Prediction of proximal femur strength by a quantitative computed tomography-based finite element method
- Creation of predicted strength data of the proximal femur according to age range in a normal population and analysis of risk factors for hip fracture-

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INTRODUCTION
Fall-related fractures are frequent in elderly patients with osteoporosis, which can result in severe disability for activities of daily living, is one of the most serious diseases in modern society. However, only 44% of all non-vertebral fractures occur in women with a T-score below 2.5. In men, this percentage is even lower (21%) [1]. However, there is a clear need for the development of more sensitive risk assessment tools, using not only bone densitometry, but also other clinical predictors of fractures. Bone densitometry can explain 60-70% of bone strength and are limited in the ability to account for complex geometry, architecture, and heterogeneity of bone. However, quantitative computed tomography (QCT)-based finite element (FE) methods (QCT/FEM) are able to perform structural analyses taking these factors into consideration to accurately predict bone strength [2-3]. Some preliminary investigations into clinical applications of these methods have been reported [4-5]. To date, however, no basic data have been available regarding predicted strength (PS) by QCT/FEM with reference to age in a normal population. To apply this method for a wide range of clinical uses, a database of PS distributions with reference to age in a normal population is essential. The purpose of this study was thus to create a database of the proximal femur by QCT/FEM in a normal population as a preliminary trial. With these data, parameters that affect PS value by QCT/FEM were also analyzed.

Materials and Methods
Participants in this study comprised individuals who participated in a health checkup program with computed tomography (CT) at the University of Tokyo hospital from January to December in 2008 and for whom scan data were available for QCT/FEM subsequent analyses. The study protocol was approved by the ethics committee in our institution, and each participant provided written informed consent in accordance with the Declaration of Helsinki. Participants included 487 men (mean age, 55.0 years; range, 40-87 years) and 237 women (mean age, 59.0 years; range, 40-83 years). Exclusion criteria included patients with any recent or current disease under treatment with an agent to alter bone turnover or bone metabolism. In addition, subjects were excluded if they had any general disease that affects bone metabolism other than osteoporosis (e.g., hyperparathyroidism, bisphosphonoid), Paget’s disease, renal osteodystrophy, Cushings’ disease, steroid-induced osteoporosis, and others), malignant diseases, and rheumatoid arthritis. Scan data of the proximal femur were isolated and taken from overall data from CT of each participant with a slice thickness of 1.25 mm and a pixel width of 0.976 mm obtained using a Light Speed Ultra16 system (GE Yokokawa Medical System, Tokyo, Japan; 120 kV, 80 mA, 512×512 matrix) with simultaneous scans of a calibration phantom (BMAS 200; Kyoto Kagaku, Kyoto, Japan) containing hydroxyapatite rods. A 3-dimensional FE model was constructed from the isolated data using Mechanical Finder software (RCCM, Tokyo, Japan). FE models were equipped with triangular shell elements with a thickness of 0.4 mm and a size of 3 mm for the outer surface of the cortical bone and tetrahedral solid elements with a size of 3 mm for the rest of the bone. We adopted two loading conditions, comprising stance and fall configurations [6]. Materially nonlinear FE analysis was performed using the Newton-Raphson method. Fracture load was defined as the load when at least one shell element failed. For each participant, height, weight, and abdominal circumference (AC) were measured, and medical history was elicited. Linear regression analysis was used to estimate the correlation between age and PS of the proximal femur as analyzed by QCT/FEM. Change in PS with age was also evaluated by grouping participants into 5-year age brackets. One-way analysis of variance was used to compare average PS of participants in each age range. In addition, a multivariate statistical technique was used to determine how PS was affected by age, height, weight, and AC. The software SPSS (SPSS Inc, Chicago, USA), was used for statistical analyses. Differences were considered significant for values of p<0.05. For highly correlated variables, variance inflation factor (VIF=1 (1-R2)) which describes multicollinearity, was computed. PS of the proximal femur was assigned to a dependent variable, while height, weight, age, and AC were assigned to independent variables. Multivariate statistical analyses were performed using stepwise method. In the analyses, when strongly correlated independent variables were included, they were excluded under a multi-collinearity of VIF<5.

RESULTS
Average PS of the proximal femur in women was lower than that in men for each age range under both stance and fall loading configurations. PS under stance configuration in men showed a negative significant correlation with age (p<0.05), but no correlation with age was found under fall configuration (p=0.678). In women, PS showed a negative significant correlation with age under both stance and fall configurations (p<0.05). In men, average PS of the 75-79 year range was significantly lower than that in the <64 year range under stance configuration. In women, average PS at 40-44 years was significantly higher than that at >55 years under stance configuration, and was significantly higher than that at <65 years under fall configuration. In men, correlation between AC and weight was very strong with R=0.860. In addition, the VIF of AC was equal to 5.756 but the VIFs of other independent values were within a range of 1 to 2, so AC was excluded. In the multivariate analysis of PS in men under stance configuration, the standardized β for height was calculated as 0.045. Because height poorly correlated with PS with p=0.348, it was excluded from the analysis. Therefore, the multivariate analysis equation for PS in men under stance configuration was expressed with a standardized β for age of -0.176 and that for weight of 0.386. Likewise, the multivariate analysis equation in men under fall configuration was expressed with a standardized β for weight of 0.201, that for height of 0.016 (p=0.760), and that for age of 0.031 (p=0.490). So, height and age correlated poor with PS, and they were excluded from the equation, which was finally expressed by a standardized β for weight of 0.212. In women, the correlation between AC and weight in women was also very strong with R=0.741 but the VIF for AC was equal to 1.874. Thus, both of these parameters could be included in the multivariate analysis equation. In the multivariate analysis of PS in women under stance configuration, the standardized β for height was calculated as 0.113 (p=0.074) and that for AC as 0.412 (p=0.412). Because height and AC poorly correlated with PS, they were excluded from the analysis equation. Therefore, the multivariate analysis equation for PS in women under stance configuration was expressed with a standardized β for age of -0.444 and that for weight of 0.331. Likewise, the multivariate analysis equation in women under fall configuration was expressed with a standardized β for height of 0.104 (p=0.124) and that for AC of 0.071 (p=0.944). Because height and AC poorly correlated with PS, they were excluded from the analysis. Therefore, the multivariate analysis equation for PS in women under fall configuration was finally expressed with a standardized β for age of -0.407 and that for weight of 0.209. Height did not significantly affect PS in either men or women.

DISCUSSION
This was the first study to investigate changes in PS of the proximal femur by QCT/FEM with age in a normal population. The number of participants in this study was small and may have been insufficient to suggest standard values for PS, but these results still contribute to creating basic standard data for PS in normal people in the future. This study obtained the following results. First, average PS of the proximal femur was lower in women than in men for all age ranges. Second, PS in men under stance configuration, and those in women under both configurations significantly decreased with age. Third, weight positively affected PS in both men and women. Whether PS by QCT/FEM correlates more closely with fracture risk for osteoporotic patients in comparison to other bone densitometries remains unclear, but the present results did not contradict any existing concept of risk factors for fragility fracture. More baseline data for PS in normal populations need to be accumulated by increasing the number of participants in studies like this. In addition, more factors that affect PS should be analyzed to estimate risk factors for osteoporotic fracture.

REFERENCES: