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ORIGINAL RESEARCH

Prevalence and Risk Factors of Osteoporosis in Chinese Postmenopausal Women Awaiting Total Knee Arthroplasty

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Background: Total knee arthroplasty (TKA) complications associated with low bone quality are challenging for orthopaedic surgeons to treat, but little is known about bone quality in Chinese postmenopausal women awaiting TKA. This study investigated the incidence of osteoporosis (OP) and explored the preoperative risk factors for OP in this population.

Methods: We retrospectively reviewed the data of Chinese postmenopausal women who were indicated for TKA between May 2017 and June 2020. The bone mineral density (BMD) of the hip and lumbar spine and multiple preoperative parameters were collected and analyzed. Binary logistic regression analysis was performed to identify independent risk factors for OP in this population.

Results: A total of 204 postmenopausal women with advanced knee OA were included in the study (age: 69.7±8.5 years; body mass index [BMI]: 25.5±4.0 kg/m2). The OP prevalence among all participants was 59.8%, and the patients aged 60–80 years had a significantly lower BMD than did the age/ethnicity-adjusted population. An age ≥60 years, a BMI<25, and the presence of a varus knee deformity were independent risk factors for preoperative OP in the postmenopausal women awaiting TKA.

Conclusion: The prevalence of OP in Chinese postmenopausal women awaiting TKA is higher than that in the age/ethnicity-adjusted normal population. An age ≥60 years, a BMI<25, and the presence of a varus knee deformity are independent risk factors that can be used to predict preoperative OP in this population.

Keywords: osteoporosis, postmenopausal women, total knee arthroplasty, Chinese, bone mineral density

Introduction

Total knee arthroplasty (TKA) has advanced significantly since it was developed. It ameliorates pain and improves the function of the knee in millions of patients suffering from knee osteoarthritis (OA) and greatly improves their quality of life.[1] However, with a steadily increasing surgery volume, multiple TKA-related complications are occurring, creating an enormous challenge for orthopaedic surgeons.[2] Decreased bone quality has been shown to increase the incidence of various TKA complications, such as periprosthetic fracture, osteolysis, and implant loosening/malposition.[3,4] Osteoporosis (OP) is regarded as the most common cause of low bone quality. Elderly/postmenopausal women comprise approximately 70–90% of TKA candidates;[5,6] moreover, this population is at high risk of OP development.[7–9]

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Anti-OP treatment before TKA has been shown to reduce the chance of TKA complications.[10] Therefore, for better outcomes in postmenopausal women awaiting TKA, it is necessary to evaluate and manage OP preoperatively.

Osteoporosis and osteoarthritis are two related diseases with different pathogeneses.[11] The exact interactive mechanism between them is complex and has not been well elucidated. Some studies have shown a positive correlation between the severity of OA and the level of bone mineral density (BMD) and that OA is a protective factor against OP,[12–14] while several researchers have instead suggested that OP exists in a considerable number of patients with advanced OA.[15,16] Dual-energy X-ray absorptiometry (DXA) scans of at least two bone sites are recommended by the International Society for Clinical Densitometry (ISCD) to diagnose osteoporosis based on the T-score. However, some studies have shown that the BMD region of interest (ROI) may be affected by orthopaedic diseases, thus resulting in the BMD not being correlated with OP and inconsistent diagnoses between different sites.[17–19] For women with advanced knee OA awaiting TKA, there is a lack of relevant evidence to determine which site can be used to appropriately evaluate OP in this population. Due to population aging, the number of Chinese postmenopausal women indicated for TKA is increasing, but little is known about the prevalence and independent risk factors for OP in this population.

More information on the preoperative bone status characteristics of Chinese postmenopausal women awaiting TKA may help surgeons select interventions more prudently and efficiently. The purposes of this study were to (1) investigate the prevalence of OP in Chinese postmenopausal women awaiting TKA, (2) determine the influence of the DXA examination site on OP detection and diagnostic discordance, and (3) identify preoperative risk factors for OP in this population to build an OP screening strategy.

Patients and Methods

Study Population

This retrospective, descriptive study was approved by the ethics committee of our hospital. All patient data were from one tertiary medical institute and treated with confidentiality. From May 2017 to June 2020, all patients indicated for TKA were routinely screened for OP using DXA 1 day before surgery. The data for these consecutive TKA candidates were searched in the electronic medical record system. The inclusion criteria were (1) postmenopausal women, (2) patients diagnosed with unilateral or bilateral advanced primary knee osteoarthritis who were scheduled for TKA, (3) patients who underwent standing anteroposterior/lateral X-ray scans of the affected knee and full-length lower limb radiography scans, (4) patients with a complete preoperative examination data of routine blood and serum biochemistry tests, and (5) patients who underwent left hip and lumbar spine DXA examinations preoperatively. The exclusion criteria were as follows: (1) patients diagnosed with secondary knee OA or OA-like diseases, such as septic arthritis, rheumatoid arthritis, gout, etc; (2) patients with a previous history of TKA; (3) patients who underwent lumbar spine or hip internal fixation/implantation or had severe spine OA, which may affect BMD measurements; (4) patients who previously had fractures affecting the lumbar spine or lower extremities; and (5) patients who were undergoing standardized anti-OP therapy.

DXA and BMD Analysis

All DXA examinations were conducted and analyzed by experienced and qualified operators. The areal BMDs (g/cm^2) of the lumbar spine (L1-L4, LS), proximal femur (PF), and femoral neck (FN) were obtained by a Discovery A scanner (Hologic Inc., Marlborough, MA, USA). The World Health Organization (WHO) classifications for osteopenia and OP were used for each bone site: normal (T-score greater than −1.0), osteopenia (T-score between −1.0 and 2.5), and osteoporosis (T-score below −2.5).[20] The white female peak BMD in the Discovery A built-in reference database was used for the T-score calculation. In accordance with the ISCD protocol,[21] the lowest T-score among multiple sites was considered the decisive T-score for a patient-level OP diagnosis. Discordance of the OP diagnosis between two sites was determined in a patient when the T-score of one site was indicative of OP and the T-score of another site was not. Hologic BMD data from the study by Zhang et al were used to compare the data from the population in this study with those of an ethnicity/age/sex-adjusted normal population.[22]

Preoperative Data Collection

Age, body mass index (BMI), comorbidities, medication use, and previous medical history were included in the demographic information. The laboratory test results obtained upon hospitalization for every participant were

collected, which included the hemoglobin level (g/L), lymphocyte count (10^9/L), prealbumin level (mg/L), total protein level (g/L), albumin level (g/L), serum calcium level (mmol/L), serum creatinine level (mmol/L), and estimated glomerular filtration rate (eGFR, mL/min/1.73 m^2). The OA grade of the affected knee was determined with the Kellgren-Lawrence (K-L) system. Bilateral OA was recorded when both knees of one patient were graded greater than K-L I according to the full-length lower limb radiograph. The knee with more severe symptoms and worse K-L grade was deemed the study knee for the patients with bilateral OA. The hip-knee-ankle (HKA) angle on the full-length lower limb radiograph (the angle formed by the mechanical femoral axis and mechanical tibial axis) was used to assess the coronal knee deformity: varus (HKA<177°), normal (177°≤HKA≤183°) and valgus (HKA>183°).[23] Knee contracture was determined when the study knee could not be fully extended actively or passively. Patellofemoral OA was defined when the study knee had a K-L grade greater than I on the lateral radiograph of the knee. Knee attrition, a severe deformity, was defined as bone loss in the medial or lateral knee compartment.[24]

Statistical Analysis

All data were analyzed with SPSS software (version 26.0; IBM, Chicago, IL). The Shapiro–Wilk test was used to assess the normality of the continuous variables. The variables were compared between groups using the independent *t*-test when the data were normally distributed. For the data with skewed distributions, the Mann–Whitney *U*-test was used for comparisons. The differences between categorical variables were assessed with the Pearson chi-square test. Binary logistic regression was conducted to identify the independent risk factors (odds ratio [OR] with 95% confidence interval [CI]) associated with OP (dependent variable) in postmenopausal women awaiting TKA, and the forward stepwise method was used to enter variables with a P-value<0.1, while variables with a P-value<0.05 remained in the model (independent variables: age, BMI, symptom duration, incidence of the bilateral knee OA, presence of a varus knee deformity, presence of a valgus knee deformity). P-values of less than 0.05 were considered statistically significant.

Results

After selection, a total of 204 postmenopausal women were included in this study. These women were mainly (79.42%) aged between 60–80 years, and 88.2% of them suffered from bilateral knee OA. The median symptom duration was eight years, and the mean ± standard deviation of age and BMI were 69.7±8.5 years and 25.5±4.0 kg/m^2. All the participants' study knees had at least K-L III grade OA, and 63.7% of all OA cases were considered severe (K-L IV). Only 4.9% of patients were classified as normal, whereas 59.8% of all women were categorized as having osteoporosis (Table 1). To further determine the age-related characteristics of OP distribution, age stratification was performed (Figure 1). There was a significantly lower incidence of OP (18.2%) and a higher incidence of normal case (13.6%) in the postmenopausal women aged <60 years than in the patients aged ≥60 years. In contrast, 63.1%, 67.9% and 60.0% of patients aged 60–70, 70–80 and ≥80 years were diagnosed with OP, respectively.

OP prevalence based on the DXA examination site is shown in Figure 2. There was an increase in OP incidence of PF and FN with patient aging, whereas the OP incidence of LS decreased after age 80. Compared with the OP prevalence at multiple sites, which is used as the gold standard for patient-level OP diagnosis proposed by ISCD, the OP incidence of LS showed no significant differences among all age groups, while the OP incidence rates in the PF and FN were significantly lower between the ages 60 and 80 years.

The discordance in OP diagnoses between different DXA exam sites is demonstrated in Table 2. When the T-score of the LS was indicative of OP, 56.76 and 76.58% of the

Table 1 Demographics and Characteristics of Women Awaiting TKA

Variables	n (%)
Age (years)	
<60	22 (10.78%)
≥60, <70	84 (41.18%)
≥70, <80	78 (38.24%)
≥80	20 (9.80%)
Knee OA side	
Double	180 (88.2%)
Single	24 (11.8%)
Kellgren-Lawrence grade of study side	
III	74 (36.3%)
IV	130 (63.7%)
Bone quality status based on the lowest T-score among multiple sites	
Osteoporosis	122 (59.8%)
Osteopenia	72 (35.3%)
Normal	10 (4.9%)

Abbreviations: TKA, total knee arthroplasty; OA, osteoarthritis.

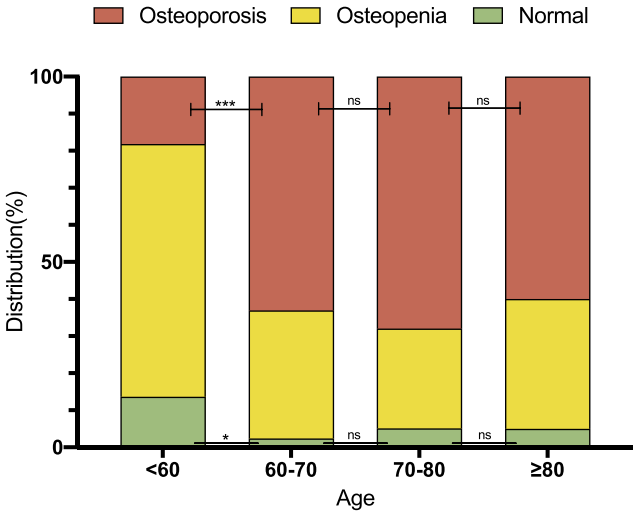

Figure 1 Distribution of bone quality status of different age groups. *P<0.05, ***P<0.001.
Abbreviation: ns, no significance.

T-scores for the FN and PF were not suggestive of the same diagnosis. Although there was less discordance between sites when the T-scores of the FN and PF were positive for OP, the absolute number of T-scores of these two sites positive for OP was much smaller than that of LS (58 and 28 vs 111).

The FN (Figure 3A) and LS (Figure 3B) BMDs for postmenopausal women of all age groups awaiting TKA were compared to those of an age/ethnicity/site-adjusted reference population of normal Chinese individuals. Both the FN and LS BMDs from the patients aged 60–80 years in this study were remarkably lower than those of the reference population.

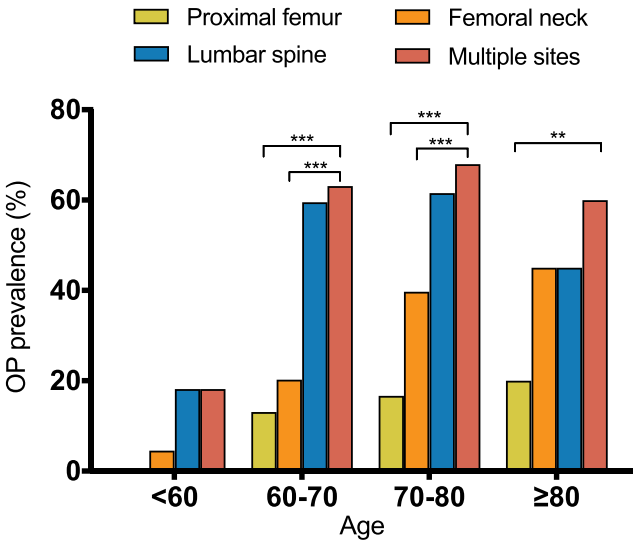

Figure 2 Osteoporosis prevalence based on different DXA examination sites. **P<0.01, ***P<0.001.
Abbreviation: OP, osteoporosis.

Table 2 The Exact Number of Different Sites Tested Positive for OP and Their Diagnostic Discordance

Site Positive for OP	Number	Percentage of Number of Site Negative for OP (n)		
		Femoral Neck	Proximal Femur	Lumbar Spine
Femoral neck	58	—	58.62% (34)	17.24% (10)
Proximal femur	28	14.29% (4)	—	7.14% (2)
Lumbar spine	111	56.76% (63)	76.58% (85)	—
Multiple sites	122	—	—	—

Abbreviation: OP, osteoporosis.

The descending trend with aging in the FN BMD was consistent between the two populations (Figure 3A), but the decreasing tendency in the LS BMD reached a plateau at the age of 60–70 years for both groups (Figure 3B).

According to the T-scores at multiple sites, the patients were classified into groups with OP or without OP, and then, the preoperative parameters were compared between the two groups (Table 3). The age (P=0.023) and the percentage of patients with varus knee deformities (P=0.025) were higher, and the BMI was lower (P=0.035) in the OP group, while the blood parameters and symptom duration showed no significant differences between groups. Binary logistic regression analysis (Table 4) revealed that an age ≥60 (OR=7.76, P<0.001), a BMI<25 (OR=1.85, P=0.048), and the presence of a knee varus deformity (OR=2.10, P=0.020) were independent risk factors associated with OP in postmenopausal women awaiting TKA.

Discussion

As the demand for total knee arthroplasty has increased to an unprecedented extent in China, perioperative complications associated with low bone quality are receiving more attention. The majority of TKA candidates are postmenopausal women, who are prone to poorer bone health and short of proper preoperative anti-osteoporosis management.[25,26] As the bone quality status of postmenopausal women awaiting TKA in China has been insufficiently studied, this study was mainly performed to investigate the prevalence and risk factors for preoperative OP in this population. We found that a significant proportion (59.8%) of women had evidence of OP, and 35.3% of patients had osteopenia. OP detection for several DXA

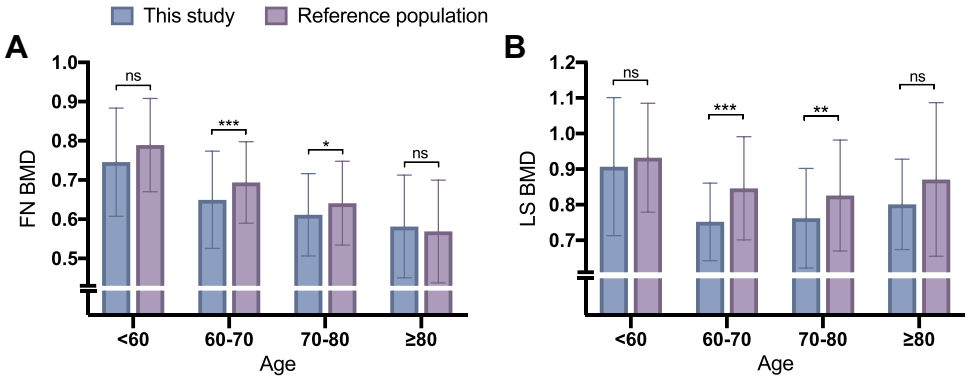

Figure 3 BMD of the femoral neck (**A**) and the lumbar spine (**B**) of different age groups compared to the age/ethnicity-adjusted reference population. *P<0.05, **P<0.01, ***P<0.001.

Abbreviations: BMD, bone mineral density; FN, femoral neck; LS, lumbar spine; ns, no significance.

sites and the discordance between them showed that the LS was a reliable BMD site for OP diagnosis in this population. Age, BMI, and the presence of varus knee deformity were found to be independent risk factors for predicting OP before TKA.

Several studies have reported the incidence of OP before TKA. In the non-Asian population, 9.6–33% of TKA candidates have been found to suffer from OP, regardless of the patient's sex,[16,27–30] and 35% of women awaiting TKA or total hip arthroplasty have been found to

Table 3 Comparison Between Non-OP and OP Women Awaiting TKA

Variables	Non-OP (n=82)	OP (n=122)	P-value
Demographics			
Age (years) *	67.85 (61.93, 74.85)	70.55 (65.48, 75.85)	**0.023**
BMI (kg/m^2)	26.21 ± 3.93	25.00 ± 4.07	**0.035**
Disease course			
Symptom duration (years) *	10.00 (5.00, 10.25)	8.00 (3.00, 10.00)	0.192
Blood nutritional marker			
Hemoglobin (g/L) *	122.00 (116.00, 129.50)	122.00 (115.00, 129.25)	0.885
Lymphocyte count (10^9/L) *	1.65 (1.40, 2.04)	1.67 (1.32, 2.03)	0.736
Prealbumin (mg/L)	213.16 ± 39.77	211.44 ± 43.89	0.777
Total protein (g/L)	68.19 ± 5.10	67.7 ± 5.04	0.509
Albumin (g/L)	41.28 ± 3.27	41.24 ± 2.90	0.916
Serum chemistry profile			
Ca^{2+} (mmol/L) *	2.26 (2.21, 2.33)	2.26 (2.21, 2.33)	0.859
Creatinine (mmol/L) *	60.00 (53.00, 66.50)	59.00 (52.00, 66.00)	0.824
eGFR (mL/min/1.73m^2) *	93.30 (86.45, 100.55)	91.95 (83.10, 98.58)	0.208
Incidence of OA-related parameters			
Bilateral knee OA	85.4% (n=70)	90.2% (n=110)	0.297
Varus deformity	56.1% (n=46)	71.3% (n=87)	**0.025**
Valgus deformity	20.7% (n=17)	15.6% (n=19)	0.343
Flexion contracture	41.5% (n=34)	41.8% (n=51)	0.961
K-L Grade IV	61.0% (n=50)	65.6% (n=80)	0.503
Patellofemoral OA	74.4% (n=61)	75.4% (n=92)	0.869
Attrition	30.5% (n=25)	26.2% (n=32)	0.506

Notes: Variables with "*" were demonstrated in median with interquartile range and compared between groups using Mann–Whitney *U*-test. Bolded values indicate statistical significance (P<0.05).

Abbreviations: OP, osteoporosis; TKA, total knee arthroplasty; BMI, body mass index; Ca^{2+}, calcium; eGFR, estimated glomerular filtration rate; OA, osteoarthritis; K-L, Kellgren-Lawrence.

Table 4 Binary Logistic Regression Analysis for the Determination of Independent OP Risk Factors in Postmenopausal Women Awaiting TKA

Variables	Odds Ratio (95% CI)	S.E.	Wald	P-value
Age (years) ≥60	7.76 (2.49–24.18)	0.58	12.51	**<0.001**
BMI (kg/m2) <25	1.85 (1.01–3.40)	0.31	3.91	**0.048**
Varus deformity	2.10 (1.13–3.92)	0.32	5.43	**0.020**

Note: Bolded values indicate statistical significance (P<0.05).
Abbreviations: OP, osteoporosis; TKA, total knee arthroplasty; BMI, body mass index; CI, confidence interval; S.E., standard error.

have OP.[15] In contrast, two Korean studies have reported OP incidence rates of 40.1 and 53.4% among women indicated for TKA.[26,31] The prevalence of OP in the Chinese women awaiting TKA in our study was higher (59.8%) than that in women of other ethnicities, especially when the patients were aged ≥60 years (60–68%). We speculate the bone health of Chinese women awaiting TKA is lower because of the ethnic BMD variance caused by genetics, physical activity levels, diet, and lifestyle factors, as Zhang et al showed that Chinese individuals have lower systematic BMD values than do non-Hispanic White, Japanese and Korean individuals.[22]

In addition to the ethnic differences, lower FN and LS BMDs were found in the women aged 60–80 years awaiting TKA than in the ethnicity/age-adjusted population (Figure 3A and B). The OP incidence of normal Chinese women aged ≥50 years ranges from 24.6% to 31.2%,[22,32,33] which is also much lower than that reported in our study. The difference may indicate a positive correlation between knee OA and OP. Im et al found that a higher degree of knee OA was associated with a lower BMD.[34] A low level of physical activity related to pain caused by advanced knee OA may lead to disuse osteoporosis. Although some investigators have shown an inverse relationship between knee OA and OP,[35,36] the study subjects were mostly Caucasian, who have significantly higher BMI values and different lifestyles than do their Chinese counterparts, and mild or moderate knee OA (KL-I/II) cases were often included in their studies, which may affect the results. The interesting phenomenon that the LS BMD of the included patients and the reference population increased after age 80 (Figure 3B) was likely caused by the natural degenerative OA change in the lumbar spine with aging.

Discordance in OP diagnoses between different DXA skeletal sites is common, and five etiologic types (physiologic, pathophysiologic, anatomic, artifactual, and technical) have been proposed.[19] Over 50% of OP diagnostic discordance has been found between the LS and FN in the normal Chinese population,[32] which is consistent with the findings of our study (Table 2). A large-scale study by Moayyeri et al showed that lower BMD for LS was more prevalent than hip in community-based individuals,[37] and they proposed that the higher velocity of bone loss at trabecular bones (typical of LS) than cortical bones (typical of FN/PF) in the postmenopausal state could be the main reason for OP diagnostic discordance. In our study, the OP prevalence based on LS in all age groups was not significantly different from that based on multiple sites, while the OP prevalence based on FN was much smaller (Figure 2), suggesting the LS alone might be used as a reliable DXA exam site for OP diagnosis in Chinese postmenopausal women awaiting TKA.

Several risk factors, including age, sex, and BMI, are associated with OP in the normal Chinese population,[38] but OP predictors specific for Chinese postmenopausal women awaiting TKA have rarely been investigated. Our study showed that the presence of a varus knee deformity was an independent risk factor for OP in this population (Tables 3 and 4), while other preoperative parameters were of little predictive value. From an anatomical perspective, an increased degree of knee varus is correlated with a larger femoral neck-shaft angle, which has been shown to be related to lower hip stresses.[39,40] The lower hip BMD possibly caused by the decreased hip stresses may partly explain our finding of the varus knee deformity as an independent OP risk factor. Moreover, Chang et al demonstrated that the degree of varus knee malalignment is significantly associated with the severity of pain and functional decline in advanced knee OA,[41] suggesting the positive relationship between varus knee and OP, to some extent, might be correlated with the decreased physical activity caused by knee function loss in TKA candidates.

The blood nutritional markers measured showed no significant differences between groups in this study, although nutritional supplementation has been shown to correlate with a higher BMD.[42] This result may suggest that nutritional status plays a limited role in developing OP

in this population, while the estrogen depletion caused by menopause and aging could be the major determinant of OP development.[43] Future studies are needed to determine the exact role of various blood parameters, including bone turnover markers and vitamin D, in the pathophysiology of OP in patients awaiting TKA.

Patients indicated for TKA are usually given inadequate attention for OP screening.[29,44] Moreover, subjects undergoing TKA may experience significant bone loss in the first 1 to 3 years postoperatively.[45,46] Given the high prevalence of preoperative OP in the subjects of our study, neglected postmenopausal women awaiting TKA may be more likely to suffer from OP-related complications. However, preoperative anti-OP treatment has been shown to lower the risk of revision and preserve periprosthetic BMD after TKA.[10,47,48] Therefore, we propose that postmenopausal women aged ≥60 years awaiting TKA who have a BMI<25 and varus knee deformity are recommended for OP screening preoperatively.

Although the COVID-19 pandemic may have influenced TKA services,[49,50] all elective TKA surgeries were canceled from February to March 2020 (the most severe period of the epidemic in China) in our hospital, and DXA protocol remained the same for all TKA candidates from April to June 2020. Therefore, we believe the pandemic has had a limited impact on the results of this study.

There are some limitations of our study. First, this is a retrospective study. Although the subjects were continuously included, the number of patients in each age group could not be matched, which may introduce selection bias. Second, some functional parameters of the knee, such as the WOMAC (The Western Ontario and McMaster Universities Osteoarthritis Index) score, were not accessible for some participants. Therefore, information about symptom-related differences between groups is not available. Third, data on bone turnover markers, vitamin D and calcium intake were not all available for the included subjects, making the analysis of these parameters between groups unfeasible. Finally, the generalizability of the results is limited because of the moderate sample size of this single-center study.

Conclusion

In summary, for Chinese postmenopausal women awaiting TKA, the prevalence of OP is higher than that in age/ethnicity-adjusted normal populations. The lumbar spine may serve as a reliable DXA exam site for OP diagnosis, while an age ≥60 years, a BMI<25, and the presence of varus knee deformity are independent risk factors that can be used to predict preoperative OP in this population.

Data Sharing Statement

The data are available upon reasonable request.

Ethical Approval

This study was approved by the ethics committee of the First Affiliated Hospital of Chongqing Medical University (No. 2020-642). Written informed consent was not needed due to the retrospective nature of this study. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki declaration and its later amendments or comparable ethical standards.

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Disclosure

The authors report no conflicts of interest in this work.

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