# Compliance and outcome of osteoporosis treatment after total knee arthroplasty

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# Abstract

**Background:** Treatment compliance is important in the treatment of osteoporosis. Our hypotheses were as follows: 1) compliance with osteoporosis treatment after total knee arthroplasty (TKA) will be high, and 2) osteoporosis treatment results after TKA will be as good as those of patients who do not undergo TKA.

**Methods and Materials:** Patients diagnosed with osteoporosis for the first time in an outpatient clinic (OPD group) and those who were diagnosed at hospitalization for TKA (TKA group) from March 2019 to December 2020 were retrospectively evaluated. Only patients treated with denoxumab were included in the study. Compliance, based on the outpatient follow-up rate after 1 year, was compared between the two groups, and the treatment outcomes were compared based on bone mineral density (BMD).

**Results:** In the OPD group, 29 of 41 patients were followed up 1 year later, and in the TKA group, all 14 patients were followed up after 1 year. In the OPD group, the BMD increased significantly. In the TKA group, there was a significant increase in BMD only in the lumbar spine. However, there were no significant between-group differences in the BMD before and after treatment.

**Conclusion:** Osteoporosis treatment compliance was significantly higher in the TKA group than in the OPD group. When denoxumab was used after TKA, there was no decrease in BMD, and osteoporosis treatment results after TKA were similar to those of the OPD group.


# Introduction

The incidence of degenerative diseases has been increasing as the population ages. Among these diseases, osteoporosis is difficult to diagnose without special examination because it is not symptomatic. In addition, treatment effectiveness is affected by treatment compliance, even when treatment is initiated after diagnosis.[1] However, if geriatric fractures occur without osteoporosis treatment, patients experience a decrease in quality of life and incur heavy medical expenses. In addition, decrease in activity due to a fracture can cause various other diseases; therefore, it is important to treat osteoporosis before a fracture occurs.

Total knee arthroplasty (TKA) is mainly performed for end-stage knee osteoarthritis (OA), which has a high prevalence in older female patients. Although the exact cause for this high prevalence remains unknown, it is consistent with the high-risk group for osteoporosis. Therefore, many patients who undergo TKA are often also diagnosed with osteoporosis. Approximately 37% of patients undergoing TKA were diagnosed with osteoporosis.[2] However, osteoporosis patients undergoing TKA tend to be undertreated; therefore, detection and treatment of these patients is important.[3–6]

Osteoporosis treatment is important for patients with nonsurgical knee OA. In such patients, osteoporosis treatment can improve clinical scores and help relieve pain. [7, 8] Treatment of osteoporosis is important even after TKA. Bone mineral density (BMD) may decrease until approximately 24 months after TKA,

thereby increasing the risk of periprosthetic fractures.[9, 10] Moreover, osteoporosis can increase the revision rate by increasing the probability of aseptic loosening after TKA; osteoporosis treatment may help in early stable fixation of the prosthesis and reduce the revision rate after TKA.[11, 12]

Compliance is an important factor for the success of osteoporosis treatment. High compliance may lower the risk of fractures.[13]. According to one study, the one-year compliance with osteoporosis treatment was approximately 50%.[14] On the other side, the probability of outpatient follow-up after 1 year of TKA is approximately 70%.[15, 16] This probability was higher than the one-year compliance with osteoporosis treatment, and we believe that osteoporosis treatment after TKA may lead to higher compliance. In addition, osteoporosis treatment after TKA may prevent the BMD decrease at 1 year after TKA. The hypotheses of this study are as follows: 1) compliance with osteoporosis treatment after TKA will be higher than compliance with that without TKA. 2) the results of osteoporosis treatment after TKA will be as good as those of the non-operation group.

## Material And Method

We retrospectively evaluated patients diagnosed with osteoporosis for the first time in an outpatient clinic (OPD group) and those diagnosed at hospitalization for TKA (TKA group) from March 2019 to December 2020. The following criteria, which are currently used as the diagnostic criteria for osteoporosis in South Korea, were used for osteoporosis diagnosis: (1) average T-score of − 2.5 or less at two or more points on the L-spine on duel energy x-ray absorptiometry (DEXA), or (2) lowest T-score of − 2.5 or less in the femur excluding the ward. Osteoporosis was defined as only one of these two conditions. Among patients diagnosed with osteoporosis, only those treated with denoxumab were included in this study because the administration method and type of drug can affect the outcome of osteoporosis treatment. [1, 17] The exclusion criteria were as follows: (1) patients undergoing treatment other than that with denoxumab, (2) patients with fractures during treatment, and (3) patients who changed medications due to complications. The effect of the treatment was confirmed based on compliance and DEXA results after 1 year. Approval from the institutional review board was prospectively obtained before the analysis (approval number: BOHUN 2022-02-014).

# Compliance

Compliance was confirmed based on the outpatient follow-up rate after 1 year of treatment. Because of the characteristics of denoxumab, the injection was administered every 6 months; therefore, follow-up loss was defined as a case wherein no DEXA tests were performed 1 year after treatment initiation or when no outpatient follow-up was performed until 3 months or more had passed after the scheduled follow-up date. Outpatient follow-up was performed at 6 weeks, 3 months, 6 months, and 12 months after TKA. In the case of osteoporosis treatment after TKA, the injection was initiated at the outpatient visit 6 weeks after TKA, and patients were followed up at 6 months and 1 year after the first injection.

# DEXA evaluation

In the DEXA evaluation (Prodigy Bone Densitometer, Madison, WI, USA), the T-score from L1 to L4, average T-score at two or more points on the L-spine, and T-score at the femur neck, femur ward, and femur total area were measured. The lowest T-score from L1 to L4, lowest average T-score at two or more points on the L-spine, lowest T-score of the femur neck, and lowest T-score of the femur total were evaluated in this study. The values of the four variables before and after 1 year of treatment were compared. In addition, the lowest value among the average T-score at two or more points on the L-spine, T-score at the femur neck, and T-score at the femur total was used as a diagnostic criterion for osteoporosis, and this value was also compared before and after treatment.

# Statistical analysis

All statistical analyses were performed using SPSS Statistics (version 22.0; IBM Corp., Armonk, NY, USA). Chi-square analysis was performed of the follow-up rate between the two groups to compare their compliance. A paired t-test was performed to compare DEXA values before and after treatment in each group, and an independent t-test was performed to analyze between-group differences. Statistical significance was set at $p < 0.05$.

## Results

The OPD group comprised 41 patients; none of these patients met the exclusion criteria. The TKA group comprised 15 patients; however, one of them had a periprosthetic fracture 3 months after TKA and was treated with teriparatide; therefore, 14 patients were included in this group. (Table 1)

Table 1
Patient demographics and 1 year follow-up

| | **OPD group (n = 41)** | **TKA group (n = 14)** |
|---|---|---|
| Sex | Male: 4<br>Female: 37 | Male: 0<br>Female: 14 |
| Age | 74.3 ± 9.2 | 75.4 ± 5.0 |
| Height (cm) | 153.3 ± 5.2 | 149.0 ± 6.5 |
| Weight (kg) | 53.6 ± 7.9 | 58.1 ± 8.1 |
| BMI | 23.1 ± 2.5 | 26.2 ± 3.4 |
| 1 year follow-up | Follow up: 29<br>Follow up loss: 12 | Follow up: 14<br>Follow up loss: 0 |
| OPD: outpatient clinic, TKA: total knee arthroplasty, BMI: body mass index | | |

# Compliance

Forty one patients were diagnosed with osteoporosis at the outpatient clinic, and denoxumab was initiated. Among them, 29 patients were followed up at the outpatient clinic after 1 year, and additional DEXA tests were performed, based on which treatment was continued or terminated. In the TKA group, all 14 patients were followed up by the outpatient clinic 1 year after TKA.

# DEXA outcome

The DEXA results after 1 year in the OPD and TKA groups were compared (Table 2). The DEXA values of the OPD group showed a statistically significant increase in the lowest T-score from L1 to L4, lowest average T-score at two or more points on the L-spine, lowest T-score of the femur neck, and lowest T-score of the femur total. In the TKA group, there was a statistically significant increase in the lowest average T-score at two or more points on the L-spine. However, there were no significant between-group differences in the DEXA results before and after treatment.

Table 2
Osteoporosis treatment outcome

| | | OPD group | TKA group | p-value |
|---|---|---|---|---|
| DEXA L-spine (lowest) | Initial | -2.83 ± 1.13 | -3.12 ± 0.69 | 0.36 |
| | After 1 year | -2.61 ± 1.09 | -2.96 ± 0.82 | 0.67 |
| | p-value | 0.01 | 0.1 | |
| DEXA L-spine more than 2 site | Initial | -2.68 ± 1.09 | -2.96 ± 0.65 | 0.42 |
| | After 1 year | -2.39 ± 1.13 | 2.69 ± 0.85 | 0.68 |
| | p-value | < 0.01 | 0.01 | |
| DEXA femur neck | Initial | -2.34 ± 0.76 | -2.23 ± 0.7 | 0.69 |
| | After 1 year | -2.24 ± 0.88 | -2.20 ± 0.81 | 0.31 |
| | p-value | 0.02 | 0.65 | |
| DEXA femur total | Initial | -2.03 ± 0.89 | -2.20 ± 0.58 | 0.1 |
| | After 1 year | -1.93 ± 0.87 | -2.16 ± 0.65 | 0.12 |
| | p-value | 0.01 | 0.49 | |
| Lowest value | Initial | -3.06 ± 0.48 | -3.14 ± 0.43 | 0.79 |
| | After 1 year | -2.87 ± 0.55 | -2.99 ± 0.58 | 0.86 |
| | p-value | < 0.01 | 0.09 | |
| Δ T-score | DEXA L-spine | 0.23 ± 0.42 | 0.16 ± 0.35 | 0.24 |
| | DEXA L-spine more than 2 site | 0.29 ± 0.31 | 0.27 ± 0.32 | 0.88 |
| | DEXA femur neck | 0.10 ± 0.20 | 0.03 ± 0.23 | 0.51 |
| | DEXA femur total | 0.10 ± 0.18 | 0.04 ± 0.23 | 0.3 |
| | Lowest value | 0.19 ± 0.29 | 0.15 ± 0.30 | 0.91 |

DEXA: dual energy X-ray absorptiometry, OPD: outpatient, TKA: total knee arthroplasty

# Discussion

The principal findings of this study were as follows: (1) patient compliance with osteoporosis treatment after TKA was high, and (2) there was no significant difference in the degree of improvement in the DEXA results between the OPD and TKA groups.

Successful osteoporosis treatment requires the selection of the appropriate treatment method and enhanced treatment compliance.[18] Low compliance is generally due to concerns regarding drug-induced adverse effects.[1] While the exact factors influencing compliance remain unknown,[17] treatment compliance is higher with injectable agents than with oral agents, and among injectable agents, compliance is generally high when injection is required once every 6 months.[14] Osteoporosis treatment compliance is higher when it is treated by a specialist and in cases of enhanced doctor-patient communication.[19–21] Further, compliance with osteoporosis treatment is higher when compliance with the treatments of concomitant diseases is high. In this study, we believed that treatment compliance in the TKA group would be high because patients in this group had increased interactions with doctors, and treatment compliance of patients who performed TKA was relatively high.

In the present study, the compliance rate in the TKA group was very high at 100%, even considering the small number of patients included. This rate was much higher than the general TKA 1-year outpatient follow-up rate of approximately 70%.[15, 16] Osteoporosis treatment compliance in the OPD group was also approximately 70% higher than the general one-year follow-up rate of 50%.[14] We believe that because the hospital involved in the study is a public hospital, treatment cost is relatively low, which can increase the follow-up rate.[22] Further, as mentioned, the high compliance rate in the TKA group may be because patients in the TKA group had more interactions with the doctor; the relatively high 1-year follow-up rate of TKA may have also affected osteoporosis treatment compliance. The use of denoxumab, which is used for injection once every 6 months and showed relatively good compliance, is also considered to be one of the reasons for the good compliance.[23]

Previous studies have demonstrated a decrease in BMD 1 year after TKA; osteoporosis treatment after TKA can prevent BMD loss.[9, 10, 24] In this study, BMD increased significantly at 1 year after treatment in the OPD group. However, in the TKA group, only the lowest average T-score at two or more points on the L-spine showed a statistically significant increase, and although there was an increase at other sites, the difference was not statistically significant. There was no statistical difference in the degree of increase in the T-scores between the two groups. The use of denoxumab after TKA was not statistically significant 1 year after TKA, but it helped prevent the decrease in BMD.

Previous studies have reported on the change in BMD when osteoporosis treatment is performed after TKA, but there is no report on the number of patients who continue to receive osteoporosis treatment. In particular, denoxumab has been reported to have high compliance; however, there are no reports on postoperative compliance. In this study, TKA increased compliance with osteoporosis treatment. While TKA is not required to increase compliance, if osteoporosis is treated after TKA, various complications, such as periprosthetic fracture, aseptic loosening, and postoperative pain can be reduced; thus,

osteoporosis treatment is required. In such cases, enhanced treatment effects can be expected because the treatment compliance is much higher than that before TKA. Moreover, osteoporosis is undertreated in a large number of patients undergoing TKA. A greater effect can be expected in the detection and treatment of patients with osteoporosis.

The present study has some limitations. First, the number of patients included in this study was small. To solve this problem, more data will be collected prospectively and additional research results will be published based on the current study. Second, the DEXA results did not indicate the BMD status around the knee implant. However, since DEXA results are generally used to indicate the outcomes of osteoporosis treatment, we believe that the overall osteoporosis treatment results in this study can be judged using DEXA evaluation. Third, as this was a retrospective study, the selection bias was likely to be high.

# Conclusion

Osteoporosis treatment compliance in the TKA group was significantly higher than that in the non-TKA group. When denoxumab was used after TKA, there was no decrease in BMD, and the treatment results were equivalent to those in the non-TKA group.

# Abbreviations

TKA: total knee arthroplasty, DEXA: duel energy x-ray absorptiometry, BMD: bone mineral density, OPD: outpatient

# Declarations


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Not applicable

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### Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

### Authors’ contributions

SHL & YYK designed this paper and performed critical revision of the manuscript. SHL coordinated the clinical study and YYK initiated and performed the study, analyzed the data, and wrote the manuscript.

SHL& JRY helped to draft the manuscript and all authors read and approved the final manuscript.

### Ethics approval and consent to participate

All methods were performed in accordance with the relevant guidelines and regulations. This article was performed under the IRB permission (Veterans Health Service Medical Center International Review Board No: BOHUN 2022-014) and informed consent was waived due to the retrospective nature of this study.

### Consents for publication

All presented cases in this report had written consents for publication

### Competing interests

The authors declare that we have no conflict of interest.

## References


1. Papaioannou A, Kennedy CC, Dolovich L, et al. Patient adherence to osteoporosis medications: problems, consequences and management strategies. Drugs Aging 2007; 24(1):37.
2. Bernatz JT, Brooks AE, Squire MW, et al. Osteoporosis Is Common and Undertreated Prior to Total Joint Arthroplasty. J Arthroplasty 2019; 34(7):1347.
3. Lingard EA, Mitchell SY, Francis RM, et al. The prevalence of osteoporosis in patients with severe hip and knee osteoarthritis awaiting joint arthroplasty. Age Ageing 2010; 39(2):234.
4. Bernatz JT, Krueger DC, Squire MW, et al. Unrecognized Osteoporosis Is Common in Patients With a Well-Functioning Total Knee Arthroplasty. J Arthroplasty 2019; 34(10):2347.
5. Ha CW, Park YB. Underestimation and undertreatment of osteoporosis in patients awaiting primary total knee arthroplasty. Arch Orthop Trauma Surg 2020; 140(8):1109.
6. Xiao PL, Hsu CJ, Ma YG, et al. Prevalence and treatment rate of osteoporosis in patients undergoing total knee and hip arthroplasty: a systematic review and meta-analysis. Arch Osteoporos 2022; 17(1):16.
7. Chang CB, Kim TK, Kang YG, et al. Prevalence of osteoporosis in female patients with advanced knee osteoarthritis undergoing total knee arthroplasty. J Korean Med Sci 2014; 29(10):1425.
8. Fu SH, Wang CY, Yang RS, et al. Bisphosphonate Use and the Risk of Undergoing Total Knee Arthroplasty in Osteoporotic Patients with Osteoarthritis: A Nationwide Cohort Study in Taiwan. J Bone Joint Surg Am 2017; 99(11):938.
9. Blaty T, Krueger D, Illgen R, et al. DXA evaluation of femoral bone mineral density and cortical width in patients with prior total knee arthroplasty. Osteoporos Int 2019; 30(2):383.
10. Prince JM, Bernatz JT, Binkley N, et al. Changes in femoral bone mineral density after total knee arthroplasty: a systematic review and meta-analysis. Arch Osteoporos 2019; 14(1):23.

11. Murahashi Y, Teramoto A, Jimbo S, et al. Denosumab prevents periprosthetic bone mineral density loss in the tibial metaphysis in total knee arthroplasty. Knee 2020; 27(2):580.
12. Thillemann TM, Pedersen AB, Mehnert F, et al. Postoperative use of bisphosphonates and risk of revision after primary total hip arthroplasty: a nationwide population-based study. Bone 2010; 46(4):946.
13. Weycker D, Macarios D, Edelsberg J, et al. Compliance with osteoporosis drug therapy and risk of fracture. Osteoporos Int 2007; 18(3):271.
14. Durden E, Pinto L, Lopez-Gonzalez L, et al. Two-year persistence and compliance with osteoporosis therapies among postmenopausal women in a commercially insured population in the United States. Arch Osteoporos 2017; 12(1):22.
15. Clohisy JC, Kamath GV, Byrd GD, et al. Patient compliance with clinical follow-up after total joint arthroplasty. J Bone Joint Surg Am 2008; 90(9):1848.
16. Yuenyongviwat V, Chunakiat S, Purngpiputtrakul P, et al. Factors Affecting Adherence to Follow-up Appointments after total knee arthroplasty. Ortop Traumatol Rehabil 2020; 22(4):245.
17. Solomon DH, Avorn J, Katz JN, et al. Compliance with osteoporosis medications. Arch Intern Med 2005; 165(20):2414.
18. Khosla S, Hofbauer LC. Osteoporosis treatment: recent developments and ongoing challenges. Lancet Diabetes Endocrinol 2017; 5(11):898.
19. Pickney CS, Arnason JA. Correlation between patient recall of bone densitometry results and subsequent treatment adherence. Osteoporos Int 2005; 16(9):1156.
20. Warriner AH, Curtis JR. Adherence to osteoporosis treatments: room for improvement. Curr Opin Rheumatol 2009; 21(4):356.
21. Huas D, Debiais F, Blotman F, et al. Compliance and treatment satisfaction of post menopausal women treated for osteoporosis. Compliance with osteoporosis treatment. BMC Womens Health 2010; 10:26.
22. Simon-Tuval T, Neumann PJ, Greenberg D. Cost-effectiveness of adherence-enhancing interventions: a systematic review. Expert Rev Pharmacoecon Outcomes Res 2016; 16(1):67.
23. Morley J, Moayyeri A, Ali L, et al. Persistence and compliance with osteoporosis therapies among postmenopausal women in the UK Clinical Practice Research Datalink. Osteoporos Int 2020; 31(3):533.
24. Soininvaara TA, Miettinen HJ, Jurvelin JS, et al. Periprosthetic femoral bone loss after total knee arthroplasty: 1-year follow-up study of 69 patients. Knee 2004; 11(4):297.