Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. ■, no. ■, 1–7, 2017

1094-6950/■:1–7/$36.00
http://dx.doi.org/10.1016/j.jocd.2017.01.005

Original Article

Quadrant Analysis of Quantitative Computed Tomography Scans of the Femoral Neck Reveals Superior Region-Specific Weakness in Young and Middle-Aged Men With Type 1 Diabetes Mellitus

Takuma Kuroda,[1] Koji Ishikawa,[,1] Takashi Nagai,[1] Tomoyasu Fukui,[2] Tsutomu Hirano,[2] and Katsunori Inagaki[1]*

[1]Department of Orthopedic Surgery, Showa University School of Medicine, Tokyo, Japan; and [2]Department of Medicine, Division of Diabetes, Metabolism, and Endocrinology, Showa University School of Medicine, Tokyo, Japan

Abstract

We have previously shown that the intertrochanter of young and middle-aged patients with type 1 diabetes mellitus (T1DM) showed higher buckling ratio (an index of cortical instability) and lower volumetric bone mineral density (vBMD). However, we have not yet reported the detailed findings regarding the mechanical and density properties of the femoral neck. Therefore, we present a subanalysis of our previous study with the aim of further evaluating the middle third of the femoral neck via quadrant quantitative computed tomography in young and middle-aged patients with T1DM. Bone parameters in 4 anatomical quadrants (superoanterior [SA], inferoanterior [IA], inferoposterior [IP], and superoposterior [SP]) were cross-sectionally evaluated in 17 male T1DM patients and 18 sex-matched healthy controls aged between 18 and 49 yr using quadrant quantitative computed tomography analysis. Patients with T1DM had a thinner cortical thickness in the SP quadrant and a significantly lower cortical vBMD in the SA quadrant than the controls. The serum insulin-like growth factor-1 values in patients with T1DM were positively correlated with the average cortical thickness in the SA quadrant and the average trabecular vBMD in the SP quadrant of the femoral neck. The cortical thickness in controls was negatively correlated with age in the SP and IP quadrants. The cortical thickness in patients with T1DM showed no correlation with age in all quadrants. The fragility of the femoral neck was remarkable in the superior region of patients with T1DM. Insulin-like growth factor-1 may play an important role in superior cortical thinning and in lowering cortical vBMD. Furthermore, in young and middle-aged men with T1DM, the structure of the femoral neck exhibits similar changes as those observed with aging.

Key Words: cortical thinning; quantitative computed tomography; region-specific weakness; type 1 diabetes mellitus.

Introduction

Type 1 diabetes mellitus (T1DM) is a lifelong condition that involves an insulin deficiency resulting from autoimmune-mediated destruction of the pancreatic β-cells. T1DM can cause many complications. One of the most common and serious complications in patients with T1DM is osteoporosis, as well as retinopathy, nephropathy, neuropathy, and cardiovascular events *(1)*. Although a number of cellular mechanisms have been proposed to explain the link between the patients with T1DM and osteoporosis *(2)*, it has now been established that defects in osteoblast differentiation and activity are the main causes of bone fragility in patients with T1DM *(3)*. Other contributing factors include insulin-like growth factor-1 (IGF-1) deficiency *(4)*, accumulation of advanced glycation end products, and

Received 08/29/16; Revised 12/26/16; Accepted 01/17/17.
*Address correspondence to: Koji Ishikawa, MD, PhD, Department of Orthopedic Surgery, Showa University School of Medicine, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8666 Japan. E-mail: o9o16979696koji@gmail.com

development of diabetes complications, which causes a further decline in bone mineral density (BMD), worsening the geometric properties within the bone, and consequently leading to an increased risk of falls *(3)*. Therefore, patients with T1DM are at increased risk for fractures compared with healthy individuals *(1)*.

Multiple studies have reported bone fragility in patients with T1DM using dual-energy X-ray absorptiometry *(5–7)* and hip structure analysis *(8)*. Recently, some studies have shown similar results using high-resolution peripheral quantitative computed tomography (QCT) *(9)* and magnetic resonance imaging *(10)*.

We have also previously shown the volumetric bone mineral density (vBMD), cross-sectional geometry, and the biomechanical parameters of the femoral bone subfractions by QCT in young and middle-aged patients with T1DM *(11)*. QCT can be used to obtain 3-dimensional measurements of BMD independently in cortical and trabecular bone compartments to determine both the cross-sectional geometry of the femoral bone and biomechanical parameters. We found that the intertrochanter of young and middle-aged patients with T1DM showed higher buckling ratio and lower vBMD. The buckling ratio is an index of cortical instability; a higher buckling ratio suggests that the cortical bone has become structurally unstable. Our previous study was the first investigation of the femoral bone using QCT in patients with T1DM *(11)*. However, our previous study had lacked detailed information regarding the mechanical and density properties in the femoral neck.

Cortical bone distribution is asymmetric within the femoral neck, thinner superior than inferior cortex *(12)*. Several studies have indicated that cortical thinning in the superior region of the femoral neck occurs with advancing age, whereas the inferior region remains relatively preserved *(13–16)*. This can be explained by the mechanics of bipedal locomotion. The differential load distribution across the femoral neck during walking leads to the asymmetric structure of the cortex *(16)*. Moreover, localized bone loss might be important in determining resistance to femoral neck fractures *(13–15)*. There have been no previous reports evaluating the regional geometry in the femoral neck in patients with T1DM. Therefore, we used quadrant QCT analysis to assess the regional differences in the mid-femoral neck of patients with T1DM. Quadrant QCT analysis provides detailed information by measuring cortical thickness, cortical vBMD, and trabecular vBMD in the anatomical quadrants of the mid-femoral neck. This is a subanalysis of our previous study *(11)*, and the aim of this study was to further evaluate the structure of the mid-femoral neck via quadrant QCT analysis in young and middle-aged patients with T1DM.

Materials and Methods

Study Subjects

The study subject group was the same as that in our previous report *(11)*. This cross-sectional study was conducted on 17 male patients with T1DM and 18 sex-matched controls aged 18–49 yr. All patients visited Showa University Hospital (Tokyo, Japan) regularly. The following exclusion criteria were applied: diabetes duration <3 mo, overt nephropathy (urine albumin-to-creatinine ratio >300 mg/g creatinine or estimated glomerular filtration rate <60 mL/min/1.73 m^2), preproliferative diabetic retinopathy or proliferative diabetic retinopathy, chronic disease apart from positive thyroid antibodies with euthyroid status, and restriction of physical activity. Participants who take calcium preparations, vitamin D, medications, or hormones known to affect bone metabolism were also not enrolled. Diabetic retinopathy was graded as simple, preproliferative, or proliferative retinopathy by ophthalmologists. The medical records of all patients were reviewed at baseline, and the duration of diabetes and mean insulin dose were calculated.

All participants provided written informed consent, and the study was approved by the ethics committee of the Showa University School of Medicine.

Background

The study patients completed questionnaires related to the following factors: physical activity (1—exercise every day, 2—exercise 2 or 3 times a week, 3—never exercise, and 4—other), calcium intake, smoking history, and alcohol intake. Weight and height were measured using standard protocols. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Blood samples and an early morning urine sample were obtained at the time of CT scanning. The value for glycated hemoglobin (HbA1c; %) was estimated as a National Glycohemoglobin Standardization Program-equivalent value (%) calculated by the following formula: HbA1c (%) = HbA1c (Japan Diabetes Society; %) + 0.4% *(17)*. Serum IGF-1 was measured by immunoradiometric assay. The Z-score of serum IGF-1 measurement was calculated via the LMS method using values appropriate for the patient's age and gender *(18)*.

QCT Scanning

The subjects underwent scanning on a SOMATOM Definition AS+ multi-detector-row CT scanner (Siemens AG, Munich, Germany) using predefined scanning conditions (X-ray energy, 120 kV; X-ray current, 200 mA; rotation speed, 1.0 s/rot; and beam pitch, 0.9) and predefined reconstruction parameters. The in-plane spatial resolution of 0.317 × 0.317 mm and reconstructed slice thickness of 2.0 mm were adjusted. To calibrate CT Hounsfield units to the equivalent bone mineral concentration, all subjects were asked to lie on a calibration phantom (Mindways Software, Austin, TX) which extended from a position covering the region from the upper margin of the L1 vertebral body to 2 cm before the lowest point on the lesser trochanter. All scanned CT data of the femoral neck were analyzed using QCT-Pro software v4.1.3 (Mindways Software).