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Prevalence of osteoporosis in patients with knee osteoarthritis awaiting total knee arthroplasty is similar to that in the general population

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Abstract

Background Osteoporosis is common in patients with knee osteoarthritis (KOA) awaiting total knee arthroplasty (TKA) and varies in different regional and ethnic. However, it is unclear whether the prevalence of osteoporosis and osteopenia in these patients is different from that in the general population. This study aims to investigate the prevalence of osteoporosis and osteopenia in both populations to help exploring the relationship between the osteoporosis and osteoarthritis, and to explore whether knee function and radiological assessments of KOA are associated with osteoporosis.

Methods In total, 249 patients diagnosed with KOA awaiting TKA were investigated in this cross-sectional study. The mean age was 70.9 ± 6.4 years. Bone mineral density (BMD) and T scores at the hip and lumbar spine were used to assess bone status using dual X-ray absorptiometry. A matched cohort from 2448 individuals in the Health Examination Center of our hospital was set as controls by matching sex, age (± 3.0 years) and BMI (± 1.0). The Kellgren-Lawrence grades (K-L grades), mechanical femorotibial angle (mFTA), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and range of motion (ROM) of the knee were measured to evaluate radiological assessments and knee function in patients awaiting TKA and used to explore the association between KOA and BMD or T score. Prevalence of osteoporosis and osteopenia were investigated in the two cohorts, and inferential statistical analyses were undertaken. The chi-squared test or Fisher's exact test was used for categorical variables while comparisons of scores were examined by ANOVA with/without Bonferroni correction or the Kruskal–Wallis test.

Results The prevalence of osteoporosis and osteopenia in patients awaiting TKA was 30.5% (76/249) and 44.2% (110/249), respectively. In the matched cohort, 72/249 (28.9%) had osteoporosis, while 98/249 (39.4%) had osteopenia. There was no significant difference in the prevalence of osteoporosis or osteopenia between the two groups ($\chi 2 = 2.603$, $P = 0.272$). mFTA was significantly correlated with BMD and T score ($P < 0.05$), while no correlation was found between K-L grade, ROM or WOMAC and BMD or T score ($P > 0.05$).

Conclusions The prevalence of osteoporosis in patients awaiting TKA was similar to that in the general population. BMD and T score were not correlated with WOMAC score or K-L grade but were correlated with mFTA.

Keywords Bone mineral density, Prevalence of osteoporosis, Osteoarthritis of knee, Arthroplasty

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Background

Knee osteoarthritis (KOA) and osteoporosis are both common musculoskeletal disorders in older adults worldwide. According to previous studies, the prevalence of symptomatic knee osteoarthritis among general population was 8.1%, while the prevalence of osteoporosis in individuals over 40 years old is 5.0% for males and 20.6% for females [1, 2]. Two decades ago, osteoporosis and KOA were thought to have an inverse correlation, meaning that patients with KOA were less likely to have osteoporosis [3–5]. However, this concept has been challenged in recent studies [6–8]. Researchers are aware that both disorders coexist in older patients and may share similar causes and pathways. For example, adipokines released by obese patients may interfere in the progression of osteoporosis and osteoarthritis [6, 9]. In addition, the existence of osteoporosis may increase complications and affect the survival time of the prosthesis in patients undergoing arthroplasty [10]. Therefore, it is essential to know the prevalence of osteoporosis in these patients to treat it as early as possible and reduce the impact of osteoporosis.

Several studies have reported the prevalence of osteoporosis in patients awaiting TKA using various diagnosis methods based on different populations in several countries. Anna et al. reported that 26% of patients had osteoporosis before arthroplasty; however, their diagnosis of osteoporosis was based on self-reported symptoms or a history of fragility fractures or treatment using bisphosphonates but not standard dual energy X-ray absorptiometry (DXA) screening [11]. After that, several research studies screened osteoporosis and osteopenia using DXA screening in patients awaiting TKA and concluded that 8.4–59.8% of patients had osteoporosis [8, 12–18]. The large differences in prevalence are due to the countries investigated and the population enrolled.

It is unclear whether there is a significant difference in the prevalence of osteoporosis among patients awaiting TKA compared to the general population. Recently, a study found that patients with moderate to severe KOA had significantly lower T scores and BMD in the KOA group than in the non-KOA group [19]. However, this study focused on different stages of KOA rather than patients awaiting TKA. Another study showed that patients awaiting TKA had a similar prevalence of osteoporosis compared with matched controls [20], but this research was conducted only in women over the age of 65. Therefore, it is necessary to know the difference in osteoporosis among all patients awaiting TKA, including men and women, and those over and under 65 years of age. The answer to this question will not only help us explore the relationship between osteoporosis and advanced KOA but also help develop individualized strategies for the treatment of both diseases. Therefore, it is necessary to compare the prevalence of osteoporosis in patients awaiting TKA with the general population matched for sex, age, and BMI.

Moreover, whether factors of KOA, including radiological assessment and knee function, are associated with osteoporosis remains controversial. Radiological grading and knee function represent stages of KOA and can affect the intensity of a patient's daily activities, thereby affecting long-term bone mass storage. Kim et al. found an inverted U-shaped association between BMD and K-L grades through a national survey [21]. In addition, Chang et al. found that lower lumbar BMD and T scores were associated with worse pain scores and knee function [16]. However, the relationship between radiological assessment or knee function and osteoporosis still requires further study for clarification.

Therefore, the aim of this study was 1). To compare the prevalence of osteoporosis in patients awaiting TKA with that in the general population. 2). To explore whether factors of KOA, such as radiological assessment and knee function, are associated with osteoporosis in these patients.

Methods

The study was approved by the institutional review board of the 2nd Affiliated Hospital of Wenzhou Medical University and conducted in compliance with national and local regulations.

Patient selection

Patients who met the following criteria were included in the study: 1). KOA was diagnosed according to Chinese Orthopedic Association criteria [22]; 2). Waiting for TKA between September 2020 and May 2022; 3). BMD examination was performed 2 weeks before TKA. The exclusion criteria were a diagnosis of inflammatory arthritis, previous TKA or THA in the contralateral knee or hip, or severe comorbidities such as stroke or metabolic bone disease.

The matched cohort

We obtained the BMD results of 2448 individuals over the age of 50 who underwent BMD measurement in the Health Examination Center of our hospital during the same period. Then, a matched cohort was created by matching sex, age (±3.0 years) and BMI (±1.0 kg/m^2) with patients awaiting TKA and set as the control group to match the major confounders of osteoporosis.

Sample size calculation

The design of this study compared study group to general population. According to the previous reports, the prevalence of osteoporosis above 65-year-old population in China was 32.0% while the prevalence of osteoporosis in postmenopausal women with KOA awaiting TKA was 59.8% [8, 23]. When the alpha value was set at 0.05 and the power value was set at 0.9, the calculated sample size was 31 (https://clincalc.com/stats/samplesize.aspx). Therefore, 38 cases ($31 \times (1 + 20\%)$) in female or male group were needed to compared the prevalence which means totally at least 76 patients in patients awaiting TKA group or control group.

Data collection

Knee osteoarthritis assessment

KOA assessment in all patients was evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score. The WOMAC score includes 3 subscales related to pain, stiffness, and function. The higher the WOMAC score, the worse the joint pain, stiffness and function. In addition, range of motion (ROM) of the knee was measured by one author (Hanle Zhang). The radiological grade of KOA was evaluated according to the Kellgren-Lawrence (K-L) grading scale (0 = none, 1 = doubtful, 2 = minimal, 3 = moderate, 4 = severe) To avoid bias, one senior orthopedic surgeon (Pei Fan) performed all radiological evaluations. The mechanical femorotibial angle (mFTA) was measured using weight-bearing lower limb X-ray. Positive degrees indicate varus, and negative degrees indicate valgus.

Osteoporosis assessment

Patients' BMD was evaluated using a DXA scan (Discovery Wi, Hologic, USA) 2 weeks or less prior to TKA, using standard protocols to measure BMD of the lumbar vertebrae (L1-L4) and proximal femur by licensed technicians with the patients in a supine position. Based on these scores, T scores were calculated based on the standard deviations of the reference BMD scores for the young Asian reference population. T scores were interpreted according to the guidelines published by the International Society for Clinical Densitometry (ISCD). The diagnosis of osteoporosis was made using the World Health Organization T score criteria. Osteoporosis was defined as a T score lower than -2.5 ($T \leq -2.5$) at either the lumbar vertebrae or proximal femur, while osteopenia was defined as a T score between -2.5 and -1.0 ($-2.5 < T < -1.0$).

Statistical analysis

Data analysis and statistics were processed using SPSS 25.0 (IBM Corp., Armonk, NY, USA). Normally distributed data are described as the mean and standard deviation. Nonnormally distributed data are reported as the mean and 95% confidence interval (CI). Comparisons of scores were examined by ANOVA with/without Bonferroni correction or the Kruskal–Wallis test depending on the results of the normality test and Levene's test. The chi-squared test or Fisher's exact test was used for categorical variables. Correlation coefficients were determined by the Spearman rank correlation test using two-tailed P values. $P < 0.05$ was set as indicating a significant difference.

Results

The demography of patients awaiting TKA and matched cohort

From September 2020 to May 2022, a total of 249 patients with BMD measurements in patients awaiting TKA was collected while a matched cohort consisting of 249 individuals was set as control (Table 1). The matched cohort exhibited similarities in terms of age ($P = 0.527$), sex ($P = 1.0$), height ($P = 0.22$), weight ($P = 0.169$) and BMI ($P = 0.921$). The demographic data of all the included objects are presented in Table 1.

The prevalence of osteoporosis and osteopenia in patients awaiting TKA was similar to that in the matched cohort

To investigate the prevalence of osteoporosis and osteopenia in patients awaiting TKA, the BMD and T score of enrolled patients were collected and analyzed. In total, there were 76/249 (30.5%) patients with osteoporosis and 110/249 (44.2%) patients with osteopenia. Only 25.3% of patients had normal T scores (Fig. 1). The numbers of patients with osteoporosis and osteopenia in men and women are shown in Table 2. Among these patients, women had a similar BMI to men ($P = 0.222$) but were younger (70.4 vs 72.2 $P = 0.008$); however, women had a significantly lower BMD than men ($P < 0.001$) (Fig. 2). Among patients over 65 years old, 67/208 (32.2%) had osteoporosis, and 89/208 (42.8%) had osteopenia.

To avoid bias in the osteoporotic analysis, a matched cohort was created to explore the prevalence of osteoporosis in the general population. The numbers of osteoporosis and osteopenia patients in the matched cohort are shown in Table 2. The BMD of the lumbar spine and proximal femur in the general population was significantly higher than that in patients awaiting TKA ($P < 0.001$) (Fig. 3). However, the prevalence of osteoporosis in the patients awaiting TKA group was similar to

Table 1 Demography of patients awaiting TKA and matched cohort

	Patients awaiting TKA			Matched cohort		
	Men (*n* = 74)	Women (*n* = 175)	Total (*n* = 249)	Men (*n* = 74)	Women (*n* = 175)	Total (*n* = 175)
Age (years)	72.2 ± 6.7	70.4 ± 6.3	70.9 ± 6.4 (55–88)	72.2 ± 7.1	69.8 ± 6.3	70.5 ± 6.6 (55–90)
Height (cm)	164.6 ± 5.8	155.5 ± 5.2	158.2 ± 6.8 (142–184)	165.4 ± 5.3	153.1 ± 5.7	156.7 ± 7.9 (135–182)
Weight (kg)	69.5 ± 8.8	63.4 ± 9.6	65.2 ± 9.7 (39–89)	70.4 ± 9.6	61.3 ± 9.5	64.0 ± 10.35 (36.5–86.0)
BMI	25.61 ± 2.90	26.19 ± 3.56	26.02 ± 3.38 (18.30–34.37)	25.67 ± 2.91	26.12 ± 3.56	25.99 ± 3.38 (18.89–33.33)
WOMAC	30.2 ± 8.9	36.7 ± 10.4	35.0 ± 10.4	\	\	\
Pain	4.7 ± 1.9	5.9 ± 2.5	5.6 ± 2.4	\	\	\
Stiffness	2.3 ± 1.1	3.0 ± 1.6	2.8 ± 1.5	\	\	\
Function	23.3 ± 7.0	27.8 ± 7.8	26.5 ± 7.8	\	\	\
K-L grade						
I	0 (0%)	0 (0%)	0 (0%)	\	\	\
2	0 (0%)	1 (0.6%)	1 (0.4%)	\	\	\
3	4 (5.4%)	22 (12.6%)	26 (10.4%)	\	\	\
4	70 (94.6%)	152 (86.8%)	222 (89.2%)	\	\	\
ROM (Degree)	116.5 ± 17.2	109.7 ± 24.1	111.7 ± 22.5 (10–153)	\	\	\
mFTA (Degree)	7.5 ± 4.8	5.6 ± 7.3	6.3 ± 6.4 (−29°- 22°)	\	\	\

Abbreviations: *BMI* body mass index, *K-L grade* Kellgren-Lawrence grade, *mFTA* mechanical femoral tibial angle, *ROM* Range of motion, *WOMAC* Western Ontario and McMaster Universities Osteoarthritis Index

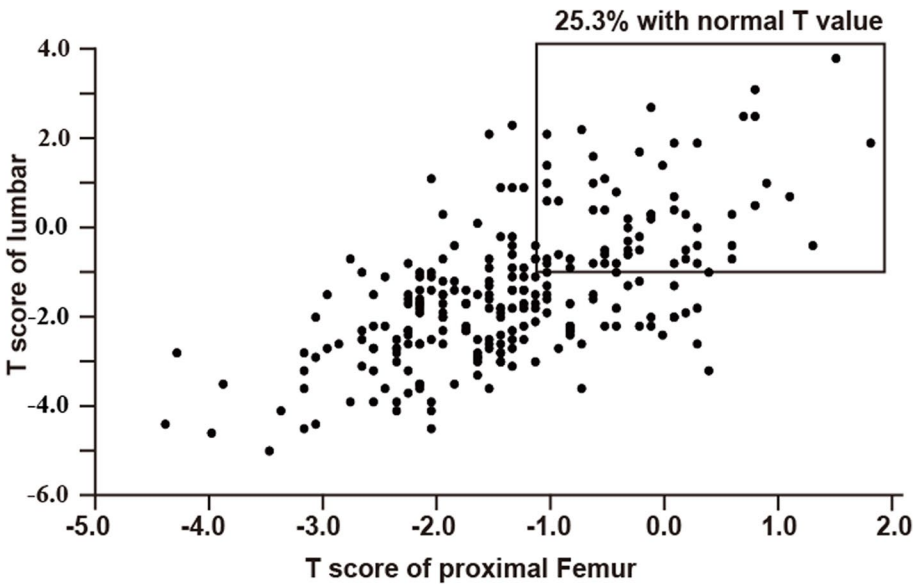

Fig. 1 T scores of the lumbar spine and proximal femur in patients awaiting TKA

that in the matched cohort (30.5% vs 28.9%), whereas the prevalence of osteopenia was 4.8% lower in the matched cohort (44.2% vs 39.4%). However, there was no significant difference in the prevalence of osteoporosis and osteopenia between patients awaiting TKA and the matched group ($\chi^2 = 2.603$, $p = 0.272$). Among patients over 65 years of age, 62/206 (30.1%) and 77/206 (37.4%) patients had osteoporosis and osteopenia, respectively, in the matched cohort.

Interestingly, although men in the awaiting TKA group had lower BMD (Fig. 4A and B), T scores were similar between the two groups ($P = 0.145$ for the lumbar spine and $P = 0.251$ for the proximal femur). Women in the matched control group also had higher BMD at the lumbar spine and proximal femur (Fig. 4C and D) but similar

Table 2 Prevalence of osteoporosis in patients awaiting TKA and the matched cohort

	KOA group			Matched Cohort		
	Men (*n* = 74)	Women (*n* = 175)	Total (*n* = 249)	Men (*n* = 74)	Women (*n* = 175)	Total (*n* = 249)
Normal	39(52.7%)	24(13.7%)	63 (25.3%)	39(52.7%)	40(22.9%)	79 (31.7%)
Osteopenia	24(32.4%)	86(49.1%)	110(44.2%)	30(40.6%)	68(38.9%)	98(39.4%)
Osteoporosis	11(14.9%)	65(37.1%)	76 (30.5%)	5(6.8%)	66 (38.3%)	72(28.9%)

Abbreviations: KOA knee osteoarthritis, *TKA* total knee arthroplasty

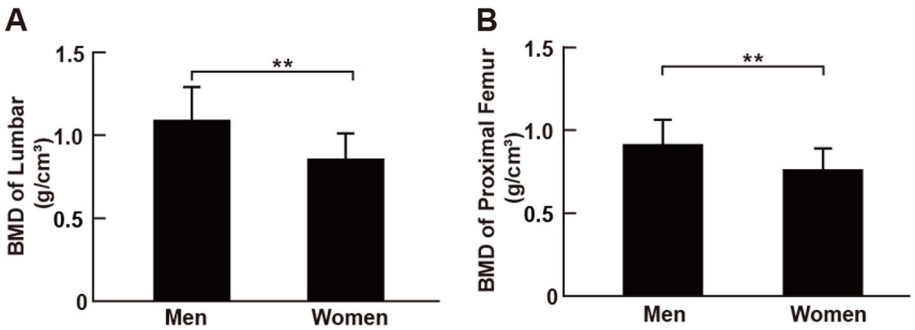

Fig. 2 BMD of men and women in patients awaiting TKA. **A** BMD of lumbar spine. **B** BMD of proximal femur. ** $P < 0.01$

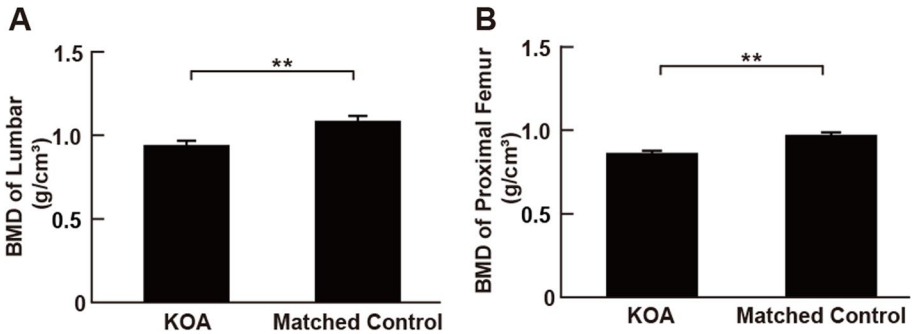

Fig. 3 BMD in patients awaiting TKA and the matched cohort. **A** BMD of lumbar spine. **B** BMD of proximal femur. ** $P < 0.01$

T scores for the lumbar spine ($P = 0.162$) and higher T scores for the proximal femur ($P < 0.001$).

Factors associated with osteoarthritis correlated with osteoporosis

To explore whether factors associated with osteoarthritis correlated with osteoporosis, K-L grades and WOMAC scores of osteoarthritis and status of osteoporosis were used for further analysis. The K-L grades of normal, osteopenia and osteoporosis patients are shown in Table 3. We found no significant difference ($P = 0.421$) in the status of osteoporosis among different K-L grades. In patients with K-L grade 4, 30.6% suffered osteoporosis. The three osteoporotic status groups did not differ significantly between the different radiological grade groups ($P = 0.982$). In addition, we compared BMD and T scores at different K-L grades, and we did not find any significant differences in BMD at the lumbar spine ($P = 0.734$) or proximal femur ($P = 0.876$) (Supplementary Figure 1). The WOMAC scores were also similar in different osteoporosis groups ($P = 0.656$) (Fig. 5). Therefore, K-L grades and WOMAC scores were not correlated with BMD or T scores.

Moreover, we explored factors associated with the T score and BMD and found that the T score and BMD were associated with sex, height, weight, and BMI but not with K-L grades or WOMAC scores (Table 4). Interestingly, mFTA scores were significantly correlated with

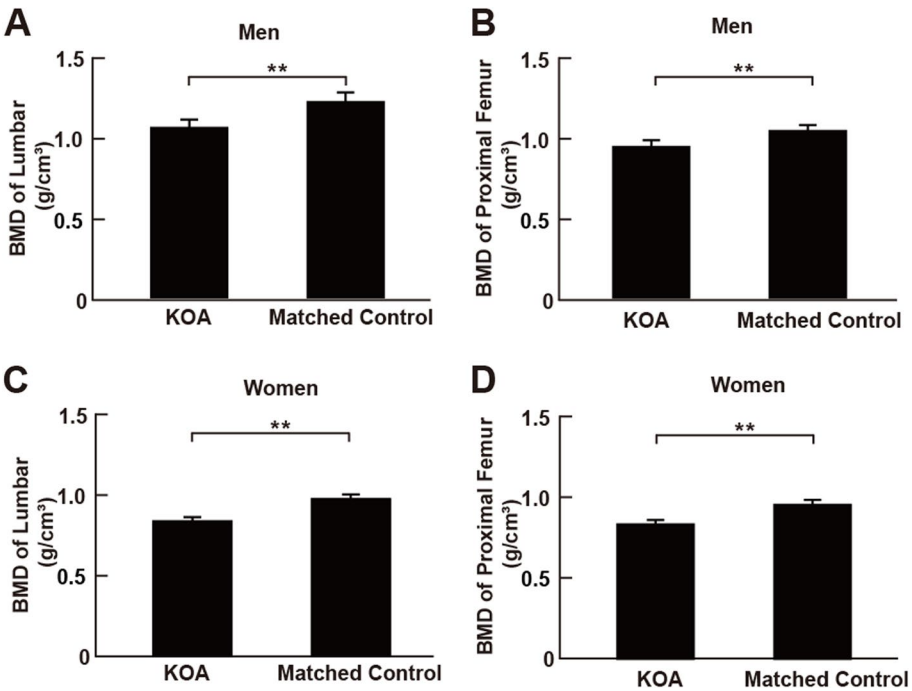

Fig. 4 BMD of men and women in patients awaiting TKA and the matched control group. **A** BMD of the lumbar spine in men; **B** BMD of the proximal femur in men; **C** BMD of the lumbar spine in women; **D** BMD of the proximal femur in women. ** $P < 0.01$

Table 3 K-L grades in normal BMD, osteopenia, and osteoporosis patients

	K-L grade			Total
	2	3	4	
Normal BMD	0	7	56	63
Osteopenia	0	12	98	110
Osteoporosis	1	7	68	76
Total	1	26	222	249

Abbreviations: *BMD* bone mineral density, *K-L grade* Kellgren-Lawrence grade

BMD and T scores, and some WOMAC subscores were found to be associated with BMD and T scores, as shown in Table 4.

Discussion

In this study, we found that the prevalence of osteoporosis was 30.5% in patients awaiting TKA, similar to the prevalence in the general population. In addition, neither the WOMAC score nor the K-L grade was associated with BMD or T score.

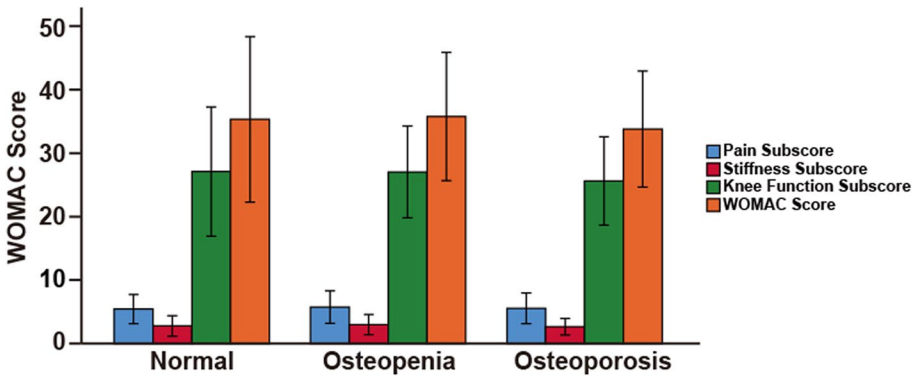

Fig. 5 WOMAC score and subscores in patients awaiting TKA grouped by osteoporosis. ** $P < 0.01$

Table 4 Correlation coefficient between BMD and T score with other factors

	Lumbar		Proximal femur	
	BMD	T Score	BMD	T Score
Sex	0.525**	0.431**	0.448**	0.285**
Height	0.501**	0.463**	0.394**	0.312**
Weight	0.478**	0.461**	0.419**	0.381**
BMI	0.221**	0.236**	0.240**	0.260**
K-L grade	0.032	0.011	−0.037	−0.066
WOMAC	0.047	−0.068	−0.018	0.017
Pain	−0.017	−0.003	−0.118	−0.099
Standing upright	−0.106	−0.121	−0.245**	−0.266**
Stiffness	0.035	0.051	−0.003	0.031
Function	0.038	0.061	−0.002	0.039
Sitting	0.219**	0.236**	0.216**	0.234**
ROM	−0.103	−0.141	−0.010	−0.038
mFTA	−0.210*	−0.179*	−0.191*	−0.181*

Abbreviations: *BMD* bone mineral density, *BMI* body mass index, *K-L grade* Kellgren-Lawrence grade, *mFTA* femorotibial angle, *ROM* range of motion, *WOMAC* Western Ontario and McMaster Universities Osteoarthritis Index

** $P < 0.01$

* $P < 0.05$

The prevalence of osteoporosis in patients awaiting TKA varies in different reports. In our study, we demonstrated that a large proportion of patients with end-stage KOA suffer from osteoporosis. It was found that 30.5% of patients awaiting TKA have osteoporosis, while 44.2% of patients have osteopenia. In patients with K-L grade 4, the percentage of osteoporosis (30.6%) was similar to the overall subjects. These data are comparable to previous reports. We summarized the prevalence of osteoporosis in Supplement Table 1. In addition, a recent systematic review also indicated that the prevalence varied from 8.4 to 59.8%, depending on the countries and participants [24]. It seems that the prevalence of osteoporosis is relatively lower in European countries than in Asian countries and may indicate the role of ethnicity and habits in osteoporosis. However, compared with another survey in China, our results were much lower than theirs (37.1% vs 59.8%) among women undergoing TKA, even though we were similar in age (70.2 ± 6.2 vs 69.7 ± 8.5). This may be due to the different living habits and environments between the two regions. Therefore, we recommend extensive investigations in China.

However, only a few studies have examined differences in the prevalence of osteoporosis between patients awaiting TKA and the general population. In our study, the prevalence of osteoporosis was similar to that of the general population when we utilized data from the Health Examination Center to create a cohort that could partially mimic the general population. In addition, compared with the report from the Chinese Center for Disease Control and Prevention, the prevalence of osteoporosis in patients over 65 years old awaiting TKA was similar to the general level (32.2% vs 32.0%) [23]. Similar to our results, Chang et al. reported that 40.1% of female patients waiting for TKA developed osteoporosis compared with 40.6% in the general population [20]. However, their research subjects focused only on women but did not include men. Based on our results and previous reports, we believe that patients awaiting TKA may have a similar prevalence of osteoporosis to the general population.

Interestingly, although the prevalence of osteoporosis was similar to that in the general population, BMD was significantly lower in the patients awaiting TKA than in the general population, both in men and women. The reasons for these results are complex. One possible reason is that pain and loss of function due to osteoarthritis may reduce daily activities, which play an important role in maintaining bone mass and lead to decreased BMD in the late stage of osteoarthritis. Some reports support this hypothesis. For example, in a national survey, Kim et al. reported that the relationship between osteoporosis and KOA was an inverted "U" and found that BMD was dramatically reduced among patients with K-L grade 4 [21]. However, more previous literature supports that BMD and osteoarthritis have opposite effects [4, 5, 25]. Therefore, the relationship and interaction between osteoarthritis and osteoporosis remains to be elucidated, and large prospective cohort studies rather than cross-sectional surveys will help answer this question.

Regarding whether factors of osteoarthritis were associated with osteoporosis, we found no correlation between BMD or T scores and K-L grades or WOMAC scores. This result is similar to Linde's report that there was no significant difference between K-L grades and T scores. However, Kim et al. reported that the BMD of the femoral neck and total hip decreased with increasing K-L grades (grades 2, 3, and 4), whereas the BMD of the lumbar spine increased with increasing K-L grades (grades 0, 1, and 2) [21]. Their findings differed from ours because we focused only on the patients awaiting TKA but not all stages of osteoarthritis. The WOMAC score can represent knee pain and function, which partially affect daily activities. Although we found no correlation between WOMAC total or subscores and osteoporosis, a study by Ha et al. showed that BMD was related to WOMAC stiffness with a weak correlation coefficient (0.087, $P < 0.001$) [26]. Furthermore, we found that the varus angle of the lower limb was associated with osteoporosis, which was also reported by other research showing that factors of osteoarthritis, such as knee varus deformity [8, 27] and

knee joint space narrowing [28], are associated with BMD.

Our research has some limitations. First, this is a single-center report, and its representation may be limited to certain regions. A large multicenter survey using a single diagnostic criterion of osteoporosis may help illustrate a more representative prevalence. Second, there may be bias in populations that represent the general population, as these populations may have a better financial condition to support their examinations at health examination centers. In addition, due to the lack of comorbidity data, knee function, and radiological assessment in the physical examination center, the cohort derived from the general population may be subject to bias. Last, this study only enrolled patients awaiting TKA, which represents the late stage of KOA. Therefore, it is difficult to provide evidence to explore the relationship between osteoporosis and different stages of osteoarthritis. Large prospective studies of different stages of KOA are still needed to elucidate the relationship between osteoarthritis and osteoporosis.

Conclusion

Osteoporosis coexists in patients with late-stage KOA. The prevalence of osteoporosis in patients awaiting TKA is similar to that in the general population, although patients awaiting TKA had lower BMD. K-L grades and WOMAC scores are not associated with BMD or T scores. However, the correlation between KOA and osteoporosis still needs further investigation. Because most patients are likely to achieve better function than before arthroplasty, future studies are needed to determine whether arthroplasty can delay the onset and progression of osteoporosis or promote BMD recovery.

Abbreviations

BMI	Body mass index
K-L grade	Kellgren-Lawrence grade
KOA	Knee osteoarthritis
mFTA	Mechanical femoral tibial angle
ROM	Range of motion
TKA	Total knee arthroplasty
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index score

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2

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Not applicable.

Authors' contributions

Study conception and design: LL and PF. Collection and assembly of data: LL, RH, ZXL, XG, YYL, HLZ, YLJ and PF. SPSS statistical analysis: LL and PF. Analysis and interpretation of data: LL and PF. Manuscript: LL, RH and PF. All authors approved the final version to be published.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The protocol of this cross-sectional study was approved by the ethics committees of the Second Affiliated Hospital of Wenzhou Medical University. Informed consent was obtained from all participates.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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