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Unrecognized Osteoporosis Is Common in Patients With a Well-Functioning Total Knee Arthroplasty

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ABSTRACT

Background: Peri-prosthetic fractures after total knee arthroplasty (TKA) are associated with poorer outcomes and high costs. We hypothesize that osteoporosis is under-recognized in the TKA population. The purpose of this study is to report osteoporosis prevalence in a healthy cohort of patients with well-functioning TKA and to compare prevalence between males and females.
Methods: This study is a cross-sectional study of 30 adults (15 males/15 females) aged 59-80 years without known bone health issues who volunteered to undergo routine dual-energy X-ray absorptiometry 2-5 years (average 3.2 ± 0.8) after primary unilateral TKA. These data plus clinical risk factors were used to estimate fracture risk via the Fracture Risk Assessment Tool and skeletal status (normal, osteopenic, osteoporotic) was determined based on the World Health Organization definition. The National Osteoporosis Foundation criteria for treatment were applied to all patients.
Results: Six of 30 (20%) patients had T-score ≤ -2.5. Eighteen of 30 (60%) patients had T-score between -1 and -2.5 and 6 (20%) patients had T-score ≥ -1. Five patients with normal or osteopenic bone mineral density (BMD) had occult vertebral fractures. Eleven of 30 (36.7%) patients met National Osteoporosis Foundation criteria for pharmacologic treatment.
Conclusion: The prevalence of occult osteoporosis meeting treatment guidelines after TKA is substantial in this sample (36.7%). BMD and osteoporosis prevalence are similar between men and women. This underappreciated prevalence of osteoporosis may contribute to peri-prosthetic fracture risk. Arthroplasty surgeons and bone health specialists must be aware of post-operative changes in bone density. These data support the further study of post-operative osteoporosis and consideration of routine BMD screening after TKA.
Level of Evidence: III.

Poor bone health is common in total knee arthroplasty (TKA) patients and is associated with poorer outcomes [1–8]. Furthermore, peri-prosthetic fractures are becoming epidemic and almost always have a fragility fracture mechanism. This suggests a relationship between peri-prosthetic fracture and osteoporotic bone. One explanation for the occurrence of peri-prosthetic fractures is that bone mineral density (BMD) decreases in the ipsilateral femur by up to 16% within 2 years after TKA (meta-analysis in submission).

Dual-energy X-ray absorptiometry (DXA) is the current clinical gold standard to measure BMD and diagnose osteoporosis. In 1994, the World Health Organization defined osteoporosis as a T-score ≤ -2.5, osteopenia between -1.0 and -2.5, and normal ≥ -1.0 as measured by DXA. However, less than 50% of patients with fragility fractures have a T-score of ≤ -2.5 [9]. Consequently, major efforts have been made to improve identification of those that do not have osteoporosis by DXA, but are nonetheless at

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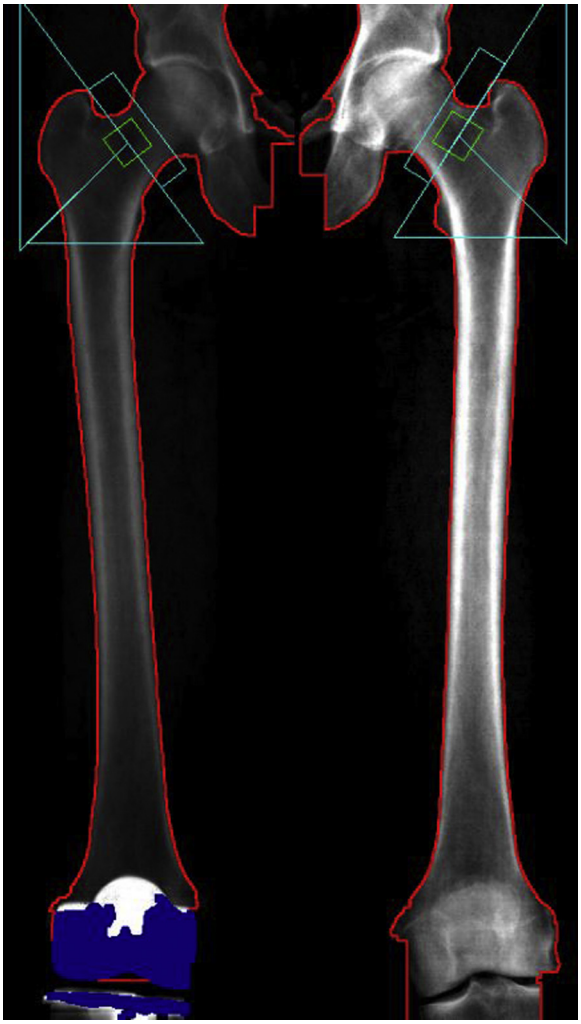

Fig. 1. Example of standard clinical hip BMD scanning in a patient with total knee arthroplasty.

elevated fracture risk. Tools like the Fracture Risk Assessment Tool (FRAX), which includes clinical risk factors for fracture and the trabecular bone score (TBS), which is a surrogate measure of bone microarchitecture, help facilitate fracture risk assessment. The addition of these tools has allowed clinicians to better determine fracture risk in osteopenic patients. Consequently, recent guidelines are moving away from using T-scores as the singular tool to determine therapeutic intervention threshold. The presence of a prior fracture identifies an individual as being at high fracture risk and is considered an indication for pharmacologic treatment by the National Osteoporosis Foundation (NOF) [10].

The senior authors observed that patients with peri-prosthetic fractures around TKAs have poor bone quality and performed a pilot method standardization and precision study using DXA to quantify BMD along the entire femur after TKA [11]. In this study, patients had standard DXA and, in this cohort, a high prevalence of osteoporosis and occult vertebral fractures was observed.

The main study question is: what is the prevalence of osteoporosis in a healthy cohort of patients after TKA? Our hypothesis is that osteoporosis is highly prevalent and under-recognized. We also aim to compare osteoporosis prevalence between males and females, and we hypothesize that it will be more prevalent in females. This study will emphasize to orthopedic surgeons the importance of assessing bone quality and assuring arthroplasty patients are receiving appropriate screening and treatment if indicated.

Methods

The study was approved by the Institutional Review Board and conducted in compliance with federal and local regulations. Thirty adults (15 males/15 females) aged 59-80 years with a unilateral primary TKA done at our university-based tertiary referral center were recruited. Sample size was selected based on that required for routine clinical DXA precision assessment. Thus, to allow calculation of precision as recommended by the International Society for Clinical Densitometry, 30 subjects were recruited [12]. Letters were sent to 84 patients from our department joint registry who pre-screened by medical record review to meet eligibility. Inclusion

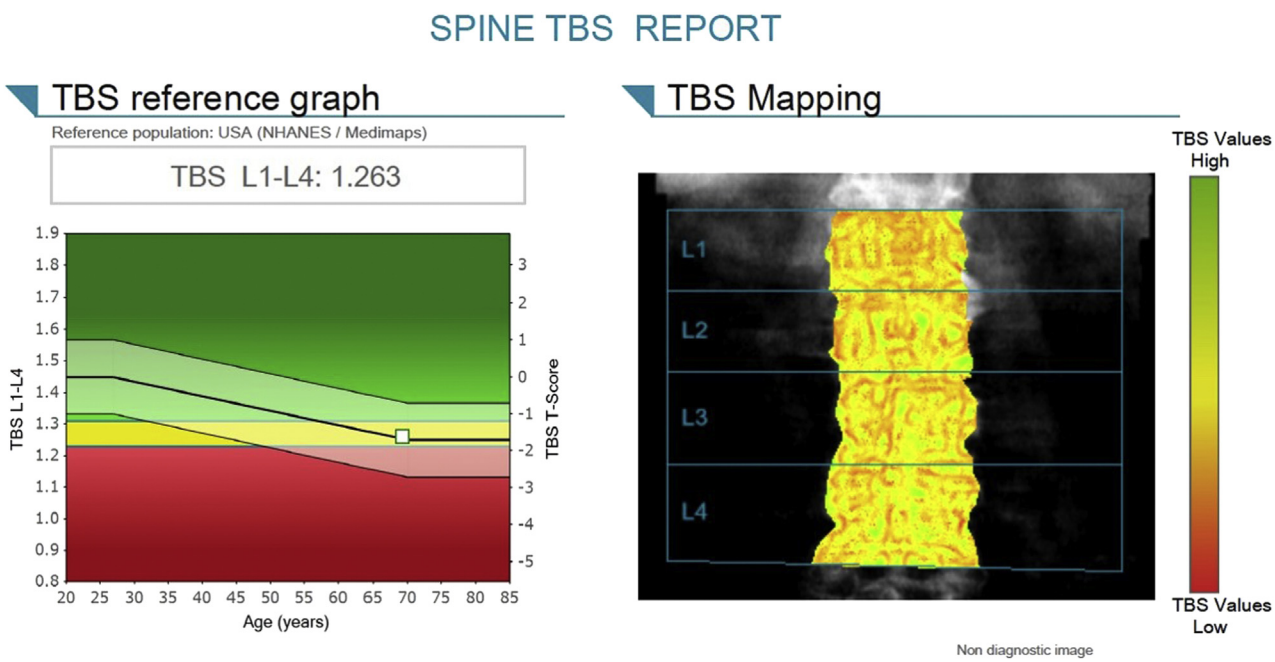

Fig. 2. Example report of spine TBS scoring and mapping.

Table 1
Clinical Risk Factors Included in the FRAX Tool [13].

1. Age
2. Gender
3. BMI
4. Previous fracture[a]
5. Parent fractured hip
6. Current smoking
7. Glucocorticoid use[b]
8. Rheumatoid arthritis
9. Secondary osteoporosis[c]
10. Alcohol 3 or more units per day
11. Femoral neck BMD, when available (g/cm^2)

BMI, body mass index; BMD, bone mineral density; FRAX, Fracture Risk Assessment Tool.
[a] Previous fracture in adult life occurring spontaneously, or a fracture arising from trauma which, in a healthy individual, would not have resulted in a fracture.
[b] Equivalent to 5 mg prednisolone daily currently or for >3 mo in the past.
[c] Secondary cause of osteoporosis: type 1 diabetes, osteogenesis imperfecta, untreated long-standing hyperthyroidism, hypogonadism or premature menopause, chronic malnutrition, or malabsorption and chronic liver disease.

criteria were patients who were 2-5 years post-surgery with excellent function as indicated by 10-point Visual Analogue Scale pain score less than 3 or 12-Item Short Form Survey physical component summary greater than 40 at the most recent follow-up. Exclusion criteria included previous hip or knee arthroplasty, previous lower extremity fracture requiring implants in the ipsilateral limb, and prolonged immobilization of the contralateral extremity. Patients with previous osteoporosis medication use, previous hormone replacement use, known metabolic bone disease, or potential secondary causes of osteoporosis (ie, malabsorption, glucocorticoid use, tobacco use) were excluded.

All patients underwent standard clinical lumbar spine, hip, and forearm BMD scanning with TBS and vertebral fracture assessment (VFA) with a Lunar iDXA densitometer (GE Healthcare, Madison, WI) (Figs. 1 and 2). All scans were acquired and analyzed in the standard clinical manner per manufacturer recommendations by one of the senior authors under the supervision of an International Society for Clinical Densitometry-certified technologist. Vertebral fractures were identified by review of the VFA images by one physician (N.B.) using the Genant visual semi-quantitative approach. These data plus clinical risk factors gathered via chart review from the institution's electronic medical record (Table 1) were used to estimate fracture risk via FRAX and skeletal status (normal, osteopenic, osteoporotic) was determined based on the World Health Organization definition. The NOF criteria for treatment were applied to all patients (Table 2).

Paired *t*-tests were used to compare demographic and BMD differences between males and females (JMP Pro v13, Carey, NC).

Results

Thirty patients (15 males/15 females) with a mean age of 68 years (range 59-80) responded to the mailed letter and participated in the study (Table 3) (52 did not respond, 2 screen-failed due to prior lower extremity fracture/implants). The average time from surgery was approximately 3 years. The average BMD at L1-L4, femoral neck, total proximal femur, and one-third radius were 1.335 (standard deviation 0.27), 0.904 (0.11), 0.941 (0.10), and 0.789 g/cm^2 (0.11), respectively. There was no significant difference between males and females in BMD at L1-L4, femoral neck, and total proximal femur, but females had significantly lower BMD at the distal one-third radius (0.989 vs 0.789 g/cm^2, $P < .0001$).

Table 2
NOF Guidelines for Pharmacologic Treatment of Osteoporosis [10].

T-score ≤2.5 at the femoral neck or spine[a]
History of hip or vertebral fracture
T-score between −1 and −2.5 at the femoral neck or spine AND a 10-y risk of hip fracture ≥3% or major osteoporotic fracture ≥20%

NOF, National Osteoporosis Foundation.
[a] After appropriate evaluation to exclude secondary causes.

Table 3
Demographics, BMD, and VFA Data of all Subjects.

	Male (n = 15)	Female (n = 15)	Total (n = 30)	*P* Value[a]
Age (y)	67.1 (5.2)	68.6 (5.5)	67.9 (5.3)	.44
BMI (kg/m^2)	30.1 (4.3)	29.9 (3.7)	30.0 (3.9)	.90
Time post-surgery (y)	3.3 (0.8)	3.3 (0.8)	3.3 (0.7)	.99
L1-L4 BMD (g/cm^2)	1.365 (0.20)	1.335 (0.27)	1.349 (0.24)	.73
Femoral neck BMD (g/cm^2)	0.942 (0.14)	0.904 (0.11)	0.923 (0.13)	.41
Total proximal femur BMD (g/cm^2)	1.003 (0.13)	0.941 (0.10)	0.972 (0.12)	.15
One-third radius BMD (g/cm^2)	0.989 (0.10)	0.789 (0.11)	0.889 (0.14)	<.0001
Lowest T-score (hip, spine, or one-third radius)	−1.2 (1.01)	−1.5 (0.97)	−1.4 (1.0)	.35
T-score ≤ −2.5	1	4	5	
Vertebral fracture	4	2	6	

Data are presented as mean (standard deviation).
BMD, bone mineral density; VFA, vertebral fracture assessment; BMI, body mass index.
[a] Comparison of males vs females.

Six of 30 (20%) patients had T-score ≤ −2.5. Eighteen of 30 (60%) patients had T-score between −1 and −2.5 and 6 (20%) patients had T-score ≥ −1. Five patients (1 male, 4 females) had a lowest T-score among average L1-L4 and proximal femur less than −2.5. Six patients (4 males, 2 females) had a vertebral fracture on VFA, 5 of which had normal or osteopenic bone by T-score.

The average FRAX risk of major osteoporotic fracture was 9.1% ± 3.7 and hip fracture was 1.5% ± 1.5. No patients had a major osteoporotic fracture risk greater than 20% but 4 had a hip fracture risk greater than 3%. After adjusting the FRAX calculation with TBS data, 2 additional (6 total) patients had hip fracture risk greater than 3%.

Eleven of 30 (36.7%) patients met NOF criteria for pharmacologic treatment. Four patients had a previous hip or vertebral fracture (Table 4). Three patients had a previous hip or vertebral fracture and a FRAX risk of hip fracture greater than 3%. Two patients had a lowest T-score less than −2.5 and FRAX risk of hip fracture greater than 3%. One patient had a lowest T-score less than −2.5 as the lone indication for treatment. One patient met 3 indications (previous hip or spine fracture, FRAX risk of hip fracture greater than 3%, and lowest T-score less than −2.5).

Discussion

The prevalence of occult osteoporosis meeting treatment guidelines after TKA in this sample of well-functioning patients is substantial (36.7%). This prevalence is likely a conservative estimate as this sample was selected to not have bone health problems or secondary causes of osteoporosis. This indicates that greater than one-third of TKA patients are potentially at elevated risk for periprosthetic fracture and other complications related to osteoporosis. Based on NOF guidelines, these patients would be indicated for anti-osteoporosis medications. In a separate study, our group found the rate of pre-operative osteoporosis prior to TKA to be 23% (Journal of Arthroplasty, accepted for publication). This difference (36.7% post-op vs 23% pre-op) suggests that there is interval decrease of overall BMD following TKA. Additionally, population-based studies have found osteoporosis prevalence in US adults over age 50 to be 10.3%, indicating that arthroplasty patients are disproportionately affected by osteoporosis [13]. The results of this study show BMD to be equal in men and women following TKA (apart from the distal one-third radius BMD being lower in

Table 4
Indications for Osteoporosis Pharmacotherapy in Patients Meeting NOF Criteria for Anti-Osteoporosis Medications (n = 11).

Indication	Previous Hip or Spine Fracture	FRAX Hip >3% or MOF >20%	T-Score ≤ −2.5	Previous Hip or Spine Fracture AND FRAX Hip >3% or MOF >20%	FRAX Hip >3% or MOF >20% AND T-Score ≤ −2.5	Previous Hip or Spine Fracture AND FRAX Hip >3% or MOF >20% AND T-Score ≤ −2.5
Number of patients	4	0	1	3	2	1

FRAX, Fracture Risk Assessment Tool; MOF, major osteoporotic fracture; NOF, National Osteoporosis Foundation.

women), whereas women in the general population are more likely to have lower BMD in the hips and spine as well [10].

Treatment with anti-osteoporosis medications has demonstrated clinical benefit following total joint arthroplasty. Bisphosphonate administration has been found to lower risk of fracture after total joint arthroplasty [14] as well as decrease revision rates after total hip arthroplasty (THA) [15]. A recent meta-analysis of 4 studies found long-term use of bisphosphonates to correlate with reduced revision rates after THA and TKA [16]. Radiographically, post-operative zoledronic acid infusion was found to maintain peri-prosthetic BMD following cementless THA [17] while teriparatide administration after TKA also increased peri-prosthetic BMD [18]. A meta-analysis of randomized controlled trials showed risedronate to be associated with significantly reduced femoral BMD loss after THA [19]. The body of literature is in need of larger, population-based research, but one study of nearly 400,000 total joint replacements found that the revision rate in TKA patients on post-operative bisphosphonates was half that of those not on bisphosphonates [20].

Osteoporosis is a systemic disease that reflects total body bone health. The effect of surgery on local bone is not well-known and may further increase the risk of post-operative complications. We conducted a meta-analysis of studies reporting peri-prosthetic BMD after TKA and found that BMD in the ipsilateral femur decreases by 15% in the first post-operative year, and this is sustained at 2 years [21]. Therefore, the BMD measured by standard DXA at the lumbar spine, hip, and distal radius may not represent the peri-prosthetic BMD. Arthroplasty surgeons and bone health specialists must be aware of post-operative changes in bone density and take this into consideration when indicating patients for surgery.

Limitations of this study include its relatively small sample size and narrow inclusion criteria. However, the criteria were intentionally selected to profile a group of patients that were doing well after surgery and thought not to be at increased risk of complication. Our study was conducted at a tertiary referral center and may not be generalizable to more community-based practices.

Conclusion

The current study finds that the prevalence of occult osteoporosis in patients with well-functioning TKA is substantial. The clinical implications of post-operative osteoporosis are under investigation but may increase the risk of peri-prosthetic fracture, subsidence, aseptic loosening, and revision surgery. The authors recommend the use of NOF screening guidelines to initiate bone health screening in select arthroplasty patients, both pre-operatively and post-operatively. Further research is required to investigate the utility and cost-effectiveness of regular BMD screening after TKA. These data support the further study of post-operative osteoporosis and consideration of BMD screening after TKA.

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