Parathyroid Hormone Injection Versus Vertebroplasty in the Treatment of Osteoporotic Vertebral Fracture in Old Age: A Retrospective Study of 58 Female Patients

Incheol Kook
Hanyang University Guri Hospital
Byeong-Jik Kang
Hanyang University Guri Hospital
Ye-Soo Park (hyparkys@hanyang.ac.kr)
Hanyang University Guri Hospital

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Abstract

Background: While the indications of parathyroid hormone (PTH) in osteoporosis prevention and management have been established, its indications in the treatment of osteoporotic vertebral fractures remain unknown. This study aimed to compare the effects of intervention (percutaneous vertebroplasty followed by anti-resorptive agents) and conservative treatment (PTH administration) in patients with osteoporotic vertebral fractures, as well as to investigate the optimal duration of PTH administration.

Methods: A retrospective study was conducted using data of patients treated for osteoporotic vertebral fractures between January 2015 and November 2019. Treatment was selected based on the patient's age, comorbidities, and patient's preference after explaining the expected advantages and disadvantages of each treatment. Group C was administered PTH injections once weekly, whereas Group I underwent vertebroplasty followed by the administration of anti-resorptive agents. Radiological and clinical parameters were analyzed between two groups.

Results: This study enrolled 58 patients (77 vertebrae). Group C included 24 patients (38 vertebrae) with average age of 77.50 ± 7.19 years (range, 65–85 years), average bone mineral density (BMD) of −3.39 ± 0.86 (range, −2.5 to −5.8), average follow-up period of 27.47 ± 7.60 weeks (range, 12–49 weeks). Group I included 34 patients (39 vertebrae) with an average age of 76.20 ± 8.67 years (range, 65–92 years), average BMD of −3.35 ± 0.91 (range, −2.5 to −5.1), average follow-up period of 30.82 ± 10.95 weeks (range, 16–59 weeks). There was no significant difference between the two groups in initial demographic, clinical and radiographic parameters. Group I showed significantly better clinical and radiological outcome during the last follow-up. Regarding side effects in Group C, two cases of dizziness (8.3%), nausea and vomiting (8.3%) were reported. In Group I, cement leakage was found in 26 vertebrae (66.7%), and cement leakage complications were observed in four patients (11.8%).

Conclusion: Conservative treatment using PTH injection demonstrated slower pain relief and lesser suppression of vertebral height loss than vertebroplasty. However, PTH injection demonstrated a lower risk of procedure-related complications. The patient's age, preference, and general condition with respect to the procedure's risk should be considered when determining treatment options for osteoporotic vertebral fracture in old age.

Introduction

Osteoporotic vertebral fracture is a typical fracture type caused by osteoporosis, with an incidence of 7.6–14% reported among women in their 60s and 30–45% among those in their 70s [1-3]. Osteoporotic vertebral fractures increase fracture risks in other vertebral bodies, and both repeated fractures and deformity progression at the fracture site can cause persistent pain and reduce the quality of life significantly [4-6]. Non-union or delayed union at the fracture site limits physical activities in the long term, and vertebral body collapse can lead to neurologic deficits; therefore, osteoporotic vertebral fractures may require operative treatment [7, 8]. Early diagnosis and treatment of osteoporotic vertebral

fractures are crucial for preventing pain and complications caused by non-union and pseudarthrosis [9]. The osteoporotic vertebral fractures treatment must not only achieve short-term goals, such as helping the patient return to his/her daily routine quickly and restoring his/her quality of life through pain control, but also achieve long-term goals, such as promoting bony union, minimizing vertebral body collapse, and preventing secondary fractures or bone density reduction [10]. An intermittent injection of parathyroid hormone (PTH) promotes the formation of the cortical bone and cancellous bone, and is thus commonly used to treat patients with severe osteoporosis who are at a high risk of osteoporotic fractures [11]. The suggestion of the use of PTH in the treatment of osteoporotic vertebral fractures is relatively recent. Short-term follow-up studies have reported that PTH improves the bony union rate, reduces the time to union more significantly than anti-resorptive agents (i.e., bisphosphonates), and produces clinical results similar to those of percutaneous vertebroplasty (VP) [10, 12, 13]. Therefore, PTH may be clinically effective and useful in treating osteoporotic vertebral fractures. However, while the indications of PTH in osteoporosis prevention and management have been established, its indications in the treatment of osteoporotic vertebral fractures are not known. Thus, this study aimed to compare the effects of an existing treatment method (percutaneous VP followed by the administration of anti-resorptive agents) and PTH administration in patients with osteoporotic vertebral fractures. Furthermore, we aimed to investigate the optimal duration of PTH administration based on clinical and radiological parameters.

Materials And Methods

This study was approved by the Institutional Review Board of our hospital. Among all the female patients aged ≥65 years, who were admitted to the hospital for osteoporotic vertebral fractures from January 2015 to November 2019, 58 patients (77 vertebrae) with a follow-up period of at least 3 months were included. Plain radiograph and physical examination were performed for female patients who visited the emergency department or an orthopedic outpatient clinic for acute lower back pain complaint. Those with suspected osteoporotic vertebral fractures were admitted to the hospital for lumbar magnetic resonance imaging (MRI) and bone densitometry.

An acute vertebral fracture was confirmed based on low signals on T1-weighted images and high signals on T2-weighted images, respectively, on lumbar MRI. The mean bone mineral density (BMD) of the L1 to L4 vertebrae and that of femoral neck was measured. The mean BMD of the two vertebral bodies with the lowest bone density was used as the lumbar BMD. For the femur, the BMD excluding that of the Ward's triangle was used. Osteoporosis was defined as a T-score ≤−2.5. Patients confirmed with osteoporotic vertebral fractures were subjected to either conservative treatment with weekly administration of 56.5 μg of teriparatide (Teribone®, Asahi Kasei Pharma Corporation, Tokyo, Japan) or an intervention consisting of percutaneous VP followed by the oral administration of anti-resorptive agents (alendronic acid, Fosamax®, Merck & Co., Inc. Kenilworth, NJ, USA). An appropriate treatment method was chosen for each patient after explaining each treatment's advantages and side effects and considering their preference, age, and general condition. In the conservative treatment group (Group C), PTH administration ceased only when their pain levels were clinically low and did not interfere with daily activities (visual analog

scale [VAS] score ≤3). There were no signs of fracture progression on follow-up plain radiographs, and radiological parameters had stabilized. Anti-resorptive agents (denosumab, Prolia®, Amgen Inc., Thousand Oaks, CA, USA) were then subcutaneously injected. The patients were examined for any side effects of PTH administration during hospital admission and outpatient follow-up. In the intervention treatment group (Group I), alendronic acid (Fosamax®), an oral anti-resorptive agent, was administered weekly following percutaneous VP. All procedures were performed by a single operator (YSP). The operator checked the patient's neurological status before performing the procedure, any cement leakage on plain radiographs, as well as any complications associated with cement leakage after the procedure. Patient's age, sex, and underlying diseases were investigated through a review of medical records, and clinical and radiological parameters were measured during hospital admission and outpatient follow-up. The exclusion criteria for patients were follow-up period <3 months, neurologic deficits at the time of their initial admission, tumor or infection at the fracture site, proof of secondary osteoporosis based on their records of underlying diseases or medication prescriptions, and history of osteoporosis treatment before receiving treatment at the present hospital.

Following hospital discharge, all patients visited the outpatient clinic 1 month after treatment. They visited the clinic monthly until 3 months after the start of the treatment, after which they visited the clinic every 3 months. Pain levels were measured using the VAS at the time of admission and during the outpatient follow-up. MRI was used at the time of admission to identify the type of acute vertebral fracture (compression fracture or stable burst fracture) and the fracture site (thoracolumbar: T9-L2, or lumbar: L3-L5). The local kyphotic angle at the fracture site and the compression rate and its changes were measured on plain radiographs during admission and outpatient follow-up. The local kyphotic angle was defined as the angle between the upper and lower endplates of the fractured vertebra. The compression rate was calculated using Mumford's method, which calculates the anterior height of the fractured vertebra by taking the mean of the anterior heights of the upper and lower vertebrae of the fractured vertebra [14].

Two examiners (ICK and BJK) independently measured radiological parameters. The measurement was repeated after 1 month to assess the intraobserver reliability.

When comparing the demographic, radiological, and clinical characteristics of the patients of the two groups, an independent t-test was used for continuous variables, and a chi-square test or Fisher's exact test was used for categorical variables. A paired t-test or Wilcoxon signed-rank test was used to examine the changes in each group's follow-up period. Intraclass correlation coefficients were used to measure the degree of agreement between the measurements of continuous radiological variables. All statistical analyses were performed using Statistical Package for the Social Sciences version 20.0 (SPSS Inc., Chicago, IL, USA). The level of statistical significance was set at $p < 0.05$.

Results

In this study, 58 patients were analyzed. Group C included 24 patients and 38 vertebrae, and Group I included 34 patients and 39 vertebrae. No significant differences in age, fracture type, fracture level, mean number of fractured vertebral bodies, BMD and initial VAS scores were found between the two groups (Table 1). While there was no difference in the mean follow-up period between the two groups, Group I showed a significantly shorter time to achieve a level of pain that did not interfere with daily activities (VAS ≤3) as compared to Group C (1.54 ± 0.74 weeks vs. 9.25 ± 5.08 weeks; $p < 0.05$). In Group C, there were significant differences between the initial and final measurements of the local kyphotic angle (10.38 ± 7.74° vs. 13.78 ± 9.40°; $p < 0.05$), height of fractured vertebra (18.76 ± 4.94 mm vs. 15.72 ± 4.92 mm; $p < 0.05$), and compression rate (22.78 ± 14.50% vs. 34.18 ± 18.09%; $p < 0.05$). Group I did not show significant differences between the initial and final measurements of the local kyphotic angle (11.64±8.03° vs. 10.68±7.81°; $p = 0.428$), height of fractured vertebra (20.77 ± 5.09 mm vs. 21.40 ± 4.26 mm; $p = 0.281$), and compression rate (25.11 ± 14.87% vs. 22.74 ± 13.99%; $P = 0.308$). There were no significant differences in the initial values of the kyphotic angle, height of fractured vertebra, and compression rate between Group C and Group I. Furthermore, no significant differences were found between Group C and Group I in the final VAS score (1.79 ± 0.77 vs. 2.08 ± 0.91; $p = 0.205$) and local kyphotic angle (13.78 ± 9.40° vs. 10.68 ± 7.81°; $p = 0.119$). However, there were significant differences between the two groups in the final height of fractured vertebra (Group C: 15.72 ± 4.92 mm vs. Group I: 21.40 ± 4.26 mm; $p < 0.05$), compression rate (Group C: 34.18 ± 18.09 vs. Group I: 22.74 ± 13.99; $p < 0.05$), and changes in compression rate (Group C: −11.39 ± 11.38% vs. Group I: 2.36 ± 14.26%; $p < 0.05$) (Fig. 1, 2).

Table 1
Demographic and initial clinical data of the participants*

	Group C	Group I	P-value
Age (years)	77.5 ± 7.2	76.20 ± 8.67	0.551
BMD	−3.4 ± 0.8	−3.35 ± 0.91	0.871
Initial VAS	8.04 ± 1.16	8.11 ± 1.23	0.821
Fracture type	14:24	18:21	0.407
(Burst:Compression)			
Fracture level	31:7	30:9	0.615
(TL:Lower lumbar)			
Number of fractures	1.6 ± 1.2	1.2 ± 0.4	0.094

*Data are presented as mean ± standard deviation

Group C, conservative group; Group I, intervention group; BMD, bone mineral density; VAS, visual analog scale; TL, thoracolumbar

In Group C, the point at which the radiological parameters did not change but stabilized was investigated. It was found that the local kyphotic angle and compression rate did not significantly change after 16.44 ± 7.37 weeks (range, 8–38 weeks). The height of fractured vertebra stabilized around 24.65 ± 8.75 weeks (range, 18– 38 weeks) (Table 2).

Table 2
Comparisons of clinical and radiological outcomes between the two groups*

	Group C	Group I	P-value
Follow-up (weeks)	27.47 ± 7.60	30.82 ± 10.95	0.123
Initial-VAS	8.04 ± 0.86	8.11 ± 1.23	0.821
Final-VAS	1.46 ± 0.90	1.13 ± 0.83	0.152
Time to acceptable VAS score ≤3 (weeks)	9.25 ± 5.08	1.54 ± 0.74	0.000†
Initial kyphotic angle (°)	10.38 ± 7.74	11.64 ± 8.03	0.486
Final kyphotic angle (°)	13.78 ± 9.40	10.68 ± 7.81	0.119
Initial vertebral height (mm)	18.76 ± 4.94	20.77 ± 5.09	0.084
Final vertebral height (mm)	15.72 ± 4.92	21.40 ± 4.26	0.000†
Initial height loss (%)	22.78 ± 14.50	25.11 ± 14.87	0.490
Final height loss (%)	34.18 ± 18.09	22.74 ± 13.99	0.000†
Change of height loss (%)	11.39 ± 11.38	2.36 ± 14.26	0.000†
Time to kyphotic angle plateau (weeks)	16.44 ± 7.37	-	
Time to vertebral height plateau (weeks)	24.65 ± 8.75	-	
Time to height loss plateau (weeks)	24.65 ± 8.75	-	

*Data are presented as mean ± standard deviation; †P < 0.05

Group C, conservative group; Group I, intervention group; VAS, visual analog scale

The measurements for the local kyphotic angle had an excellent interobserver reliability of 0.846. The height of the fractured vertebra and compression rate also showed excellent interobserver reliability. Moreover, the intraobserver reliability for the measurements obtained after 1 month by two examiners was rated as “excellent” to “very good” (Table 3).

Table 3
Interobserver and intraobserver reliability of radiologic parameters

	Interobserver	Intraobserver (ICK/BJK)
Initial kyphotic angle (°)	0.846	0.784/0.805
Final kyphotic angle (°)	0.875	0.794/0.871
Initial vertebral height (mm)	0.808	0.859/0.789
Final vertebral height (mm)	0.845	0.802/0.794
Initial height loss (%)	0.828	0.851/0.823
Final height loss (%)	0.837	0.823/0.830
ICK/BJK, two examiners independently measuring the radiological parameters		

Regarding complications and side effects, there were two cases (8.3%) of dizziness and two (8.3%) of nausea in Group C (Table 4). Dizziness, nausea, and vomiting were all transient symptoms that improved without treatment and were not severe enough to cease treatment. In Group I, 26 of the 39 vertebral bodies (66.7%) showed cement leakage on plain radiographs, and four (15.5%) of these vertebral bodies had severe complications.

In one case, the cemented foreign body was removed under general anesthesia because of acute chest pain and heart failure induced by the leaked cement that entered the heart through the bloodstream following percutaneous VP. In another case, the leaked cement caused pulmonary thromboembolism, and two cases showed neurologic deficits (Table 4). Both cases of neurologic deficits showed transient motor weakness and paresthesia in the dermatome that disappeared within a few weeks of follow-up (Fig 3).

Table 4
Complications reported in both groups

	Group C (n = 24)	Group I (n = 34)
Cardiovascular (%)	0 (0%)	1* (2.94%)
Respiratory (%)	0 (0%)	1† (2.94%)
Neurology (%)	0 (0%)	2 (5.88%)
Dizziness (%)	2 (8.33%)	0 (0%)
Nausea or Vomiting (%)	2 (8.33%)	0 (0%)
*cardiac foreign body; †pulmonary thromboembolism		

Discussion

PTH is a bone forming agent that significantly reduces the risk of osteoporotic vertebral fracture and treats it effectively, especially in multiple level fractures [6, 15, 16]. While previous studies reported that conversion to anti-resorptive agents is necessary after 2 years of PTH administration for the treatment of osteoporosis, there is no standard duration of PTH administration established for acute osteoporotic vertebral fractures [17-19]. This study compared the conservative treatment group (Group C) and the intervention treatment group (Group I). Group C was administered PTH weekly until VAS scores reached ≤3 and radiological parameters had stabilized, followed by administration of anti-resorptive agents, whereas Group I was administered oral anti-resorptive agents after percutaneous VP. Group C required an average of 9.25 ± 5.08 weeks (range, 4–22 weeks) to achieve VAS scores ≤3 and 16.44 ± 7.37 to 24.65 ± 8.75 weeks for the stabilization of radiological parameters.

Although percutaneous VP is commonly used to treat osteoporotic vertebral fractures, studies have reported that patients still experience difficulty in returning to a daily routine after this procedure [20, 21]. Although percutaneous VP is effective in relieving acute pain, it has certain limitations. Percutaneous VP showed no significant difference in symptom relief when compared to conservative treatment at 12 months after the onset of a fracture and no evident symptom relief when compared to a sham procedure [22-25]. There have been reports of interruption of bony union at the fracture site by the injected bone cement and occurrence of re-fracture at the site of cement injection [26]. The leakage of the cement injected into a fractured vertebra can cause unexpectedly severe complications [27]. In a study that compared the findings from a 3-month follow-up of patients undergoing PTH treatment or percutaneous VP, the latter significantly relieved pain in the first week and increased the height of the fractured vertebra at 3 months after the onset of the fracture. However, it did not show a significant difference in the pain level and the ability to perform daily activities after 3 months when compared to PTH treatment. Moreover, there were lower medical expenditures reported in the PTH group as compared to the percutaneous VP group [10].

Previous studies on PTH examined patients with osteoporotic vertebral fractures without dividing them according to the severity of osteoporosis, and these studies only included patients with fractures of a single vertebral body. In such cases, a sample population may predominantly consist of patients with mild to moderate osteoporotic vertebral fractures. Hence, it may appear as if the patients responded well to conservative palliative treatments, such as simple bed rest, thus limiting an accurate assessment of the effects of different treatments. In the present study, a treatment plan was selected after considering patients' general conditions, BMD and number of fractured vertebral bodies. The current retrospective study setting included treatment groups resembling real-world patients more closely. Group C had a higher mean number of fractured vertebral bodies as compared to Group I (1.58 vs. 1.15), although the difference was not statistically significant. Including severe patients with the lowest BMD (T-score: −5.8) in Group C also emphasized the close setting to the real world.

It took an average of 9.25 weeks for the pain to reduce to a level that did not interfere with daily activities. However, it took 4–6 months (16.44–24.65 weeks) until the radiological parameters stabilized. A study that used plain radiographs and computed tomography to assess the continuity of cancellous bone showed that bony union took an average of 2.8 months to reach bony union through the weekly administration of PTH [13]. In our study, the local kyphotic angle, height of fractured vertebra, and compression rate were used instead of cancellous bone continuity to assess bony union, and the time to achieve bony union differed from that reported in previous studies. The results of this study suggest that it is advisable to continue the use of PTH in patients with osteoporotic vertebral fractures even after their VAS scores improve. Based on previous reports, it may be necessary to maintain PTH administration for 3–6 months after the initial administration. While percutaneous VP is an effective treatment option for acute osteoporotic vertebral fractures, its use is limited in patients with multiple vertebral fractures or underlying diseases, elderly patients, and cases where patients or their legal guardians do not consent to the operation. Percutaneous VP poses a severe risk of cement embolisms in patients with cardiovascular diseases.

Therefore, cement leakage and the resulting complications have been considered severe problems with percutaneous VP. Cement leakage may be asymptomatic, or it may cause complications such as pulmonary thromboembolism, nerve root and cord compression, and neurologic deficits [27, 28]. These complications were observed in this study as well. In most cases of cement leakage, patients experience no symptoms or only mild and transient symptoms. However, as observed in previous studies and this study, cement leakage can also cause lethal complications such as pulmonary thromboembolism and cement migration to the heart. These complications would most likely require additional procedures or operations, which not only places a physical burden on elderly patients, but also increases the duration of hospital stay and medical expenses. Although several protocols have been proposed to prevent cement leakage, extra caution is required when injecting cement in patients with severe osteoporotic vertebral fractures, as they are at a significant risk of cement leakage [29-31]. A previous study reported that the group receiving PTH for 3 months had significantly lower medical expenditures than the group undergoing percutaneous VP. This suggested that PTH is a good treatment option in elderly patients with severe osteoporotic vertebral fractures [10]. In this study, two cases of dizziness and two of nausea or vomiting were reported in the group that was administered PTH. However, these symptoms were not severe enough to cease treatment and were relieved through conservative treatment. The two most commonly reported side effects of PTH are dizziness and lower leg cramps. Other common side effects include nausea, arthralgia, fatigue, headache, and hypertension [32, 33]. A previous study reported that these side effects usually start in the early treatment period and rarely occur after 3 months of treatment [17]. This report is consistent with the results of the present study in which side effects occurred in the early treatment period and were relieved with conservative treatment. Hence, it is necessary to inform patients before starting the treatment that the aforementioned symptoms, albeit mild, may occur in the early treatment period in order to form a therapeutic relationship and ensure high compliance of the patients.

The limitations of this study include the single-center retrospective design, small sample size and relatively short follow-up period. A prospective randomized controlled trial for patients with severe osteoporotic vertebral fractures is warranted to understand the differences between PTH and conventional procedures, and to establish a more precise standard for PTH administration.

Conclusions

Conservative treatment using PTH in osteoporotic vertebral fractures achieves pain relief more slowly and prevents fracture site compression to a limited extent as compared to intervention procedures. However, it achieves evident symptom relief and does not cause side effects usually resulting from anesthesia and surgical procedures. Therefore, conservative treatment using PTH may be performed as a new and effective treatment method in patients with severe osteoporotic vertebral fractures who are of advanced age or show poor general conditions. When choosing an appropriate treatment method for osteoporotic vertebral fractures, it may be advisable to consider the patient's age, general conditions, and preferences regarding the treatment and the risks of surgery.

Abbreviations

PTH: Parathyroid hormone; VP: vertebroplasty; MRI: Magnetic resonance imaging; VAS: Visual analog scale

Declarations

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Authors' contributions

ICK, BJK and YSP contributed equally to this work. Scientific idea: YSP; Project planning: YSP; Manuscript writing: ICK, BJK; Manuscript revision: BJK, YSP; All authors read and approved the final manuscript.

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Availability of data and materials

The data used and analyzed during the current study is available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Medical Ethical Committee of Hanyang university Guri hospital has approved the research ethics approval (IRB No: 2020-06-044). All included patients consented to participate in this study and a signed consent form was obtained from each subject before analysis. All procedures were conducted according to the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

Department of Orthopedic Surgery, Guri Hospital, Hanyang University College of Medicine, Guri-si, Korea

References

1. Melton LJ, 3rd, Kan SH, Frye MA, Wahner HW, O'Fallon WM, Riggs BL: **Epidemiology of vertebral fractures in women**. *Am J Epidemiol* 1989, **129**(5):1000-1011.
2. Kitazawa A, Kushida K, Yamazaki K, Inoue T: **Prevalence of vertebral fractures in a population-based sample in Japan**. *J Bone Miner Metab* 2001, **19**(2):115-118.
3. Cho M, Moon S-H, Lee J-H, Lee JH: **Investigation of Comorbidity, Trauma History, and Osteoporotic Fractures in the Postmenopausal Population: A Nationwide, Observational, and Cross-Sectional Study of Korean Orthopedic Outpatient Clinics**. *Asian Spine J* 2019, **13**(5):779-785.
4. Lindsay R, Silverman SL, Cooper C, Hanley DA, Barton I, Broy SB, Licata A, Benhamou L, Geusens P, Flowers K *et al*: **Risk of new vertebral fracture in the year following a fracture**. *Jama* 2001, **285**(3):320-323.
5. Silverman SL, Minshall ME, Shen W, Harper KD, Xie S: **The relationship of health-related quality of life to prevalent and incident vertebral fractures in postmenopausal women with osteoporosis: results from the Multiple Outcomes of Raloxifene Evaluation Study**. *Arthritis Rheum* 2001, **44**(11):2611-2619.
6. Gallagher JC, Genant HK, Crans GG, Vargas SJ, Krege JH: **Teriparatide reduces the fracture risk associated with increasing number and severity of osteoporotic fractures**. *J Clin Endocrinol Metab* 2005, **90**(3):1583-1587.

7. Matsumoto T, Hoshino M, Tsujio T, Terai H, Namikawa T, Matsumura A, Kato M, Toyoda H, Suzuki A, Takayama K *et al*: **Prognostic factors for reduction of activities of daily living following osteoporotic vertebral fractures**. *Spine (Phila Pa 1976)* 2012, **37**(13):1115-1121.
8. Kashii M, Yamazaki R, Yamashita T, Okuda S, Fujimori T, Nagamoto Y, Tamura Y, Oda T, Ohwada T, Yoshikawa H *et al*: **Surgical treatment for osteoporotic vertebral collapse with neurological deficits: retrospective comparative study of three procedures–anterior surgery versus posterior spinal shorting osteotomy versus posterior spinal fusion using vertebroplasty**. *Eur Spine J* 2013, **22**(7):1633-1642.
9. Ikeda S, Nakamura E, Narusawa K, Fukuda F, Matsumoto H, Nakai K, Sakata T, Yoshioka T, Fujino Y, Sakai A: **Comparison of once-weekly teriparatide and alendronate against new osteoporotic vertebral fractures at week 12**. *J Bone Miner Metab* 2020, **38**(1):44-53.
10. Ma Y, Wu X, Xiao X, Ma Y, Feng L, Yan W, Chen J, Yang D: **Effects of teriparatide versus percutaneous vertebroplasty on pain relief, quality of life and cost-effectiveness in postmenopausal females with acute osteoporotic vertebral compression fracture: A prospective cohort study**. *Bone* 2020, **131**:115154.
11. Bodenner D, Redman C, Riggs A: **Teriparatide in the management of osteoporosis**. *Clin Interv Aging* 2007, **2**(4):499-507.
12. Iwata A, Kanayama M, Oha F, Hashimoto T, Iwasaki N: **Effect of teriparatide (rh-PTH 1-34) versus bisphosphonate on the healing of osteoporotic vertebral compression fracture: A retrospective comparative study**. *BMC Musculoskelet Disord* 2017, **18**(1):148.
13. Shigenobu K, Hashimoto T, Kanayama M, Ohha H, Yamane S: **The efficacy of osteoporotic treatment in patients with new spinal vertebral compression fracture pain, ADL, QOL, bone metabolism and fracture-healing - In comparison with weekly teriparatide with bisphosphonate**. *Bone Rep* 2019, **11**:100217.
14. Mumford J, Weinstein JN, Spratt KF, Goel VK: **Thoracolumbar burst fractures. The clinical efficacy and outcome of nonoperative management**. *Spine (Phila Pa 1976)* 1993, **18**(8):955-970.
15. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, Hodsman AB, Eriksen EF, Ish-Shalom S, Genant HK *et al*: **Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis**. *N Engl J Med* 2001, **344**(19):1434-1441.
16. Kitaguchi K, Kashii M, Ebina K, Sasaki S, Tsukamoto Y, Yoshikawa H, Murase T: **Effects of Weekly Teriparatide Administration for Vertebral Stability and Bony Union in Patients with Acute Osteoporotic Vertebral Fractures**. *Asian Spine J* 2019, **13**(5):763-771.
17. Minisola S, Cipriani C, Grotta GD, Colangelo L, Occhiuto M, Biondi P, Sonato C, Vigna E, Cilli M, Pepe J: **Update on the safety and efficacy of teriparatide in the treatment of osteoporosis**. *Ther Adv Musculoskelet Dis* 2019, **11**:1759720x19877994.
18. Cosman F, Crittenden DB, Ferrari S, Lewiecki EM, Jaller-Raad J, Zerbini C, Milmont CE, Meisner PD, Libanati C, Grauer A: **Romosozumab FRAME Study: A Post Hoc Analysis of the Role of Regional Background Fracture Risk on Nonvertebral Fracture Outcome**. *J Bone Miner Res* 2018, **33**(8):1407-1416.

19. Eastell R, Walsh JS: **Anabolic treatment for osteoporosis: teriparatide**. *Clin Cases Miner Bone Metab* 2017, **14**(2):173-178.
20. Venmans A, Klazen CA, Lohle PN, Mali WP, van Rooij WJ: **Natural history of pain in patients with conservatively treated osteoporotic vertebral compression fractures: results from VERTOS II**. *AJNR Am J Neuroradiol* 2012, **33**(3):519-521.
21. Jung HJ, Park YS, Seo HY, Lee JC, An KC, Kim JH, Shin BJ, Kang TW, Park SY: **Quality of Life in Patients with Osteoporotic Vertebral Compression Fractures**. *J Bone Metab* 2017, **24**(3):187-196.
22. Wardlaw D, Cummings SR, Van Meirhaeghe J, Bastian L, Tillman JB, Ranstam J, Eastell R, Shabe P, Talmadge K, Boonen S: **Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial**. *Lancet* 2009, **373**(9668):1016-1024.
23. He D, Yu W, Chen Z, Li L, Zhu K, Fan S: **Pathogenesis of the intravertebral vacuum of Kümmell's disease**. *Exp Ther Med* 2016, **12**(2):879-882.
24. Kallmes DF, Comstock BA, Heagerty PJ, Turner JA, Wilson DJ, Diamond TH, Edwards R, Gray LA, Stout L, Owen S *et al*: **A randomized trial of vertebroplasty for osteoporotic spinal fractures**. *N Engl J Med* 2009, **361**(6):569-579.
25. Buchbinder R, Osborne RH, Ebeling PR, Wark JD, Mitchell P, Wriedt C, Graves S, Staples MP, Murphy B: **A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures**. *N Engl J Med* 2009, **361**(6):557-568.
26. Lin WC, Lee YC, Lee CH, Kuo YL, Cheng YF, Lui CC, Cheng TT: **Refractures in cemented vertebrae after percutaneous vertebroplasty: a retrospective analysis**. *Eur Spine J* 2008, **17**(4):592-599.
27. Teng MM, Cheng H, Ho DM, Chang CY: **Intraspinal leakage of bone cement after vertebroplasty: a report of 3 cases**. *AJNR Am J Neuroradiol* 2006, **27**(1):224-229.
28. Schmidt R, Cakir B, Mattes T, Wegener M, Puhl W, Richter M: **Cement leakage during vertebroplasty: an underestimated problem?***Eur Spine J* 2005, **14**(5):466-473.
29. Kwon HM, Lee SP, Baek JW, Kim SH: **Appropriate Cement Volume in Vertebroplasty: A Multivariate Analysis with Short-Term Follow-Up**. *Korean J Neurotrauma* 2016, **12**(2):128-134.
30. Zhan Y, Jiang J, Liao H, Tan H, Yang K: **Risk Factors for Cement Leakage After Vertebroplasty or Kyphoplasty: A Meta-Analysis of Published Evidence**. *World Neurosurg* 2017, **101**:633-642.
31. Ding J, Zhang Q, Zhu J, Tao W, Wu Q, Chen L, Shi P, Zhang H: **Risk factors for predicting cement leakage following percutaneous vertebroplasty for osteoporotic vertebral compression fractures**. *Eur Spine J* 2016, **25**(11):3411-3417.
32. Rajzbaum G, Jakob F, Karras D, Ljunggren O, Lems WF, Langdahl BL, Fahrleitner-Pammer A, Walsh JB, Gibson A, Tynan AJ *et al*: **Characterization of patients in the European Forsteo Observational Study (EFOS): postmenopausal women entering teriparatide treatment in a community setting**. *Curr Med Res Opin* 2008, **24**(2):377-384.
33. Obermayer-Pietsch BM, Marin F, McCloskey EV, Hadji P, Farrerons J, Boonen S, Audran M, Barker C, Anastasilakis AD, Fraser WD *et al*: **Effects of two years of daily teriparatide treatment on BMD in**

postmenopausal women with severe osteoporosis with and without prior antiresorptive treatment. *J Bone Miner Res* 2008, **23**(10):1591-1600.

Figures

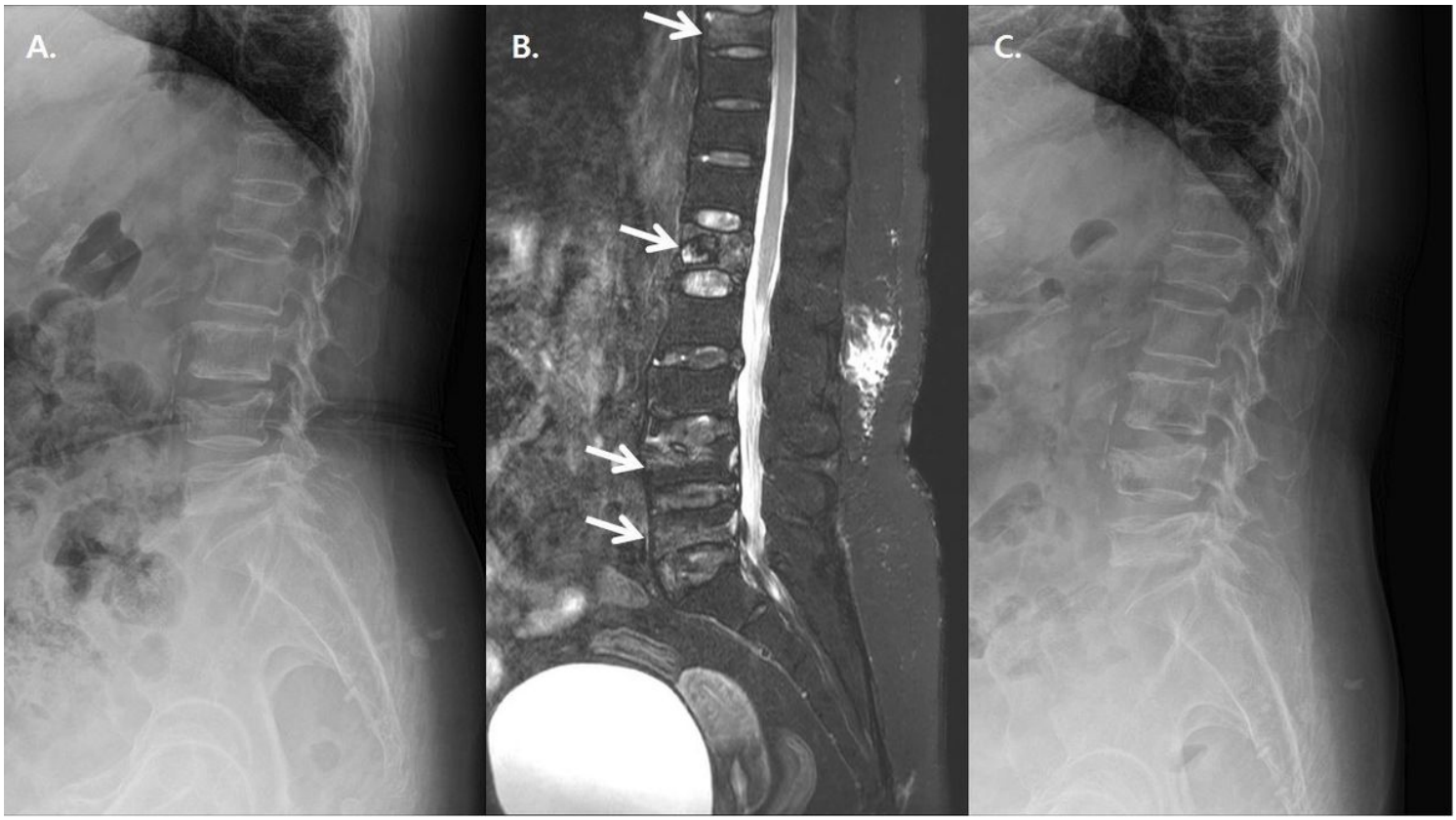
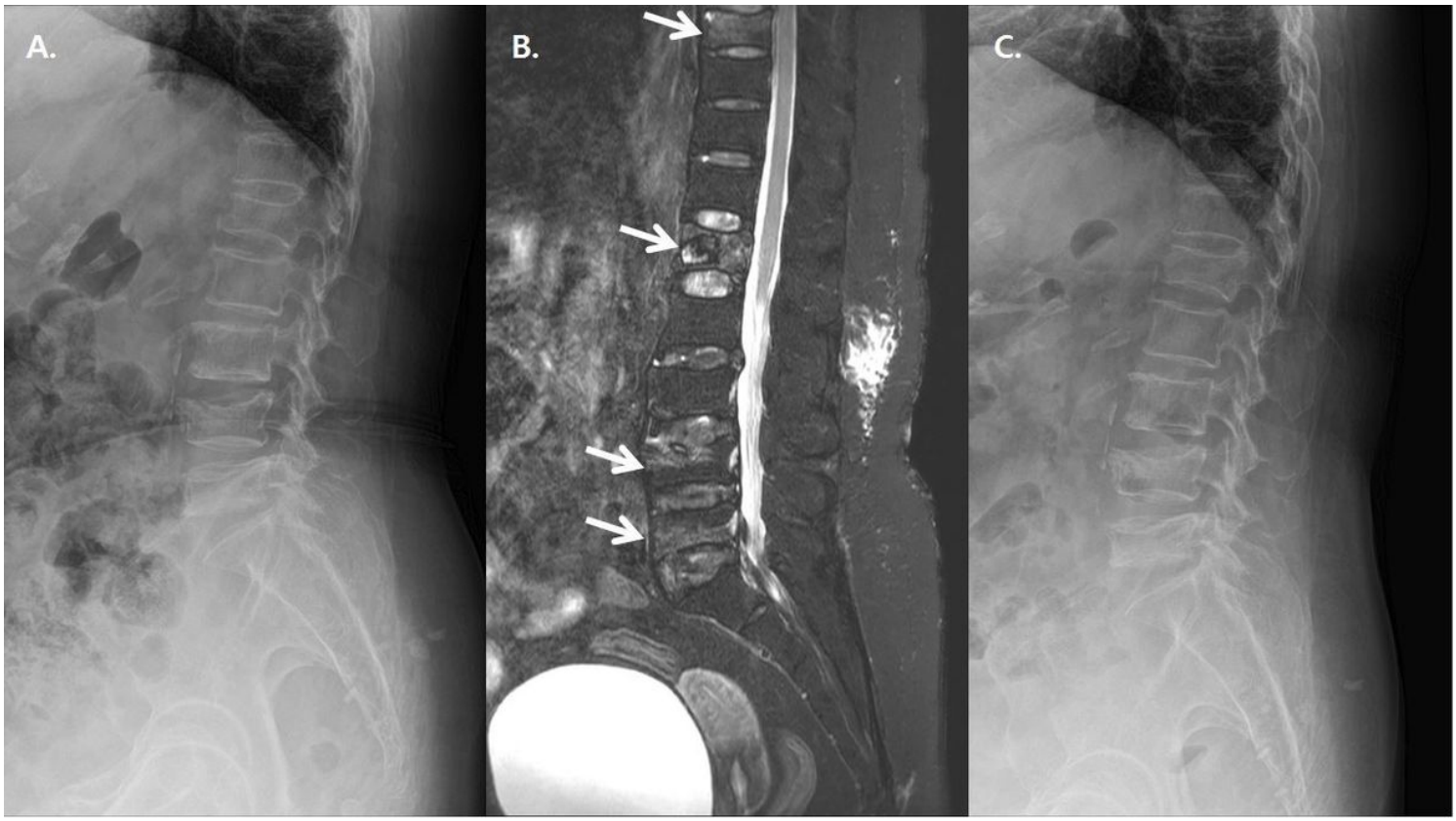


Figure 1

Case of a 77-year-old woman visiting the emergency room for lower back pain caused by falling from a height of 0.5 m. Initial radiograph and T2-weighted magnetic resonance imaging show acute fractures at T9, L1, L4, and L5 (arrow) with a height loss of 16.26%, 29.48%, 30.06%, and 22.56%, respectively (A, B). Five months after PTH injection, plain radiograph shows height loss at T9, L1, L4, and L5 levels of 11.28%, 21.68%, 26.24%, and 19.07%, respectively (C).



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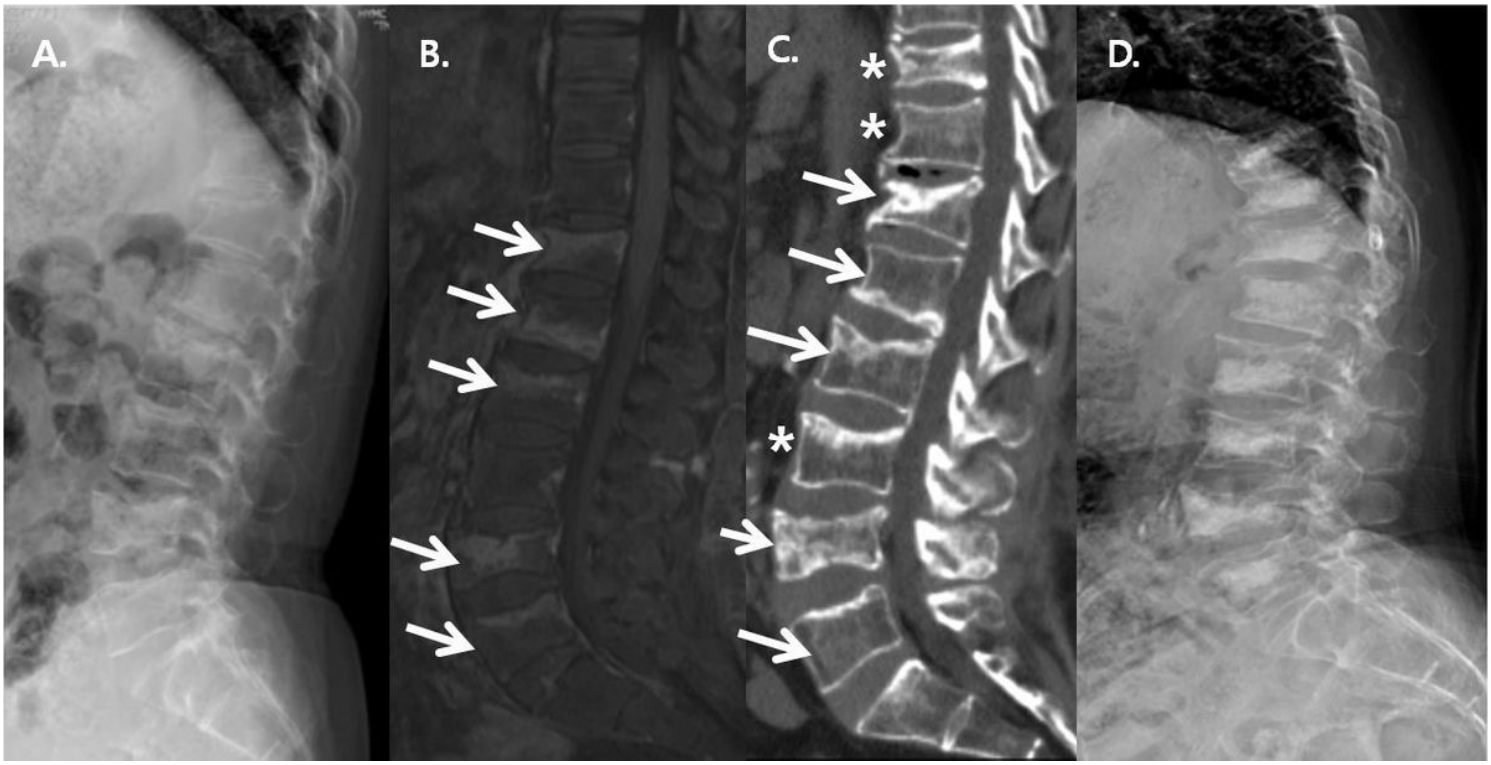
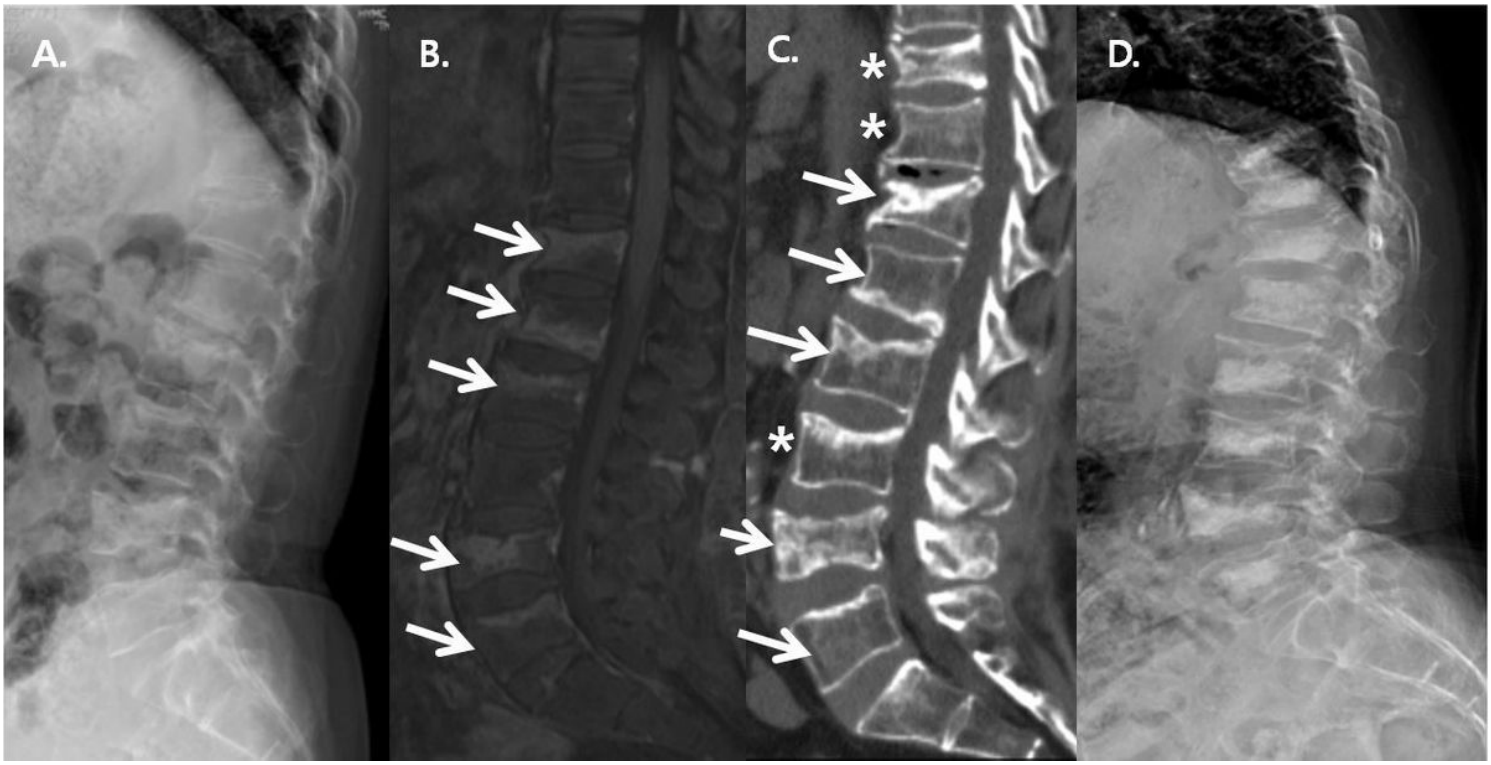


Figure 2

Case of a 68-year-old woman visiting the orthopedic outpatient clinic for lower back pain caused by slippage from the staircase. Initial radiograph and T2-weighted magnetic resonance imaging show acute fractures at T12, L1, L2, L4, and L5 (arrow) (A, B). Computed tomography 1 month after admission shows newly developed fractures at T10, T11, and L3 (asterisk) with the progression of the fractures from the pre-existing level (arrow) (C). After undergoing vertebroplasty from T10 to L5, plain radiograph shows cement injected in the vertebral bodies from T10 to L5 (D).



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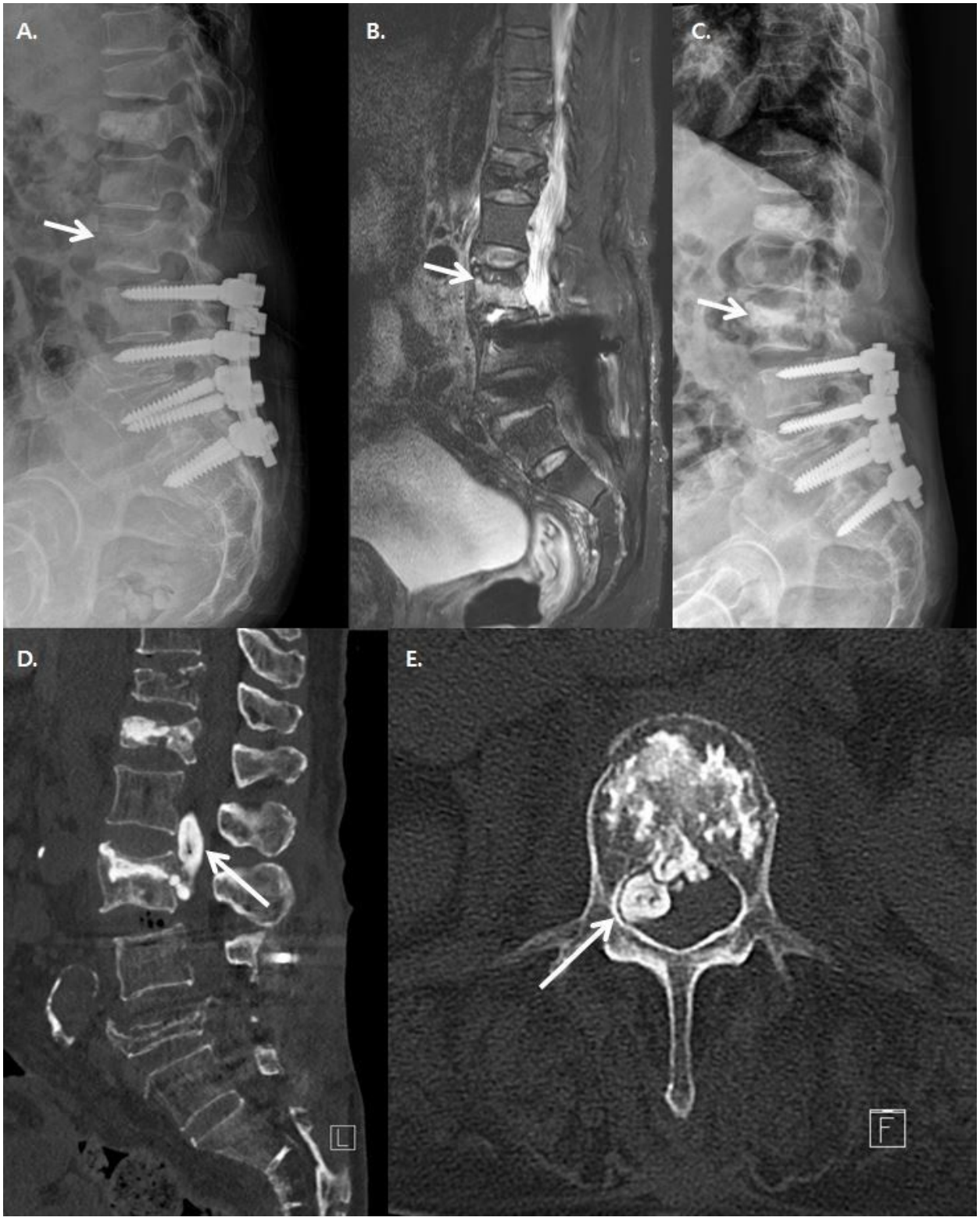
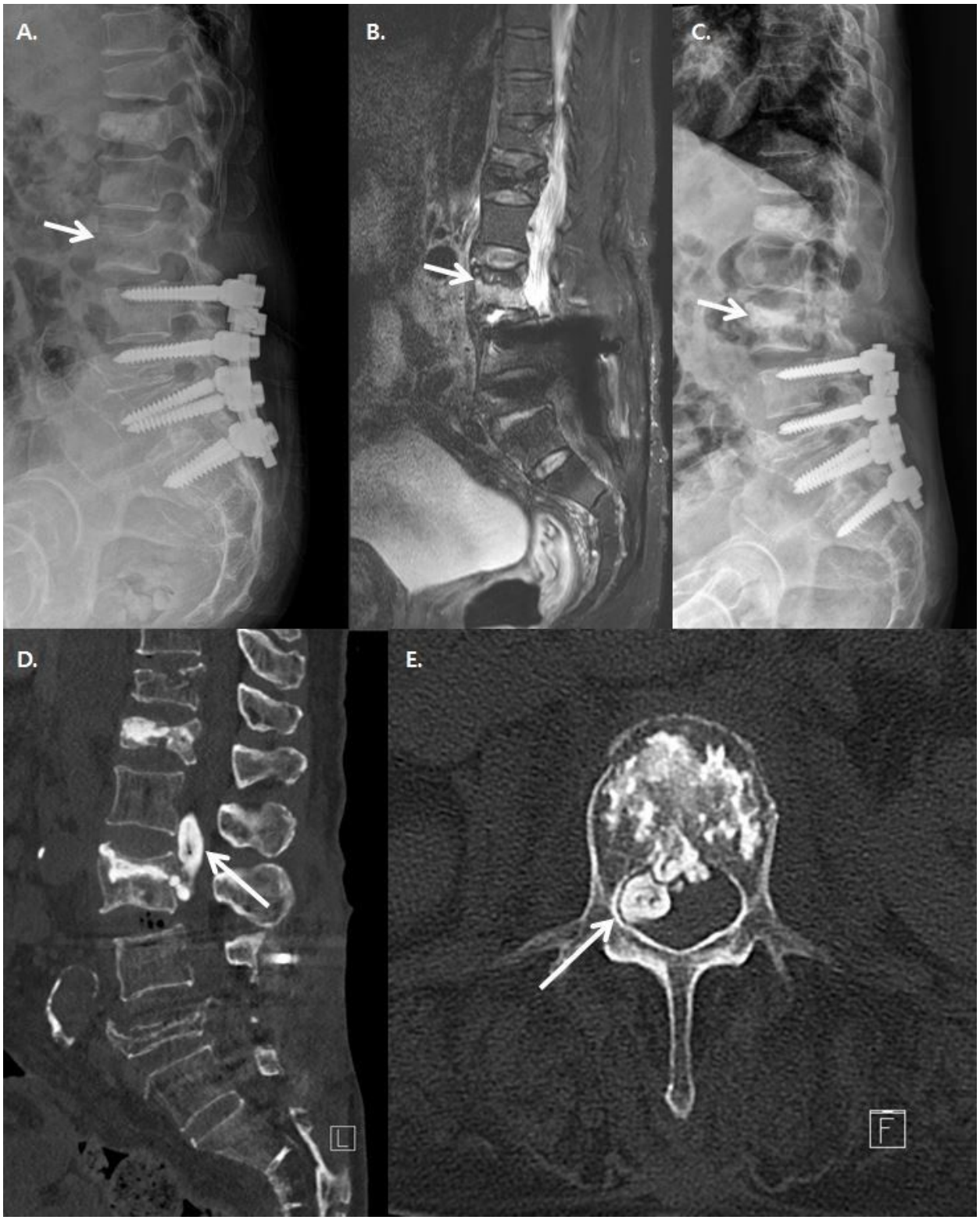


Figure 3

Case of a 79-year-old woman visiting the emergency room for lower back pain caused by slippage from ground level. Patient had undergone vertebroplasty of T12 and posterior fusion and pedicle screw fixation from L3 to S1 15 years ago because of L4 burst fracture and T12 compression fracture in a car accident. She was diagnosed as osteopenia (T-score: -1.4) at that time. Initial radiograph and T2-weighted magnetic resonance imaging show acute compression fracture at L2 (arrow) (A, B). Postoperative plain

radiograph shows cement injected at the L2 vertebral body (arrow) (C). Postoperative computed tomography shows leaked cement right side of spinal canal at L1-L2 level (D, E). Patient showed transient motor weakness of right hip flexor muscle with hypoesthesia on anterior aspect of right thigh. Her motor weakness improved within a week and was discharged as an independent ambulation status.



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