Teriparatide increases the insertional torque of pedicle screws during fusion surgery in patients with postmenopausal osteoporosis

Clinical article

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Object. The object of this study was to examine the efficacy of preoperative teriparatide treatment for increasing the insertional torque of pedicle screws during fusion surgery in postmenopausal women with osteoporosis.

Methods. Fusion surgery for the thoracic and/or lumbar spine was performed in 29 postmenopausal women with osteoporosis aged 65–82 years (mean 72.2 years). The patients were divided into 2 groups based on whether they were treated with teriparatide (n = 13) or not (n = 16) before the surgery. In the teriparatide-treated group, patients received preoperative teriparatide therapy as either a daily (20 µg/day, n = 7) or a weekly (56.5 µg/week, n = 6) injection for a mean of 61.4 days and a minimum of 31 days. During surgery, the insertional torque was measured in 212 screws inserted from T-7 to L-5 and compared between the 2 groups. The correlation between the insertional torque and the duration of preoperative teriparatide treatment was also investigated.

Results. The mean insertional torque value in the teriparatide group was 1.28 ± 0.42 Nm, which was significantly higher than in the control group (1.08 ± 0.52 Nm, p < 0.01). There was no significant difference between the daily and the weekly teriparatide groups with respect to mean insertional torque value (1.34 ± 0.50 Nm and 1.18 ± 0.43 Nm, respectively, p = 0.07). There was negligible correlation between insertional torque and duration of preoperative teriparatide treatment (r² = 0.05, p < 0.01).

Conclusions. Teriparatide injections beginning at least 1 month prior to surgery were effective in increasing the insertional torque of pedicle screws during surgery in patients with postmenopausal osteoporosis. Preoperative teriparatide treatment might be an option for maximizing the purchase of the pedicle screws to the bone at the time of fusion surgery.

(http://thejns.org/doi/abs/10.3171/2014.5.SPINE13656)

Key Words • insertional torque • teriparatide • osteoporosis • pedicle screw • fusion surgery • technique

Use of pedicle screws has become common in spinal surgery. Despite their clinical usefulness, they are associated with mechanical problems, such as implant breakage, screw loosening, and other related failures, sometimes requiring revision surgery. Loosening of pedicle screws is a common complication that can lead to pseudarthrosis, and it represents a major patient safety concern. The frequency of screw loosening reported in the literature varies from 0.6% to 27%.3,33,39,47 To decrease the frequency of screw loosening, several different concepts have been tried, including altering screw design.5,21,23,41 Screw augmentation, using bone cement or allograft, is reported to have biomechanical advantages.1,3,27,32,43 Still, fixation in the osteoporotic spine remains a difficult challenge, with a risk of failure by loosening or pullout of the pedicle screw. Osteoporosis is a very important risk factor because bone mineral density (BMD) is reported to be highly correlated with the stability of the pedicle screw.2,26 In the treatment of osteoporosis, bisphosphonates are the first-line medications for inhibiting osteoclast-mediated bone resorption, but recently intermittent administration of parathyroid hormone (PTH) has provided a new approach for the treatment of osteoporosis. Intermittently administered PTH is recognized to
have potent anabolic effects on bone remodeling, and recombinant human PTH-(1–34) (teriparatide) has already been approved as a treatment for severe osteoporosis in the United States, Europe, and Japan.\textsuperscript{3,8,31,32} 

Treatment using teriparatide is associated with a significant increase of bone mass in the lumbar spine.\textsuperscript{14,26,28,44} We previously reported that teriparatide administered daily for 2 months before surgery reduced the incidence of pedicle screw loosening after instrumented lumbar fusion in postmenopausal women with osteoporosis, suggesting that teriparatide increased not only bone mass, but also the quality of the pedicle cortex.\textsuperscript{34} However, a clinical study of the effect of teriparatide on pedicle screw insertional torque in postmenopausal women with osteoporosis has not yet been reported. The purpose of the current prospective study was to examine the efficacy of preoperative teriparatide for affecting insertional torque of pedicle screws investigated during fusion surgery in postmenopausal women with osteoporosis.

**Methods**

**Patients**

The protocols for human procedures used in this study were approved by the ethics committee of Kitasato University. Twenty-nine postmenopausal women with osteoporosis (mean age [SD] 72.2 ± 4.7 years, range 65–82 years) underwent lumbar and/or thoracic fusion surgery at Kitasato University East Hospital between January 2012 and August 2013. Informed consent for participation in this study was obtained from each of the participants. Osteoporosis was diagnosed in all of the women based on Japanese criteria and preoperative BMD, which was examined in the lumbar spine, femoral neck, or calcaneus by dual-energy x-ray absorptiometry (DEXA).\textsuperscript{10,37,46} Patients who had previously undergone spinal surgery or were diagnosed with bone metastases or infections were excluded. Patients who used products for osteogenesis, osteoinduction, or osteoconduction, except for teriparatide, were also excluded.

A summary of the patients’ clinical and demographic characteristics is shown in Table 1. All patients underwent fusion surgery with pedicle screws using the CD Horizon Solera Spinal System (Medtronic).

**Teriparatide Treatment and Marker Assessment**

The 29 patients were divided into 2 groups based on a physician’s prescription: 16 patients were allocated to a control group without medication for osteoporosis and the remaining 13 patients were allocated to a teriparatide treatment group. Patients in the teriparatide group were treated with a daily subcutaneous injection of 20 μg (n = 7, Eli Lilly) or a weekly subcutaneous injection of 56.5 μg (n = 6, Asahi Kasei Pharma Corporation). These 2 dosing regimens have received Ministry of Health, Labour and Welfare approval for severe osteoporosis in Japan. Patients decided which type of teriparatide to use after informed consent about usage rules, effectiveness based on evidence, complications, and cost. Patients who refused or were determined by a physician not to be ap-
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Fig. 1. Insertional torque was measured using a calibrated torque wrench with a specially designed connector (Medtronic).

1 at L-4 in the teriparatide group. These were excluded because the precise measurement of violation degree, which was assessed postoperatively by CT using Fu's grading system, was Grade III, which means the screw extended more than 2 mm beyond the cortex. The mean insertional torque was compared between the 2 groups using measurements obtained for a total of 212 screws. Also, insertional torque was compared among screws of different diameter and length in similar size. For this comparison, we divided the screws into 2 groups based on length (25–35 mm and 40–45 mm) and into 3 groups based on major diameter (3.5–4.0 mm, 4.5–5.5 mm, and 6.5–7.5 mm).

The correlation between insertional torque and duration of preoperative teriparatide treatment was investigated. This correlation was also investigated in the 2 subgroups: patients treated with once-daily teriparatide and those treated with once-weekly teriparatide.

Statistical Analysis

Statistical analysis was performed using JMP Pro version 9 (SAS Institute Inc.). The data are presented as the mean ± SD. The differences between the groups and the subgroups were calculated using analysis of variance and the chi-square test. The level of significance was set at p = 0.05.

Results

There were no significant differences between the control and teriparatide groups in the patients’ ages at surgery or diagnosis, or in the surgical methods used (Table 1). There were no significant between-group differences in preoperative BMD and baseline levels of intact PINP and TRACP5b, indicating no difference in remodeling between the groups prior to teriparatide treatment. The mean number of fused levels was significantly greater in the teriparatide group (4.2 ± 2.0) compared with controls (2.3 ± 1.7), but the distribution of pedicle screws at each level did not differ significantly between the 2 groups (p = 0.94; Table 2). The mean duration of teriparatide treatment was 61 ± 26.3 days in the teriparatide group. The number of fused levels was not significantly different between the subgroups treated with daily and weekly teriparatide injections.

The mean insertional torque in the teriparatide group (1.28 ± 0.42 Nm) was significantly higher than in the control group, which was 1.08 ± 0.52 Nm (p < 0.01; Fig. 2). There was no significant difference in insertional torque between the daily (1.34 ± 0.50 Nm) and weekly (1.18 ± 0.43 Nm) teriparatide subgroups (p = 0.07).

Figure 3 upper shows the insertional torque values for screws stratified by length (25–35 vs 40–45 mm). In the teriparatide group, the mean torque value for the longer screws was significantly greater than that for the shorter screws.

TABLE 2: Distribution of pedicle screw insertion levels

<table>
<thead>
<tr>
<th>Level</th>
<th>Control</th>
<th>Teriparatide</th>
<th>Total</th>
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<td>4</td>
<td>6</td>
</tr>
<tr>
<td>T-8</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>T-9</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>T-10</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>T-11</td>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>T-12</td>
<td>6</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
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<td>12</td>
<td>14</td>
<td>26</td>
</tr>
<tr>
<td>L-2</td>
<td>8</td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>L-3</td>
<td>14</td>
<td>19</td>
<td>33</td>
</tr>
<tr>
<td>L-4</td>
<td>18</td>
<td>19</td>
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<td>17</td>
<td>31</td>
</tr>
<tr>
<td>total</td>
<td>87</td>
<td>125</td>
<td>212</td>
</tr>
</tbody>
</table>

* Values represent numbers of pedicle screws. The distribution of pedicle screws at each level did not differ significantly between the 2 groups (p = 0.94).

Fig. 2. The insertional torque in the teriparatide group was 1.28 ± 0.42 Nm, which was significantly higher than in the control group, which was 1.08 ± 0.52 Nm (p < 0.01). The data are presented as the mean ± SD. *p < 0.01.
screws (1.44 ± 0.56 vs 1.14 ± 0.38 Nm, respectively, p < 0.01). In the control group, there was no significant difference between the 2 length categories. Insertional torque was significantly greater in the teriparatide group compared with controls (p = 0.03 and p < 0.01, respectively). The insertional torque was also compared among screws of 3 different diameter categories (Fig. 3 lower). In both patient groups, screws with a larger diameter had greater insertional torque. The between-group difference was statistically significant for the largest diameter category (1.14 ± 0.63 Nm vs 1.49 ± 0.56 Nm, *p < 0.01).

**Fig. 3.** Upper: Insertional torque of screws stratified by length. In the teriparatide group, the insertional torque of the longer screws was significantly greater than the torque of the shorter screws (1.44 ± 0.56 Nm vs 1.14 ± 0.38 Nm, *p < 0.01). In the control group, there was no significant difference between the 2 length categories. Insertional torque was significantly greater in the teriparatide group than the control group for both screw lengths (*p < 0.05 and **p < 0.01). Lower: Insertional torque was compared for screws in 3 different diameter categories (3.5–4.0 mm, 4.5–5.5 mm, and 6.5–7.5 mm). In both control and teriparatide groups, screws with a larger diameter had greater insertional torque. The between-group difference was statistically significant for the largest diameter category (1.14 ± 0.63 Nm vs 1.49 ± 0.56 Nm, *p < 0.01).”

In Fig. 3, we compared insertional torque for screws of different lengths and different diameters. In previous reports, biomechanical strength of pedicle screws evaluated by pullout testing was closely linked with the screw’s diameter and length. Based on these results, we compared insertional torque in 2 screw length categories and 3 diameter categories individually. Insertional torque did not differ significantly between the 2 length categories in the control group, but longer screws showed significantly greater insertional torque in the teriparatide group. Also, the correlation between insertional torque and the duration of preoperative teriparatide treatment showed negligible correlation (r² = 0.05, p < 0.01). Subgroup analysis showed negligible correlation between these two variables for both the daily and weekly treatment subgroups (r² = 0.08, p < 0.01, and r² = 0.03, p < 0.01, respectively).

**Discussion**

In this study, postmenopausal women with osteoporosis underwent instrumented fusion surgery with or without receiving at least 1 month of preoperative teriparatide treatment. Daily or weekly subcutaneous injection of teriparatide significantly increased pedicle screw insertional torque during surgery compared with the values in patients who did not receive preoperative teriparatide therapy (controls). Our study provides the first insight into the possible effects of teriparatide treatment on the insertional torque of pedicle screws in patients with postmenopausal osteoporosis. Previous papers reported that the biomechanical pullout strength of pedicle screw fixation was in direct proportion to the torque at the time of screw insertion. Previous papers have also shown that insertional torque is significantly lower in patients with osteoporosis than in those without osteoporosis, with a negative relationship reported between insertional torque and the grade of osteoporosis. In Fig. 3, we compared insertional torque for screws of different lengths and different diameters. In previous reports, biomechanical strength of pedicle screws evaluated by pullout testing was closely linked with the screw’s diameter and length. Based on these results, we compared insertional torque in 2 screw length categories and 3 diameter categories individually. Insertional torque did not differ significantly between the 2 length categories in the control group, but longer screws showed significantly greater insertional torque in the teriparatide group. Also,

![Image](image.png)

**Fig. 4.** Scatter plots for insertional torque versus the duration of preoperative teriparatide treatment. Gray circles indicate once-daily teriparatide; white circles indicate once-weekly teriparatide. There was negligible correlation (r² = 0.05, p < 0.01).
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Insertional torque was significantly greater in the teriparatide group than in controls for both screw length categories. These results indicate that teriparatide affects insertional torque regardless of screw length, but the effect is greater with longer screws. On the other hand, insertional torque was directly proportional to screw diameter in both groups, consistent with previous reports. Mean torque was greater in the teriparatide group for all diameters, but a statistically significant difference was noted only for the largest diameter category (6.5–7.5 mm). These results may depend on the difference of the area of the bone-screw interface; a smaller-diameter screw may have too small an interface to be affected by teriparatide within 1–4 months of treatment. These evaluations suggest that the insertional torque increases in screws that are longer and thicker, which have a more extensive screw-bone interface, an important factor for biomechanical strength of the pedicle screw.49

Bone mineral density is one of the important indicators used to evaluate the degree of osteoporosis, and pedicle screw pullout strength is highly correlated with BMD.13 The positive correlation between BMD and the insertional torque shown in previous studies suggests that preoperative assessment of BMD may be useful in determining the ultimate strength of screw fixation in patients in whom osteoporosis is suspected.2,20,22,29,35 Based on these previous papers, the insertional torque can be affected by osteoporosis treatments via increased BMD. In this study, we investigated BMD before treatment with teriparatide. There was no significant difference between the teriparatide treatment group and the control group, indicating that the severity of osteoporosis in the groups was similar.

Intermittent administration of PTH is reported to have potent anabolic effects on bone remodeling.25 Because this treatment increases bone mass and reduces the risk of osteoporotic vertebral fractures, teriparatide already has been approved as a treatment for severe osteoporosis in the United States, Europe, and Japan.22 The Japanese trial reported that injection of 56.5 μg teriparatide weekly for 72 weeks increased lumbar BMD by 6.4%,30 and injection of 20 μg once daily for 48 weeks increased lumbar BMD by 9.9%.26 On the other hand, a randomized trial performed in 168 centers in 9 countries reported that daily injection of 100 μg of teriparatide increased lumbar BMD by only 6.9% after 72 weeks.12 Intermittent administration of PTH is recognized to have potent anabolic effects on bone remodeling, but the optimum dosing interval is still controversial. In this study, we used 2 dosing regimens for teriparatide, daily injection of 20 μg or weekly injection of 56.5 μg; both are approved in Japan. Teriparatide was administered for a minimum of 31 days and a maximum of 117 days (mean 61.4 days). A change of BMD has never been reported with such short-term administration, and this treatment duration might be too short to result in a BMD increase. However, in addition to its effect on BMD, teriparatide has been reported to affect both cancellous and cortical structure in earlier stages of treatment.19 In cancellous bone, teriparatide is reported to increase bone volume and improve trabecular architecture via “intratrabecular tunneling,” which increases the number and connectivity of trabeculae.18,25 In cortical bone, teriparatide increases both cortical porosity and thickness at the same time, which maintains cortical bone strength.16,17,19 These structural changes have been confirmed at 6 months after teriparatide treatment using high-resolution CT,21 and could be induced earlier than a measurable increase of BMD, accounting for the increase of insertional torque found in this study following a mean duration of treatment of 61.4 days.

Our study has some limitations. First, the study was not a randomized controlled trial and the sample size was small, with limited treatment duration. In this study, treatment duration differed from patient to patient, and there was no correlation between insertional torque and treatment duration. A randomized controlled trial involving a larger number of patients or screws and longer treatment duration should be encouraged in the future. Second, preoperative BMD after teriparatide treatment was not evaluated. We only compared BMD between the 2 groups before teriparatide treatment, and there was no significant difference. The change in BMD after teriparatide treatment for less than 3 months has not been previously reported. Whether increased insertional torque could be predicted by pretreatment BMD prior to surgery is an important issue that is not addressed in this paper. Further evaluation with BMD monitoring is required.

Conclusions

Teriparatide treatment for at least 1 month prior to surgery was effective in increasing the insertional torque of pedicle screws during surgery in patients with postmenopausal osteoporosis. Preoperative teriparatide therapy could be an option for maximizing the purchase of pedicle screws in the bone at the time of fusion surgery.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Inoue, Ohtori. Acquisition of data: Inoue, Ueno, Nakazawa, Imura, Saito. Analysis and interpretation of data: Inoue, Ueno, Saito, Uchida. Drafting the
article: Inoue, Toyone, Takahira, Takaso. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Inoue. Statistical analysis: Inoue. Administrative/technical/material support: Uchida. Study supervision: Takaso.

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Manuscript submitted July 14, 2013. Accepted May 5, 2014.

Please include this information when citing this paper: published online June 6, 2014; DOI: 10.3171/2014.5.SPINE13656.

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