学 位 論 文 の 要 旨

氏名　　清原　信昭

学 位 論 文 名　Discordance Between Prevalent Vertebral Fracture and Vertebral Strength Estimated by the Finite Element Method Based on Quantitative Computed Tomography in Patients With Type 2 Diabetes Mellitus

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著 者 名　Nobuaki Kiyohara, Masahiro Yamamoto, and Toshitsugu Sugimoto

論 文 内 容 の 要 旨

INTRODUCTION

Meta-analyses have demonstrated that patients with type 2 diabetes mellitus (T2DM) are at increased risk of hip fracture compared with non-T2DM subjects. However, assessing the bone fragility in patients with T2DM by bone mineral density (BMD) is difficult because BMD at any site is not significantly associated with the presence of vertebral fractures (VFs). Bone strength is a composite of both BMD and bone quality, and these findings suggest that the patients with T2DM might have a poor bone quality that is not apparent in the BMD measurements.

The finite element method (FEM) is a computational analytical tool for a complex system such as the stress analysis of a structure. The quantitative computed tomography-based FEM (QCT-based FEM) was superior to BMD for assessing the bone strength of vertebrae because QCT-based FEM can estimate the integrated bone strength which consists of BMD and bone structure (one of a component of bone quality). To clarify whether the bone strength of T2DM patients can be estimated by QCT-based FEM, we investigated the relationship between the presence of VFs and the bone strength index calculated by QCT-based FEM in T2DM patients.

MATERIALS AND METHODS

A total of 146 Japanese patients with T2DM were enrolled [54 postmenopausal women (age range 47-84 years) and 92 men (age range 51-88 years)]. All of these patients underwent BMD measurements using a QDR-4500 system (Hologic, Waltham, MA) for the diagnosis of osteoporosis and multi-detector computed tomography (MDCT) scans (the Aquilion 64, Toshiba Medical Systems Corporation, Otawara, Japan) to exclude secondary diabetes. Conventional thoracic and lumbar radiographs using lateral and anterior-posterior projections were obtained. A VF was diagnosed according to a reduction of $\geq$ 20% as defined by the Genant visual criteria.

The FEM procedure in this study was performed according to the protocol of the previous study for nondiabetic subjects to compare with the results from this population. QCT data were embedded into an image that was diverted from MDCT scan. A 3-dimensional FEM of the vertebral body was constructed with 2-mm tetrahedral elements and 2-mm triangular plates from the CT image using Mechanical Finder software (Mitsubishi Space Software, Tokyo, Japan). The ash density of each voxel was assigned using the linear regression equation created from the values of the calibration phantom. Young's modulus and the yield stress of each element were calculated from the equations proposed for nondiabetic subjects according to a previous study.

Complete restraint to all nodes of the lower end of the vertebral model was applied as boundary conditions for the simulation of VF. The bone strength was calculated every 50 N under the condition of uniaxial and uniformly distributed compression to the upper site of the vertebrae. The vertebral yield and VFs were determined by the occurrence of the yield and failure in at least one element. The fracture load was defined as the vertebral strength index.

The statistical analyses were conducted using StatView (Abacus Concepts, Inc., Berkeley, CA, USA). Multiple logistic regression analysis was performed after adjusting for the confounding variables. *P*-values of less than 0.05 were considered to be significant.

This study was approved by the Ethics Committee of Shimane University and review board of our institution the Shimane University Institutional Committee on Ethics and written informed consent was obtained from all subjects.

RESULTS AND DISCUSSION

In total, 20 women (37.0%) and 39 men (42.4%) had VFs. Six women (11.1%) and 12 men (13.0%) had grade 2 or 3 VFs and multiple prevalent VFs. Logistic regression analysis that

adjusted for age, spine BMD, BMI, HbA1c, and duration of T2DM did not reveal a significant relationship between any of the severities of the VFs defined by the grade or number and the vertebral strength index.

The estimation of the skeletal strength of the vertebrae by QCT-based FEM is well established in non-diabetic subjects. However, FEM using a patient's own material properties has not been achieved because the determination of the material properties requires invasive procedures such as a bending strength test. According to a published protocol, the values obtained from nondiabetic subjects were used as the bone material properties of T2DM patients in this study because no specific values are available for patients with T2DM. Taken together, substituting these values may lead to false results. In addition, this finding indirectly suggests that patients with T2DM have deteriorated bone material properties compared with nondiabetic subjects, which may underlie the bone fragility in T2DM.

CONCLUSION

The presence of VFs in T2DM patients was not significantly associated with the vertebral strength index calculated by QCT-based FEM based on an established standard protocol when the parameters derived from nondiabetic subjects were applied to the bone material properties of diabetic patients. This finding suggests that the bone material properties of T2DM individuals could be deteriorated compared to nondiabetic subjects.