MS ID#: AMJSPORTS/2020/312314

MS TITLE: Effect of high tibial osteotomy on the distribution of subchondral bone density across the proximal tibial articular surface of the knee with medial compartment osteoarthritis

Koji Iwasaki, MD, PhD [1], Eiji Kondo, MD, PhD [2], Shinji Matsubara, MD, PhD [3], Masatake Matsuoka, MD, PhD [3], Kaori Endo, MD, PhD [3], Isao Yokota, PhD, M.P.H[4], Tomohiro Onodera, MD, PhD [3], Norimasa Iwasaki, MD, PhD [3]

[1] Department of Functional Reconstruction for the Knee Joint, Faculty of Medicine, Hokkaido University, Sapporo, Japan

[2] Centre for Sports Medicine, Hokkaido University Hospital, Sapporo, Japan

[3] Department of Orthopaedic Surgery, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

[4] Department of Biostatics, Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Correspondence to: Eiji Kondo, MD, PhD.

North-15, West-7, Sapporo, Hokkaido 060-8638, Japan

Tel: +81-11-706-5934; Fax: +81-11-706-6054

Email: eijik@med.hokudai.ac.jp

Effect of high tibial osteotomy on the distribution of subchondral bone density across the proximal tibial articular surface of the knee with medial compartment osteoarthritis

Abstract

Background: The effect of high tibial osteotomy (HTO) on the stress distribution across the knee joint is not completely understood. The subchondral bone density is considered to reflect the pattern of stress distribution across a joint surface.

Purpose: To assess the distribution of subchondral bone density across the proximal tibia in nonarthritic knees and in the knees of patients with osteoarthritis before and after HTO.

Methods: We retrospectively collected radiographic and computed tomography (CT) data from 16 nonarthritic subjects (control group) and 17 patients with OA (OA group). Data from the OA group were collected before and 1.5 year after HTO. The subchondral bone density of the proximal tibia was assessed with CT–osteoabsorptiometry. The locations and percentages represented by high-density areas on the articular surface were quantitatively analyzed.

Results: The ratio of the high-density area of the medial compartment to the total high-density area (medial ratio) was significantly higher in preoperative OA patients (mean, 80.1%) than in control subjects (61.3%) ($p < 0.001$). After HTO, the medial ratio decreased significantly (to 75.1%, $p = 0.035$, in comparison with preoperative values) and was significantly correlated with the hip–knee–ankle angle (HKA) in both the control ($r = -0.551$, $p = 0.033$) and OA groups ($r = -0.528$, $p = 0.043$). The change in medial ratio after HTO was significantly correlated with the change in HKA (r = 0.587, p = 0.035). In the medial compartment, the high-density area in most lateral areas of four divided subregions increased after HTO, but that of the other medial three subregions decreased.

Conclusions: In this exploratory study, HTO shifted the high-density area of the medial compartment of the proximal tibial articular surface toward the lateral compartment. In contrast, the high-density area of the most lateral region of the medial compartment decreased after HTO. This change in subchondral bone density may result from the change in stress distribution.

Clinical relevance: Assuming that the subchondral bone density is a surrogate for stress, HTO shifts the stress from the medial compartment to the lateral compartment but increases the stress on the most lateral region of the medial compartment.

Key terms: high tibial osteotomy, knee, osteoarthritis, stress distribution, CT–osteoabsorptiometry, alignment

What is known about the subject: HTO has been suggested to decrease the stress on the medial compartment of the knee joint. However, the effect of HTO on the stress distribution across the knee joint is not completely understood.

What this study adds to existing knowledge: HTO decreases the stress on the medial compartment of the proximal tibial articular surface and shifts the distribution of stress toward the lateral compartment. Moreover, the stress on the medial compartment does not decrease across the whole area after HTO and actually increases at the most lateral region.

Introduction

Biomechanical risk factors for knee osteoarthritis (OA), such as obesity, trauma, malalignment, meniscal deficiency, and muscle weakness, increase the mechanical stress across the knee joint. Some of these factors are believed to be important and potentially modifiable factors that determine the site[45] and severity[45] of knee OA. Identifying the distribution of mechanical stress across the knee joint would thus contribute to the prediction and management of OA progression.

Malalignment of the lower limbs is a strong risk factor for progression of knee OA, and one of the few risk factors that can be modified *a posteriori.* Valgus high tibial osteotomy (HTO) is an established surgical procedure that can be used to treat medial knee OA. HTO reduces loading of the medial compartment and, thereby, slows disease progression. Because it extends the healthy life expectancy of the knee, HTO is widely used as a treatment option for medial OA with varus alignment.[3, 10, 16] The relationships among leg alignment, medial compartment loading, and change in medial compartment loading after HTO have been examined in a cadaveric study,[1] finite element analyses,[36, 52] and three-dimensional (3-D) gait analyses by assessing the knee adduction moment (KAM)[7, 15, 29]; however, how the distribution of the actual stress within each compartment changes after HTO remains unclear.

The distribution of the subchondral bone mineral density is thought to be correlated with the distribution of stress over the joint surface; because of the varying degrees of mineralization over the surface of a joint, a materialized field of stress is observed.[42] Computed tomography (CT)–osteoabsorptiometry was developed by Müller-Gerbl et al. as an analytical method to assess the long-term stress distribution over individual joints in living participants by measuring the subchondral bone mineral density.[31, 32] This method generates a precise map of the distribution pattern of subchondral bone density over various articular surfaces. Our previous studies involving this method have evaluated the distribution of subchondral bone density to assess the pattern of stress distribution at the wrist, elbow,[34] and the glenohumeral,[12, 46] patellofemoral,[37] and ankle joints[41] in normal people, those with pathological conditions, and athletes. The distribution pattern of subchondral bone density over the knee joint has been suggested to be related to the presence of knee OA[19, 39]; however, it is unclear whether leg alignment affects the distribution of bone density. Furthermore, whether or how the distribution pattern of subchondral bone density changes on the articular surface across the knee joint after HTO is yet to be elucidated.

Using CT–osteoabsorptiometry, a precise map of the subchondral bone density distribution across the knee joint could provide insight into the stress distribution across the articular surface of the knee joint with and without OA and the change in the stress distribution after HTO. Thus, we hypothesize that valgus HTO leads to a reduction in the *in vivo* subchondral bone density on the medial compartment of the femorotibial joint in the case of varus OA of the knee. The aims of this exploratory study were: (1) to evaluate the distribution pattern of subchondral bone density across the proximal tibia in patients with and without OA, (2) to assess changes in the pattern of bone density distribution in patients with OA before and after HTO, and (3) to clarify the correlation of leg alignment with changes in bone density distribution.

Methods

Study design

This study was approved by the institutional review board of Hokkaido university hospital (017-0163). We retrospectively recruited all patients who underwent HTO for medial compartment OA between April 2013 and March 2017 at our institution. All operations were performed by a senior orthopedic surgeon (EK) who had over 20 years of experience in performing knee surgery. The OA group included patients who underwent medial open wedge HTO (OWHTO) for medial compartment OA. Indications for OWHTO in our hospital were: (1) moderate varus leg alignment (HKA of $>-10°$) and (2) absence of OA in the patellofemoral joint (Kellgren–Lawrence [KL] grade[21] ≥ II) or anterior knee pain. Exclusion criteria were: (1) lateral knee OA (KL grade ≥ II) or lateral knee pain, (2) not completing a follow-up period of at least 1 year, (3) having no metal removal after HTO, (4) loss of >15° of knee extension before and after HTO, (5) knee range of motion of <130° before and after HTO, (6) anterior cruciate ligament insufficiency or varus/valgus instability of >10°, (7) medial meniscal injury ≥ grade 3 (Lotysch and Mink's magnetic resonance imaging [MRI] grading system[5, 30]) or any tear of the medial meniscus for which partial meniscectomy or other repair was performed, and (8) any lateral meniscal injury. Finally, we evaluated 17 knees in 16 patients in the OA group (Figure 1).

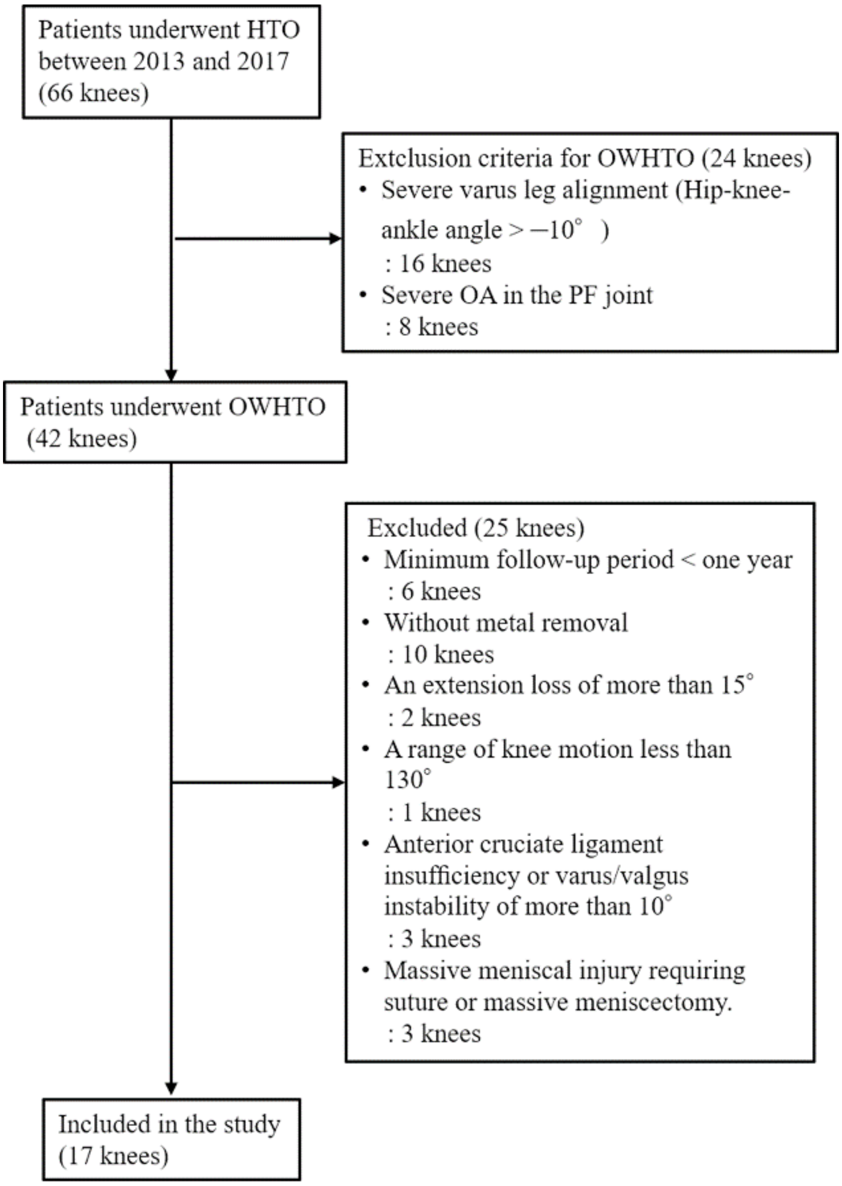


Figure 1. Flowchart of study enrollment

Abbreviations: HTO, high tibial osteotomy; OA, osteoarthritis; OWHTO, open wedge HTO.

We also collected the data of 16 patients who underwent simultaneous radiographical and CT examinations of bilateral knees for comparison of ipsilateral knee trauma between April 2013 and March 2017 as control subjects. The uninjured contralateral knee was used as control. Inclusion criteria for the control group were (1) knee OA (KL grade ≤ 1) in the contralateral knee and (2) patients aged 15–30 years at the time of CT scanning. Exclusion criteria for the control group were (1) current pain in the contralateral knee and (2) previous surgery in the contralateral knee.

Postoperative clinical and radiological evaluations were performed around 1.5 years (mean: 17.4 months, range: 14–25 months) after OWHTO and immediately after removal of the locking plate.

Preoperative planning

Miniaci's method was used for preoperative planning as previously reported.[33, 43, 49] To calculate an appropriate angle of the medial opening wedge, a long line, [A], was drawn from the center of the femoral head through the 65% lateral from the medial edge of the tibial plateau on the lateral tibial plateau. Another line, [B], was then drawn from the hinge point [P] to the center of the talar dome, and its length was measured. An arc, [C], the center and the radius of which are the hinge point P and line B, respectively, was then drawn so that the arc crossed line A. A line, [D], was then drawn from the hinge point to the crossing point between line A and the arc C. The angle formed between lines B and D provides the medial opening angle, which is identical to the correction angle of the lower limb alignment.

Surgical technique

Surgery was performed as previously described.[40, 43, 49] The proximal tibia was exposed through a 7-cm medial longitudinal incision. Further, after the complete release of the distal attachment of the superficial medial collateral ligament, three pairs of Kirshner wires (K-wires) were inserted into the tibia so that each inserted K-wire precisely reached the proximal tibiofibular joint using the parallel guide. We then performed a biplanar osteotomy of the tibia, after which the oblique osteotomy site was gradually opened—according to the preoperative planning angle—using a specially-designed spreader (Olympus Terumo Biomaterials, Tokyo, Japan). Under fluoroscopic control, we set a long straight metal rod to connect the center of femoral head and ankle, then measured the transection point of the rod through the tibial plateau. This was expressed as a percentage of the tibial width from medial-to-lateral. We confirmed the transection point of 65%.[11] Two wedged beta-tricalcium phosphate spacers (Osferion 60; Olympus Terumo Biomaterials) were implanted into the anterior part and posterior part of the opening space in a parallel fashion. We fixed the tibia with a locking plate (Tomofix; DePuy Synthes, Raynham, MA, USA, or TriS Medial HTO plate system; Olympus Terumo Biomaterials) by inserting eight locking screws.

Each patient underwent an additional procedure approximately 1 year (mean: 13.4 months, range: 12–15 months) after the initial surgery to remove the locking plate. Arthroscopic evaluation was performed simultaneously to evaluate the status of the meniscus after HTO.

Evaluation criteria

Clinical evaluation

Patients were evaluated according to the Japanese Orthopaedic Association (JOA) knee scoring system (total, 100 points),[4, 50] which is the standard knee subjective score used in clinics in Japan. The JOA knee score consists of four categories: “pain on walking” (0–30 points), “pain on ascending and descending stairs” (0–25 points), “range of motion” (0–35 points), and “joint effusion” (0–10 points).

Meniscus status evaluation

To compare meniscus status before and after HTO, an examiner (KI) evaluated the arthroscopic images at HTO as well as at plate removal and MRI images before HTO as well as after plate removal according to the Lotysch and Mink’s MRI grading system.[30] The change in meniscal status after HTO was graded according to three categories: deterioration, no change, and improvement.

Radiological evaluations

Standing anteroposterior and lateral radiographs of the knee and full-length anteroposterior radiographs of the whole lower limb with the knee in full extension were acquired. The radiological stage of OA was assessed according to the KL grading system.[21] We measured HKA on anteroposterior radiographs of the whole lower limb taken with a long cassette in the one-leg standing position. We also calculated the percentage of mechanical axis (%MA) as follows: A line was drawn between the center of the femoral head and the center of the tibial plafond; the medial edge of the tibia plateau was defined as 0% and the lateral edge as 100%, and the %MA was the point at which the line passed across the tibial plateau.[8, 20, 35, 38, 51] The posterior tibial slope (PTS) was measured as the angle between a line perpendicular to the mid-diaphysis of the tibia and the posterior inclination of the medial tibial plateau on the lateral view.

Computed tomography–osteoabsorptiometry

A high-resolution helical CT scanner (Aquilion One/ViSION Edition; Toshiba Medical Systems, Japan) was used to acquire axial images of the knee. Patients rested in a supine position with their knees extended during imaging. Slice thickness and interval were set at 0.5 mm. Acquired CT data were transferred to a personal computer. Sagittal and coronal slices at 1.0-mm intervals and 3-D bone models were generated from axial CT data with the use of commercial software (Ziocube®; Ziosoft, Inc., Tokyo, Japan). We determined the sagittal and coronal axes by reference to the epicondylar axis of the distal femoral condyle at the axial slice. By reference to sagittal and coronal CT images and a 3-D CT image of the articular surface of the proximal tibia, an outline of the medial and lateral compartment of proximal tibial articular surface was manually selected to include the entire subchondral bone layer of the articular surface in all slices.[12] Then the subchondral bone density of each generated sagittal slice was analyzed with our noncommercial software (OsteoDens 4.0) developed at our institution.[12, 17, 37, 41, 46] The maximum increment point in Hounsfield units from the joint surface as the starting point of the region of interest, and the maximum point in Hounsfield units was selected automatically in the 2.5-mm region of interest from the starting point (Supplementary file). We determined the radiodensity of the identified subchondral bone region at each coordinate point at 1-mm intervals. Then, a two-dimensional image that mapped the distribution of subchondral bone density was obtained by stacking sagittal slices (Figure 2A, 2B). The differences between the maximum and minimum values in Hounsfield units on the mapping images were divided into nine grades, and a surface mapping image was generated through the use of these grades to produce a color scale, in which red and violet indicated the greatest and lowest bone densities, respectively. Selected areas of the medial and lateral plateaus included the cortical bone or bony spur at the periphery of the articular surface because it was impossible to exclude the cortical bone or bony spur using the software. However, these features were carefully removed manually from the target area of analysis in subsequent quantitative analysis.[12]

Quantitative analysis of the obtained mapping data focused on the location of the high-density area (HDA) of the articular surface. The HDA was defined as the region containing the coordinate points representing the top 20% of Hounsfield unit values out of the total area of the medial and lateral compartments. The medial ratio was calculated as the ratio of the HDA of the medial compartment to the total HDA of both compartments. The medial compartment of the proximal tibia was divided into four subregions of equal width in the coronal direction, denoted M1 to M4 from the medial-to-lateral sides. The lateral compartment was divided equivalently, denoted L1 to L4 from the medial-to-lateral sides (Figure 2C). The percentage of each subregion represented by the HDA was calculated (%HDA).

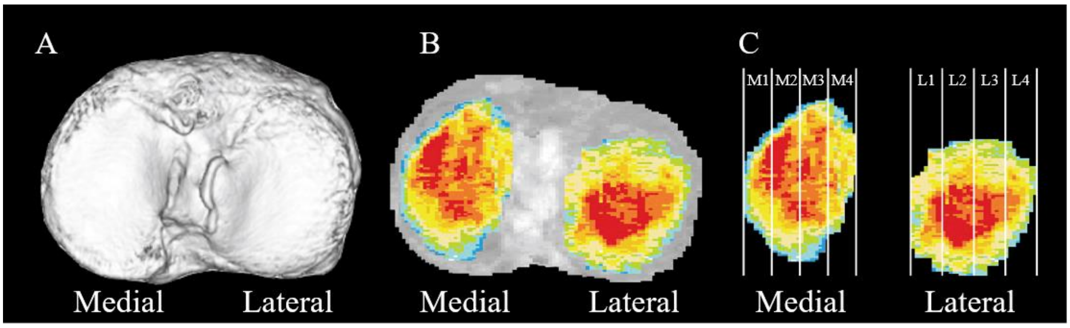


Figure 2. Identification of the subchondral bone regions of the proximal tibia using a customized software. (A, B) The subchondral bone density of the selected region was automatically measured at each coordinate point in each 1.0-mm sagittal slice. (C) Images of the areas used for quantitative analysis of the bone density mapping data for the medial and lateral compartments of the proximal tibia.

Definitions: M1–M4, subregions of the medial compartment of the proximal tibia, divided equally from the medial side to the lateral side; L1–L4, subregions of the lateral compartment, divided equally from the medial side to the lateral side.

Statistical analysis

Statistical analyses were performed using JMP Pro 14.0 (SAS Institute Inc., Cary, NC, USA). The significance level was set at $p = 0.05$. Means and 95% confidence intervals (CIs) for the changes after surgery in patients with OA were calculated. We compared controls and patients with OA before and after surgery by using Student's *t* test, and we compared the patients with OA before and after surgery by using a paired *t* test. Pearson's correlation was used to evaluate the relationship between medial ratio and other factors (age, body mass index [BMI], HKA, %MA, and PTS) to compare controls with preoperative patients. In addition, we compared changes from preoperative to postoperative values (denoted by "Δ") of the medial ratio and other variables using Pearson's correlation. These factors were selected because they are believed to influence the distribution of subchondral bone density[19, 45, 47] or the biomechanics of the knee joint.[44]

The reproducibility of data was evaluated using our noncommercial software (OsteoDens 4.0). Intra- and interobserver reliability were assessed on three randomly selected knees from the control group and each OA group. Two observers (KI and SM) independently measured %HDA in these six knees; a total of 48 subregions were measured twice in a blinded manner at 1 month intervals. The intraclass correlation coefficients for intraobserver reliability were 0.922 (KI) and 0.913 (SM), respectively, and the intraclass correlation coefficient for interobserver reproducibility was 0.917.

Results

Age, BMI, HKA, and %MA were significantly different between the control and preoperative OA groups (*P* < .001, *P* = .026, *P* < .001, and *P* < .001, respectively; Table 1). The medial ratio was 31% higher in the preoperative OA group than in the control group (*P* < .001).

After HTO, JOA score improved by 33% (P < .001). The sum of "pain on walking" and "pain on ascending and descending stairs" subcategory scores improved by 56% (P < .001). Significant differences in HKA, %MA, and PTS between the preoperative and postoperative OA groups (P < .001, P < .001, and P = .019, respectively). The medial ratio decreased by 6% after HTO, respectively (P = .035; Table 1).

In the comparison between the patients with OA after surgery and the controls, leg alignment was significantly more valgus in the patients (5.0 degrees valgus in HKA) compared with the controls (1.5 degrees varus; *P* < .001). The medial ratio was 21%

higher in the patients than that in the controls (P = .008).

Table 1. Patient characteristics, OA grade, leg alignment, clinical outcomes, and medial ratio[a]

Characteristic	Controls (n = 16)	Patients with OA (n = 17)		Comparison: preop with control	Comparison: preop with postop		Comparison: postop with control
		Preoperative	Postoperative	*P* value	Mean change	*P* value	*P* value
Age, years	20.8 (18.1–23.4)	58.9 (54.8–63.0)	n/a	<.001	n/a	n/a	n/a
Male:female ratio	8:8	6:11	n/a	.393	n/a	n/a	n/a
BMI, kg/m^2	24.0 (21.8–26.2)	27.0 (25.1–28.9)	n/a	.026	n/a	n/a	n/a
KL grades (III and IV)	n/a	16:1	16:1	n/a	n/a	.99	n/a
HKA, degrees	−1.5 (−3.4–0.4)	−6.1 (–8.0–−4.2)	5.0 (4.1–5.8)	<.001	9.9 (7.6–12.2)	<.001	<.001
%MA, %	43.8 (37.3–50.3)	22.8 (14.9–30.7)	68.8 (65.3–72.3)	<.001	45.4 (36.7–54.0)	<.001	<.001
PTS, degrees	9.9 (8.2–11.6)	11.5 (9.7–13.7)	13.1 (10.8–15.4)	.191	1.6 (0.3–2.8)	.019	.025
JOA knee score, points							
Total	n/a	68.8 (61.3–76.2)	91.6 (86.6–96.5)	n/a	22.7 (17.3–28.3)	<.001	n/a

Pain on walking	n/a	19.6 (17.2–21.9)	29.1 (27.7–30.5)	n/a	9.6 (6.8–12.3)	<.001	n/a
Pain on ascending and descending stairs	n/a	13.6 (11.0–16.3)	22.7 (21.0–24.5)	n/a	9.1 (6.5–11.6)	<.001	n/a
Range of motion	n/a	28.6 (26.5–30.8)	30.9 (28.4–33.4)	n/a	2.3 (0.5–4.0)	.02	n/a
Joint effusion	n/a	6.8 (4.6–9.1)	8.3 (7.1–10.2)	n/a	1.8 (0.1–3.5)	.04	n/a
Medial ratio,[b] %	61.3 (55.7–66.9)	80.1 (72.3–85.6)	75.1 (67.8–83.5)	<.001	4.4 (0.6–8.1)	.035	.008

[a]Data are reported as means (95% confidence intervals) or ratios.
[b]Medial ratio: The ratio of high-density area (HDA) of the medial compartment in relation to the total HDA of both compartments. HDA: 20% highest area in Hounsfield unit values out of the sum of the medial and lateral compartments. Varus alignment was a negative value of HKA, and valgus alignment was a positive value.
n/a, not applicable. OA, osteoarthritis. BMI, Body mass index. KL, Kellgren–Lawrence. HKA, Hip–knee–ankle angle. %MA, Percentage of mechanical axis. PTS, Posterior tibial slope. JOA, Japanese Orthopedic Association (knee score: total, 100 points). Preop: before HTO. Postop: 1 year after HTO.

In arthroscopic evaluation after HTO, meniscal status was graded “no change” in both medial and lateral compartments in all cases. However, Lotysch and Mink’s MRI grading of meniscal status was unchanged in both medial and lateral compartments after HTO.

Of the parameters that differed significantly between the control and preoperative OA groups, age, HKA. and %MA were found to be significantly correlated with the medial ratio (Table 2). Only HKA was found to be significantly correlated with the medial ratio in both the control and OA groups (Figure 3).

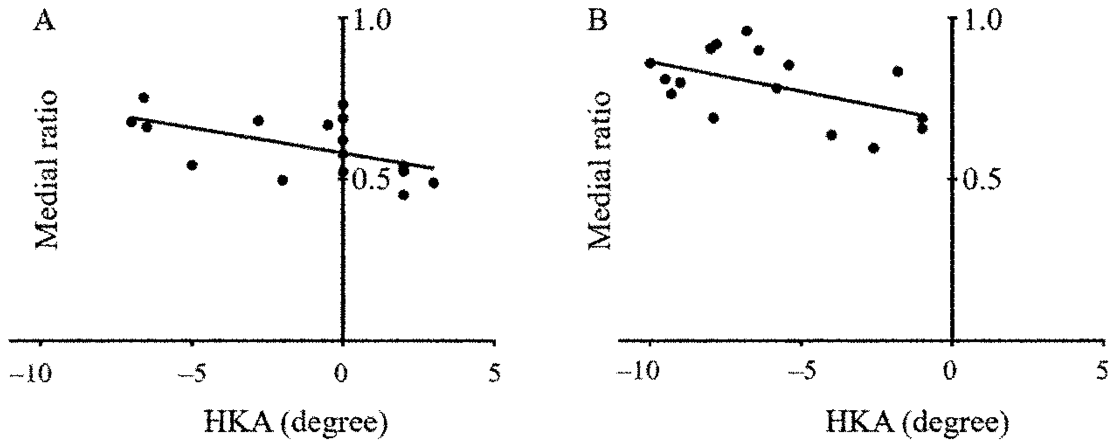
Table 2. Statistical analysis: Pearson correlation (r) between medial ratio and demographic data in controls and patients with osteoarthritis[a]

Characteristic	Controls		Patients	
	r	*P* value	r	*P* value
Age	0.122	.670	0.671	.009
BMI	−0.144	.609	−0.077	.785
HKA	−0.551	.033	−0.528	.043
%MA	−0.558	.031	−0.432	.108
PTS	−0.126	.654	−0.217	.438

[a]Medial ratio: The ratio of high-density area (HDA) of the medial compartment relative to the total HDA of both compartments. HDA: 20% highest area in Hounsfield unit values out of the sum of the medial and lateral compartments.

BMI, Body mass index. HKA, Hip–knee–ankle angle. %MA, Percentage of mechanical axis. PTS, Posterior tibial slope.

Figure 3. Relationship between hip–knee–ankle angle (HKA) and medial ratio. (A) Control group: Pearson correlation analysis showing a significant negative correlation between HKA and medial ratio (Pearson r = −0.551; $P < 0.033$). (B) OA group: Pearson correlation analysis showing a significant negative correlation between HKA and medial ratio (Pearson r = −0.528; $P < 0.043$). Medial ratio: The ratio of high-density area (HDA) of the medial compartment in relation to the total HDA of both compartments. HDA: 20% highest area in Hounsfield units values out of the sum of the medial and lateral compartments.



Of the patients' characteristics, including age, BMI, sex, and JOA knee score, none showed a significant correlation with Δmedial ratio. In contrast, of the parameters that were changed after HTO, only ΔHKA was significantly correlated with the Δmedial ratio (P = .035; Table 3). In addition, there was no significant correlation between ΔHKA and functional knee score.

Table 3. Statistical analysis: Pearson correlation coefficients and partial correlation coefficients between Δmedial ratio and demographic data in patients with osteoarthritis before and after HTO[a]

Characteristic	Correlation coefficient	P value	Partial correlation coefficient
Pre-HTO HKA	−0.338	.259	−0.431
Pre-HTO PTS	0.0002	.999	0.151
Post-HTO HKA	0.432	.140	0.415
Post-HTO PTS	0.009	.999	0.031
ΔHKA	0.587	.035	0.539
ΔPTS	0.018	.930	0.151

[a] Medial ratio: The ratio of high-density area (HDA) of the medial compartment in relation to the total HDA of both compartments.
HDA: 20% highest area in Hounsfield unit values out of the sum of the medial and lateral compartments. HTO, High tibial osteotomy. HKA, Hip–knee–ankle angle. PTS, Posterior

tibial slope. Post-HTO refers to 1 year after HTO. Δ: the value of the change before and after HTO.

Subregional %HDA analysis revealed %HDA of the M2 and M3 regions to be significantly higher among patients with OA than controls (*P* = .011 and *P* < .001, respectively). The %HDA of all four subregions of the lateral compartment was significantly lower in patients with OA than controls (for M1, *P* < .001; for M2, *P* = .013; for M3, *P* =.005; and for M4, *P* = .005; Table 4). After HTO, the %HDA of M2 and M3 decreased by 23% (P = .009) and 20% (P = .017), respectively. whereas that of M4 increased by 19% (P = .014). In the lateral compartment, the %HDA of L2 and L3 increased by 52% (P =.026) and 74% (P = .006).

Table 4. Subregional analysis of %HDA[a]

Subregion	Controls	Patients with OA		*P* value	
		Preoperative values	Postoperative values	Comparison: Preop with control	Preop–postop change
M1	6.2 (4.6–7.9)	9.5 (6.5–12.6)	7.0 (3.9–10.2)	.051	.112
M2	18.9 (16.4–21.3)	23.4 (20.8–26.0)	18.1 (13.8–22.5)	.011	.009
M3	21.6 (19.8–23.3)	29.0 (26.5–31.6)	23.2 (18.5–28.0)	<.001	.017
M4	16.1 (13.0–19.1)	18.1 (15.1–21.0)	21.6 (18.3–24.9)	.323	.014
L1	12.1 (9.9–14.3)	5.4 (3.5–7.3)	8.1 (4.0–12.1)	<.001	.132
L2	13.5 (11.4–15.6)	9.1 (6.3–12.0)	13.8 (9.4–18.3)	.013	.026
L3	9.0 (6.6–11.4)	4.2 (1.8–6.6)	7.3 (3.7–10.9)	.005	.006
L4	2.7 (1.2–4.2)	0.5 (0.1–0.8)	1.6 (0.2–3.0)	.005	.095

[a]Data are reported as means (95% confidence intervals).

HDA: 20% Highest area in Hounsfield unit values out of the sum of the medial and lateral compartments. %HDA: The percentage of the HDA in each subregion. OA, osteoarthritis. HTO, High tibial osteotomy. Preop: before HTO. Postop: 1 year after HTO. M1–M4: Subregions of the medial compartment of the proximal tibia, divided equally from the medial side to the lateral side. L1–L4: Subregions of the lateral compartment, divided equally from the medial side to the lateral side.

Discussion

In this study, we demonstrated that the medial ratio, defined as the ratio of the medial HDA to the total HDA of the proximal tibia, was increased among patients with OA and varus deformity but decreased significantly after valgus HTO. Furthermore, we discovered that leg alignment was significantly correlated to medial ratio in healthy individuals as well as patients with OA and that the degree of correction of alignment after HTO was correlated to the change in medial ratio.

According to the results of previous studies involving dual-energy X-ray absorptiometry (DEXA), leg alignment was correlated with bone mineral density (BMD) of the proximal tibia[2, 25, 47] as well as with the decrease in BMD of the medial compartment after HTO.[2, 25] These findings are similar to the results of our study. However, DEXA is used to evaluate BMD of the periarticular bone but does not distinguish the subchondral bone plate from trabecular bone of the articular surface or from bone spurs or cortical bone. In addition, according to the results of one experimental study, BMD of subchondral bone and trabecular bone changed differently over time,[6] which suggests the difficulty of evaluating the change in the BMD of subchondral bone precisely with DEXA. In contrast, in CT–osteoabsorptiometry, bone spurs can be hidden in the region of interest so that the focus is on the subchondral bone plate of the articular surface. This was believed to be an advantage in our study.

Previous studies involving CT–osteoabsorptiometry have indicated that the distribution pattern of subchondral bone density reflects the distribution of the resultant stresses acting on a joint surface under actual loading conditions.[12, 17, 18, 31, 32, 34, 37, 41, 46] We found the medial ratio to be higher in OA patients than healthy individuals, decreasing after HTO in the former. Moreover, the JOA knee scores improved, particularly in the pain subcategories, after HTO. These results indicated that HTO reduces the stress distribution pattern across the medial compartment of the proximal tibial articular surface.

The correlation between ΔHKA and Δmedial ratio was weak ($r = 0.587$), which indicates that the change in leg alignment explained the small variance (~35%) in the Δmedial ratio. Other factors not evaluated in this study, including physical characteristics (e.g., muscle strength, pelvic width), kinetics (i.e., dynamic alignment), and postoperative activity, might explain the rest of the variance in the Δmedial ratio. Our results demonstrated that HKA, but not age and BMI, was significantly correlated with the medial ratio in both healthy individuals and patients with OA, and that only ΔHKA was significantly correlated with the Δmedial ratio among variances (age, sex, BMI, JOA knee score, and pre-, postoperative and Δ values of HKA and PTS). In addition, a 3-D motion analysis study demonstrated that among the changes in the mechanical axis angle, PTS, gait speed, and lateral trunk lean, only the change in the mechanical axis angle was significantly correlated with the change in KAM during level walking before and after HTO.[28] Thus we can conclude that leg alignment is an important factor influencing the stress distribution pattern across the proximal tibial articular surface.

The comparison between the patients postoperatively and the controls revealed that although the patients had valgus alignment more than did controls, the medial ratio was still higher in the patients postoperatively. A possible explanation for this dissociation between the alignment and the medial ratio is the influence of OA itself on the subchondral bone density.[19, 39] Another possible explanation is that the distribution of bone density 1.5 years after HTO was not the final distribution of bone density after HTO, inasmuch as the DEXA study mentioned earlier demonstrated that a medial-to-lateral ratio of femoral and tibial condyle BMD was still changing 1 year after HTO.[25] Further study is needed to clarify when the final distribution of subchondral bone density is established.

The results of our subregional analysis of HDA distribution pattern before and after HTO demonstrated that, of the four subregions in the medial compartment, %HDA of M2 and M3 decreased after HTO, whereas M4 was the only region of the medial compartment to exhibit increased %HDA. These results suggested that stress on the most lateral region of the medial compartment increases after HTO. A finite element study has reported that shear stress on the lateral region in the medial compartment increases as lateral joint line obliquity increasing.[36] This might be a reason for the paradoxical observation that the stress increases on the most lateral region only but decreases for all other regions. Further study is required to clarify whether this effect influences long-term clinical outcomes; however, surgeons should consider the risk of progression of OA at the most lateral region of the medial compartment after HTO due to increased mechanical stress, especially in cases where changes in OA have occurred in this region. In this study, the mean medial ratio was higher in the OA (80.1%) than control group (61.3%), which is consistent with a previous biomechanical study in which the percentage of total loading attributable to medial compartment loading was 66% in the control group (with normal alignment) compared with 74.5% in patients with OA at the first peak of the KAM.[26] The similarity between the medial ratio of this study and the medial compartment loading ratio in the previous study[26] provides some support and verification of the reliability of CT–

osteoabsorptiometry as a method for evaluating stress distribution.[12, 17, 18, 31, 32, 34, 37, 41, 46]

There are different opinions about the leg alignment after HTO. Some authors recommend HKA of 3°–5° valgus,[13, 14] others suggest 8°–10° valgus.[9, 24] Fujisawa et al. suggests %MA of 65%–70%.[11] However, the medial compartment loading correlated with the tibiofemoral alignment in the dynamic single-limb loading ($R^2 = 0.59$) with varus malalignment,[27] indicating that same leg alignment does not indicate the same distribution pattern of the joint loading. Therefore, it is thought to be desirable that the postoperative leg alignment of each patient is decided considering the distribution of the joint loading. Further investigation including of the distribution pattern of subchondral bone density and kinematic analysis including KAM can be useful for elucidating the optimal leg alignment of each patient who underwent HTO.

This study has several limitations that should be acknowledged. First, we did not directly measure the stresses and the overall bone density in the knee. Instead, the distribution of subchondral bone density in the knee joint was assessed according to the CT–osteoabsorptiometry method.[31, 32] Furthermore, the absolute value of stress at each analysis point was not elucidated. Therefore, it should be kept in mind that the stress distribution evaluated by the CT–osteoabsorptiometry method does not reflect actual stress at the analysis points. Second, there was a significant difference in age between the

OA and control groups (mean difference 38.1 years). This study reveals that age is correlated with the medial ratio in patients with OA but not in healthy individuals. However, leg alignment was found to be correlated with medial ratio in both groups. This indicates that age might influence the distribution of subchondral bone density as strongly as varus alignment. Third, we evaluated patients with OA after the removal of metal component. Finite element analysis has been used to demonstrate the stress shielding effect of the HTO plate on the bone around the plate[22]; however, the mechanisms underlying this effect on the articular surface are unclear. Moreover, regardless of the stress shielding effect of the HTO plate, this study reveals that the distribution of subchondral bone density differs significantly before and 1.5 years after HTO. A fourth limitation was the small sample size. We included the patients who underwent OWHTO and excluded those with meniscus injury, joint instability, patellofemoral OA, and lateral OA. Our results may have consequently been affected by the inclusion of patients only with good outcomes, especially in view of the small sample size. At our institution, however, we perform closed HTO[23] for patients with severe varus OA (HKA $\leq -10°$) or patellofemoral OA (KL grade $\geq$ II). In general, closed HTO necessitates fibular osteotomy, which itself might affect stress distribution across the knee joint.[48] Each exclusion criterion was believed to be a contraindication to HTO or a factor other than HTO that affects the stress distribution. We thus believed that the inclusion and exclusion criteria were necessary for this study to evaluate the influence of HTO alone on the distribution of subchondral bone density as accurately as possible. Despite these limitations, the results presented here provide fundamental clarification of the stress distribution over the knee joint.

In conclusion, we demonstrated that the distribution pattern of the HDA shifted from the medial-to-lateral compartment after HTO. We discovered that leg alignment was correlated with the distribution of subchondral bone density among nonarthritic individuals and patients with OA, and that the degree of alignment correction after HTO was correlated with the change in the distribution of the HDA. Moreover, we found that the HDA of the most lateral region in the medial compartment decreased after HTO.

These findings suggest that HTO reduces the stress on the medial compartment of the proximal tibial articular surface in knees with varus OA by shifting the stress toward the lateral compartment, and that the stress on the most lateral region of the medial compartment increases after HTO, inasmuch as the change in subchondral bone density results from the change in stress distribution.

References

1. Agneskirchner JD, Hurschler C, Wrann CD, Lobenhoffer P. The effects of valgus medial opening wedge high tibial osteotomy on articular cartilage pressure of the knee: a biomechanical study. *Arthroscopy.* 2007;23(8):852-861.
2. Akamatsu Y, Koshino T, Saito T, Wada J. Changes in osteosclerosis of the osteoarthritic knee after high tibial osteotomy. *Clin Orthop Relat Res.* 1997(334):207-214.
3. Akizuki S, Shibakawa A, Takizawa T, Yamazaki I, Horiuchi H. The long-term outcome of high tibial osteotomy: a ten- to 20-year follow-up. *J Bone Joint Surg Br.* 2008;90(5):592-596.
4. Aoki Y, Yasuda K, Mikami S, Ohmoto H, Majima T, Minami A. Inverted V-shaped high tibial osteotomy compared with closing-wedge high tibial osteotomy for osteoarthritis of the knee. Ten-year follow-up result. *J Bone Joint Surg Br.* 2006;88(10):1336-1340.
5. Crues JV, Mink J, Levy TL, Lotysch M, Stoller DW. Meniscal tears of the knee: accuracy of MR imaging. *Radiology.* 1987;164:445-448.
6. Dedrick DK, Goldstein SA, Brandt KD, O'Connor BL, Goulet RW, Albrecht M. A longitudinal study of subchondral plate and trabecular bone in cruciate-deficient dogs with osteoarthritis followed up for 54 months. *Arthritis Rheum.* 1993;36(10):1460-1467.
7. Deie M, Hoso T, Shimada N, et al. Differences between opening versus closing high tibial osteotomy on clinical outcomes and gait analysis. *Knee.* 2014;21(6):1046-1051.
8. Elson DW, Petheram TG, Dawson MJ. High reliability in digital planning of medial opening wedge high tibial osteotomy, using Miniaci's method. *Knee Surg Sports Traumatol Arthrosc.* 2015;23:2041-2048.
9. Engel GM, Lippert FG, 3rd. Valgus tibial osteotomy: avoiding the pitfalls. *Clin Orthop Relat Res.* 1981(160):137-143.
10. Floerkemeier S, Staubli AE, Schroeter S, Goldhahn S, Lobenhoffer P. Outcome after high tibial open-wedge osteotomy: a retrospective evaluation of 533 patients. *Knee Surg Sports Traumatol Arthrosc.* 2013;21(1):170-180.
11. Fujisawa Y, Masuhara K, Shiomi S. The effect of high tibial osteotomy on osteoarthritis of the knee. An arthroscopic study of 54 knee joints. *Orthop Clin North Am.* 1979;10(3):585-608.
12. Funakoshi T, Furushima K, Momma D, et al. Alteration of stress distribution

patterns in symptomatic valgus instability of the elbow in baseball players: A computed tomography osteoabsorptiometry study. *Am J Sports Med.* 2016;44:989-994.

13. Goutallier D, Hernigou P, Medevielle D, Debeyre J. [Outcome at more than 10 years of 93 tibial osteotomies for internal arthritis in genu varum (or the predominant influence of the frontal angular correction)]. *Rev Chir Orthop Reparatrice Appar Mot.* 1986;72(2):101-113.

14. Hernigou P, Medevielle D, Debeyre J, Goutallier D. Proximal tibial osteotomy for osteoarthritis with varus deformity. A ten to thirteen-year follow-up study. *J Bone Joint Surg Am.* 1987;69(3):332-354.

15. Hurwitz DE, Ryals AB, Case JP, Block JA, Andriacchi TP. The knee adduction moment during gait in subjects with knee osteoarthritis is more closely correlated with static alignment than radiographic disease severity, toe out angle and pain. *J Orthop Res.* 2002;20(1):101-107.

16. Insall JN, Joseph DM, Msika C. High tibial osteotomy for varus gonarthrosis. A long-term follow-up study. *J Bone Joint Surg Am.* 1984;66(7):1040-1048.

17. Irie T, Takahashi D, Asano T, et al. Is there an association between borderline-to-mild dysplasia and hip osteoarthritis? Analysis of CT osteoabsorptiometry. *Clin Orthop Relat Res.* 2018;476(7):1455-1465.

18. Iwasaki N, Minami A, Miyazawa T, Kaneda K. Force distribution through the wrist joint in patients with different stages of Kienbock's disease: using computed tomography osteoabsorptiometry. *J Hand Surg Am.* 2000;25(5):870-876.

19. Johnston JD, Masri BA, Wilson DR. Computed tomography topographic mapping of subchondral density (CT-TOMASD) in osteoarthritic and normal knees: methodological development and preliminary findings. *Osteoarthritis Cartilage.* 2009;17:1319-1326.

20. Jones LD, Brown CP, Jackson W, Monk AP, Price AJ. Assessing accuracy requirements in high tibial osteotomy: a theoretical, computer-based model using AP radiographs. *Knee Surg Sports Traumatol Arthrosc.* 2017;25:2952-2956.

21. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis.* 1957;16(4):494-502.

22. Koh YG, Lee JA, Lee HY, Chun HJ, Kim HJ, Kang KT. Design optimization of high tibial osteotomy plates using finite element analysis for improved biomechanical effect. *J Orthop Surg Res.* 2019;14(1):1-10.

23. Kondo E, Yasuda K, Yabuuchi K, et al. Inverted V-shaped high tibial osteotomy for medial osteoarthritic knees with severe varus deformity. *Arthrosc Tech.*

2018;7(10):e999-e1012.

24. Koshino T, Morii T, Wada J, Saito H, Ozawa N, Noyori K. High tibial osteotomy with fixation by a blade plate for medial compartment osteoarthritis of the knee. *Orthop Clin North Am.* 1989;20(2):227-243.

25. Kosior P, Czuraszkiewicz L, Tarczynska M, Mazurkiewicz T, Gaweda K. The evaluation of knee bone mineral density following open-wedge high tibial osteotomy. *J Appl Biomech.* 2012;28(4):359-365.

26. Kumar D, Manal KT, Rudolph KS. Knee joint loading during gait in healthy controls and individuals with knee osteoarthritis. *Osteoarthritis Cartilage.* 2013;21(2):298-305.

27. Kutzner I, Bender A, Dymke J, Duda G, Von Roth P, Bergmann G. Mediolateral force distribution at the knee joint shifts across activities and is driven by tibiofemoral alignment. *Bone and Joint Journal.* 2017;99B(6):779-787.

28. Leitch KM, Birmingham TB, Dunning CE, Giffin JR. Medial opening wedge high tibial osteotomy alters knee moments in multiple planes during walking and stair ascent. *Gait Posture.* 2015;42:165-171.

29. Lind M, McClelland J, Wittwer JE, Whitehead TS, Feller JA, Webster KE. Gait analysis of walking before and after medial opening wedge high tibial osteotomy. *Knee Surg Sports Traumatol Arthrosc.* 2013;21:74-81.

30. Lotysch M MJ, Crues JV, Schwartz SA. Magnetic resonance imaging in the detection of meniscal injuries. *Magn Reson Imaging.* 1986;4:185.

31. Müller-Gerbl M, Putz R, Hodapp N, Schulte E, Wimmer B. Computed tomography-osteoabsorptiometry for assessing the density distribution of subchondral bone as a measure of long-term mechanical adaptation in individual joints. *Skeletal Radiol.* 1989;18:507-512.

32. Müller ‐ Gerbl M, Putz R, Kenn R. Demonstration of subchondral bone density patterns by three ‐ dimensional ct osteoabsorptiometry as a noninvasive method for in vivo assessment of individual long ‐ term stresses in joints. *J Bone Miner Res.* 1992;7:S411-S418.

33. Miniaci A, Ballmer FT, Ballmer PM, Jakob RP. Proximal tibial osteotomy. A new fixation device. *Clin Orthop Relat Res.* 1989(246):250-259.

34. Momma D, Iwasaki N, Oizumi N. Alterations in stress distribution patterns through the forearm joint surface of the elbow in baseball players assessed using computed tomography osteoabsorptiometry. *J Orthop Sci.* 2012;17:253-260.

35. Moore J, Mychaltchouk L, Lavoie F. Applicability of a modified angular correction measurement method for open-wedge high tibial osteotomy. *Knee Surg*

Sports Traumatol Arthrosc. 2017;25:846-852.

36. Nakayama H, Schröter S, Yamamoto C, et al. Large correction in opening wedge high tibial osteotomy with resultant joint-line obliquity induces excessive shear stress on the articular cartilage. *Knee Surg Sports Traumatol Arthrosc.* 2018;26:1873-1878.

37. Nishida K, Iwasaki N, Fujisaki K, et al. Distribution of bone mineral density at osteochondral donor sites in the patellofemoral joint among baseball players and controls. *Am J Sports Med.* 2012;40:909-914.

38. Ogata K, Yoshii I, Kawamura H, Miura H, Arizono T, Sugioka Y. Standing radiographs cannot determine the correction in high tibial osteotomy. *J Bone Joint Surg Br.* 1991;73(6):927-931.

39. Omoumi P, Babel H, Jolles BM, Favre J. Quantitative regional and sub-regional analysis of femoral and tibial subchondral bone mineral density (sBMD) using computed tomography (CT): comparison of non-osteoarthritic (OA) and severe OA knees. *Osteoarthritis Cartilage.* 2017;25:1850-1857.

40. Onodera J, Kondo E, Omizu N, Ueda D, Yagi T, Yasuda K. Beta-tricalcium phosphate shows superior absorption rate and osteoconductivity compared to hydroxyapatite in open-wedge high tibial osteotomy. *Knee Surg Sports Traumatol Arthrosc.* 2014;22(11):2763-2770.

41. Onodera T, Majima T, Iwasaki N, Kamishima T, Kasahara Y, Minami A. Long-term stress distribution patterns of the ankle joint in varus knee alignment assessed by computed tomography osteoabsorptiometry. *Int Orthop.* 2012;36:1871-1876.

42. Pauwels F. *Biomechanics of the Locomotor Apparatus*. Berlin, Heidelberg: Springer Berlin Heidelberg; 1980.

43. Sato D, Kondo E, Yabuuchi K, et al. Assessment of valgus laxity after release of the medial structure in medial open-wedge high tibial osteotomy: an in vivo biomechanical study using quantitative valgus stress radiography. *BMC Musculoskelet Disord.* 2019;20(1):481.

44. Schatka I, Weiler A, Jung TM, Walter TC, Gwinner C. High tibial slope correlates with increased posterior tibial translation in healthy knees. *Knee Surg Sports Traumatol Arthrosc.* 2018;26(9):2697-2703.

45. Sharma L. Local factors in osteoarthritis. *Curr Opin Rheumatol.* 2001;13(5):441-446.

46. Shimizu T, Iwasaki N, Nishida K, Minami A, Funakoshi T. Glenoid stress distribution in baseball players using computed tomography osteoabsorptiometry: a pilot study. *Clin Orthop Relat Res.* 2012;470(6):1534-1539.

47. Wada M, Maezawa Y, Baba H, Shimada S, Sasaki S, Nose Y. Relationships among bone mineral densities, static alignment and dynamic load in patients with medial compartment knee osteoarthritis. *Rheumatology (Oxford).* 2001;40(5):499-505.

48. Wang X, Wei L, Lv Z, et al. Proximal fibular osteotomy: a new surgery for pain relief and improvement of joint function in patients with knee osteoarthritis. *J Int Med Res.* 2017;45(1):282-289.

49. Yabuuchi K, Kondo E, Onodera J, et al. Clinical outcomes and complications during and after medial open-wedge high tibial osteotomy using a locking plate: A 3- to 7-Year Follow-up Study. *Orthop J Sports Med.* 2020;8(6):2325967120922535.

50. Yasuda K, Majima T, Tsuchida T, Kaneda K. A ten- to 15-year follow-up observation of high tibial osteotomy in medial compartment osteoarthrosis. *Clin Orthop Relat Res.* 1992(282):186-195.

51. Yin Y, Li S, Zhang R, Guo J, Hou Z, Zhang Y. What is the relationship between the "Fujisawa point" and postoperative knee valgus angle? A theoretical, computer-based study. *Knee.* 2020;27(1):183-191.

52. Zheng K, Scholes CJ, Chen J, Parker D, Li Q. Multiobjective optimization of cartilage stress for non-invasive, patient-specific recommendations of high tibial osteotomy correction angle – a novel method to investigate alignment correction. *Med Eng Phys.* 2017;42:26-34.