Review
Future Rheumatology

Contribution of total knee arthroplasty to increased bone mineral density

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Although several studies describe a significant decrease in postoperative bone mineral density of up to 44% adjacent to the implants after total knee arthroplasty, most reports demonstrated that the decrease in bone mineral density did not continue after 2 years. Most patients may show a reduction in activity levels in the first 6 months after surgery, gradually returning to the preoperative level within the next 6 months, and then show an improvement over the preoperative level by 2 years postoperatively. Namely, although bone density initially decreases after total knee arthroplasty, this procedure contributes to increased bone mineral density approximately 1–2 years postoperatively. Our results suggest that total knee arthroplasty may contribute to a reduction of the risk of later hip fractures. In addition, it may reduce the risk of lifestyle-related diseases, including diabetes mellitus, hypertension and hyperlipemia, by allowing increased mobility, resulting in better bone quality.

Total knee arthroplasty (TKA) and total hip arthroplasty (THA) have become widely accepted as two of the most effective interventions to eliminate the pain and disability caused by degenerative joint disease, such as advanced knee osteoarthritis and rheumatoid arthritis. Both TKA and THA have become more durable and reliable, owing to improvements in surgical technique and in prosthetic implant materials and designs [1–5]. The biological quality and integrity of the surrounding host bone has become increasingly important, as newer prostheses may provide 25 years of good implant function. TKA implantation alters the mechanical loading of both the femur and tibia, causing the bone to adjust its mineral density and structure to meet the new mechanical demands [6,7].

Due to pain, individuals with degenerative joint disease do not load their bone as much as those with healthy joints. Therefore, the increase in activity after joint arthroplasty may have an effect on bone mineral density (BMD). Conversely, several studies describe a significant decrease in postoperative BMD of up to 44% adjacent to the implants after TKA [8–16]. Prosthesis-related bone loss is thought to occur mainly as a result of stress-shielding, although immobilization in combination with local bone and tissue reactions to operative trauma have separate effects on bone loss [9,10,14,16]. Theoretically, component loosening or increased risk of periprosthetic fractures could occur in patients with greater postoperative bone loss. Therefore, the most important issue is whether the bone loss continues. This review will focus on the contribution of TKA to increasing BMD, including a discussion of our recent studies.

Factors affecting BMD

Bone mineral density can be influenced by systemic factors, medications, exercise and mechanical loading [17]. Mechanical loading is the most important of these factors, since TKA can increase activity owing to pain relief and improved joint function. There have been several studies of the relationship between mechanical loading and TKA [18–22]. In normally aligned valgus knees, the tibial metaphyseal bone has a higher BMD on the medial side [18]. This was supported by the observation that during walking, approximately 70% of the total load is typically transmitted through the medial compartment in the normal knee joint [19].

Degenerative joint disease and severe osteoarthritis leads to relative sclerosis beneath the loaded condyle and relative porosis beneath the unloaded condyle, with the strongest bone being found on the concave side of the deformity [20]. The tibial BMD of the medial compartment has been shown to be significantly higher than that of the lateral compartment in both mild and severe varus osteoarthritis [21,22]. In the valgus knee, it would be of higher density in the lateral compartment.

Keywords

beneficial effects ■ bone mineral density ■ broadband ultrasound attenuation ■ contribution ■ dual x-ray absorptiometry ■ total knee arthroplasty

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Knee alignment is also an important factor that affects loading of the knee joint and, thus, BMD. Soininvaara *et al.* reported bone remodeling tending toward similar values in the medial metaphysis and between the medial and lateral compartments [7]. These results may reflect a more physiological alignment of the knee joint and more optimal loading conditions. Li and Nilsson reported a similar association between bone remodeling and knee alignment [23].

Baseline BMD

We have found that the baseline BMD of the medial proximal tibia varies substantially among our patients, which may be explained by degenerative changes. The mechanical and morphological properties of the proximal tibia differ as a result of bone remodeling due to misalignment, progressive subluxation, metaphyseal microfractures and altered activity levels [7]. Many patients with osteoarthritis of the knee are relatively immobile owing to pain and the deformity of the joint, and therefore lose the beneficial effects of weight bearing on BMD. The stage of the degenerative process has been shown to be associated with large variations in BMD values [24,25].

Evaluation of BMD following TKA

Traditionally, the results of TKA have been evaluated based on the postoperative clinical status (knee function, stability, range of motion and pain) and plain radiographs. However, quantitative evaluation of periprosthetic bone density from plain radiographs is not possible, as they detect only the presence or absence of gross bone loss [13]. Quantitative computerized tomography was used to evaluate the changes of BMD at a different joint; however, it also allows the detection of losses [6].

Dual x-ray absorptiometry (DXA) can provide reproducible, high-quality measurements of periprosthetic BMD. Dedicated software is available to allow measurement of bone density adjacent to metal implants [12,13,26,27]. Soininvaara *et al.* performed single-photon-emission computed tomography analysis using ^{99m}Tc-labeled methylene diphosphonate, which has affinity for hydroxyapatite uptake, which is correlated with the activity of osteoblasts [28]. Owing to the close relationship between osteoblastic and osteoclastic activity, increased diphosphonate uptake represents increased bone metabolism. Ishii and Matsuda used broadband ultrasound attenuation (BUA) through the calcaneus to assess patients' bone quality [29,30]. Ultrasonography provides information not only on bone density, but also on architecture and elasticity [31–33].

The precision of BMD measurement

There are variable factors to affect the precision of BMD measurement, such as baseline BMD, size and position of regions of interest, software used, background compensation and so on. Therefore, it is very difficult to control these factors and to make the measurements comparable. Bone quality after joint replacement is usually evaluated using DXA. DXA measurements correlate strongly with the ash content of the bone and are seven-times more accurate than visual evaluation [34]. Namely, DXA can provide reproducible, high-quality measurements of periprosthetic BMD. Commercial software allows the measurement of bone density adjacent to metal implants, as confirmed with an average precision error of 1.3–3.1% [12,13,15,34].

Changes in BMD after arthroplasty

Although many studies have evaluated BMD after total joint arthroplasty, most mainly considered periprosthetic BMD to check loosening of the components [11,34–40]. In addition, some studies examined the changes in BMD at different sites after total joint replacement [41,42].

A prospective 1-year DXA study of 69 patients revealed a tendency for major bone loss to occur in the distal femur during the first 3 months after cemented TKA [6]. Reductions in BMD continued for up to 12 months, although the changes were minor after 6 months. Reduction in BMD was significant in the medial metaphyseal and diaphyseal regions of interest. Bone loss in the diaphysis probably represents operation-induced loss and bone loss due to postoperative disuse, which is most pronounced during the first 3 months after surgery. In the medial metaphysis, the decreases were less than 5% during the first 6 months and quite modest at 1 year (below 6.6%). In another study, Spittlehouse *et al.* reported bone loss with a 5% reduction at 6 months and with 0% bone loss at 1 year [13], which had also been reported previously [15]. Changes in the proximal tibial BMD that were not statistically significant have also been described [23]. Tibial bone loss is caused by load changes on the metaphyseal bone beneath the tibial implant, while higher degrees of bone loss in femoral bone are induced by stress-shielding in periprosthetic bone [13,15,26].

Spittlehouse *et al.* reported the greatest BMD decrease (16%) in the distal anterior femur over the first 6 months postoperatively in 16 patients

with uncemented TKA [13]. These reductions in BMD were most significant during the early postoperative phase, which may be related to postoperative stress-shielding. Early bone loss may be accelerated by operative trauma and postoperative immobilization, as well as by the altered mechanical situation.

The clinical and functional status of the knee joint, evaluated using the Hospital for Special Surgery Score [43], improved steadily and significantly during the follow-up period. Paradoxically, the major improvement in the clinical and functional status of the knee was insufficient to overcome the overriding postoperative early-phase stress-shielding phenomenon.

From a clinical viewpoint, high BMD is considered to provide better support for bone implant fixation. A number of cementing techniques, as well as uncemented arthroplasty and numerous implant modifications, have been introduced to improve the quality of the primary arthroplasty. Bone loss occurs with all designs of TKA, and the prevalence of bone loss seems to be independent of the fixation method.

In another study, rapid bone loss was observed during the first 6 months postoperatively in periprosthetic femoral metaphyseal BMD. During the follow-up period, decreases in all femoral parameters were significant (all $p < 0.001$), reaching up to 25.5%. By contrast, tibial periprosthetic BMD values remained close to those at baseline [28]. Petersen *et al.* followed eight patients after uncemented TKA for 5 years with DXA and reported an average decrease of 36% of BMD behind the anterior flange of the femoral component [11]. The decrease in BMD did not continue after 2 years [16]. Karbowski *et al.* found a 21.5% decrease of distal femoral BMD in 12 patients 9 months after cemented TKA [15]. Apparently, a decrease in BMD of the distal femur of 20–40% occurs within 1 year after TKA due to stress-shielding, independent of the type of fixation of the femoral component.

The changes in BMD in different joints have been evaluated by quantitative computed tomography. Adolphson *et al.* reported decreases in vertebral bone density and in BMD of the distal femur and proximal tibia after THA [41,42]. Ruegsegger *et al.* also reported temporary loss of bone density in the tibia after THA [44]. Ishii *et al.* evaluated changes in the BMD of the proximal femur after TKA using DXA [45]. They concluded that the BMD of the proximal femur declined inconsistently in most patients during the first 6 months, but by 1 year the BMD was almost equivalent to that before surgery. In addition, BMD was within the expected 4% age-related loss in 81% of hips on the operative side and 82% on the nonoperative side. These results are consistent with the hypothesis that the increased mobility of patients after TKA, leading to increased activity levels, may increase hip BMD.

Furthermore, Ishii *et al.* evaluated the bone quality of the hip using BUA through the calcaneus after TKA, during 2 years of follow-up [29]. They demonstrated that TKA patients had a significantly higher BUA at the heel than a hip-fracture group, and that increased activity may maintain or improve bone quality by relieving the pain after TKA.

Hans *et al.* concluded that ultrasonographic measurements of the calcaneus can predict the risk of hip fracture in elderly women, as well as DXA of the hip [31], and Stewart *et al.* reported that ultrasonographic heel measurement was a better discriminator of hip fracture than DXA of the hip [46].

In a study evaluating BUA, Porter *et al.* concluded that improving bone strength in elderly women may reduce the incidence of hip fracture [47]. These studies suggest that TKA may contribute to a reduction of the risk of later hip fracture, by allowing increased mobility and maintaining or improving bone quality.

In another study, Petersen *et al.* followed eight patients after uncemented TKA for 5 years with DXA and reported an average decrease of 36% in BMD behind the anterior flange of the femoral component [11]. The decrease in BMD did not continue after 2 years. van Loon *et al.* reported that BMD in the lumbar spine and both femoral necks of patients 1 year after cemented TKA was similar to the general preoperative BMD [16]. The patients' general mobility 1 year after surgery was roughly comparable with their preoperative status. In addition, TKA patients in whom the activities of daily life could be correlated with general BMD of the lumbar spine and hips showed improvement in postoperative mobility status compared with mobility prior to surgery.

Recently, we reported the relationship between TKA and BMD of the calcaneus in 40 TKA patients using BUA [30]; the follow-up was 2 years. Knee function was assessed using the Hospital for Special Surgery knee score. The score improved from 45 ± 15 to 91 ± 7 (average ± 1 standard deviation). Bone quality after total joint replacement is usually evaluated using DXA. Although precise, this method provides almost no information on bone microarchitecture or elasticity. Ultrasonography not only provides information

Executive summary

Factors affecting bone mineral density after total knee arthroplasty

- Bone mineral density (BMD) can be influenced by systemic factors, medications, exercise and mechanical loading.
- Mechanical loading is the most important of these factors, since total knee arthroplasty (TKA) can increase activity due to pain relief and improved joint function.

Baseline BMD

- The stage of the degenerative process has been shown to be associated with large variations in BMD values.

Evaluation of BMD following TKA

- Although quantitative computerized tomography (QCT) was used to evaluate the changes of BMD at a different joint, QCT allows the detection of losses.
- Dual x-ray absorptiometry can provide reproducible, high-quality measurements of periprosthetic BMD. Dedicated software is available to allow measurement of bone density adjacent to metal implants.
- Single photon emission computed tomography analysis using ^{99m}Tc-labeled methylene diphosphonate, which has affinity for hydroxyapatite, has an uptake that is correlated with the activity of osteoblasts.
- Broadband ultrasound attenuation provides information on not only bone density but also architecture and elasticity.

Changes in BMD after arthroplasty

- Although several studies describe a significant decrease in postoperative BMD of up to 44% adjacent to the implants after TKA, the decrease in BMD did not continue after 2 years.
- Most patients may show a reduction in activity levels in the first 6 months after surgery, gradually returning to the preoperative level within the next 6 months, and then show an improvement over the preoperative level by 2 years postoperatively.

Future of the objective beneficial affects of TKA

- TKA may contribute to a decrease in the risk of later hip fracture, by allowing increased mobility and maintaining or improving bone quality.
- TKA may reduce the risk of lifestyle-related disease, including obesity, diabetes mellitus, hypertension and hyperlipemia.
- We surgeons should find out the additional benefit for patients that received a TKA.

on bone density, but also on architecture and elasticity. Therefore, BUA was used to evaluate bone quality in this study.

The BMD was measured preoperatively and 1, 3 and 6 months, and 1 and 2 years after TKA. Maximum rates of bone resorption in patients with osteoporosis have been reported to be between approximately 1 and 3% annually. The present study defined the bone resorption rate at a 2% decrease per year according to previous reports [32,45]. The BUA decrease in the first 6 months, and gradually return to the preoperative level in the next 6 months, and achieve improved preoperative level by 2 years postoperatively (**Table 1**). Despite a predicted age-related loss of 4% during 2 years, 52% of the patients 1 year postoperatively and 78% of the patients 2 years postoperatively had BMD higher than preoperative level. In addition, 55 and 85% of patients had a BMD that was within the expected 4% age-related loss.

Considering that clinical outcome was excellent after 2 years surgery in this study, these results suggested that most patients may show a reduction in activity levels in the first 6 months after surgery, gradually returning to the preoperative level within the next 6 months, and then show an improvement over the preoperative level by 2 years postoperatively.

Conclusion

Published reports and our results suggest that although bone density decreases initially after TKA, TKA contributes to increased BMD approximately 1–2 years postoperatively. A study period of 1 year following surgery is probably insufficient to trace the significance of increased BMD.

Although the prime indication for recommending TKA will continue to be pain, it is important for surgeons to recognize the objective beneficial effects of TKA in addition to pain

Table 1. Changes in broadband ultrasound attenuation (dB/MHz) at the heel in total knee arthroplasty.

	Preoperative	Postoperative				
		1 month	*3 months*	*6 months*	*1 year*	*2 years*
Mean BUA ± 1 SD	47.1 ± 15.4	45.8 ± 16.2	46.7 ± 15.5	46.7 ± 15.2	47.8 ± 13.5	53.1 ± 8.9

BUA: Broadband ultrasound attenuation; SD: Standard deviation.

relief. First, TKA may contribute to a reduction of the risk of later hip fractures [29]. Second, it may reduce the risk of lifestyle-related diseases, including diabetes mellitus, hypertension and hyperlipemia, by allowing increased mobility, which results in better bone quality.

Future perspective

Total knee arthroplasty and total hip arthroplasty have become more reliable procedures to improve the joint function due to relief of pain; however, we should not be satisfied. It is very important to study the objective beneficial effects of TKA in addition to pain relief. Ishii *et al.* suggested that TKA might contribute to a decrease in the risk of later hip fracture, by allowing increased mobility and maintaining or improving bone quality. At present, we investigate the relationship between TKA and the lifestyle-related diseases. TKA may reduce the risk of lifestyle-related disease, including obesity, diabetes mellitus, hypertension and hyperlipemia. Furthermore, there is a possibility of it effecting metabolic syndrome. Surgeons need to determine the additional benefit for patients who have received a TKA.

Table 2. Changes in broadband ultrasound attenuation at 1 and 2 years postoperatively.

Postoperative	Preoperative	Within expected 4% age-related loss
1 year	21/40 (52%)	22/40 (55%)
2 year	31/40 (78%)	34/40 (85%)

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