Weekly injection of teriparatide for bone ingrowth after cementless total knee arthroplasty

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ABSTRACT

Purpose. To compare bone mineral density (BMD) in patients with or without weekly injection of teriparatide to promote bone ingrowth after cementless total knee arthroplasty (TKA).

Methods. Records of 8 men and 32 women (mean age, 75.6 years) who underwent cementless TKA for medial knee osteoarthritis with (n=20) or without (n=20) once-weekly subcutaneous/hypodermic injection of teriparatide for 48 weeks were reviewed. BMD and bone volume/total volume (BV/TV) of the bone-prosthesis interface of the proximal tibia in 6 regions of interest (ROI) were assessed at 3, 6, 9, and 12 months using multi-detector computed tomography.

Results. Patients with or without weekly injection of teriparatide after cementless TKA were comparable in terms of baseline characteristics and pre- and post-operative knee range of motion and Knee Society knee and function scores. In ROI 1 (medial), ROI 3 (anteromedial), and ROI 4 (posteromedial), the BV/TV increased throughout the postoperative period in patients with weekly injection of teriparatide and declined after 6 months in patients without weekly injection of teriparatide. These 3 ROIs of the 2 groups differed significantly only in BMD at 6, 9, and 12 months. In ROI 2 (lateral), ROI 5 (anterolateral), and ROI 6 (posterolateral), both BV/TV and BMD showed a decreasing trend, and these 3 ROIs of the 2 groups did not differ significantly.

Conclusion. Weekly injection of teriparatide after cementless TKA promoted bone ingrowth mostly in the medial aspect of the bone-prosthesis interface.

Key words: arthroplasty, replacement, knee; bone density; teriparatide

INTRODUCTION

The parathyroid hormone (PTH) drug—PTH 1-34 (teriparatide) [Teribon; Asahi Kasei Pharma Corporation, Tokyo, Japan]—is produced by chemical synthesis of the N-terminal 34 amino acids comprising the active region of human PTH. It has been approved...
for clinical use in Japan since 2011. Weekly injection of teriparatide can promote new bone formation and reduce the incidence of new bone fractures in osteoporosis patients. It promotes ossification remodelling and induces fibrous bone replacement by lamellar bone and its transformation to cortical bone. Teriparatide is effective in promoting fracture healing, but its effects in the early postoperative period are not well known. Bone mineral density (BMD) of the proximal tibia decreases following total knee arthroplasty (TKA) as a result of shear-stress shielding, particularly during the first postoperative year. This study compared BMD in TKA patients with or without weekly injection of teriparatide to promote bone ingrowth after cementless TKA.

MATERIALS AND METHODS

This study was approved by the institutional review board of our hospital. Informed consent was obtained from each patient. Records of 8 men and 32 women (mean age, 75.6 years) who underwent cementless TKA for medial knee osteoarthritis by a single surgeon between October 2012 and January 2013, followed by having (n=20) or not having (n=20) once-weekly subcutaneous/hypodermic injection of teriparatide for 48 weeks were reviewed. The TKA was minimally invasive, with a skin incision of 6 to 11 cm. A trabecular tantalum modular tibia component (Nexgen CR-Flex; Zimmer, Warsaw [IN], USA) was used. The posterior cruciate ligament was retained. Walking was allowed on day 1. Patients with postoperative malalignment or radiolucency were excluded.

According to the American Society for Bone and Mineral Research, BMD (bone mineral content/total volume [BMC/TV]) and bone volume/total volume (BV/TV) of the bone-prosthesis interface of the proximal tibia were assessed at 3, 6, 9, and 12 months using multi-detector computed tomography. A cylinder made of cortical bone–like material and filled with cancellous bone–like material was placed under the knee. The cancellous trabecular structure was reconstructed with 3-dimensional osteomorphometry software (TRI/3D-BON64; RATOC System Engineering, Tokyo, Japan).

To avoid inaccurate delineation caused by artefacts from the prosthesis, the bone-prosthesis interface of the proximal tibia was divided into 6 regions of interest (ROI) consisting of 2 cylindrical volumes, each 16 mm in diameter and 8 mm in height, with their tops 0.6 mm below the medial or lateral peg, with each further divided into 2 half-cylinders: ROI 1 (medial), ROI 2 (lateral), ROI 3 (anteromedial), ROI 4 (posteromedial), ROI 5 (anterolateral), and ROI 6 (posterolateral) [Fig. 1]. Ossification density was assessed at 3, 6, 9, and 12 months.

Ossification density of the 2 groups at each time point was compared using the paired t-test. A p value of <0.05 was considered statistically significant.

RESULTS

Patients with or without weekly injection of teriparatide after cementless TKA were comparable in terms of baseline characteristics and pre- and postoperative knee range of motion and Knee Society knee and function scores (Table). No patient had bone fracture around the knee prosthesis.

In ROI 1 (medial), ROI 3 (anteromedial), and ROI 4 (posteromedial), the BV/TV increased throughout the postoperative period in patients with weekly injection of teriparatide and declined after 6 months in patients without weekly injection of teriparatide. These 3 ROIs of the 2 groups differed significantly only in BMD at 6, 9, and 12 months (Fig. 2).

In ROI 2 (lateral), ROI 5 (anterolateral), and ROI 6 (posterolateral), both BV/TV and BMD showed a
decreasing trend, and these 3 ROIs of the 2 groups did not differ significantly (Fig. 2).

**DISCUSSION**

Cemented TKA may result in complications such as cement toxicity, residual cement particles, and loosening due to cement degradation. Cementless TKA enables bone ingrowth in hydroxyapatite-coated components.\(^{13}\) Porous tantalum tibial components resemble cancellous bone and have a high coefficient of friction,\(^{14}\) high porosity, and low elastic modulus. The motion of tibial components assessed by radiostereometric analysis has been reported. Trabecular metal is migratory at 3 months but stable at 1 year.\(^{15}\) Tibial components migrate initially and then stabilise, and migration tends to be greater in patients with low bone density.\(^{16}\)

Bone strength is determined by bone density and bone quality,\(^{17}\) which is governed by the properties of the bone material and structure (microstructure). Abnormality in bone microstructure tends to occur with accelerated bone resorption, and most osteoporosis treatments aim to inhibit bone resorption using bisphosphonate and selective oestrogen receptor modulators. Teriparatide improves bone density, microstructure, and material properties by promoting ossification remodelling and has been recommended as the first treatment drug for osteoporosis.\(^{18}\) Nonetheless, weekly injection of teriparatide results in more side effects than bone resorption inhibitors (vitamin D and calcium preparations), although most are mild and transient. In a Japanese study of 290 patients treated with weekly injection of teriparatide, 127 developed adverse effects of nausea (n=54, 18.6%), vomiting (n=25, 8.6%), headache (n=22, 7.6%), and/or fatigue (n=18, 6.2%), but 52 (18.1%) of 288 patients in the placebo group also reported adverse effects.\(^{19}\)

Weekly injection of teriparatide, unlike daily administration, increases bone mass (BV/TV) through inhibition of bone resorption together with bone formation.\(^{19,20}\) Bone density correlates strongly with tibial component migration; the decrease in bone density of the proximal tibia is most significant (up to 23%) during the first 6 months after TKA.\(^{21}\)

In patients with weekly injection of teriparatide, BMD increased significantly more in ROI 1 (medial), ROI 3 (anteromedial), and ROI 4 (posteromedial).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Weekly injection of teriparatide after TKA</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=20)</td>
<td>No (n=20)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>74.13±7.40</td>
<td>77.13±6.15</td>
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<tr>
<td>No. of males:females</td>
<td>4:16</td>
<td>4:16</td>
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<td>Body mass index (kg/m²)</td>
<td>26.96±2.43</td>
<td>24.80±4.21</td>
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<td>Preop bone volume/total volume (%)</td>
<td>48.31±9.72</td>
<td>46.73±5.29</td>
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<td>Preop bone mineral density (mg/cm³)</td>
<td>121.2±6.48</td>
<td>123.7±4.01</td>
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<td>Knee Society knee score</td>
<td>Preop</td>
<td>13.88±8.31</td>
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<td></td>
<td>Postop</td>
<td>88.00±9.41</td>
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<tr>
<td>Knee Society function score</td>
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<td>62.50±11.95</td>
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<tr>
<td></td>
<td>Postop</td>
<td>79.38±10.16</td>
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<tr>
<td>Knee extension</td>
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<tr>
<td></td>
<td>Postop</td>
<td>1.25º±3.54º</td>
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<tr>
<td>Knee flexion</td>
<td>Preop</td>
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<td></td>
<td>Postop</td>
<td>129.38º±9.43º</td>
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<td>Femoral angle (β)</td>
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<td>Tibial angle (γ)</td>
<td>0.82º±2.42º</td>
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<tr>
<td></td>
<td>Tibial angle (δ)</td>
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</tr>
</tbody>
</table>

* Data are presented as mean±SD or no. of patients

† In the central portion 10 mm under the tibia
Figure 2  Comparison of patients with or without weekly injection of teriparatide in terms of bone volume/total volume (BV/TV) and bone mineral density (bone mineral contents/total volume [BMC/TV]) in the 6 regions of interest (ROI): (a) ROI 1 (medial), (b) ROI 2 (lateral), (c) ROI 3 (anteromedial), (d) ROI 4 (posteromedial), (e) ROI 5 (anterolateral), and (f) ROI 6 (posterolateral).
REFERENCES


