CLINICAL ARTICLE

Anatomical Imaging Study on Uneven Settlement of the Proximal Tibia

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Objective: Uneven settlement of the proximal tibia significantly contributes to the onset and progression of medial compartment knee OA; however, the specific location and variations of proximal tibial deformity remain unclear. Therefore, this study aimed to explore the effects of the anatomic morphology of different tibial regions on proximal tibial vara and proximal tibial microstructural changes with age in both sexes to reveal the pattern of uneven settlement of the proximal tibia.

Methods: In this retrospective study, we reviewed the radiographs of 414 patients (789 legs) between May and September 2021. The medial proximal tibial angle (MPTA) and four anatomic angles of the tibia (i.e., the tibial plateau-epiphyseal line [PT-EL] angle, epiphyseal line-tibial platform [EL-PF] angle, epiphyseal axis inclination angle [EAIA], and subepiphyseal axis inclination angle [SAIA]) were measured. The effect of each angle on MPTA and their changes with age in both sexes were investigated using Pearson's correlation coefficient and multiple linear regression.

Results: In females, PT-EL angle, EL-PF angle, and SAIA negatively correlated with MPTA ($r = -0.325$, -0.246, and -0.502; $p < 0.05$), and EAIA positively correlated with MPTA ($r = 0.099$, $p < 0.05$). Regression analysis showed that the correlations between MPTA and PT-EL angle, EL-PF angle, and SAIA were significant ($\beta = -1.003$, -0.013, and -0.971; adjusted $R^2 = 0.979$). Furthermore, MPTA negatively correlated with age ($r = -0.202$, $p < 0.05$); PT-EL angle and EAIA positively correlated with age ($r = 0.237$ and 0.142, $p < 0.05$). Regression analysis showed that only the correlation between PT-EL angle and age was significant ($\beta = 5.635$, $p < 0.05$). In males, PT-EL angle, EL-PF angle, and SAIA negatively correlated with MPTA ($r = -0.270$, -0.267, and -0.533; $p < 0.05$), and EAIA positively correlated with MPTA ($r = 0.135$, $p < 0.05$). Regression analysis showed that the correlations between MPTA and PT-EL angle, EL-PF angle, and SAIA were significant ($\beta = -0.992$, -0.017, and -0.958; adjusted $R^2 = 0.970$). However, there was no significant correlation between age and any of the measured angles ($p > 0.05$).

Conclusions: Proximal tibial vara is affected by the anatomic morphology of the epiphyseal and subepiphyseal regions. In females, the uneven settlement of the epiphysis progresses with age and may be responsible for dynamic varus deformity of the proximal tibia.

Key words: Knee Osteoarthritis; Proximal Tibial Vara; Radiological Anatomy; Uneven Settlement

Introduction

Knee osteoarthritis (OA) is the leading cause of lower limb dysfunction in the middle-aged and geriatric populations,[1–3] affecting the medial compartment more commonly than the lateral.[4,5] Varus limb alignment significantly contributes to the onset and progression of medial compartment knee OA, which usually requires surgical correction at more advanced stages.[6,7]

Among the variables associated with varus alignment, only the medial proximal tibial angle (MPTA) has been reported to be significantly associated with the progression of joint space narrowing in the medial compartment, the

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odds of which increase by 21% for every 1° decrease in MPTA.[8] MPTA reflects an overall morphological varus inclination of the tibial articular surface relative to the mechanical axis of the tibia. However, the specific location and variations of proximal tibial deformity remain unclear.

Lu et al.[9] reported a significant correlation between MPTA and age in females; however, no such correlation was found in males. This study suggested several potential causes of tibial varus and reported the dynamic changes seen in both men and women. Zhang et al. proposed the theory of uneven settlement of the tibial plateau and reported a significant correlation between the settlement of the medial tibial plateau and the Kellgren–Lawrence (K–L) classification of knee OA.[10–12] This theory states that subsidence of the medial tibial plateau may progress, causing structural changes in the cancellous bone, which may be precipitated by an uneven distributed mechanical load and a decrease in the bone mass with aging.[13,14]

The proximal epiphysis, which is demarcated from the metaphysis by the epiphyseal line, contains the most cancellous bone in the proximal tibia. Varus deformity of the epiphysis due to a long-term load is associated with knee OA.[15] Interestingly, Kawasaki et al.[16] reported that besides varus inclination, a medial shift of the tibial articular surface also contributes to proximal tibial vara. Therefore, further research is necessary to clarify the structural changes in different tibial regions and their contribution to overall varus deformity in the proximal tibia, to investigate the mechanobiological basis of knee OA.

As such, this study aimed to (i) explore the effects of the anatomic morphology of different tibial regions on proximal tibial vara and (ii) illustrate age-related proximal tibial microstructural changes in both sexes to reveal the pattern of uneven settlement of the proximal tibia. We hypothesized that an uneven settlement of the tibial plateau occurs mainly in the epiphyseal region, which progresses with age in females, while in males, proximal tibial vara may form during development.

Methods

Study Participants

We retrospectively reviewed the weight-bearing, full-leg anteroposterior radiographs obtained in our hospital between 1st May 2021 and 30th September 2021 through a picture archiving and communication system (Beijing Tianjian Yuan Da Technology Co. Ltd., China). The study participants were selected based on the following inclusion and exclusion criteria:

i. Inclusion criteria: (1) age >18 years; (2) radiographs showing the standard anteroposterior view with the patella visible in the midline and approximately one-third to one-half overlap of the fibular head with the lateral edge of the proximal tibia; and (3) varus alignment of the lower extremity, that is, a hip–knee angle of <180°.
ii. Exclusion criteria: (1) extension deficit of the observed knee joint; (2) history of injury or surgery in either lower extremity; (3) skeletal dysplasia or osteopathy involving the lower extremities; and (4) blurring articular surface outline or epiphyseal line on the radiographs.

Based on these criteria, 414 patients (789 knees) were finally included in the statistical analysis (Figure 1).

Radiological Measurements

The requirement for informed consent was waived because of the retrospective nature of this study. This study was approved by the institutional review board of the Third Hospital of Hebei Medical University (IRB number: 2021–056-1). The films were taken according to the patient's medical needs, not for our research. All data were fully anonymized before we accessed

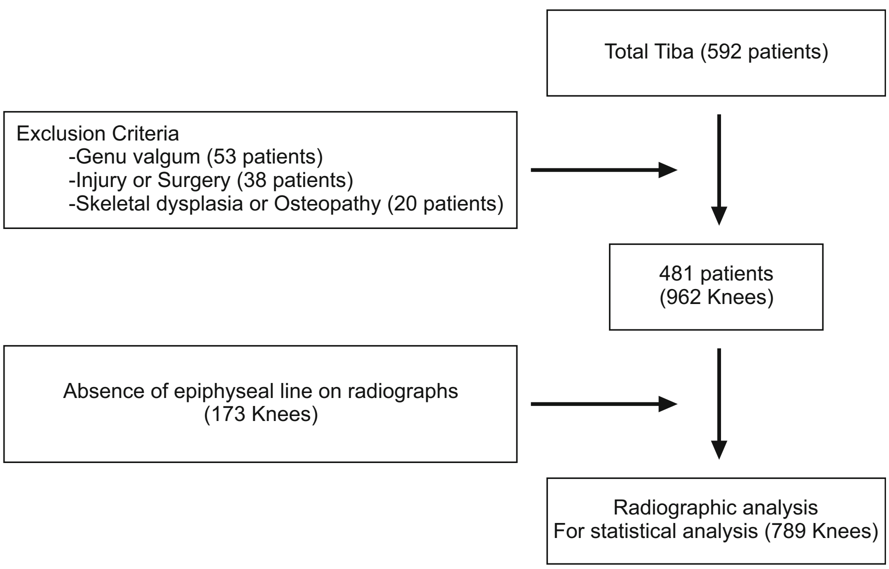

FIGURE 1 Flowchart illustrating the enrollment procedure

them, without personal details included, and no patient consent was requested. The radiographs were marked and measured using RadiAnt DICOM Viewer (v4.6.9 Medixant, Poznan-Poland). The radiological measurements of the tibia included: (1) MPTA: the medial angle between the line tangent to the tibial plateau and the mechanical axis of the tibia[12]; (2) the tibial plateau-epiphyseal line (PT-EL) angle: the angle between the tibial plateau and the proximal epiphyseal line (Figure 2); (3) the epiphyseal line-tibial platform (EL-PF) angle: the angle between the proximal epiphyseal line and the tibial plafond (Figure 3); (4) the epiphyseal axis inclination angle (EAIA): the angle between the line perpendicular to the proximal epiphyseal line and the line connecting the midpoints of the proximal epiphyseal line and tibial plateau (Figure 4); and (5) the sub-epiphyseal axis inclination angle (SAIA): the angle between the line perpendicular to the proximal epiphyseal line and the line connecting the midpoints of the proximal epiphyseal line and tibial plafond (Figure 5).

Two investigators performed radiological measurements twice at 1-week intervals for 50 randomly selected patients. Intra-observer and inter-observer reliabilities were

FIGURE 2 PT-EL angle is defined as the angle between the tibial plateau and proximal epiphyseal line. (A) Anteroposterior radiograph; (B) schematic diagram. PT-EL, tibial plateau-epiphyseal line

FIGURE 3 EL-PF angle is defined as the angle between the proximal epiphyseal line and tibial plafond. (A) Anteroposterior radiograph; (B) schematic diagram. EL-PF, epiphyseal line-tibial platform

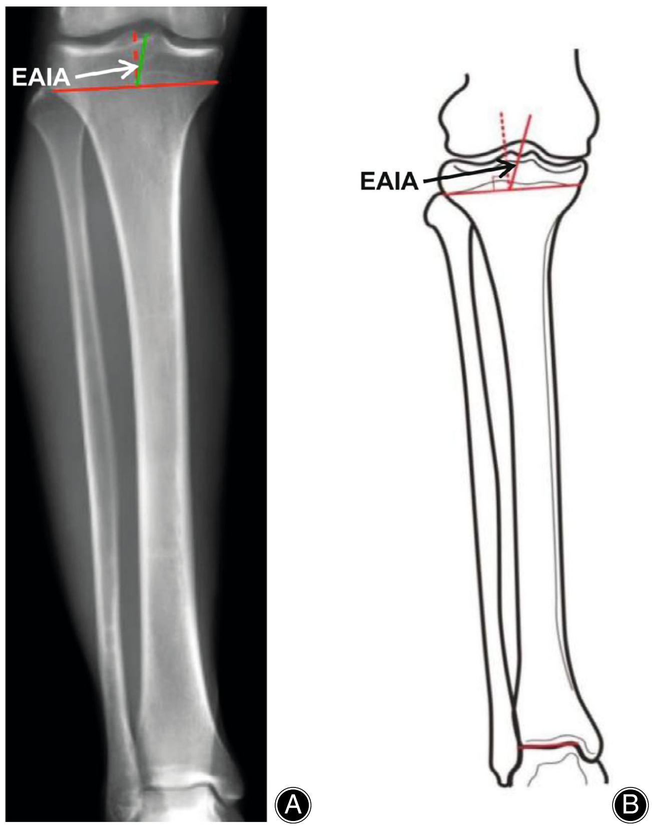

FIGURE 4 EAIA is defined as the angle between the line connecting the midpoints of the tibial plateau and proximal epiphyseal line, and the line perpendicular to the proximal epiphyseal line. (A) Anteroposterior radiograph; (B) schematic diagram. EAIA, epiphyseal axis inclination angle

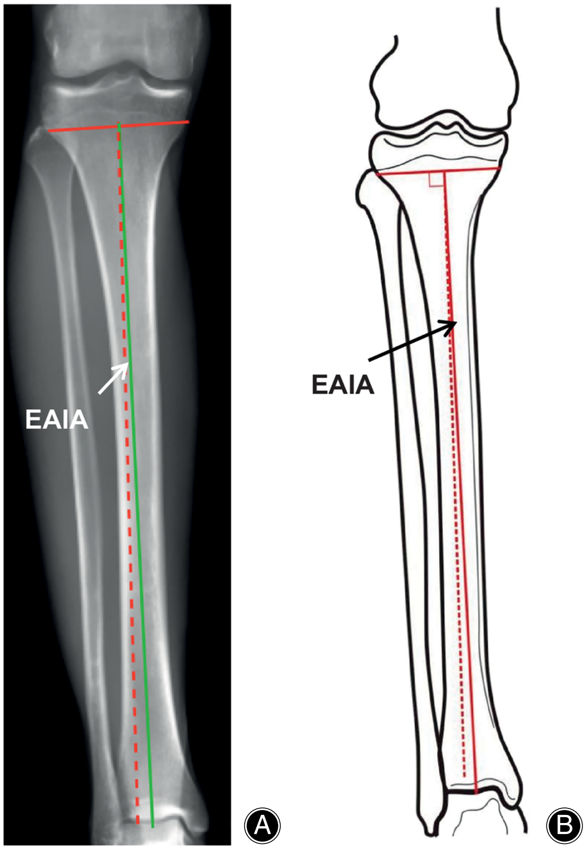

FIGURE 5 SAIA is defined as the angle between the line connecting the midpoints of the proximal epiphyseal line and tibial plafond, and the line perpendicular to the proximal epiphyseal line. (A) Anteroposterior radiograph; (B) schematic diagram. SAIA, subepiphyseal axis inclination angle

estimated by intraclass correlation coefficients (ICCs), with an ICC of >0.8 considered excellent reliability. Based on satisfactory intra- and inter-observer reliabilities (ICCs > 0.9) for each measurement, the radiological measurements from the same investigator were analyzed.

Statistical Methods

Statistical analyses were performed with IBM SPSS 25.0 (IBM Corp., Armonk, NY, USA) software for Windows. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. Continuous variables following a normal distribution were expressed as the mean ± standard deviation. Pearson's correlation coefficients were calculated, and multiple regression analyses were conducted to examine age-related changes in the four structural variables of the tibia (PT-EL angle, EL-PF angle, EAIA, SAIA) and their relationships with MPTA in both sexes. The level of significance was defined as $\alpha = 0.05$.

TABLE 1 Descriptive statistical data

Parameters	Female ($n = 547$)	Male ($n = 242$)
Age (years)	58.6 ± 11.4	57.1 ± 14.5
MPTA (°)	86.1 ± 2.4	85.9 ± 2.4
PT-EL angle (°)	3.8 ± 2.7	3.2 ± 2.6
EL-PF angle (°)	−0.5 ± 5.2	0.2 ± 4.7
EAIA (°)	5.1 ± 3.5	5.6 ± 3.2
SAIA (°)	1.2 ± 3.0	1.4 ± 3.0

Abbreviations: EAIA, epiphyseal axis inclination angle; EL-PF, epiphyseal line-tibial platform; MPTA, medial proximal tibial angle; PT-EL, tibial plateau-epiphyseal line; SAIA, subepiphyseal axis inclination angle.

Results

Baseline Characteristics

We enrolled a total of 414 patients (789 legs), including 287 females (547 legs) with an average age of 58.6 ± 11.4 years and 127 males (242 knees) with an average age of 57.1 ± 14.5 years. Detailed statistics are listed in Table 1.

Correlations between Variables

Pearson's correlation coefficients for evaluating the relationship between age and tibial variables showed a significant correlation of MPTA, PT-EL angle, and EAIA with age in females ($r = -0.202$, 0.237, and 0.142, respectively; $p < 0.01$). The two remaining variables (SAIA and EL-PF) in females and all the variables in males did not correlate with age ($p > 0.05$) (Table 2). In females, multivariate linear regression analysis of the four structural variables indicated that only the PT-EL angle significantly correlated with age ($\beta = 5.635$, $p < 0.01$; Table 3).

Bisexual Age-Based Analysis

Further analyses of the effects of the four structural variables on MPTA were conducted. Pearson's correlation coefficients demonstrated a significant correlation between all four

TABLE 2 Univariate correlation between tibial variables and MPTA based on sex

	Female ($n = 547$)		Male ($n = 242$)	
Parameters	Pearson's correlation coefficient (r)	p-value	Pearson's correlation coefficient (r)	p-value
PT-EL angle	−0.325	<0.001	−0.270	<0.001
EL-PF angle	−0.246	<0.001	−0.267	<0.001
EAIA	0.099	0.021	0.135	0.035
SAIA	−0.502	<0.001	−0.533	<0.001

Abbreviations: EAIA, epiphyseal axis inclination angle; EL-PF, epiphyseal line-tibial platform; MPTA, medial proximal tibial angle; PT-EL, tibial plateau-epiphyseal line; SAIA, subepiphyseal axis inclination angle.

TABLE 3 Multivariate correlation between tibial variables and MPTA based on sex

Parameters	Regression coefficient	95% CI		*p*-value
Female ($n = 547$)				
PT-EL angle	−1.003	−1.018	−0.988	<0.001
EL-PF angle	−0.013	−0.020	−0.005	0.001
EAIA	0.006	−0.003	0.016	0.204
SAIA	−0.971	−0.986	−0.956	<0.001
Male ($n = 242$)				
PT-EL angle	−0.992	−1.019	−0.965	<0.001
EL-PF angle	−0.017	−0.031	−0.004	0.013
EAIA	0.017	0.000	0.035	0.056
SAIA	−0.958	−0.985	−0.932	<0.001

Abbreviations: EAIA, epiphyseal axis inclination angle; EL-PF, epiphyseal line-tibial platform; MPTA, medial proximal tibial angle; PT-EL, tibial plateau-epiphyseal line; SAIA, subepiphyseal axis inclination angle.

variables and MPTA in both males and females ($p < 0.05$). In contrast, multivariate linear regression analysis revealed a negative correlation of PT-EL and EL-PF angles and SAIA with MPTA in both sexes (females: $\beta = -1.003$, -0.013, and -0.971, respectively; male: $\beta = -0.992$, -0.017, and -0.958, respectively; $p < 0.05$); however, there was a lack of significant correlation between EAIA and MPTA ($p > 0.05$).

Discussion

The most important finding of the present study was that the PT-EL angle, EL-PF angle, and SAIA correlated negatively with MPTA, whereas EAIA correlated positively with MPTA. Multiple linear regression analysis revealed that the above-mentioned negative correlations were significant in both females and males. Furthermore, MPTA correlated negatively with age, whereas the PT-EL and EAIA angles correlated positively with age. However, no significant correlation was noted between age and the measured angles in males.

Morphological Indicators of the Tibia

The tibia is the primary weight-bearing structure of the knee joint, receiving a maximum load of approximately three times the body weight during normal gait, with the medial tibial plateau receiving about 60% of that load.[17] Additionally, in both Eastern and Western populations, developmental varus of the tibia is prevalent to some degree,[18–20] which may cause greater differences in the load distribution of the medial and lateral tibial plateaus. As age increases, bone mineral density and mechanical strength decline, causing corresponding changes in the load-bearing bone settlement.[13,14] According to Wolff's law and the theory of mechanical regulation of bone, bones eventually adapt to the mechanical load and undergo structural changes. Interestingly, although increased stress within a certain range can promote bone formation, an excessive pathological load leads to an imbalance in bone homeostasis.[21] Therefore, an uneven stress distribution may initiate uneven settlement of the medial and lateral tibial plateaus. This can aggravate proximal tibial varus, causing an inward displacement of the force line of the lower limb, thereby increasing the load on the medial compartment further, creating a vicious circle. Currently, patients with knee osteoarthritis due to obvious proximal tibial varus primarily undergo a high tibial osteotomy, which corrects the lower limb force line, redistributes the internal and lateral compartment load, and slows the uneven settlement of the medial compartment. However, in the early stages, an effective means to redistribute the tibial load and prevent the occurrence and progression of uneven settlement is lacking. Therefore, it is vital to first identify the location of proximal tibial settlement and its influence on the overall tibial morphology, which can serve as a foundation for further research on proximal tibial microstructural changes and osteoarthritis-related pathological changes.

The proximal tibia, demarcated by the epiphysis line, can be further subdivided into the epiphysis and subepiphysis. These two regions are unique in their developmental origin and microstructure. The epiphyseal region, dominated by cancellous bone, is the first to conduct and buffer the stress, dispersing the stress load to protect the articular cartilage and transmitting the load to the denser and greater load-bearing cortical bone.[22,23] In the subepiphysis, the following changes are seen: the diameter gradually decreases, the proportion of cancellous bone declines, and the cortical bone steadily thickens. The proximal tibial cancellous bone density varies by region. In patients with knee osteoarthritis, bone density in the medial region of the epiphysis increases in response to a lower limb force line and stress distribution.[24–27] Therefore, we hypothesized that the uneven settlement of the proximal tibia occurs mainly in the epiphysis. In this study, taking the proximal tibial epiphyseal line as the boundary, the tibia was divided into upper and lower regions. Morphological changes in each region were reflected using four imaging measurements, and the composition of proximal tibial varus was subsequently analyzed. While the PT-EL angle reflects the vertical changes of the tibial plateau relative to the epiphyseal line, the EAIA reflects the corresponding horizontal changes, which together affect the anatomical morphology of the tibial epiphysis. Similarly, the EL-PF angle and SAIA reflect the vertical and horizontal changes in the distal tibial articular surface in relation to the proximal epiphyseal line, respectively, which together affect the anatomical morphology of the epiphyseal area.

In this study, multiple linear regression analysis revealed a significant correlation of the PT-EL angle, EL-PF angle, and SAIA with MPTA in both males and females, suggesting that epiphyseal varus, subepiphyseal varus, and subepiphyseal shift are the main factors affecting proximal tibial varus. Several studies have demonstrated an inward inclination and horizontal displacement of the articular surface of the plateau. Kawasaki et al.[16] reported that in patients with severe proximal tibial varus, the greater the intraarticular displacement of the tibia, the greater the separation of the tibial anatomical and mechanical axes at the proximal end. In this study, the EAIA, which reflects the medial shift of the tibial articular surface relative to the epiphyseal line, positively correlated with MPTA. This indicates that an increased shift of the tibial articular surface will lead to a greater proximal medial angle of the tibia and lesser proximal tibial inward migration. This result contradicts the report by Kawasaki et al.[16] possibly due to differences in the methods and references used to set the indicators. Specifically, they used the integral anatomical and mechanical axes as the reference to set the tibial articular surface inclination angle and inward migration distance, ignoring the combined effect of the morphological changes in the subepiphyseal region on the anatomical and mechanical axes of the tibia. Therefore, we presume the tibia is divided into different anatomical areas, for each of which corresponding morphological indexes were set. This could give an in-depth and accurate reflection of the causes and factors influencing proximal tibial varus; measuring the medial angle of the proximal tibia with the tibial mechanical axis as the reference is better than with the tibial anatomical axis as the reference. However, in the multivariate regression analysis in this study, the influence of EAIA on MPTA was not significant, and it may only be a minor factor among others influencing proximal tibial varus.

Age-Related Proximal Tibial Structural Changes

This study analyzed the correlation of age and sex with proximal tibial varus. Although MPTA correlated negatively with age in women, it did not significantly correlate with age in men (Table 4). This is consistent with the report by Lu et al.,[9] which suggested that proximal tibial varus increases with age in women but not in men. This study further analyzed the relationship between morphological changes in different tibial regions and age. In males, the PT-EL angle, EL-PF angle, EAIA, and SAIA had no significant correlation with age (Table 4), suggesting that the morphology of the epiphyseal and subepiphyseal regions did not change significantly with age in males. In females, univariate correlation analysis revealed that both PT-EL angle and EAIA correlated positively with age, while EL-PF angle and SAIA did not (Table 4), suggesting that the area above the epiphyseal line of the proximal tibia underwent uneven settlement and shifted with age, while the area below the epiphyseal line did not. In contrast, multivariate regression analysis demonstrated that only the PT-EL angle significantly correlated with age in females (Table 5). These results suggest that the proximal tibial epiphysis in females shows uneven settlement with age, which may be responsible for the dynamic change in proximal tibial varus. Therefore, the crux is that the epiphysis is the main site of uneven tibial settlement in female patients.

TABLE 4 Univariate correlation between tibial variables and age by sex

Parameters	Female ($n = 547$) Pearson's correlation coefficient (*r*)	Female ($n = 547$) *p*-value	Male ($n = 242$) Pearson's correlation coefficient (*r*)	Male ($n = 242$) *p*-value
MPTA	−0.202	<0.001	−0.058	0.368
PT-EL angle	0.237	<0.001	0.078	0.226
EL-PF angle	−0.030	0.480	−0.037	0.569
EAIA	0.142	0.001	−0.015	0.815
SAIA	−0.078	0.067	−0.095	0.139

Abbreviations: EAIA, epiphyseal axis inclination angle; EL-PF, epiphyseal line-tibial platform; MPTA, medial proximal tibial angle; PT-EL, tibial plateau-epiphyseal line; SAIA, subepiphyseal axis inclination angle.

TABLE 5 Multivariate correlation between tibial variables and age in females

Parameters	Regression coefficient	95% CI		*p*-value
PT-EL angle	5.635	0.853	1.765	<0.001
EL-PF angle	1.288	−0.079	0.380	0.198
EAIA	1.918	−0.007	0.587	0.056
SAIA	1.862	−0.025	0.918	0.063

Abbreviations: EAIA, epiphyseal axis inclination angle; EL-PF, epiphyseal line-tibial platform; MPTA, medial proximal tibial angle; PT-EL, tibial plateau-epiphyseal line; SAIA, subepiphyseal axis inclination angle.

Sex-Related Differences

Maeda et al.[28] reported that the thickness of both the medial and lateral cortices of the proximal tibial epiphysis in geriatric women was greater than that in young women. In contrast, in geriatric men, only the medial cortex was thicker, which may result from cortical bone remodeling under axial stress. Higano et al.[29] reported that a thicker medial cortex of the proximal tibia before the onset of knee osteoarthritis is associated with the progression of arthritis and that cortical thickness can be used as an indicator of stress distribution and related morphological changes. Therefore, we suggest that age-related changes in the area below the epiphyseal line of the proximal tibia in both males and females may result from cortical bone remodeling and thickening without any significant morphological changes in this area due to enhanced cortical bone support.

The pathological process of uneven settlement of the proximal tibia remains unclear. In this study, an uneven settlement was found in the epiphysis, showing only dynamic changes in women. This provides an important basis for elucidating its mechanism and relationship with knee osteoarthritis in the future. The metaphysis is primarily composed of cancellous bone, which is susceptible to osteoporosis, especially in perimenopausal women.[30] Furthermore, a link between osteoporosis and osteoarthritis has been reported. Previous studies have shown that the incidence of osteoarthritis and osteoporosis in women is significantly higher than that in men.[31,32] Akamatsu et al.[33] reported that lower limb BMD in postmenopausal women was associated with more severe proximal tibial introversion. Based on the results of this study and previous literature, we inferred that bone mass loss and osteoporosis might play an important role in the uneven settlement of the proximal tibial epiphysis in females, which needs validation through clinical and basic experiments.

Strengths and Limitations

This retrospective cross-sectional study has some limitations. First, the indicators set in the analysis considered the area from the proximal epiphyseal line to the distal articular surface as a whole, ignoring the anatomical changes below the proximal epiphyseal line. Second, factors such as weight, height, and bone mineral density were not included in this study, nor were the risk factors for tibial morphological changes screened and analyzed; therefore, the correlation between tibial imaging parameters and age is confounded. In addition, due to the measurement on two-dimensional images, there may be errors in the positioning of anatomical markers, selection of midpoints, and measurement of angles.

Despite these limitations, our study demonstrated that dividing the tibia into different anatomic regions along the epiphysis and setting the corresponding parameters can reflect the composition of uneven settlement more accurately. Furthermore, we confirmed that the location of uneven settlement is the epiphysis and that dynamic changes were only observed in women, which provides an important basis to further elucidate its mechanism and relationship with knee osteoarthritis, which highlights the novelty of this study. As part of a theoretical study on uneven settlement of the proximal tibia, our study will prompt subsequent investigations that seek to further clarify the pathological process of this condition through imaging, mechanobiology, and molecular biology techniques.

Conclusion

Proximal tibial vara (MPTA decrease) was influenced by changes in the PT-EL angle, EL-PF angle, and SAIA. Epiphyseal varus, subepiphyseal varus, and subepiphyseal shift were the main factors affecting proximal tibial varus. In females, uneven settlement of the epiphysis progressed with age, whereas no obvious changes were observed in males. Our findings provide a theoretical basis for uneven settlement of the proximal tibia. More attention should be paid to aging patients, especially females.

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Author Contributions

All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Conceptualization*, *Data Curation*, *Formal Analysis*, *Investigation*, *Project Administration*, *Resources*, *and Writing—Original Draft*: Zhijie Wang. *Methodology*: Yi Zheng. *Software*: Decheng Meng. *Supervision*: Handi Li. *Validation*: Chenni Ji. *Visualization and Writing—Review and Editing*: Juan Wang.

Ethics Statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent

Approval from the Institutional Review Board was obtained and in keeping with the policies for a retrospective review (IRB number: 2021–056-1). Informed consent was not required.

References

1. Vina ER, Kwoh CK. Epidemiology of osteoarthritis: literature update. Curr Opin Rheumatol. 2018;30:160–7.
2. Sun X, Zhen X, Hu X, Li Y, Gu S, Gu Y, et al. Osteoarthritis in the middle-aged and elderly in China: prevalence and influencing factors. Int J Environ Res Public Health. 2019;16:4701.
3. Hawker GA. Osteoarthritis is a serious disease. Clin Exp Rheumatol. 2019; 37(Suppl 120):3–6.
4. Chang AH, Lee SJ, Zhao H, Ren Y, Zhang LQ. Impaired varus-valgus proprioception and neuromuscular stabilization in medial knee osteoarthritis. J Biomech. 2014;47:360–6.
5. Dell'Isola A, Steultjens M. Classification of patients with knee osteoarthritis in clinical phenotypes: data from the osteoarthritis initiative. PLoS One. 2018;13: e0191045.
6. Wang Y, Nguyen UDT, Lane NE, Lu N, Wei J, Lei G, et al. Knee osteoarthritis, potential mediators, and risk of all-cause mortality: data from the osteoarthritis initiative. Arthritis Care Res (Hoboken). 2021;73:566–73.
7. Collins JE, Neogi T, Losina E. Trajectories of structural disease progression in knee osteoarthritis. Arthritis Care Res (Hoboken). 2021;73:1354–62.
8. Palmer JS, Jones LD, Monk AP, Nevitt M, Lynch J, Beard DJ, et al. Varus alignment of the proximal tibia is associated with structural progression in early to moderate varus osteoarthritis of the knee. Knee Surg Sports Traumatol Arthrosc. 2020;28:3279–86.
9. Lu Y, Zheng ZL, Lv J, Hao RZ, Yang YP, Zhang YZ. Relationships between morphological changes of lower limbs and gender during medial compartment knee osteoarthritis. Orthop Surg. 2019;11:835–44.
10. Dong T, Chen W, Zhang F, Yin B, Tian Y, Zhang Y. Radiographic measures of settlement phenomenon in patients with medial compartment knee osteoarthritis. Clin Rheumatol. 2016;35:1573–8.
11. Wang J, Lv HZ, Chen W, Fan MK, Li M, Zhang YZ. Anatomical adaptation of fibula and its mechanism of proximal partial fibulectomy associated with medial compartment knee osteoarthritis. Orthop Surg. 2019;11:204–11.
12. Paley D, Tetsworth K. Mechanical axis deviation of the lower limbs. Preoperative planning of uniapical angular deformities of the tibia or femur. Clin Orthop Relat Res. 1992;280:48–64.
13. Yin Y, Zhang R, Jin L, Li S, Hou Z, Zhang Y. The hip morphology changes with ageing in Asian population. Biomed Res Int. 2018;2018:1507979.

14. Wei J, Chen W, Wang H, Wang J, Cheng L, Zhang Y. Application of non-uniform settlement theory in spine degenerative kyphosis. J Hebei Med Univ. 2019;40:54–7. (in Chinese).
15. Ruppel ME, Miller LM, Burr DB. The effect of the microscopic and nanoscale structure on bone fragility. Osteoporos Int. 2008;19:1251–65.
16. Kawasaki M, Nagamine R, Chen W, Ma Y, Sakai A, Suguro T. Proximal tibia vara involves the medial shift of the tibial articular surface. J Orthop Surg (Hong Kong). 2020;28:2309499020902592.
17. Ishibashi K, Sasaki E, Ota S, Oyama T, Chiba D, Yamamoto Y, et al. Bone marrow lesion severity was associated with proximal tibial inclination in early knee osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 2022;30:668–79.
18. Bellemans J, Colyn W, Vandenneucker H, Victor J. The Chitranjan Ranawat award: is neutral mechanical alignment normal for all patients? The concept of constitutional varus. Clin Orthop Relat Res. 2012;470:45–53.
19. Song MH, Yoo SH, Kang SW, Kim YJ, Park GT, Pyeun YS. Errata to "coronal alignment of the lower limb and the incidence of constitutional Varus knee in Korean females". Knee Surg Relat Res. 2015;27:197.
20. Teichtahl AJ, Cicuttini FM, Abram F, Wang Y, Pelletier JP, Dodin P, et al. Meniscal extrusion and bone marrow lesions are associated with incident and progressive knee osteoarthritis. Osteoarthr Cartil. 2017;25:1076–83.
21. Pearson OM, Lieberman DE. The aging of Wolff's "law": ontogeny and responses to mechanical loading in cortical bone. Am J Phys Anthropol. 2004; Suppl 39:63–99.
22. Hess S, Moser LB, Amsler F, Behrend H, Hirschmann MT. Highly variable coronal tibial and femoral alignment in osteoarthritic knees: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2019;27:1368–77.
23. Fonseca H, Moreira-Gonçalves D, Coriolano HJ, Duarte JA. Bone quality: the determinants of bone strength and fragility. Sports Med. 2014;44:37–53.
24. Thorp LE, Wimmer MA, Block JA, Moisio KC, Shott S, Goker B, et al. Bone mineral density in the proximal tibia varies as a function of static alignment and knee adduction angular momentum in individuals with medial knee osteoarthritis. Bone. 2006;39:1116–22.
25. Burnett WD, Kontulainen SA, McLennan CE, Hazel D, Talmo C, Wilson DR, et al. Proximal tibial trabecular bone mineral density is related to pain in patients with osteoarthritis. Arthritis Res Ther. 2017;19:200.
26. Burnett WD, Kontulainen SA, McLennan CE, Hazel D, Talmo C, Hunter DJ, et al. Knee osteoarthritis patients with severe nocturnal pain have altered proximal tibial subchondral bone mineral density. Osteoarthr Cartil. 2015;23: 1483–90.
27. Sannmann F, Laredo JD, Chappard C, Engelke K. Impact of meniscal coverage on subchondral bone mineral density of the proximal tibia in female subjects - a cross-sectional in vivo study using QCT. Bone. 2020;134: 115292.
28. Maeda K, Mochizuki T, Kobayashi K, Tanifuji O, Someya K, Hokari S, et al. Cortical thickness of the tibial diaphysis reveals age- and sex-related characteristics between non-obese healthy young and elderly subjects depending on the tibial regions. J Exp Orthop. 2020;7:78.
29. Higano Y, Hayami T, Omori G, Koga Y, Endo K, Endo N. The varus alignment and morphologic alterations of proximal tibia affect the onset of medial knee osteoarthritis in rural Japanese women: case control study from the longitudinal evaluation of Matsudai knee osteoarthritis survey. J Orthop Sci. 2016;21: 166–71.
30. Tosi LL, Boyan BD, Boskey AL. Does sex matter in musculoskeletal health? The influence of sex and gender on musculoskeletal health. J Bone Joint Surg Am. 2005;87:1631–47.
31. Jones CD. Gender differences in patellofemoral joint biomechanics. Clin Orthop Relat Res. 2004;419:317 (author 317–318).
32. Ritter MA, Harty LD, Davis KE, Meding JB, Berend ME. Predicting range of motion after total knee arthroplasty. Clustering, log-linear regression, and regression tree analysis. J Bone Joint Surg Am. 2003;85: 1278–85.
33. Akamatsu Y, Kumagai K, Kobayashi H, Tsuji M, Saito T. Effect of increased coronal inclination of the tibial plateau after opening-wedge high tibial osteotomy. Art Ther. 2018;34:2158–2169.e2.