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Treatment of Osteoporosis after Hip Fracture: Survey of the Korean Hip Society

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Purpose: To assess current practice in the treatment of osteoporosis in patients who underwent treatment for hip fracture in South Korea.

Materials and Methods: A survey of 97 members of the Korean Hip Society, orthopedic hip surgeons who administer treatment for hip fractures in South Korea, was conducted. The survey was conducted for assessment of demographic data and perceptions regarding the management of osteoporosis in patients who have undergone treatment for hip fracture. Analysis of the data was performed using descriptive statistical methods.

Results: The majority of participants were between the age of 41 and 50 years, and 74% were practicing in tertiary hospitals. Testing for serum vitamin D levels (82%) was the most commonly performed laboratory test. Calcium and vitamin D were prescribed for more than 80% of patients by 47% and 52% of participants, respectively. Denosumab was the most commonly used first-line treatment option for osteoporosis in hip fracture patients. Bisphosphonate was most often perceived as the cause of atypical femoral fractures, and the most appropriate time for reoperation was postoperative 12 months. Teriparatide was most preferred after cessation of bisphosphonate and only prescribing calcium and vitamin D was most common in high-risk patients for prevention of atypical femoral fracture.

Conclusion: The results of this study that surveyed orthopedic hip surgeons showed that most participants followed the current strategy for management of osteoporosis. Because the end result of osteoporosis is a bone fracture, active involvement of orthopedic surgeons is important in treating this condition.

Keywords: Osteoporosis, Hip fractures, Orthopedic surgeons, Drug therapy, Republic of Korea

INTRODUCTION

Although treatment for osteoporosis is often administered in other sectors of medicine including endocrinology, geriatric, and gynecology, treatment of osteoporotic fractures is most often administered by orthopedic surgeons[1]. In particular, hip fracture, the most life-threatening osteoporotic fracture, is treated mainly by hip surgeons with surgery[2]. However, some studies have reported that medical treatment of osteoporosis is neglected by many orthopedic surgeons[3-5]. Prevention of second fracture is of utmost importance in patients who have suffered from previous osteoporotic fractures. The findings of a recent meta-analysis demonstrated the significant effect of osteoporotic medications on secondary prevention[6]. According to the

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previous prospective cohort study reported in 2007, the most common barrier in treatment of osteoporosis after hip fracture was a reluctance of patients[7]. This finding was probably related to the lack of awareness regarding the impact of osteoporosis on fragility fractures[8].

Previously, limited media coverage of osteoporosis might have been related to a lack of awareness of the disease, its clinical implications following a low-energy trauma fracture, and the benefits of treatment for prevention of future fractures[9,10]. However, a growing body of literature and exposure in the media has led to a recent increase in awareness of osteoporosis and related fractures[11-13]. Orthopedic surgeons should attempt to expand their awareness of osteoporosis treatment, particularly for patients who have suffered from previous osteoporotic fractures. The purpose of this study was to evaluate current practice in the treatment of osteoporosis in patients who have undergone treatment for hip fracture in South Korea.

MATERIALS AND METHODS

Members of the Korean Hip Society (KHS) are orthopedic hip surgeons involved in treatment of hip fractures in South Korea. A survey of members of KHS on the management of osteoporosis in patients who have undergone treatment for hip fracture was conducted. Among the 568 KHS members, 97 surgeons (17%) participated in this survey.

Survey questionnaires included basic demographic data on the surgeons. Age groups from 30 to over 60 years old were stratified. The levels of medical institutions where surgeons were practicing were categorized as tertiary hospitals (≥500 beds), general hospitals (100-500 beds), hospitals (30-100 beds), and clinics (≤30 beds). Surgeons were also asked whether they were involved in educating orthopedic residents. A short-answer question regarding the duration of treatment as an orthopedic surgeon was included.

The survey on the general treatment of osteoporosis in patients with hip fracture included the following items: routine laboratory tests for management of osteoporosis, the rate of prescribing calcium and vitamin D in hip fracture patients, the first-line treatment option for prevention of secondary fracture, whether to prescribe different medications for patients who experienced an osteoporotic fracture compared to osteoporotic patients without fractures, and management after cessation of denosumab for treatment of osteoporosis. Items related to perception of osteoporotic medications were as follows: the most important factor in the occurrence of atypical femoral fracture (AFF), the number of AFF patients encountered by each surgeon in a month, timing of determining the reoperation for delayed union after the index operation on complete AFF, management of osteoporosis after cessation of bisphosphonate in AFF patients, and management of osteoporosis during a drug holiday in patients who are susceptible to AFF.

All surveys were conducted through google forms and analysis and charting were performed using Microsoft Excel 2016 (Microsoft Corp.). Because this study was managed by the KHS, participation through email was encouraged. A descriptive statistical method was used for presentation of results.

RESULTS

The most common age range of the participants was 41 to 50 years (40%), followed by 31 to 40 years (24%), 51 to 60 years (24%), and over 61 years (12%). The most common type of medical institution where the surgeons are practicing was tertiary hospitals (74%), followed by general hospitals (21%), hospitals (4%), and clinics (1%). Involvement in education and training of orthopedic residents was reported by 86% of the participants. The mean duration of orthopedic treatment as a hip specialist was 15.3±9.8 years (range, 1-40 years).

The mean number of hip fracture surgeries per month was 10 to 20 cases for 41%, more than 20 cases for 39%, 5 to 10 cases for 12%, and less than five cases for 7%. The most common laboratory tests routinely performed in hip fracture patients were serum vitamin D level for 82% followed by carboxy-terminal telopeptide of collagen I (CTX) for 61% (Fig. 1).

According to 52% of the responders, there was no difference in prescribing osteoporosis medications in patients with osteoporotic fracture compared to patients who have osteoporosis without fracture.

Regarding calcium supplementation, 47% of responders reported prescribing calcium in over 80% of patients with osteoporotic fracture, while 18% prescribed calcium in less than 20% of patients. Vitamin D was prescribed in over 80% of patients with osteoporotic fracture by 52% of the responders while 13% prescribed vitamin D in less than 20% of patients.

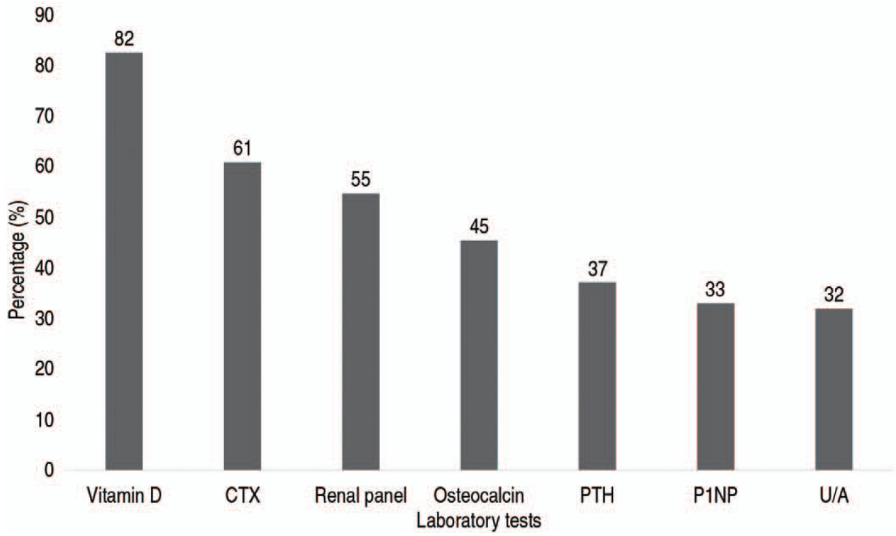

Fig. 1. Laboratory tests performed in hip fracture patients. CTX: carboxy-terminal telopeptide of collagen I, PTH: parathyroid hormone, P1NP: procollagen type I N propeptide, U/A: urinalysis.

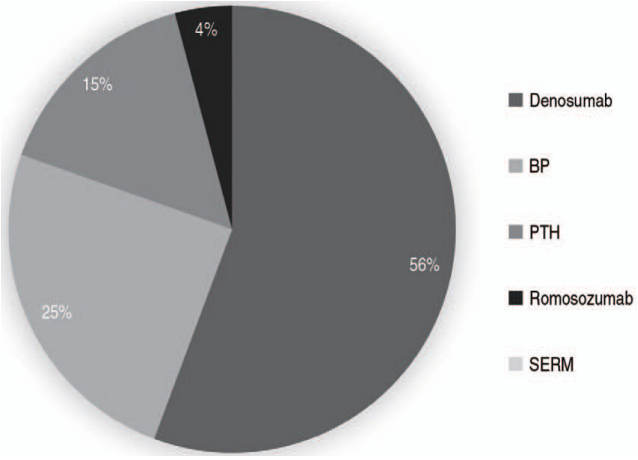

Fig. 2. First-line treatment option for osteoporosis in hip fracture patients. BP: bisphosphonate, PTH: parathyroid hormone, SERM: selective estrogen receptor modulator.

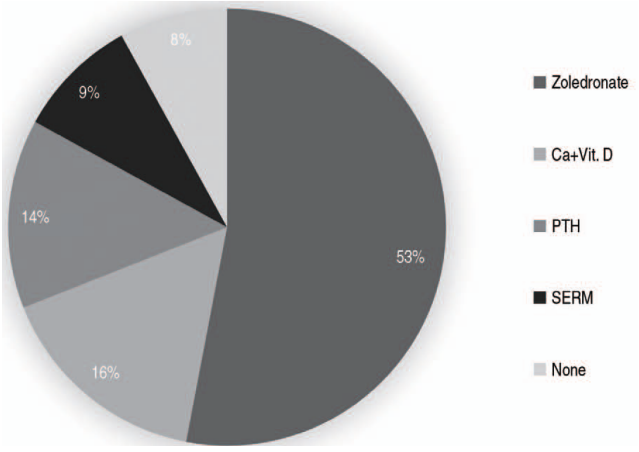

Fig. 3. Osteoporosis medication in patients with rebound phenomenon after cessation of denosumab. Ca+Vit. D: calcium and vitamin D, PTH: parathyroid hormone, SERM: selective estrogen receptor modulator.

Denosumab was the most common first-line treatment option for osteoporosis in hip fracture patients for prevention of secondary fracture, followed by bisphosphonates and parathyroid hormone (PTH). None of the participants chose selective estrogen receptor modulator (SERM) as the first-line treatment (Fig. 2).

To prevent rebound phenomenon after cessation of denosumab, zoledronate was the most commonly preferred medication (53%) followed by only calcium and vitamin D (16%), PTH (14%), and SERM (9%) (Fig. 3).

The mean number of patients with AFF treated per month was 1.7 patients (range, 0-15 patients). Bisphosphonate was the most important reason for AFF, as reported by 78% of the hip surgeons, and the remaining 22% responded that femoral bowing was the most important factor. None of the participants answered that denosumab, obesity, and high activity level were the most important recognized factors for AFF (Fig. 4). Postoperative 12 months was reported as the timing to determine the necessity of reoperation in case of delayed union by 43%, while 21% reported six months and 19% reported nine months as the appropriate timing.

Regarding the treatment strategy after cessation of bisphosphonate in patients with AFF, PTH was preferred as an osteoporosis medication by 78% of the responders (Fig. 5). For prevention of AFF in high-risk patients, prescription of only calcium and vitamin D was most common, as reported by 32% followed by

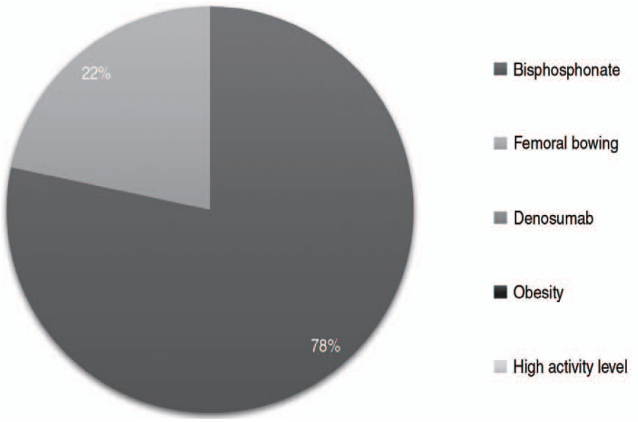

Fig. 4. The most important recognized factor for atypical femoral fracture.

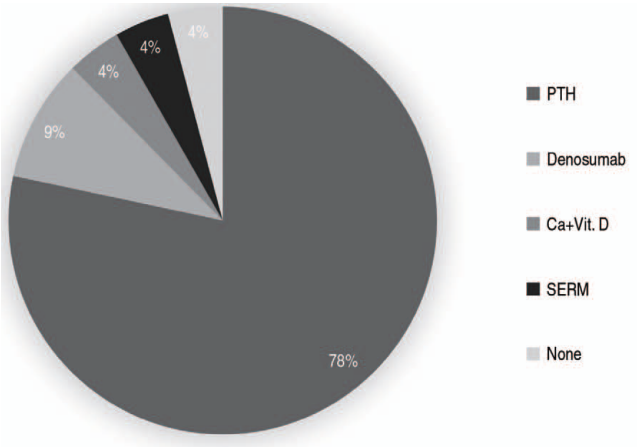

Fig. 5. Preferred osteoporosis medications after cessation of bisphosphonate in patients with atypical femoral fracture. PTH: parathyroid hormone, Ca+Vit. D: calcium and vitamin D, SERM: selective estrogen receptor modulator.

SERM by 24%, PTH by 18%, and denosumab by 16% (Fig. 6).

DISCUSSION

Evaluating the current status in the perspective of clinicians is crucial in the effort to enhance the management of osteoporosis and prevent second fractures. In this survey, vitamin D test and denosumab were the most common laboratory test and the first-line osteoporosis medication, respectively. Zoledronate was used most often to prevent rebound phenomenon after cessation of denosumab. Use of bisphosphonate and femoral bowing were regarded as the main reasons for AFF. One year was most commonly determined as appropriate timing to consider reoperation in the case of

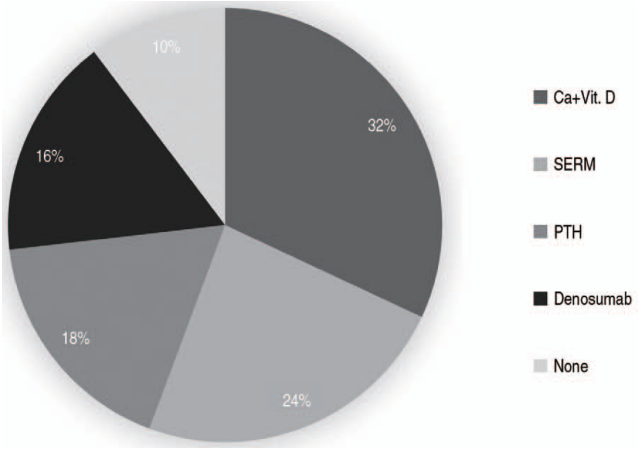

Fig. 6. Preferred osteoporosis medications in patients with high-risk of atypical femoral fracture. Ca+Vit. D: calcium and vitamin D, SERM: selective estrogen receptor modulator, PTH: parathyroid hormone.

delayed union after AFF. Calcium and vitamin D were most commonly preferred for prevention of AFF. After AFF, PTH was the most commonly preferred osteoporosis medication.

Blood tests for osteoporosis included complete blood counts, calcium, phosphorus, alkaline phosphatase, creatinine, vitamin D, thyroid stimulating hormone, liver enzymes, PTH, and bone turnover markers including CTX, P1NP (procollagen type I N propeptide), NTX (N-telopeptide of type 1 collagen), DPD (deoxypyridinoline), and PYD (pyridinoline)[14,15]. Testing for vitamin D was the most commonly performed test in this study. In the form of serum 25-OH-D, vitamin D plays an essential role in maintaining the levels of calcium and PTH. A serum 25 hydroxyvitamin D test is currently recommended for patients who have osteoporosis and who might benefit from vitamin D replacement[16]. According to the National Osteoporosis Society (NOS), less than 30 nmol/L of 25-OH-D is deficient and 30-50 nmol/L may be insufficient in some patients[8]. Although the effectiveness of vitamin D as a tool for use in evaluation of osteoporosis has been widely accepted, vitamin D supplementation as a treatment is more controversial. The findings of a meta-analysis conducted by the National Osteoporosis Foundation (NOF) demonstrated that supplementation with calcium plus vitamin D resulted in a 15% reduction in total fractures and a 30% reduction in hip fractures[17]. In contrast, some studies on the oral supplementation of vitamin D with or without calcium have reported no effect on bone mineral density (BMD) increase[18,19] or fracture prevention regardless of the rise in serum vitamin D levels[20,21]. This may be related

to aging-related declines of hepatic and renal function, which can affect hydroxylation of vitamin D[22]. In this regard, more potent vitamin D analogues, such as alfacalcidol, have been considered as an alternative to vitamin D in treatment of osteoporosis[23].

In this study, denosumab was the most popular medication for the first-line treatment of osteoporosis. The 3-year FREEDOM trial, the most prominent study that led to the current popularity of denosumab, reported a substantial reduction of osteoporotic fractures in denosumab-treated patients[24]. Compared to bisphosphonates, BMD was further increased by denosumab at 12 months at all fracture sites with lower levels of bone turnover markers[25]. Although no cases of osteonecrosis of the jaw (ONJ) or AFF were included in the FREEDOM trial[24], two AFFs[26] and 13 ONJ[27] were identified in FREEDOM Extension. More importantly, the rebound increase of bone turnover markers and elevated risk of multiple vertebral fractures necessitated the awareness of rebound phenomenon after discontinuation of denosumab[28,29]. To avoid rebound phenomenon, zoledronate was used most often after cessation of denosumab in the current study. Administration of bisphosphonate has been an effective strategy in the effort to overcome rebound phenomenon[30]. However there is still a challenge in patients with renal insufficiency, AFF, or ONJ, which proscribe the use of potent bisphosphonates[31]. Conduct of more extensive studies on the rebound phenomenon of denosumab discontinuation is warranted.

AFF, which was introduced as a detrimental effect of long-term bisphosphonate treatment, is a challenging fracture due to the high rate of nonunion. The results of this study indicated that bisphosphonate (78%) and femoral bowing (22%) were the main causes of AFF. Many recent studies have reported on a relation between geometrical features of the femur and the occurrence and location of AFF. Severe anterolateral bowing of the femur is related to AFFs, and to diaphyseal AFFs in particular[32-36]. The reported effect of bisphosphonate in bone microstructure is a lower number of Haversion canals, larger osteon diameter, and a lower proportion of osteocyte lacunae[37-39]. While femoral bowing represents the mechanical factor of AFF as in stress fracture, long-term use of bisphosphonates represents the biological factor of AFF. In the study comparing 196 cases of AFF with 94 cases of typical proximal femur fractures by Lim et al.[40], the adjusted odds ratios for bisphosphonate use, coronal femoral curvature, and sagittal femoral curvature in development of AFF were 25.65 (95% confidence interval [CI] 10.74-61.28), 1.23 (95% CI 1.04-1.45), and 1.25 (95% CI 1.09-1.44), respectively. However, recent studies have suggested a close relation between femoral bowing and atypical fractures of the femoral shaft rather than atypical subtrochanteric fractures[32,41]. Specialized strategies for prevention of AFF should be implemented in patients with long-term bisphosphonate use or severe femoral bowing.

While intramedullary nailing of the femur continues to be the mainstay of treatment for complete and high-risk incomplete AFFs, there is still controversy regarding medical treatment[42]. According to general agreement, antiresorptive therapy should be discontinued following the diagnosis of AFFs[43,44]. Considering only AFFs and not the typical femoral fractures that can be prevented by treatment with bisphosphonates, simply ending bisphosphonate treatment would lead to a decrease in the annual risk of AFF by 70%[45]. In this study, along with discontinuing antiresorptives, 78% of hip surgeons preferred to use PTH as osteoporosis medication. This might be due to the fact that PTH is not only effective in enhancing BMD but also aids in union of AFF. Findings from a recent meta-analysis supported the use of PTH in treatment of AFF due to lower risk of nonunion and delayed union compared to the control group[46]. However, some studies have reported that sequential therapy consisting of alendronate followed by PTH is related to a temporary decline of hip BMD[47,48]. Therefore, caution is required when planning sequential therapy for patients who underwent long-term alendronate therapy prior to hip fracture.

Regarding prevention of AFF, calcium and vitamin D supplementation without prescription of osteoporotic medication was the most common option chosen in this survey. A drug holiday for bisphosphonates is currently widely accepted for the prevention of AFF[49]. During the drug holiday, regular follow-up with bone turnover markers or DXA (dualenergy X-ray absorptiometry) is sufficient for patients with a low risk of developing osteoporotic fractures. Switching antiresoprtives to anabolic agents is recommended for patients with a high risk of AFF along with thigh pain. Continuation of bisphosphonates with reassessment for the potential for administration of other treatments is recommended for patients with a relatively low risk of AFF but a

high risk of osteoporotic fractures without stress reaction[50]. With the development of novel anabolic agents and accumulating evidence of their effects in AFF, it appears that the indications for use of anabolic agents as alternatives to bisphosphonates will increase in the future.

CONCLUSION

In this survey study, management of osteoporosis by orthopedic hip surgeons was largely in compliance with the current up-to-date management strategy. Because fracture is the final outcome of osteoporosis, orthopedic surgeons should be active participants in the treatment of osteoporosis.

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Conflict of Interest

Young-Kyun Lee has been an editorial board member since January 2023, but had no role in the decision to publish this article. No potential conflict of interest relevant to this article was reported.

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