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Teriparatide Improves Fracture Healing and Early Functional Recovery in Treatment of Osteoporotic Intertrochanteric Fractures

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Abstract: Osteoporotic intertrochanteric fractures result in serious health problems and decrease health-related quality of life (HRQoL). Faster time-to-union is important for early return to daily activities and reduction of complications. Teriparatide has been shown to accelerate fracture healing, but the literature is sparse on this topic. The aim of this study is to assess whether teriparatide accelerates fracture healing.

Between 2008 and 2014, patients with osteoporotic intertrochanteric fractures who underwent surgical interventions were enrolled in this retrospective cohort study. Group 1 included patients who were not on any osteoporosis medication prior to fracture and who postoperatively received only calcium and vitamin D; patients in Group 2 were not on any osteoporosis medication prior to fracture, and received teriparatide and calcium and vitamin D postoperatively. Patients in Group 3 were those who were on alendronate prior to fracture and postfracture received teriparatide as well as calcium and vitamin D. Demographics, time-to-union, HRQoL (short-form health survey [SF]-12 physical component summary [PCS] and SF-12 mental component summary [MCS]), morbidities, mortalities, and radiographic and functional outcomes between groups were compared.

A total of 189 patients were enrolled in this study. There were 83 patients in Group 1, 47 patients in Group 2, and 59 patients in Group 3. A significantly shorter time-to-union was found in the teriparatide-treated groups (mean, 13.6, 12.3, and 10.6 weeks, respectively [$P = 0.002$]). With regard to SF-12 PCS, the scores were significantly better in teriparatide-treated groups at 3 months (mean, 19, 28, and 29, respectively [$P = 0.002$]) and 6 months (mean, 28, 37, and 38, respectively [$P = 0.008$]). Similar inter-group differences were noted when comparing the pain scores, the ability to get around the house, the ability to get out of the house, and the ability to go shopping at 3 and 6 months. Complications and mortality were also markedly reduced in the teriparatide-treated groups.

Postoperative use of teriparatide for 6 months appears to be an effective adjunct therapy in the treatment of patients with osteoporotic intertrochanteric fractures. However, because of the limited power of the study, a prospective, randomized, large-scale cohort study is still required for determining the efficacy of teriparatide.

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Abbreviations: AO/OTA = Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association, AP = anteroposterior, ASA = American Society of Anesthesiologists, BMD = bone mineral density, BMI = body mass index, DHS = dynamic hip screw, DXA = dual-energy X-ray absorptiometry, HRQoL = health-related quality of life, PTH = parathyroid hormone, SF-12 MCS = short-form health survey mental component summary, SF-12 PCS = short-form health survey physical component summary, TAD = tip-apex distance.

INTRODUCTION

Osteoporotic hip fracture is a serious medical problem and a notable burden on the healthcare system.[1–3] Many patients will experience significant functional loss, poor health-related quality of life (HRQoL), and higher mortality rate.[4–6] Previous studies have estimated the cost burden of osteoporosis-related fractures in the United States to be 13.7 to 20.3 billion dollars and 72% of this were due to hip fractures.[2,7] In Taiwan, the elderly (defined as age $\geq$ 65 years) will account for 14% and 20% of the total population by 2018 and 2025, respectively.[8] Chen et al[3] performed a nationwide cohort study and concluded that the number of osteoporotic hip fractures in Taiwan is expected to increase 2.7-fold by 2035. The goal of treatment is to allow pain relief, early return to daily activities, and prevent complications.[8,9] Despite advances in surgical technique and implant design, age-related decreases in bone regenerative capacity and poor bone stock remain problematic.[9–12]

Recently, there has been heightened interest in using osteoanabolic agents for osteoporosis treatment. Controlled trials have shown that recombinant parathyroid hormone (teriparatide) may play a valuable role in the treatment of fractures.[9,12–14] The concept of the so-called ''anabolic window'' refers to the ability of teriparatide to stimulate processes of bone formation before bone resorption.[12–14] In contrast to antiresorptive drugs, an acceleration of fracture healing and improved bone strength by directly stimulating proliferation and differentiation of osteoprogenitor cells have been demonstrated in teriparatide-treated animals.[14–17] In some human trials, it appears to lessen the risk of nonunion[18] and enhance

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fracture healing.[19–22] Theoretically, the positive impact of teriparatide on fracture healing is important for early return to daily activities and morbidity and mortality reduction in patients with osteoporotic intertrochanteric fractures. However, the literature is sparse on this topic. This retrospective study aims to assess whether teriparatide improves osteoporotic intertrochanteric fracture healing. Additional correlation analyses were also conducted to determine the role of supplementary teriparatide in functional and HRQoL recovery as well as reduction of complications.

METHODS

Since 2008, all patients who underwent surgery for osteoporotic intertrochanteric fractures at the author's institution were routinely enrolled in our osteoporosis management program. The merits and risks of osteoporosis treatment based on the World Health Organization guidelines[23] were explained to the patients. Pharmacologic management including calcium and vitamin D supplementation, antiresorptive drugs (alendronate, ibandronic acid, zoledronic acid, denosumab, and raloxifene), and osteoanabolic drugs (teriparatide) was offered. The choice of osteoporosis treatments was decided by the patients themselves (no blinding or randomization) due to regulatory and financial constraints. For the patients who chose recombinant parathyroid hormone (teriparatide), 20 μg/d was given subcutaneously for 18 months beginning on the day of surgery. Drug administration information was documented in our computerized database.

We identified all patients who had intertrochanteric fractures (AO/OTA 31-A1) and who underwent surgery using a dynamic hip screw (DHS) between January 2008 and August 2014. To minimize implant-related confounding factors, patients treated with intramedullary devices such as Gamma nails were not included in this study. A portion of the patients were already taking antiresorptives prior to sustaining their intertrochanteric fracture. The most commonly used drug was alendronate. In order to minimize drug-related variables, we limited this subgroup to alendronate users only. Patients who had received raloxifene, denosumab, ibandronic acid, and zoledronic acid were excluded.

Patients who met the following criteria were also excluded: patients with delirium or dementia and cannot decide their choice of osteoporosis treatments and cannot cooperate to assess the functional outcomes; minimum follow-up of <12 months; subjects with multiple fractures, pathologic fractures, previous ipsilateral hip or femur surgeries, or fractures of the contralateral hip; musculoskeletal conditions that altered bone conditions such as arthrogryposis multiplex congenita, poliomyelitis, cerebral palsy, developmental abnormality, and Down syndrome; patients with contraindications to the use of teriparatide; patients who developed complications related to teriparatide such as generalized weakness and hypercalcemia; patients who were taking teriparatide before the surgery or who had minimum treatment course of <12 months; those who were not ambulatory preoperatively; and incomplete medical records, radiographic analyses, and clinical functional assessments.

The patients were then divided into 3 subgroups: Group 1, patients who were not taking any medication for osteoporosis before the fracture and postfracture received only calcium and vitamin D supplementation (600 mg of calcium and 800 international units of vitamin D3 per day). Group 2, patients who were not taking any medication for osteoporosis before the fracture, and postoperatively received teriparatide and calcium and vitamin D supplementation. Group 3, patients who were taking alendronate before the fracture and received subsequent teriparatide therapy and calcium and vitamin D supplementation after surgery. To determine adequate sample size, a priori power analysis using the hypothesis test with a power of 90% and a significance of 0.05 was done. Based on the report of Vergar et al[5] and Orive et al[6] and using short form-12 health status instrument physical component summary (SF-12 PCS) as the primary variable. The assumption that the mean changes in SF-12 PCS among patients with hip fracture was 9 with a standard deviation of 8, the sample size calculation indicated that 44 patients would be required in each group.

Radiographic Assessment

All patients enrolled in this study had bone mineral density (BMD) measurements made on the contralateral hip (using the Hologic DXA QDR 4500, Hologic Inc., Waltham, MA), and radiographic examinations, including anteroposterior (AP) view of pelvis, AP and lateral views of the affected hip prior to surgery and at 1 day, 2 weeks, 4 weeks and then monthly postoperation until the fracture had healed. Fracture union was defined as recanalization of the trabeculae or visible bridging callus on both radiograph views[24]; delayed union was defined as no signs of fracture healing for 24 weeks[24]; and nonunion was defined as the absence of bone union 36 weeks postoperatively.[24] The tip-apex distance was measured using AP and lateral radiographs of the affected hip.[25] The initial postoperative and the last follow-up radiographs were compared, a decrease in the neck-shaft angle was measured as varus collapse,[24] and the telescoping of the lag screw was measured as lag screw sliding.[26] The magnitude of bone shortening was measured using the method established by Leung et al.[27] Failure of treatment was recognized if any of the following events occurred: penetration of the lag screw into the hip joint; breakage of the barrel-plate or its screws; or patient underwent a second operation due to any other cause of implant failure.[24] The radiographic assessments and BMD of the opposite hip were reviewed and analyzed by an independent surgeon. The intraobserver reliability was assessed according to the method described by Konigsberg et al[28] and was found to be good to very good in this study.

Clinical Assessment

Preoperative surgical risk was categorized according to the classification of the American Society of Anesthesiologists (ASA).[29] The hip pain was graded on a 4-point scale: (1) no pain; (2) mild pain, not affecting walking or requiring regular analgesic medication; (3) moderate pain, affecting walking and/or requiring regular medication; and (4) severe pain.[24] Postoperative functional scores were calculated using the mobility score of Parker and Palmer.[30] Information on general HRQoL was obtained using the 12-item short form health survey (short-form [SF]-12 physical component summary [PCS] and SF-12 mental component summary [MCS]).[31] Each subscale is scored from 0 to 100, with higher scores representing better functions. Assessment was performed at 3, 6, 9, and 12 months postoperatively. The pain scores and functional scores were reviewed and analyzed by a research associate. This retrospective study was approved by the Ethics Committee and Institutional Review Board of the Chang Gung Memorial Hospital (102-5918B), and all patients provided signed informed consent.

Statistical Analysis

All data were recorded into an Excel spreadsheet (Microsoft Corp, Redmond, WA) and subsequently copied to a statistical analysis software SPSS version 13.0 (SPSS Inc., Chicago, IL). Statistical analysis was performed by an independent statistician blinded to group allocations. One-way ANOVA test was employed for continuous variables. Scheffe post hoc test was performed for subgroups comparison. The level of statistical significance was set at $P < 0.05$. Where appropriate, the χ^2 test or the Fisher exact test was used for categorical variables with the level of statistical significance set at $P < 0.05$.

RESULTS

A total of 255 patients (255 hips) met our inclusion criteria. Among them, 29 patients had incomplete data and 37 patients were lost to follow-up. These patients were excluded; 83 patients were in Group 1 (no meds pre-op, calcium and vitamin D supplementation only post-op), 47 patients were in Group 2 (no meds pre-op, teriparatide post-op), and 59 patients were in Group 3 (alendronate pre-op, teriparatide post-op).

A total of 189 patients were available for analysis, consisting of 61 men and 128 women with a mean age of 82 years (range, 65–89 years) at the time of surgery. The mean body height was 157 cm (range, 138–176 cm), the mean body weight was 54 kg (range, 38–89 kg), and the mean body mass index (BMI) was 23 kg/m^2 (range, 19–36 kg/m^2). In Group 1, 62 patients were ASA class II and 21 were ASA class III; Group 2 including 32 ASA class II and 15 ASA class III; Group 3 including 42 ASA class II and 17 ASA class III. No statistical differences of ASA classification exists among the 3 groups. Demographically, there were no statistical differences in sex, age at time of operation, BMI, BMD of contralateral hip, delay between admission and surgery, duration of surgery, and duration of hospital stay (Table 1). The mean of duration of analgesic use after surgery in Groups 1, 2, and 3 were 24.3, 15.1, and 16.1 weeks, respectively ($P < 0.001$). Scheffe post hoc test revealed that differences existed between Groups 1 and 2, between Groups 1 and 3, but not between Groups 2 and 3 ($P < 0.001$, $P < 0.001$, and $P = 0.78$, respectively; Table 1). The mean union time in Groups 1, 2, and 3 was 13.6, 12.3, and 10.6 weeks, respectively ($P = 0.002$). Scheffe post hoc test revealed that differences existed between Groups 1 and 2, between Groups 1 and 3, and between Groups 2 and 3 ($P < 0.001$, $P < 0.001$, and $P = 0.03$, respectively; Table 1).

With regard to radiographic analyses, there were significant differences in overall varus collapse ($5^\circ \pm 2^\circ$ vs $2^\circ \pm 1^\circ$ vs $2^\circ \pm 1^\circ$, $P < 0.001$). Scheffe post hoc test showed differences between Groups 1 and 2 and between Groups 1 and 3 ($P < 0.001$ and $P < 0.001$, respectively). However, no significant differences could be detected between Groups 2 and 3 ($P = 0.99$). The sliding of the lag screw and the shortening of the femoral were also significantly different among 3 groups ($P < 0.001$ and $P < 0.001$, respectively; Table 1). Scheffe post hoc test showed statistically significant differences in patients who received teriparatide. However, no statistically significance could be

TABLE 1. Demographic and Radiographic Data of Patients

Variables	Group 1 (n = 83)	Group 2 (n = 47)	Group 3 (n = 59)	*P* Value
Demographic data				
Sex				0.31
Male	22 (27%)	18 (38%)	21 (36%)	
Female	61 (73%)	29 (62%)	38 (64%)	
Age at time of operation, y	81 ± 8	82 ± 10	81 ± 8	0.81
Body height, cm	155 ± 9	156 ± 8	154 ± 9	0.54
Body weight, kg	54 ± 11	56 ± 11	54 ± 10	0.67
Body mass index, kg/m^2	22.4 ± 3.9	22.9 ± 4.4	22.8 ± 3.1	0.48
BMD of contralateral hip, T-score	−3.9 ± 1.2	−4.2 ± 1.3	−3.9 ± 1.1	0.44
ASA classification				0.71
ASA I	–	–	–	
ASA II	62 (75%)	32 (68%)	42 (72%)	
ASA III	21 (25%)	15 (32%)	17 (28%)	
Delay between admission and surgery, h	23 ± 11	22 ± 9	23 ± 12	0.76
Duration of surgery, min	91 ± 14	89 ± 12	91 ± 13	0.79
Duration of hospital stay, d	8 ± 1	8 ± 1	8 ± 1	0.85
Duration of analgesic use after the surgery, wk	24.3 ± 8.3*	15.1 ± 4.2	16.1 ± 6.7	**<0.001**
Union time, wk	13.6 ± 1.5*	12.3 ± 1.3	10.6 ± 1.3	**0.002**
Radiographic data				
Tip apex distance, mm	21 ± 2	22 ± 2	22 ± 2	0.77
Varus collapse, degrees	5 ± 2*	2 ± 1	2 ± 1	**<0.001**
Sliding of lag screw, mm	6 ± 2*	3 ± 1	3 ± 1	**<0.001**
Femoral shortening, mm	8 ± 6*	2 ± 1	2 ± 1	**<0.001**

Group 1: patients without supplementary pharmacologic treatment. Group 2: patients treated with teriparatide. Group 3: patients treated with sequential teriparatide. Values are shown as mean ± standard deviation or given as the n (%). *P* values for between-group comparisons were determined by the chi-squared test and Fisher exact test for categorical variables and 1-way ANOVA test for continuous variables.

ASA = American Society of Anesthesiologist, BMD = bone mineral density.

*Statistically significant among groups, bold digits indicate *P* value <0.05.

found between patients without and with antiresorptive drugs prior to teriparatide therapy ($P = 0.98$ and $P = 0.94$, respectively; Table 1).

Sixteen patients in Group 1, 2 patients in Group 2, and 3 patients in Group 3 died during the follow-up period due to reasons unrelated to the operation ($P < 0.001$). Implant cut-out occurred in 12 hips ($P < 0.001$). Eleven of these were patients in Group 1, 9 hips were treated with bipolar hemiarthroplasty and 2 with total hip arthroplasty. One patient in Group 2 had the lag screw cut out of the femoral head in a fall that occurred 7 weeks after surgery, and underwent bipolar hemiarthroplasty. There was no significant difference in the rate of superficial wound infection, deep wound infection, pneumonia, urinary tract infection, delayed union, nonunion, implant failure, or subsequent fractures among the groups. However, when comparing the cut-out of lag screw among the 3 groups, there were differences between individuals in Groups 1 and 2, and between those in Groups 1 and 3. However, no differences were noted between Groups 2 and 3. Similar intergroup differences were seen when comparing the overall morbidity and mortality (Table 2).

Decreases in SF-12 PCS scores were worse in Group 1 at 3 months (mean, 19, 28, and 29, respectively; $P = 0.002$) and 6 months (mean, 28, 37, and 38, respectively; $P = 0.008$) postoperation. However, Scheffe post hoc test showed no differences between Groups 2 and 3. The scores of SF-12 PCS of the 3 groups did not differ at 9 and 12 months ($P = 0.56$ and $P = 0.79$, respectively; Table 3). Similar intergroup differences were noted when comparing the hip pain scores at 3 months (mean, 2.8, 1.9, and 1.8, respectively [$P < 0.001$]) and 6 months (mean, 2.5, 1.6, and 1.6, respectively [$P < 0.001$]) (Figure 1), the ability to get around the house at 3 months (mean, 1.1, 1.8, and 1.8, respectively [$P < 0.001$]) and 6 months (mean, 1.8, 2.7, and 2.7, respectively [$P < 0.001$]) (Figure 2), the ability to get out of the house at 3 months (mean, 0.4, 0.7, and 0.9, respectively [$P < 0.001$]) and 6 months (mean, 0.8, 1.5, and 1.6, respectively [$P < 0.001$]) (Figure 3), and the ability to go shopping at 3 months (mean, 0.2, 0.7, and 0.8, respectively [$P < 0.001$]) and 6 months (mean, 0.3, 0.8, and 1.0, respectively [$P < 0.001$]) (Figure 4). The difference in scores among 3 groups did not achieve statistical significance at the postoperation periods of 9 and 12 months. With regard to SF-12 MCS, there were no significant differences among the groups. With regard to the ability to get around the house, patients in Groups 2 and 3 recovered to baseline level at postoperative 6 months ($P = 0.146$ and $P = 0.205$, respectively). Group 1 recovered to baseline level at postoperative 9 months ($P = 0.111$). Regarding the ability to get out of the house and the ability to go shopping, however, none of the groups had recovered to baseline level by postoperative 12 months. Similarly, lowered scores in SF-12 PCS persisted in all 3 groups during the entire study period. With regard to SF-12 MCS, there were no significant differences in either group between each time point (postoperative 3, 6, 9, and 12 months) and preinjury.

DISCUSSION

In several studies, teriparatide appeared effective in improving BMD and reducing the rate of subsequent osteoporotic fracture.[18] Recently, there has been heightened interest in the effect of osteoanabolic agents (teriparatide) on acceleration of fracture healing. In contrast to antiresorptive drugs, direct stimulation of bone formation may not only increase bone strength but also facilitate fracture healing.[9,13] In animal studies, teriparatide has shown efficacy in enhancing the mechanical properties of fracture callus, improving bone-implant contact, and accelerating fracture-healing.[14–17] Faster fracture-healing in association with teriparatide has been demonstrated in case reports and clinical trials.[18–22] Aspenberg et al[21] reported a prospective, randomized, double-blind study of 102 postmenopausal women and concluded that teriparatide shortened the time of healing of distal radial fracture as compared with placebo. Bashutski et al[22] reported a randomized clinical trial of 40 patients with periodontitis. Compared with placebo, patients receiving 20 μg/d teriparatide for 6 weeks had greater resolution of alveolar bone defects, and more rapid

TABLE 2. Postoperative Complications of Patients

Variables	Group 1 (n = 83)	Group 2 (n = 47)	Group 3 (n = 59)	*P* Value
Postoperative complications				
Superficial wound infection	6 (7%)	3 (6%)	4 (7%)	0.98
Deep wound infection	–	–	–	
Pneumonia	13 (16%)	4 (9%)	3 (5%)	0.11
Urinary tract infection	17 (20%)	4 (9%)	5 (8%)	0.06
Delayed union	–	–	–	
Nonunion	–	–	–	
Cutting of the lag screw	11 (13%)*	1 (2%)	0	**0.002**
Implant failure	–	–	–	
Overall morbidity	47*	12	12	**<0.001**
Mortality	16 (19%)*	2 (4%)	3 (5%)	**0.007**
Subsequent fracture				
Vertebral fracture	15 (18%)	5 (11%)	6 (10%)	0.312
Hip fracture	6 (7%)	2 (4%)	1 (2%)	0.307
Wrist fracture	6 (7%)	3 (6%)	3 (5%)	0.875

Group 1: patients without supplementary pharmacologic treatment. Group 2: patients treated with teriparatide. Group 3: patients treated with sequential teriparatide. Values are shown as mean (standard deviation) or given as the n (%). *P* values for between-group comparisons were determined by the chi-squared test and Fisher exact test.

*Statistically significant among groups, bold digit indicate *P* value <0.05.

TABLE 3. Clinical Outcome Measures of Patients

	SF-12 PCS				SF-12 MCS			
	Group 1 (n = 83)	Group 2 (n = 47)	Group 3 (n = 59)	*P* Value	Group 1 (n = 83)	Group 2 (n = 47)	Group 3 (n = 59)	*P* Value
Preinjury	46 ± 8	46 ± 9	46 ± 10	0.881	58 ± 13	59 ± 12	59 ± 11	0.903
3 mo	19 ± 8*	28 ± 11	29 ± 11	0.002	51 ± 11	51 ± 11	52 ± 12	0.864
6 mo	28 ± 10*	37 ± 11	38 ± 11	0.008	53 ± 10	54 ± 9	53 ± 10	0.793
9 mo	35 ± 10	39 ± 11	40 ± 10	0.564	53 ± 11	52 ± 11	52 ± 12	0.771
12 mo	41 ± 11	44 ± 12	45 ± 10	0.794	53 ± 11	54 ± 11	55 ± 11	0.882

Group 1: patients without supplementary pharmacologic treatment. Group 2: patients treated with teriparatide. Group 3: patients treated with sequential teriparatide. Values are shown as mean ± standard deviation (*P* value). *P* values for between-group comparison were determined by 1-way ANOVA tests.

MCS = mental component summary, PCS = physical component summary, SF-12 = short-form-12.

*Statistically significant (*P* value < 0.05).

osseous wound healing in the oral cavity. Animal studies, as well as clinical data, suggest that the main clinical advantages of using teriparatide are the acceleration of fracture healing and bone formation enhancement. However, to our knowledge, there is little in the literature regarding the role of teriparatide on the management of osteoporotic intertrochanteric fractures.

In this study, we excluded patients receiving any antiresorptive medication other than alendronate prior to surgery to avoid confounding factors from different medications. In order to avoid confounding factors from different implant and fracture patterns, the present study was focused on AO type 31-A1 fractures and limited to patients treated using a DHS. Under these strict inclusion criteria, we analyzed the effects of teriparatide on patients with osteoporotic intertrochanteric fractures and demonstrated an acceleration of time-to-union for patients with fractures who received teriparatide treatment. This study also found that teriparatide significantly improved SF-12 PCS, relieved pain, decreased analgesic use after surgery and increased mobility score at the postoperative periods of 3 and 6 months, and provided a lower morbidity and mortality rate as compared with the control group.

A high rate of cut-out of the lag screw (13%) was noted in Group 1 (no teriparatide). Patients enrolled in this study had low BMD (mean T-score, −3.9, −4.2, and −3.9, respectively [*P* value = 0.44]). The poor bone stock results in insufficient contact between fracture fragments and decreases pull-out strength of implants, an excessive sliding of the lag screw occurs and leads to femoral shortening, varus collapse of the proximal fragment, and subsequent cut-out of the lag screw.[24,32] In order to address this problem, several techniques using cement and autograft have been developed in order to augment bone stock or to enhance the implant-bone interface.[9–11,24] Although cement-augmentation has been widely used for osteoporotic intertrochanteric fractures, it has its own set of failure modes and makes subsequent revision surgeries more complex and technically demanding.[24] Autogenous bone graft

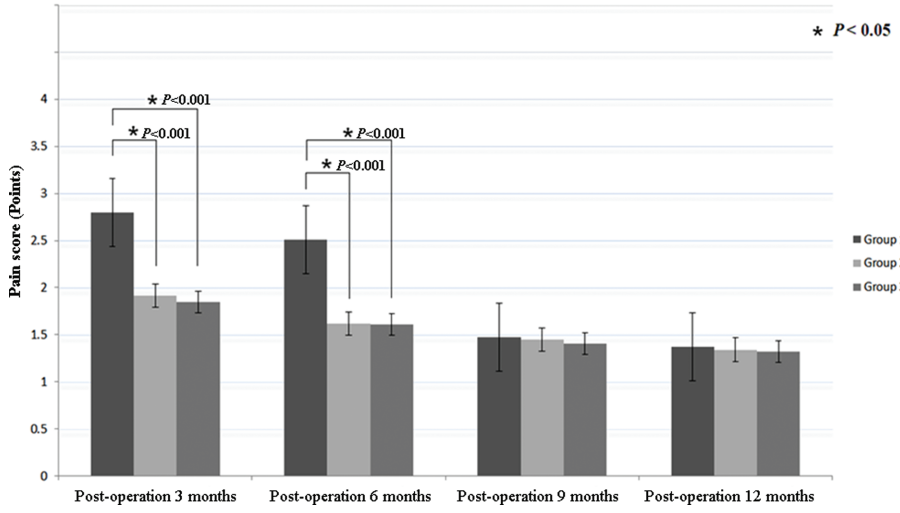

FIGURE 1. Mean hip pain scores. Differences of mean hip pain scores were found among the 3 groups at the postoperation periods of 3 and 6 mo. Mean pain scores at the postoperation periods of 3 mo in Groups 1, 2, and 3 were 2.8, 1.9, and 1.8, respectively. The Scheffe post hoc test revealed that there were differences between Groups 1 and 2 and between Groups 1 and 3 ($P < 0.001$ and $P < 0.001$, respectively). No such differences could be detected between Groups 2 and 3 ($P = 0.80$). Similar intergroup differences were noted at postoperation 6 mo.

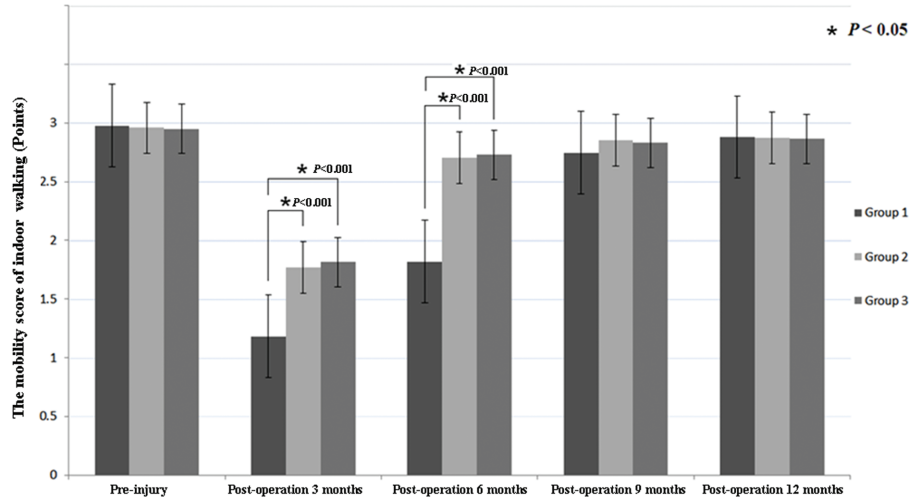

FIGURE 2. Mobility score of Parker and Palmer preinjury, at postoperation 3 mo, at postoperation 6 mo, at postoperation 9 mo, and at postoperation 12 mo for the ability to get about the house (indoor walking). Evaluation of the ability to indoor walking. The ability was graded on a 4-point scale: (0) not at all; (1) with help from another person; (2) with a walking aid; and (3) no difficulty and no aid.[30] The score of the ability to get around the house was significantly worse in Group 1 at postoperation 3 and 6 mo ($P < 0.001$ and $P < 0.001$, respectively). Scheffe post hoc test revealed no differences between individuals in Groups 2 and 3 at postoperation 3 and 6 mo ($P = 0.90$ and $P = 0.98$, respectively). The scores of the 3 groups did not differ at 9 and 12 mo ($P = 0.31$ and $P = 0.97$, respectively).

is desirable because of its biological characteristics, but there are concerns regarding the poor mechanical properties and donor-site morbidity.[11] Conversely, significant reduction of sliding of lag screw, femoral shortening, varus collapse, and incidence of cut-out of the lag screw was noted in patients who received teriparatide (Table 1). Tao et al[33] study 27 female Sprague–Dawley rats and concluded that 8 weeks of teriparatide use provides a positive effect on repair of femoral metaphyseal defect. This positive effect provides sufficient contact between fracture fragments to decreases excessive sliding of the lag screw and prevents subsequent complications. Concerns exist regarding teriparatide-induced osteosarcoma. Long-term usage and high dose teriparatide contributes to a high incidence of osteosarcoma in Fischer 344 (F344) rats, but no such effect was detected in other animal models and in human trials.[34] Despite higher cost and relatively poor compliance compared with other antiosteoporotic drugs, teriparatide may be a valuable supplemental treatment to enhance fracture healing for osteoporotic intertrochanteric fracture, where poor bone stock and poor bone regenerative capacity challenge orthopedic surgeons.[35] However, it should be mentioned that there are many other factors that influence patients' outcome (e.g., quality of surgery, orthogeriatric co-management).

The influence of sequential osteoanabolic therapy following antiresorptive drugs is an important area of research. Several studies have shown that beneficial effects on BMD and

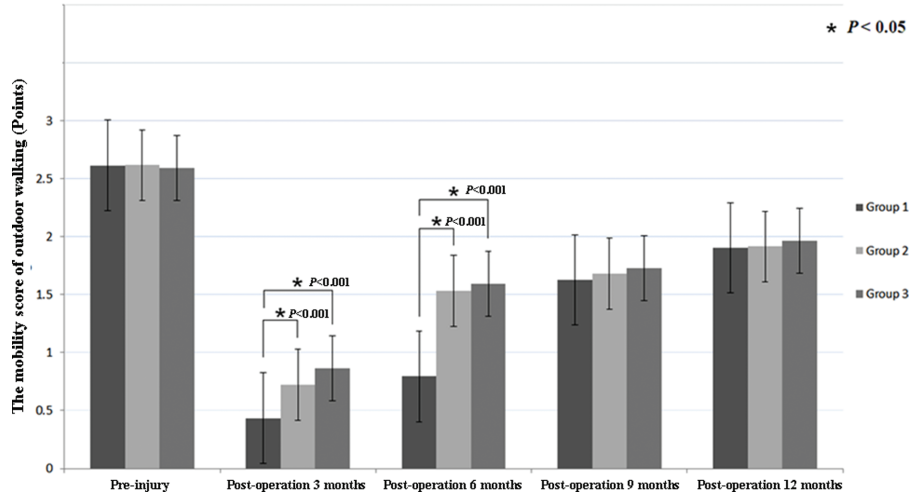

FIGURE 3. Mobility score of Parker and Palmer preinjury, at postoperation 3 mo, at postoperation 6 mo, at postoperation 9 mo, and at postoperation 12 mo for the ability to get out of the house (outdoor walking). Evaluation of the ability to outdoor walking. The ability was graded on a 4-point scale: (0) not at all; (1) with help from another person; (2) with a walking aid; and (3) no difficulty and no aid.[30] Significant differences were noted at postoperation 3 and 6 mo between patients without teriparatide therapy and those with teriparatide therapy ($P < 0.001$ and $P < 0.001$, respectively).

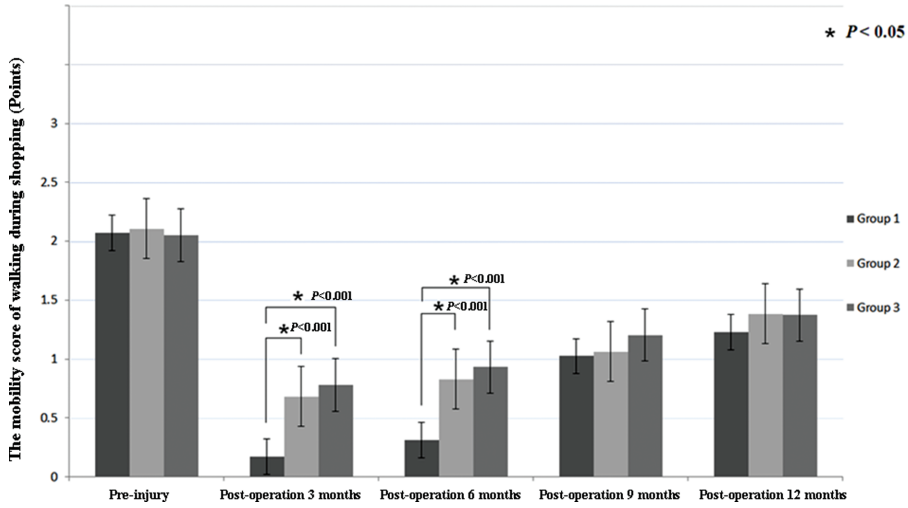

FIGURE 4. Mobility score of Parker and Palmer preinjury, at postoperation 3 mo, at postoperation 6 mo, at postoperation 9 mo, and at postoperation 12 mo for the ability to go shopping (walking during shopping). Evaluation of the ability to walking during shopping. The ability was graded on a 4-point scale: (0) not at all; (1) with help from another person; (2) with a walking aid; and (3) no difficulty and no aid.[30] For patients without teriparatide therapy, the mean score of the ability to go shopping was significantly lower than the scores in other groups at postoperation 3 and 6 mo ($P < 0.001$ and $P < 0.001$, respectively).

improvement of bone strength occur in patients who had been treated with alendronate prior to teriparatide.[36–40] In addition, the duration of previous alendronate treatment and the time interval between alendronate and teriparatide did not affect the BMD at any skeletal sites.[41–43] Miller et al[44] found that pronounced responses to increased serum level of the bone formation marker (procollagen type 1 amino-terminal propeptide) in alendronate-treated patients were seen as soon as 1 month after the treatment. The early anabolic effects in sequential teriparatide treatment may contribute to shorter time of fracture healing. Our results were compatible with that concluded by Miller et al. In this study, patients who had been treated with alendronate prior to teriparatide had the shortest time of fracture-healing. However, with regard to HRQoL (Table 3), pain relief (Figure 1), and mobility scores (Figures 2–4), no superior responses at postoperative 3 and 6 months in Group 3 were found as compared with Group 2. The most plausible reason for this circumstance is that the union time in both teriparatide-treated groups was <12 weeks. When fractures were healed, patients were able to perform daily activities and had a better HRQoL compared with patients who did not have fracture-healing.

Several limitations in this study must be acknowledged. First, this is a retrospective study with all the inherent weakness and biases of such study designs. Second, the number of patients was small. We excluded patients receiving raloxifene, denosumab, ibandronic acid, and zoledronic acid (any medication other than alendronate) prior to teriparatide to avoid confounding factors from different medication. The strict inclusion criteria for this investigation were designed to limit the variables in the study, but it also reduced the numbers of subjects and limited the power of the study to detect a clinically significant difference. Regarding the role of teriparatide in recovery of HRQoL, although we had more than adequate sample size (44 hips were theoretically required per group) to detect a difference of SF-12 PCS, this study may still be underpowered to demonstrate significant differences. Third, we did not make BMD measurements on the patients at 12 months. This may have been important but it was not in our treatment protocol. Fourth, we did not measure the vitamin D levels at baseline and at the end of therapy. Again, it was not routine in our treatment protocol. Finally, there are 2 different recombinant parathyroid hormones (PTH1-34 and PTH1-84). At present, only teriparatide (recombinant PTH1-34) is available in Taiwan. Although recombinant PTH1-84 also demonstrated clinical effects on fracture healing in postmenopausal women,[45] the authors are not aware of any comparative studies regarding anabolic effects between the 2 drugs.

CONCLUSION

In this retrospective study, 6 months of teriparatide use after surgery was associated with faster fracture-healing, better HRQoL, and less complications. However, a prospective, randomized, large-scale cohort study is still necessary to determine the efficacy of teriparatide in osteoporotic intertrochanteric fractures.

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