

THE EFFECTS OF TYPE II DIABETES ON TRABECULAR MICROARCHITECTURE AND BIOMECHANICAL PROPERTIES AS ASSESSED BY μ CT and FEA IN ANIMAL MODELS

*Myong-Hyun Baek¹, Ye-Yeon Won¹, Wen-Quan Cui¹, Tae-Bong Yun¹, Kwang-Kyun Kim², Yoon-Suck Chung³

¹Department of Orthopaedic Surgery and Biomechanics Research Center, Ajou University, Korea

²Department of Orthopaedic Surgery, Kong-Ju Medical Center

³Department of Endocrinology and Metabolism, Ajou University, Korea

*San5 Wonchon-dong Youngtong-gu Suwon-City; Tel: 82-31-219-4536; Fax: 82-31-216-4536; E-mail: mct@ajou.ac.kr

Introduction:

Uncontrolled conditions in type II diabetes have severe consequences on skeletal health, including suppressed skeletal development, increased incidence of osteopenia and osteoporosis[1]. Although several studies have shown that type II diabetes is not associated with lower bone mineral density (BMD)[2,3], recent studies indicate that diabetes itself is associated with increased risk of fracture of the hip, proximal humerus, and foot. A better understanding of the factors that determine bone strength is not only depended on bone quantity as measured by BMD, but also depended on bone quality. It has been shown that trabecular microarchitecture play a important role in determining bone quality. To date, the effects of type II diabetes on trabecular microarchitecture and biomechanical properties are less clear. Otsuka Long Evans Tokushima Fatty (OLETF) rat is a useful animal model of type II diabetes with obesity, similar to the progression from onset of youth to adult maturity human diabetes conditions.

Therefore, the objective of this study was to investigate the effects of both type II diabetes on the bone strength of proximal femur in OLETF and Long Evans Tokushima Otsuka (LETO) rat models as a control using μ CT and μ FEA.

Materials and Methods:

Animal

Fourteen, 12 weeks old OLETF rats and LETO rats were housed in a room maintained at 22.2°C with 12-h light and 12-h dark cycles. The animals were divided 2 groups, with 7 rats per group, and two rats were housed per cage. The OLETF rats were diabetic group and LETO rats were control group. At the end of the 51 weeks, the rats were killed, and the femur were harvested and stored in saline-soaked gauze at -20° until required for analysis. All samples were scanned in the proximal femur using a μ CT (SKYSCAN, Skyscan-1072, Belgium) at a spatial resolution of 17.09 μ m, 1024 x 1024 pixel matrices (Fig. 1).

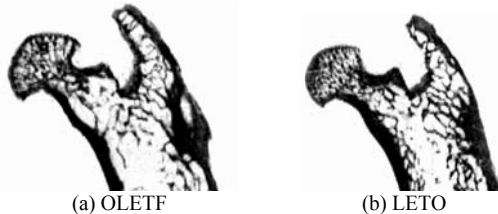


Fig. 1 Micro-images of the rat femur.

Micro-CT Scanning

All animals were scanned with a high-resolution micro-computed tomography system (micro-CT, SKYSCAN, Skyscan-1072, Belgium) at a spatial resolution of 21.31 μ m. The morphometry indices were determined by ANT software (Skyscan, Belgium) such as trabecular thickness (Tb.Th), trabecular separation (Tb.Sp), bone volume fraction (BV/TV), structure model index (SMI) and trabecular number (Tb.N) [4].

Finite Element Model and Analysis

Reconstruction images of femur were converted to micro FE models by converting the voxels (size 84.45 x 84.45 x 84.45 μ m) that represent bone tissue to equally shaped 8-node brick elements using the hexahedron meshing technique [5, 6]. To limit the computational requirements of the FE analyses, micro-images were resampled at an isotropic size of 84.45 μ m prior to converting the three-dimensional bone volume directly into hexahedron-based FE meshes. For all models,

element material properties were assumed to be isotropic, linear elastic, and uniform with a tissue Young's modulus of 1 GPa and a tissue Poisson's ratio of 0.3. Boundary conditions for the FE model were applied to represent the situation in a compressive-test setup with a 1%-strain level, in which the bottom face the displacements in the z-direction are unconstrained, all other faces of the cube were constrained.

The FE-problems for the hexahedron models were solved using a commercial software package (ABAQUS 6.4, Inc) (Fig. 2). The mechanical parameters calculated were apparent stress (σ_a)(Table 2).

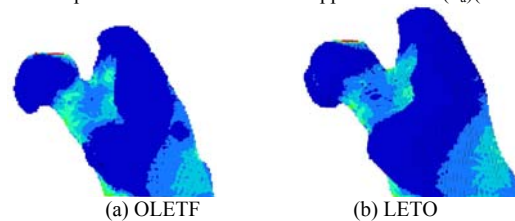


Fig. 2 Finite element analysis showing stress distribution of the rat femur in two groups.

Results:

As for the microstructure parameters, specifically, there was a 4.87%, 9.42% and 8.20% of reduction in Tb.Th, BV/TV and Tb.N, a 13.72% and 4.13% of increase in Tb.SP and SMI in LETO group when compared with those of OLETF group. However, there was no significant difference in Tb.Th and SMI. The ultimate stress of LETO group was higher than that of OLETF group, but difference was insignificant.

Table 2. Comparison of histomorphometry and mechanical property indices of rat femur between groups

	Tb.Th (mm)	Tb.Sp (mm)	BV/TV (%)	SMI	Tb.N (1/mm)	σ_a (MPa)
OLETF	0.066	0.225	31.308	1.198	3.451	118
LETO	0.069	0.198	34.568	1.151	3.760	129
P-value	0.060	0.008*	0.003*	0.273	0.018*	0.095

P-value <0.05 is considered to be significant.

Discussion:

In conclusion, in addition to BMD, both type II diabetes and obesity had adverse effects on the microstructural and biomechanical properties of trabecular bone of the proximal femur in OLETF rats model. Therefore, trabecular microstructure should be added to predict the fracture risk for diabetes-induced osteoporosis.

References:

- [1] E. Balint. et al, Bone 2, pp.21-28, 2001.
- [2] E. Barrett-Connor, T. Holbrook, JAMA. 16, pp. 3333-3337, 1992.
- [3] J. Christensen, O. Svendsen, Osteoporos Int. 10, pp. 307-311.
- [4] A. Parfitt. et al, J Bone and Miner Res. 2, p p. 595-608, 1987
- [5] B. van Rietbergen. et al, J. Biomech 28, pp. 69-81, 1995
- [6] Ulrich. et al. J Biomech. 31, pp.1187-1192, 1998.
- [7] D. Ulrich. et al, Bone 25, pp. 55-60, 1999