Varus osteoarthritic knees show a different trend of medial cortical bone thickness with associations in the alignment and tibial morphology from those in healthy knees

Keisuke Maeda[1], Tomoharu Mochizuki[1], Osamu Tanifuji[1], Shigeru Takagi[1], Hiroyuki Kawashima[1]
[1]Niigata University, Japan
Email: m07a076c@gmail.com

Disclosures: Keisuke Maeda (N), Tomoharu Mochizuki (N), Osamu Tanifuji (N), Shigeru Takagi (N), Hiroyuki Kawashima (N)

INTRODUCTION: Cortical bone thickness (CBT) varies with the mechanical loads applied to the bone. Therefore, it is an optimal parameter for assessing structural adaptation due to biological factors and mechanical use. The CBT of the tibia is assumed to change under the influence of the loading environment, including aging, bone mineral density, bone morphology, and whole lower extremity alignment. In a 21-year longitudinal epidemiological study, Higano et al.reported that an increase in the medial CBT of the proximal tibia was a risk factor for the development of knee osteoarthritis (OA) in the longitudinal epidemiological study using two-dimensional (2D) X-rays. Previous studies using the CBT to examine the pathomechanism of knee OA measured using 2D X-rays. If automatic three-dimensional (3D) measurement of the CBT is possible, even a small difference in millimeters can be detected with a higher degree of accuracy. Since the difference in CBT between healthy and osteoarthritic knees is estimated to be a few millimeters, accurate verification by applying 3D cortical thickness assessment will lead to a better understanding of the pathomechanism of knee OA. To date, it has been difficult to accurately measure 3D-CBT; however, Treece et al. reported a highly accurate method that can precisely estimate CBT from clinical low-resolution CT data. Bone morphology and whole lower extremity alignment probably influence CBT; however, there have been few reports on the relationship between the tibial CBT and bone morphology and whole lower extremity alignment. The purpose of this study was to clarify (1) the differences in the CBT of the tibial diaphysis between healthy and osteoarthritic knees; and (2) the influence of whole lower extremity alignment and MCT inclination on tibial CBT. The hypotheses were as follows: (1) the medial CBT in varus knee OA shows a different trend from healthy knees; and (2) the medial CBT of the proximal tibia correlates with standing lower extremity alignment and MCT inclination.

METHODS: The study assessed 60 subjects with varus knee osteoarthritis (OA) and 53 healthy elderly subjects. For the varus knee OA (age > 50 years), exclusion criteria is participants with diseases affecting the CBT, such as skeletal dysplasia, infections, bone metabolic diseases, and those without CT or BMI data were excluded. The lower extremities of 60 patients with varus knee OA (22 males and 38 females), randomly selected from 1,120 knees aged 50 years or older, were included.The mean ± SD (range) age of males and females was 74 ± 8 (54 to 86) years and 74 ± 7 (61 to 87) years, respectively. For the healthy subjects, a total of 107 elderly Japanese volunteers who had no knee complaints or histories of joint disease or major injury in the lower extremity were publicly recruited. Out of 100 healthy elderly patients (50 males and 50 females) with grades 0–1 according to the Kellgren-Lawrence (K-L) classification and the absence of radiographic knee OA, 53 elderly (aged >50 years) Japanese volunteers (28 males and 25 females) were randomly selected for this study. The average age ± standard deviation (SD) (range) of the elderly males and females was 71 ± 6 years (61 to 83 years) and 68 ± 6 years (60 to 83 years), respectively. The CBT of the tibial diaphysis was automatically calculated in 3D space using the high-resolution measurements reported by Treece et al., which allowed for accurate estimates of the CBT based on an estimate of cortical density. The method uses a complex model-based fit approach with a mathematical model of the anatomy and imaging system, calculates from thousands of data points across the bone surface, and performs assessments using semi-automatic segmentation. The number of measurement points per subject was 2,752–11,296, depending on the tibial length and bone mineral density. Regarding accuracy, Treece et al. tested the validity of the constant-density assumption by measuring the true density of cadaveric femurs on high-resolution CT, which had approximately seven times the resolution of low-resolution scans. They reported that the CBT estimates were accurate by up to 0.3 mm. An anatomical coordinate system for the tibia was constructed using original software. Twenty-four regions were created by combining six heights (most proximal, 63%–70%; proximal, 57%–63%; central proximal, 50%–57%; central distal, 43%–50%; distal, 37%–43%; and most distal, 30%–37%) and four areas of the axial plane (xy-plane) at 90° (medial, anterior, lateral, and posterior). Each of the 24 regions comprised cortical thickness data from 20 to 948 points. The cortical thickness in each of the 24 regions was compared among the four groups categorized by sex and OA (OA males, OA females, healthy males, and healthy females). When the data were compared, standardized values rather than actual values were applied. Standardized values divided by tibial length (CBT/tibial length) were applied because the CBT is influenced by body constitution (body weight and height). To ensure the precision and test–retest reliability of the measurement of CBT in 3D space through all processes, two researchers performed two measurements as one set on 10 subjects randomly selected from each group. In the test–retest reliability (SPSS version 21, SPSS Inc., Chicago, IL, USA), intraobserver reproducibility via the intraclass correlation coefficient of the two measurements was 0.925 ($p < 0.001$) for researcher #1 and 0.998 ($p < 0.001$) for researcher #2. Inter-observer reproducibility via the interclass correlation coefficient was 0.989 ($p = 0.001$). A 3D lower extremity alignment assessment system (Knee CAS, LEXI Inc., Tokyo, Japan) using biplanar long-leg X-rays (0°, 60°) was developed to evaluate the femorotibial angle (FTA). The femoral and tibial coordinate systems in the 3D skeletal model were determined as described by Sato et al. The matching error of the 3D to 2D image registration technique was within a range of 0.7 mm in rotation and 0.5 mm in translation. The best-fitting "approximation plane" in the MCT was determined by the least-squares method, using eight points digitized on the MCT. The digitization points did not include osteophytes or large deformities such as excessive concavity to obtain high precision and reproducibility. The approximation plane of the MCT and the normal vector were mathematically calculated. The angle between the normal vector and each axis was the minimum angle in 3D space between the x-axis of the tibial coordinate system and the crossing line consisting of the approximation plane of the MCT and the xz-plane of the tibial coordinate system, defined as the coronal angle of the MCT. The mean and maximum differences were set as 1.1° for precision. The intra- and interobserver reproducibilities, expressed as intra- and interclass correlation coefficients, were 0.958 and 0.893, respectively.This study was performed in accordance with a protocol approved by the Institutional Review Board of Niigata University (IRB number 2015–2351). All participants provided written or verbal informed consent for participation in the study and for the use of their data.

RESULTS: The healthy group showed a trend of thicker CBT in the lateral areas than in the medial areas in the mediolateral comparison within each group as the structural characteristics [male: most distal ($p = 0.026$); female: proximal ($p = 0.008$), distal ($p = 0.049$)]. In contrast, the OA group showed a thicker CBT in the medial areas than in the lateral areas from the most proximal to the central proximal height [OA males: total ($p = 0.001$), most proximal ($p < 0.001$), central distal ($p = 0.008$), distal ($p = 0.023$); OA females: most proximal ($p < 0.001$), proximal ($p = 0.001$)].No sex differences were found in the Medial/Lateral ratios in either the healthy or OA groups. In the comparison between the healthy and OA groups, the Medial/Lateral ratio was significantly higher for both OA males and OA females in the total and most proximal heights.

Regarding the correlation between FTA and CBT, there was no significant difference in OA males, but OA females showed a significant weak positive correlation in four regions [most proximal-medial (CC = 0.365, $p = 0.026$): proximal-medial (CC = 0.369, $p = 0.023$), central distal-lateral (CC = 0.337, $p = 0.038$), and distal-lateral (CC = 0.354, $p = 0.029$)]. No significant differences were found in most regions in the healthy group.Regarding the correlation between MCT inclination and CBT, males with OA showed significant positive correlations in the proximal-medial regions [most proximal-medial (CC = 0.594, $p = 0.004$) and proximal-medial (CC = 0.61, $p = 0.003$)]. Females with OA showed a significantly positive correlation mainly in the medial areas [total-medial (CC = 0.409, $p = 0.011$), most proximal-medial (CC = 0.554, $p < 0.001$), proximal-medial (CC = 0.368, $p = 0.023$), central proximal-medial (CC = 0.375, $p = 0.020$), and central distal-medial (CC = 0.380, $p = 0.019$)]. No significant correlation was observed in the healthy group.

DISCUSSION: The most important findings of this study were as follows: (1) the CBT in osteoarthritic knees showed a different trend from that in healthy knees, especially for medial areas; and (2) the medial CBT of the proximal tibia correlated with the FTA and MCT inclination in the OA group.

SIGNIFICANCE/CLINICAL RELEVANCE: In terms of clinical relevance, accurate verification using 3D-CBT, whole lower extremity alignment, and MCT inclination will lead to a better understanding of the pathological mechanism of knee OA.