared to hip fracture. In contrast, hip fracture is more associated with clinical risk factors and BMD. The death rate increased to 32% before adjustment and to 20% after adjustment in patients with a low TBS score [29].

In conclusion, increased osteoporotic fracture rate in Type 2 DM is probably associated with deteriorated bone quality. Hip geometry, cortical porosity, and TBS are clinically useful and measurable bone quality imaging parameters.

Conflicts of interest

None.

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