


CLINICAL ARTICLE

Medium Activity Prevents Periprosthetic Bone Mass Loss in the Medial Metaphyseal Region of the Tibia after Posterior-Stabilized TKA: A 5-Year Follow-up Study of 110 Knees

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Objective: The bone mass around the prosthesis plays an important role in the stability of the prosthesis. This study aimed to assess the effect of postoperative activity on bone mineral density (BMD) in the proximal tibia 5 years after total knee arthroplasty (TKA). To provide a scientific guidance for postoperative functional exercise.

Methods: 110 patients underwent unilateral primary TKA were divided into three groups based on the University of California Los Angeles (UCLA) activity scale: low activity group (LA group, UCLA = 4, 5); medium activity group (MA group, UCLA = 6, 7); and high activity group (HA group, UCLA = 8, 9). The primary observation was a comparison of the BMD and BMD change percentage (Δ BMD (%)) in the periprosthetic tibia among the LA, MA and HA groups at 1 year, 3 years and 5 years. The secondary observations were radiographic evaluation (prosthetic stability, periprosthetic fractures, aseptic loosening and periprosthetic joint infection) and clinical evaluation (Knee Society Score (KSS), visual analogue score scores and range of motion (ROM)). A one-way ANOVA was used to compare the clinical scores and BMD among the three groups.

Results: The BMD of medial region decreased by 10.80%, 12.64%, 13.61% at 1, 3, and 5 years respectively; these were 5.72%, 6.26%, 7.83% in lateral region and 1.42%, 1.78%, 3.28% in diaphyseal region. For medial metaphyseal region, the BMD of the MA group was significantly greater than that of the LA and HA groups at 1 and 3 years (108.9 ± 5.2 vs. 106.1 ± 6.69 vs. 105.4 ± 5.2 and 108.5 ± 6.0 vs. 101.2 ± 6.76 vs. 103.0 ± 6.8 , $P < 0.01$ and $P < 0.001$), and the BMD changes (Δ BMD (%)) in the MA group were significantly smaller than those in the LA and HA groups (8.75 ± 5.36 vs. 11.92 ± 5.49 vs. 12.70 ± 5.21 and 9.11 ± 5.11 vs. 16.04 ± 4.79 vs. 14.82 ± 4.26 , $P < 0.01$ and $P < 0.001$).

Regarding secondary observations, all of the prostheses were assessed as stable, without periprosthetic fractures, aseptic loosening and periprosthetic joint infection. Regarding KSS scores, there was no significant difference among the three groups. However, the VAS and ROM of the HA group were better than those of the MA and LA groups (1.65 ± 0.79 vs. 2.63 ± 0.77 vs. 3.00 ± 1.17 , $p < 0.001$, and 111.90 ± 9.17 vs. 110.20 ± 6.78 vs. 102.90 ± 8.48 , $P < 0.001$).

Conclusion: Medium activity prevented periprosthetic bone loss in the medial metaphyseal region of the tibia after posterior-stabilized TKA, and moderate-intensity exercise is recommended for patients after TKA to reduce periprosthetic bone loss.

Key words: Activity level; Bone loss; Bone mineral density; Prosthetic loosening; Total knee arthroplasty

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Received 26 May 2021; accepted 8 June 2022

Orthopaedic Surgery 2022;14:2210-2218 • DOI: 10.1111/os.13386

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Introduction

Total knee arthroplasty (TKA) is a common procedure to treat patients with knee osteoarthritis. Prosthesis subsidence and aseptic prosthesis loosening are the main reasons for total knee arthroplasty revision, which bring great pain and heavy burden to patients. The TKA revision rate at 10 years as reported in the major arthroplasty registries was approximately 5%.¹ TKA has a good postoperative efficacy, but postoperative prosthesis loosening will seriously reduce the postoperative rehabilitation effect, which is an important factor leading to postoperative knee pain and reducing the satisfaction rate of patients. Aseptic prosthesis loosening usually occurs in patients with osteoporosis or decreased bone mineral density around the prosthesis.

Periprosthetic bone quality is an important factor in maintaining prosthesis stability and preventing prosthesis migration, and periprosthetic bone loss increases the risk of prosthesis loosening and revision rates. Bone mineral density (BMD) is an important measure of bone strength and quality.^{2,3} BMD is usually used to measure bone quality in clinical studies. Soininvaara *et al.*⁴ reported on 69 patients who underwent TKA with a follow-up of 1 year that an average decrease in bone density of 17.1% (mean range of 12.1%–22.8%) was measured adjacent to the prosthesis at the 12-month follow-up. Murahashi *et al.*⁵ reported on 28 patients in a prospective cohort study that the BMD of the proximal medial tibia decreased drastically at 12 months after TKA (–19.7%) in the control group. Other studies found that the bone mineral density of the proximal medial tibia decreased drastically by 19.7% at 12 months after TKA, and there was a rapid and significant 15% decrease in BMD in the first 6 months to 24 months after TKA.⁶ Bone loss after total knee arthroplasty may lead to periprosthetic loosening and fractures. Therefore, how to reduce bone loss and increase bone mass is a very important topic.

Bone mass and bone density are related to multiple factors, such as age, sex, body weight, muscle strength, and activity level.⁷ There are studies suggesting that activity level is an important factor affecting bone density. Troy *et al.*⁸ declared that physical activity is an important contributor to bone quality and high-impact exercises such as jumping or hopping, or resistance training combined with high- or odd-impact activities, are most consistently effective for bone. Highly active patients had increased survival at the 5-year minimum follow-up compared to lower activity patients after TKA.⁹ Many studies have shown that patient activity level improves after TKA and many patients do return to sports.^{10,11} However, the impact of a patient's activity level following TKA remains controversial, with some surgeons concerned about increased polyethylene wear, aseptic loosening, and revisions, and other surgeons supported higher activity level to improve life quality. Little is known about the effect of patient activity on bone quality and bone mass of knee after TKA.

Ng *et al.*¹² reported that older men who engaged in high-intensity exercise maintained greater BMD, indicating that appropriate physical exercise was beneficial to maintain bone density. Gallo *et al.*¹³ reported that high levels of physical activity and a high historical level of physical activity were associated with a greater risk of reoperation, indicating that high activity levels after TKA increased the risk of prosthesis instability and revision. Petersen *et al.*¹⁴ revealed that decreased load led to rapid bone loss, while increased load led to an increase in BMD in the tibial condyles. The activity level of the body is closely related to bone mineral density, higher activity level is beneficial to improve bone mineral density. However, the relationship between post-TKA activity and the bone mineral density around the prosthesis has not been reported, so we wonder whether post-TKA activity affects the bone mineral density around the prosthesis. In this study, the postoperative activity level of patients and the periprosthetic BMD in tibia were recorded for 5 years follow up. The purpose of the present study was to: (i) clarify the change of periprosthetic BMD in the proximal tibia after TKA in the medium term; (ii) evaluate the relationship between patient activity and periprosthetic BMD in the proximal tibia; and (iii) provide reference for rehabilitation exercise of patients after TKA.

Materials and Methods

Inclusion and Exclusion Criteria

Patients were selected using the following inclusion criteria: (i) age ≥ 50 years old; (ii) diagnosis of knee osteoarthritis following the International Classification of Diseases 9th Revision (ICD-9); (iii) undergoing primary and unilateral TKA under epidural anesthesia; (iv) a PS prosthesis used; and (v) complete data, including clinical evaluations and radiographic examinations. The exclusion criteria included: (i) knee varus deformity greater than 15° or knee valgus deformity; (ii) the use of drugs that affect BMD; (iii) body mass index (BMI) greater than 30; (iv) surgery performed on the other knee within 5 years; and (v) postoperative infection and other serious diseases and complications.

Study Design

The present study was retrospectively conducted from January 2010 to December 2015. The study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Sun Yat-Sen University (code number [2011] 57), and all of the procedures followed the principles of the Helsinki Declaration. All of the information for this study was acquired by directly interviewing the patients by telephone and by reviewing the medical records at our hospital.

Patient Characteristics

A total of 120 patients underwent primary TKA with a posterior stabilized (PS) prosthesis (DePuy Synthes, P.F.C. Sigma, Warsaw, IN, USA) from January 2010 to December 2015 and were enrolled in this study. All of the

patients were informed of the study purpose and follow-up requirements, and all of the patients signed informed consent forms.

Operative Procedure

The patients received unilateral primary cemented TKA by the same experienced surgeon using epidural anesthesia at the Department of Joint Surgery of the First Affiliated Hospital of Sun Yat-Sen University. A PS prosthesis with patellar resurfacing was used.

A longitudinal incision was made in the anterior midline of the knee. The skin, fascia, and quadriceps tendon were incised to expose the articular cavity. Part of the subpatellar fat pad and meniscus were removed, and the anterior cruciate ligament was cut off.

Femoral condyle osteotomy was performed intramedullary. Proximal tibial osteotomy was performed extramedullary. Then the medial and lateral meniscus and osteophyte of the posterior femur was cleaned, and the tense tissue released. The femoral and tibial test models were implanted according to size. The mechanical axis of the lower limb and flexion/extension gap was then evaluated. Lastly, the knee joint was thoroughly rinsed, and the knee prosthesis was installed with bone cement. A drainage tube was placed, and the device was engaged by negative pressure. The pneumatic tourniquet was used with pressure at 55–75 kPa for about 60 min.

UCLA Activity Scale

In this study, the activity levels of patients were assessed by the UCLA activity scale at 1, 3, and 5 years postoperatively. In clinical practice, patients returned to normal activities six months to one year after surgery, and the patients' movement patterns and activity levels remained unchanged for at least five years after surgery. Therefore, the average value of the UCLA activity scale at 1, 3 and 5 years after surgery was used as the patients' activity level in this study. The UCLA Activity Scale^{15–17} is a simple scale ranging from 1 to 10. The patient indicates her or his most appropriate activity level, with 1 defined as “no physical activity, dependent on others” and 10 defined as “regular participation in impact sports.”¹⁸

Patients were divided into three groups based on their UCLA Activity Scale scores: low activity group (LA group, UCLA score = 4, 5); medium activity group (MA group, UCLA score = 6, 7); and high activity group (HA group, UCLA score = 8, 9). There were 33 patients in the LA group, 51 patients in the MA group, and 26 patients in the HA group.

Method for Measuring BMD

Dual X-ray absorptiometry (DXA) is the gold standard for evaluating BMD, but it is not used in routine examinations after TKA. Hernandez-Vaquero *et al.*¹⁹ reported a method based on digital X-ray images to evaluate BMD, and the consistency between BMD measured by DXA and relative BMD (rBMD) measured by this method was approximately 0.72 to

0.92. Therefore, this method was used to evaluate BMD in this study. Postoperative X-rays of the lower limb were performed for BMD measurement at 1 week, 3 months, 1 year, 3 years, and 5 years after surgery.

To ensure the comparability between the X-ray images, all X-rays were obtained on the same machine, and the patients' knee joints were controlled in a neutral position to reduce errors caused by differences in the position of the knee. Knee flexion was minimized by fixing the tibial tubercle at the lower end of the knee. Rotation was controlled by fixing the heel and the first and second toes (Fig. 1A). Three regions of interest (ROIs) were chosen as the measured regions in the tibia: the medial metaphyseal region (R1), lateral metaphyseal region (R2), and diaphyseal region (R3) (Fig. 1B). ImageJ software (version 1.8, National Institutes of Health, Bethesda, MD, USA) was used to measure the mean grayscale value in the established regions of the radiographs. The measured grayscale value of each designated region was calibrated using the following formula: $G_{C,R} = [255(G_R - G_a)] / (G_f - G_a)$, where $G_{C,R}$ was the calibrated grayscale value, also representing the rBMD in a given region; G_R was the grayscale value within an ROI; G_a was the value of air on the radiograph; and G_f was the grayscale value of the femoral component.

Demographic and Clinical Subject Characteristics

Data on sex, age, course of the disease, operation time, blood loss, BMI, hospital stay, and range of motion (ROM) were obtained through the medical records system of the hospital. All of the patients were clinically evaluated with respect to knee function using the Knee Society Score (KSS)²⁰ and visual analogue score (VAS). The secondary observations were radiographic evaluations (prosthetic stability, periprosthetic fractures, aseptic loosening and periprosthetic joint infection) and clinical evaluations (KSS scores, VAS scores and ROM).

Knee Society Score

The KSS is an instrument for evaluating functional ability in TKA. The KSS contains questions in two sections: knee joint (pain, range of motion, stability) and function (walking distance, ability to climb stairs). When calculating the score, deductions are made for assistive devices and flexion contractures, misalignment, or extension lag. Final scores range from 0 to 100. A score <60 is considered poor, 60–69 is fair, 70–84 is good, and 85–100 is excellent.

VAS Score

The visual analog scale (VAS) is a validated, subjective measure of acute and chronic pain. Scores are recorded by making a handwritten mark on a 10-cm line that represents a continuum between “no pain” and “worst pain.”

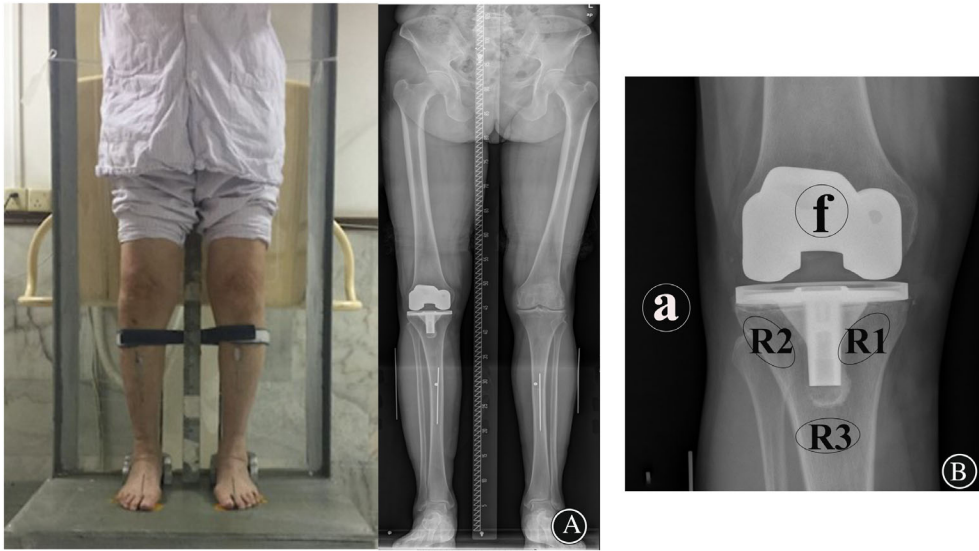


Fig. 1 (A) Schematic diagram of lower limb x-ray photography, the patients' knee joint was controlled in a neutral position by black bind to reduce errors caused by differences in the position of the knee. Knee flexion was minimized by fixing the tibial tubercle at the lower end of the knee. Rotation was controlled by fixing the heel and the first and second toes. (B) rBMD was measured at 3 regions of interest around the tibial component on X-ray film, R1: medial metaphyseal region, R2: lateral metaphyseal region, R3: diaphyseal region. Regions a and f measured the gray values of air and metal in the femoral prosthesis, respectively, to adjust the bone density. The measured area avoided cement, cortical bone, and the fibula head

Statistical Analysis

All of the statistical analyses were performed using SPSS software, version 21.0 (SPSS Inc., Chicago, IL, USA). The Shapiro–Wilk test was used to confirm that the data were normally distributed. One-way ANOVA was used to compare the clinical scores and BMD among the three groups. The unpaired *t*-test was used for statistical analysis of continuous variables between groups. Significance was defined as $P < 0.05$.

Results

Study Flow and Patient Characteristics

A total of 120 consecutive patients (120 knees) were initially identified. After applying the inclusion criteria, 110 cases (110 knees) were eligible for our study. Ten patients were excluded (one patient died of myocardial infarction, five patients were unable to visit our hospital because of comorbidities (myocardial infarction in two, cerebral infarction in one, brain hemorrhage in one, and lung cancer in one), and four patients were lost to follow-up because they recovered well after the operation and did not want to return to the hospital again). Finally, the data of 110 patients (33 in the low activity group, 51 in the medium activity group, and 26 in the high activity group) were included in the study and analyzed.

All of the patients were followed up for 5 years, and the data collection was complete. A flow diagram is presented in Fig. 2. There were five men and 28 women in the LA group, with an average age of 66.7 years old. There were

10 men and 41 women in the MA group, with an average age of 66.1 years old. There were five men and 21 women in the HA group, with an average age of 67.4 years old. The mean preoperative KSS (clinical score) was 48.9 (range, 44.3–53.5), 51.1 (range, 47.0–55.1) and 52.3 (range, 44.8–59.8) for the LA, MA and HA groups, respectively; the mean preoperative KSS (functional score) was 31.6 (range, 25.2–38.1), 27.0 (range, 22.1–31.8) and 31.5 (range, 22.9–39.9) for the LA, MA and HA groups, respectively. The preoperative ROMs were 169.0 (range, 167.2–170.8), 170.1 (range, 168.9–171.4), and 169.0 (range, 167.2–170.8) in the LA, MA and HA groups, respectively. The preoperative rBMDs were 151.7 (147.0–156.4), 153.6 (150.2–157.1), and 153.6 (150.2–157.1) in the LA, MA and HA groups, respectively. The demographic and clinical subject characteristics are shown in Table 1. There were no significant differences in demographic data or preoperative rBMDs among the three groups ($P > 0.05$).

Primary Observations

Bone Mineral Density

Compared with the baseline, a significant reduction in rBMD was found at the medial metaphyseal region (R1), lateral metaphyseal region (R2) and distal region (R3) in all groups. As shown in Fig. 3, the rBMD of R1, R2 and R3 decreased by 7.9%, 4.8% and 1.4%, respectively, at 3 months; decreased by 10.8%, 5.7% and 1.4%, respectively, at 1 year; decreased by 12.6%, 6.2% and 1.8%, respectively, at 3 years; and decreased by 13.6%, 7.8% and 3.3%, respectively, at 5 years.

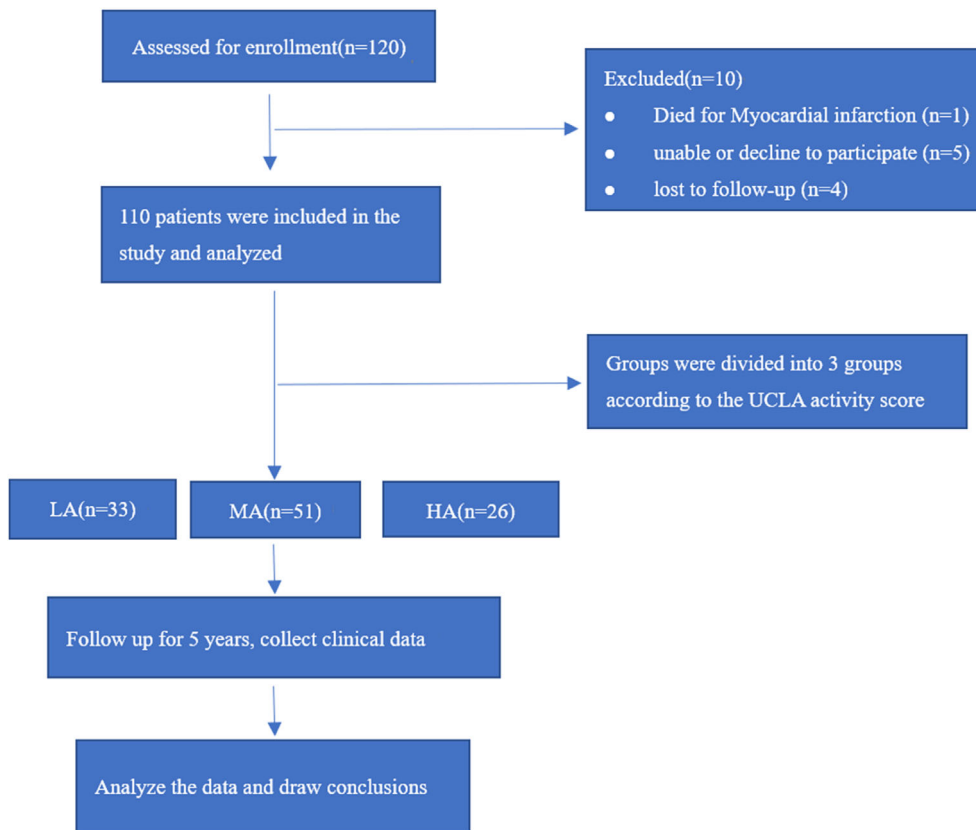


Fig. 2 Flow diagram of the study. LA, low activity; MA, medium activity; HA, high activity

TABLE 1 Demographic and clinical subject characteristics

Variables	LA group (n = 33)	MA group (n = 51)	HA group (n = 26)	F	P
Gender (male/female)	M5/F28	M10/F41	M5/F21	–	–
Age (years)	66.7 (64–69)	66.1 (63–68)	67.4 (65–69)	0.29	0.75
BMI (kg/m ²)	27.3 (26.0–28.7)	26.0 (25.0–27.0)	26.9 (25.8–28.1)	1.68	0.19
Disease Course (years)	9.5 (7.7–11.4)	10.1 (8.6–11.7)	10.0 (8.3–11.7)	0.13	0.87
Operation time (min)	157.3 (149.1–165.5)	158.6 (153.7–163.5)	147.3 (138.9–155.7)	6.26	0.06
Blood loss (mL)	81.5 (71.7–91.3)	83.0 (75.8–90.3)	81.2 (71.1–91.2)	0.10	0.94
Hospital stay (days)	11.3 (10.5–12.1)	11.7 (10.9–12.4)	11.9 (10.3–13.4)	0.28	0.75
Preoperative rBMD	151.7 (147.0–156.4)	153.6 (150.2–157.1)	153.6 (150.2–157.1)	0.34	0.72
Preoperative ROM (°)	169.0 (167.2–170.8)	170.1 (168.9–171.4)	169.0 (167.2–170.8)	0.95	0.45
Preoperative KSS score					
clinical score (point)	48.9 (44.3–53.5)	51.1 (47.0–55.1)	52.3 (44.8–59.8)	0.38	0.68
function score (point)	31.6 (25.2–38.1)	27.0 (22.1–31.8)	31.5 (22.9–39.9)	0.85	0.43
VAS (point)	6.27 (5.0–7.0)	6.18 (5.0–7.0)	6.35 (5.8–7.0)	0.25	0.77

Values are presented as mean (95% confidence interval) or numbers.; Abbreviations: BMI, body mass index; HA, high activity; KSS, Knee Society Score; LA, low activity; MA, medium activity; rBMD, relative bone mineral density; ROM, range of motion; VAS, visual analogue scale.

For the medial metaphyseal region (R1), the rBMD of the MA group was significantly greater than that of the LA and HA groups at 1 and 3 years postoperatively (108.9 ± 5.2 vs. 106.1 ± 6.69 vs. 105.4 ± 5.2 , $F = 4.24$, $P < 0.01$ and 108.5 ± 6.0 vs. 101.2 ± 6.76 vs. 103.0 ± 6.8 , $F = 12.23$, $P < 0.0001$; Fig. 4A, Table 2), and the rBMD changes (Δ BMD (%)) in the MA group were significantly smaller

than those in the LA and HA groups ($8.75\% \pm 5.36\%$ vs. $11.92\% \pm 5.49\%$ vs. $12.70\% \pm 5.21\%$, $F = 6.02$, $p < 0.01$ and $9.11\% \pm 5.11\%$ vs. $16.04 \pm 4.79\%$ vs. $14.82\% \pm 4.26\%$, $F = 24.5$, $P < 0.0001$; Fig. 4B, Table 3). However, in the lateral region (R2) and distal region (R3), there were no significant differences among the LA, MA, and HA groups for rBMD and Δ BMD (%) ($P > 0.05$; Tables 2 and 3).

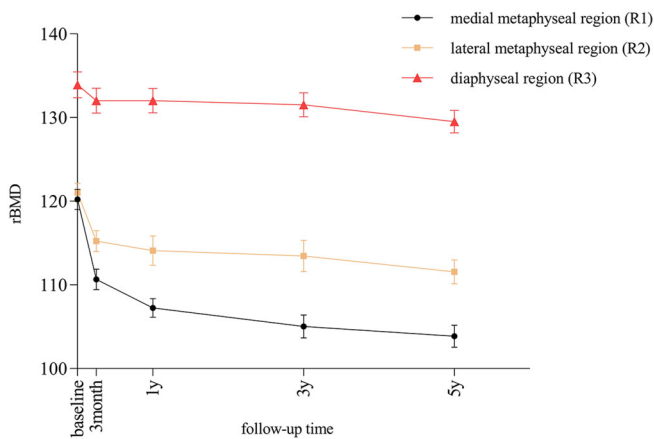


Fig. 3 All 110 patients' average rBMD change curve in R1, R2 and R3 within 5 follow-up years. The rBMD decreased over time significantly and the most severe at medial region (R1)

Secondary Observations

Radiographic Evaluation

At the endpoint, all prostheses were assessed as stable without loosening, subsidence or radiolucent lines. Comparing the LA, MA and HA groups, the KSS (clinical scores and functional scores) was 92.45 ± 6.03 and 89.09 ± 3.41 vs. 91.73 ± 6.78 and 90.00 ± 4.70 vs. 93.69 ± 5.24 and 89.81 ± 4.99 respectively. No statistical significance was found for these data ($P > 0.05$). The VAS was higher in the LA group than in the MA group and was higher in the MA group than in the HA group (3.00 ± 1.17 vs. 2.63 ± 0.77 vs. 1.65 ± 0.79 , $F = 16.49$, $P < 0.001$). The ROM was greater in the HA group than in the MA group and greater in the MA

group than in the LA group (111.90 ± 9.17 vs. 110.20 ± 6.78 vs. 102.90 ± 8.48 , $F = 11.92$, $P < 0.001$). These secondary observations are presented in Table 4.

Discussion

The main objective of this clinical study was to explore the relationship between patient activity and periprosthetic BMD in the tibia after TKA. This 5 years follow-up study of 110 patients revealed that compared with the LA and HA groups, patients in the MA group got better BMD and less bone loss, that is to say, BMD loss was minimal at medium activity level and increased at low and high activity level. Thus, we believe that post-TKA activity is an important factor affecting bone mineral density, and medium activity is conducive to reducing bone loss. This provides scientific guidance for postoperative functional exercise.

Periprosthetic BMD Decreased during Follow-Up Time

Regarding the primary observation, BMD decreased significantly during follow-up after surgery, and the decrease was more pronounced in the medial tibia than lateral or diaphyseal region (Fig. 3). These results were consistent with previous research,²¹⁻²³ which declared that bone mineral density decreased after total knee arthroplasty and was believed to affect prosthetic fixation. Li and Nilsson²⁴ reported on 28 patients who underwent TKA with a follow-up of 2 years that bone density temporarily decreased by 13% in the first three months after TKA due to a general metabolic reaction of the skeleton to the operative trauma combined with the effect of the postoperative immobilization. Ritter *et al.*²⁵ observed that non-failing knees of TKA showed a significant decrease (range from 7.3% to 17.4%) in density across tibial regions at seven-year follow-up on standardized radiographs.

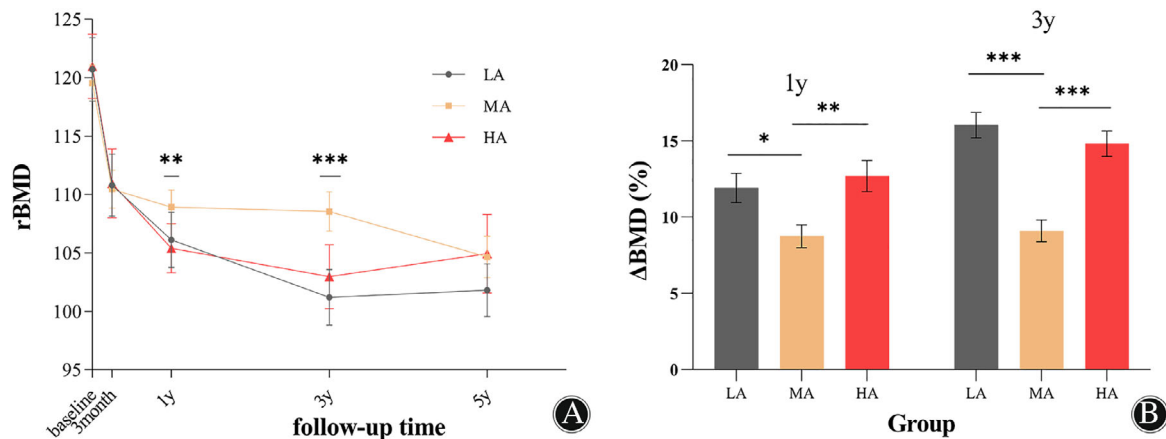


Fig. 4 Figures showed the effect of activity level on medial rBMD. A: shows the average rBMD change curve over time. The average rBMD of LA MA and HA groups declined over time but the rBMD of MA group was significantly higher than LA and HA groups at 1 and 3 years. There was no significant difference between LA group and HA group. B: shows the Δ BMD (%) among LA MA and HA groups at 1 year and 3 years. The Δ BMD (%) of MA group was significantly lower than LA and HA group both at 1 year and 3 years. There was no significant difference between LA and HA groups. *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$

TABLE 2 The rBMD of 3 ROIs at 1 year, 3 years and 5 years

ROIs	Groups	n	baseline			3 months			1 year			3 years			5 years		
			rBMD	F	P	rBMD	F	P	rBMD	F	P	rBMD	F	P	rBMD	F	P
R1	LA	33	120.7 ± 7.6	0.59	110.8 ± 7.46	0.94	106.1 ± 6.69	101.2 ± 6.76	101.8 ± 6.36	<0.001	104.7 ± 6.3	12.23	101.2 ± 6.76	101.8 ± 6.36	0.12		
	MA	51	119.6 ± 5.4	0.53	110.4 ± 5.8	0.06	108.9 ± 5.2	108.5 ± 6.0	104.7 ± 6.3		104.9 ± 8.3	2.15	108.5 ± 6.0	104.7 ± 6.3			
	HA	26	121.0 ± 6.8		110.9 ± 7.3		105.4 ± 5.2	103.0 ± 6.8	104.9 ± 8.3		112.3 ± 7.8	0.58	103.0 ± 6.8	104.9 ± 8.3			
R2	LA	33	121.3 ± 6.9	0.21	115.7 ± 8.0	0.40	114.0 ± 8.9	112.8 ± 10.3	112.3 ± 7.8	0.51	110.7 ± 6.9	0.55	112.8 ± 10.3	110.7 ± 6.9	0.58		
	MA	51	120.1 ± 5.5	1.31	114.3 ± 6.5	0.91	112.6 ± 9.8	112.8 ± 9.2	110.7 ± 6.9		110.7 ± 6.9	0.55	112.8 ± 9.2	110.7 ± 6.9			
	HA	26	122.6 ± 5.3		116.3 ± 5.5		117.1 ± 8.6	115.4 ± 10.6	110.7 ± 6.9		112.2 ± 8.6	0.55	115.4 ± 10.6	110.7 ± 6.9			
R3	LA	33	133.9 ± 8.1	0.28	132.1 ± 7.6	0.99	132.0 ± 7.8	131.6 ± 6.7	129.4 ± 6.1	0.41	128.9 ± 7.8	0.59	131.6 ± 6.7	129.4 ± 6.1	0.55		
	MA	51	132.9 ± 8.4	1.28	131.9 ± 8.0	0.01	130.8 ± 7.6	130.7 ± 8.3	128.9 ± 7.8		128.9 ± 7.8	0.59	130.7 ± 8.3	128.9 ± 7.8			
	HA	26	136.0 ± 7.9		132.1 ± 8.1		134.4 ± 7.9	133.1 ± 7.5	128.9 ± 7.8		130.8 ± 7.2	0.59	133.1 ± 7.5	128.9 ± 7.8			

Abbreviations: HA, high activity; LA, low activity; MA, medium activity; ROIs, range of interests; rBMD, relative bone mineral density. Bold indicates highlight the p value.

TABLE 3 The rBMD changes (ΔBMD (%)) of 3 ROIs at 1 year, 3 years and 5 years

ROIs	Group	1 year			3 years			5 years		
		ΔBMD (%)	F	p	ΔBMD (%)	F	p	ΔBMD (%)	F	p
R1	LA	11.92 ± 5.49	6.02	0.003	16.04 ± 4.79	24.5	<0.0001	15.44 ± 6.06	2.82	0.06
	MA	8.75 ± 5.36			9.11 ± 5.11			12.36 ± 5.29		
	HA	12.70 ± 5.21			14.82 ± 4.26			13.14 ± 6.66		
R2	LA	5.97 ± 6.12	0.53	0.59	6.96 ± 6.97	1.19	0.30	7.27 ± 6.05	1.11	0.33
	MA	6.15 ± 7.52			5.94 ± 7.33			7.70 ± 5.21		
	HA	4.38 ± 6.66			5.81 ± 8.06			8.39 ± 7.26		
R3	LA	1.22 ± 4.86	0.06	0.94	1.55 ± 3.99	0.13	0.87	3.11 ± 5.01	0.32	0.72
	MA	1.47 ± 3.96			1.56 ± 4.61			2.85 ± 4.65		
	HA	1.16 ± 3.61			2.05 ± 3.98			3.75 ± 4.17		

Abbreviations: HA, high activity; LA, low activity; MA, medium activity; ROIs, range of interests; rBMD, relative bone mineral density. Bold indicates highlight the p value.

TABLE 4 Clinical outcomes at the endpoint of the study

	LA Group (n = 33)	MA Group (n = 51)	HA Group (n = 26)	F	P
KSS					
Clinical scores (point)	92.45 ± 6.03	91.73 ± 6.78	93.69 ± 5.24	0.86	0.42
Functional scores (point)	89.09 ± 3.41	90.00 ± 4.70	89.81 ± 4.99	0.44	0.65
VAS (point)	3.00 ± 1.17	2.63 ± 0.77	1.65 ± 0.79	16.49	<0.001
ROM (°)	102.90 ± 8.48	110.20 ± 6.78	111.90 ± 9.17	11.92	<0.001

Abbreviations: HA, high activity; KSS, Knee Society Score; LA, low activity; MA, medium activity; ROM, range of motion; VAS, visual analogue scale.

The results of our study were similar to those observed in these studies. In the present study, we found that compared with baseline, the rBMD of R1, R2 and R3 decreased by 7.9%, 4.8% and 1.4%, respectively, at 3 months; decreased by 10.8%, 5.7% and 1.4%, respectively, at 1 year; decreased by 12.6%, 6.2% and 1.8%, respectively, at 3 years; and decreased by 13.6%, 7.8% and 3.3%, respectively, at 5 years.

We speculate that there are multiple factors contributing to the loss of bone mineral density: First, it is stress shielding effect. The knee implant have a strong stress shielding effect on tibial plateau, and the stress shielding effect is considered to be the most important cause of bone loss;^{6,26–28} second, the heat generated during intraoperative osteotomy causes thermal cauterization of the tibial cancellous bone, resulting in the death of a large number of bone cells; third, the formation of prosthesis debris for a long time postoperatively causes aseptic inflammation of the bone-prosthesis interface, resulting in osteocyte death.

Bone Loss Was Smaller at Medium Activity Level than Low and High Activity Level

More importantly, we found the BMD of the MA group was significantly greater than that of the LA and HA groups (Fig. 4A, $p < 0.01$), and the percentage of BMD decrease (Δ BMD (%)) of the MA group was significantly smaller than that in the LA and HA groups (Fig. 4B, $P < 0.01$) at 1 and 3 years postoperatively. These results indicated that post-TKA activity level is an important factor affecting bone mineral density, and appropriate activity level is conducive to reducing bone loss and increasing bone mass.

Regular physical exercise has been recommended as a low-cost and safe nonpharmacological strategy to prevent bone loss in older people. It has long been established that, to improve bone density, bone tissue must be subjected to mechanical loads higher than the intensity of daily activity (bone adaptation).^{29,30} One explanation was that high activity increased the compressive stress and mechanical load on the knee joint; then the stress and wear at the prosthesis-bone interface were increased, and bone loss appeared gradually due to the stress shielding effect;^{31,32} conversely, low activity led to osteoporosis according to Wolff's law. Therefore, appropriate rehabilitation (medium activity level) should be considered a major rehabilitation exercise pattern for patients.

Patient activity had a significant effect on bone mineral density, it was founded that the effect of activity on BMD was significant in the medial region but not in the lateral or diaphyseal region. We speculated that TKA corrected the lower limb alignment so that the load of the knee joint was mainly concentrated on the medial metaphyseal region; so activity mainly affected the BMD at the medial region. The diaphyseal region was far from the articular surface, and activity had limited effect on it.

Clinical Results among LA, MA and HA Groups

During the 5-year follow-up period, no prosthesis displacement or periprosthetic joint infection was observed. Regarding clinical assessment (KSS scores), there was no significant difference among the three groups. However, for VAS and ROM, the HA group was better than the LA and MA groups. Higher activity levels were associated with better ROM of the knee, less pain sensation and better satisfaction. Therefore, an appropriate increase in activity level can reduce pain, increase ROM and improve patient satisfaction.

Despite activity being encouraged for patients, there are no standard criteria for the recommended quantity of activity after TKA. This current study found that the medium activity level was beneficial to reduce bone loss and could help to increase the stability of the prosthesis. It is recommended that patients should engage in a moderate level of exercise after TKA, which not only results in excellent clinical outcomes but also helps to maintain bone mass and prosthesis stability.

Strengths and Limitations

This study has several strengths. First, the study was followed up for as long as 5 years. Second, the relationship between postoperative activity level and periprosthetic bone density was discussed, and it was found that moderate postoperative activity level was beneficial to reduce periprosthetic bone loss, and provided a scientific reference for postoperative functional exercise. Third, the use of X-rays to measure bone density is simple and effective.

There are some limitations of our study. First, the number of participants in the study was limited, and more samples are needed to confirm the conclusions. Second, the sex distribution was atypical, with 81.8% women. However, according to relevant statistics, the ratio of men to women

with knee osteoarthritis is approximately 1:7; thus, women represent the majority. Third, rBMD measured on standard X-ray images is a relative value not the real BMD measured by DXA. Hernandez-Vaquero *et al.*¹⁹ proved that the relationship between the rBMD measured on standard X-ray images and the true BMD measured by DXA is linear; therefore, rBMD could serve as an alternative to BMD.

Conclusion

This study revealed that postoperative activity is an important factor affecting bone mineral density, and medium activity prevented periprosthetic bone loss in the medial metaphyseal region of the tibia after posterior-stabilized TKA. This provided a scientific reference for functional exercise after TKA.

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