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ORIGINAL ARTICLE

Teriparatide improves volumetric bone mineral density and fine bone structure in the UIV+1 vertebra, and reduces bone failure type PJK after surgery for adult spinal deformity

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Abstract

Summary We conducted a prospective comparative study of the effect of teriparatide therapy for preventing vertebral-failure-type PJK after reconstructive surgery for adult spinal deformity. Prophylactic teriparatide improved the volumetric bone mineral density and fine bone structure of the vertebra above the upper-instrumented vertebra and reduced the incidence of vertebral-failure-type PJK.

Introduction Proximal junctional kyphosis (PJK) is a complication after corrective surgery for spinal deformity. This study sought to determine whether teriparatide (TP) is an effective prophylactic against PJK type 2 (vertebral fracture) in surgically treated patients with adult spinal deformity (ASD).

Methods Forty-three patients who started TP therapy immediately after surgery and 33 patients who did not receive TP were enrolled in this prospective case series. These patients were female, over 50, surgically treated for ASD, and followed for at least 2 years. Preoperative and postoperative standing whole-spine X-rays and dual-energy X-ray absorptiometry scans, and multidetector CT images obtained before and 6 months after surgery were used to analyze the bone strength in the vertebra above the upper-instrumented vertebra (UIV+1).

Results Mean age was 67.9 years. After 6 months of treatment, mean hip-bone mineral density (BMD) increased from 0.721 to 0.771 g/cm^2 in the TP group and decreased from 0.759 to 0.729 g/cm^2 in the control group. This percent BMD change between groups was significant ($p < 0.05$). The volumetric BMD (326 to 366 mg/cm^3) and bone mineral content (BMC) (553 to 622 mg) at UIV+1 were also significantly increased in TP group. The bone volume/tissue volume ratio increased from 46 to 54 % in the TP group, and the trabecular bone thickness and number increased by 14 and 5 %, respectively. At the 2-year follow-up, the PJK type 2 incidence was significantly lower in the TP group (4.6 %) than in the control group (15.2 %; $p = .02$).

Conclusions Prophylactic TP treatment improved the volumetric BMD and fine bone structure at UIV+1 and reduced the PJK-type 2 incidence.

Keywords Adult spinal deformity · Osteoporosis · PJK · Teriparatide

Introduction

Proximal junctional kyphosis (PJK) can occur in adults and adolescents after scoliosis surgery [1–19]. We define proximal junctional failure (PJF) as any serious PJK requiring revision surgery. A postoperative increase in junctional stress concentration can cause the soft tissue and ligaments, the bone, or the bone implant interface to fail [14–19]. We previously identified a preexisting low bone mineral density (BMD) as a significant risk factor for PJK [14–16, 20]. We also previously described a categorization system for PJK (or PJF) based on severity and type. In this system, PJK resulting from disc and ligamentous failure is type 1, from bone failure is type 2, and from implant/bone interface failure is type 3 [16]. Among these categories, type 2 PJK is the most problematic and often requires revision surgery [14–16, 20].

Teriparatide (TP), a recombinant human parathyroid hormone (PTH 1–34), is a skeletal anabolic agent used to treat

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osteoporosis patients with a high risk of fracture [21, 22]. Although several reports suggest that TP therapy increases BMD, little is known about TP's prophylactic effect against the vertebral fracture type PJK.

Bone strength depends on the bone density and bone quality; bone quality is defined as the sum of the structural and material properties of the trabecular bone as well as the structural and material properties of the cortical bone [23–25]. An accurate BMD determination is an important diagnostic indicator for osteoporosis and for assessing a patient's response to treatment [26, 27]. Most studies on TP's effects have assessed two-dimensional BMD by dual-energy X-ray absorptiometry (DXA) scans [28, 29]. Although the DXA evaluation of BMD is useful, it does not provide information about the bone's trabecular structure; DXA-assessed BMD provides only a partial description of the bone strength and fracture resistance [26, 30]. Lumbar or hip DXA is widely used to measure BMD in adults [28, 29]. On the other hand, Lochmüller et al. reported that lumbar DXA has no relevant correlation to the failure load of the thoracic spine [26]. We previously reported that DXA scores are discordant between the hip and spine in patients with adult spinal deformity (ASD) [20]. Recently, the effects of TP were also investigated by several other techniques, including histomorphometry and peripheral quantitative computed tomography (pQCT) [22, 28]. Quantitative assessments of the macrostructural characteristics of bone such as geometry, and of the microstructural characteristics such as the trabecular volume and the trabecular spacing, number, and connectivity, may improve our ability to estimate bone strength, verify the effect of osteoporosis treatment, and predict fractures [21, 25, 26]. Therefore, here, we measured the bone quality by multidetector CT (MDCT). To our knowledge, the prophylactic effect of TP against adjacent vertebral fracture in surgically treated ASD patients has not been reported. We hypothesized that prophylactic TP treatment would decrease the incidence of adjacent vertebral fracture PJK in patients after surgery for ASD.

Materials and methods

Patient sample

We prospectively enrolled 43 consecutive female adults with ASD who underwent corrective surgery at our institution and had osteoporosis or osteopenia, and received TP therapy immediately after surgery (TP group). We compared the clinical outcome, radiographic parameters, and incidence of PJK/PJF in the TP group with those of a control group consisting of 33 consecutive adult female patients with osteoporosis or osteopenia who underwent surgery for ASD just prior to the beginning of this study and who did not receive TP therapy. The lead author performed the surgery in all cases, using the same surgical methods, from 2010 to 2014 (2010–2012, control group; 2012–2014, TP group). All of the patients in the TP group received 20 mcg TP subcutaneously once a day from the day after surgery to 18 months after surgery. In the TP group, 18 of the 43 patients had a DXA score lower than −2.5 and received vitamin D and calcium, whereas in the control group, 14 of the 33 patients received vitamin D and calcium. The mean age was 67.9 years (range 62–78; TP group 68.8 years and control group 66.7 years; $p = 0.78$).

Inclusion criteria

1. Females over 50 years of age with ASD
2. Osteoporosis or osteopenia (T-score < −1.0)
3. Posterior long instrumented fusion (minimum of 5 fused vertebrae)
4. An upper-instrumented vertebra (UIV) of T9 or T10
5. Complete radiographic data
6. Minimum follow-up of 2 years

Exclusion criteria

1. Patients who required 3-column osteotomy
2. Patients who were not diagnosed with osteoporosis/osteopenia or were not at risk for surgical/drug-induced osteoporosis
3. Patients with a history of a hypersensitivity reaction or another contraindication to TP, such as Paget's disease, hypercalcemia or hypocalcemia, bone cancer, bone metastases, radiation treatment to the skeleton, or hyperparathyroidism with a creatinine clearance <30 mL/min

Radiographic data acquisition

1. Standing anteroposterior and lateral whole-spine X-rays were taken immediately before and after surgery and 6 months, 12 months, and 2 years after surgery.
2. Multidetector CT (MDCT) scans of the UIV, UIV+1, and UIV+2 vertebrae were taken prior to and 6 months after surgery. MDCT scans were performed with an Aquilion 64 CT scanner (Toshiba, Tokyo, Japan) using a standard protocol (120 kV, 250 mA, collimation of 0.5 mm, and reconstruction index of 0.3 mm), a 200-mm field of view, and a 512- × 512-pixel matrix. Specific regions of interest (ROIs) were defined within the UIV+1 vertebra for morphometric analysis. All of the MDCT imaging data were transferred to a workstation at the authors' institution and were blinded; the data were then analyzed at an independent institution. All of the MDCT data were analyzed using the TRI/3D-BON (RATOC System Engineering Co., Tokyo JAPAN) 3D image analysis software. We performed image thresholding using a discriminant analysis

method based on the density histogram of a selected ROI to ensure a consistent threshold across all subjects. Isolated small particles in the marrow space and isolated small holes in the bone were removed with a cluster-labeling algorithm to delete small noise in the binary extraction. The following measurement parameters were calculated in 3D: the bone volume fraction (bone volume/total volume; %), trabecular thickness (μm), trabecular number, trabecular separation (μm), trabecular bone pattern factor (Δbone surface/Δbone volume), bone-marrow space star volume, trabecular star volume, and structure model index (SMI). The star volume is defined as the mean volume of all of the parts of an object that can be seen, unobscured, in all directions from a particular point inside the object. The SMI is used to evaluate whether trabecular bone is rod-like or plate-like; a smaller value indicates a more plate-like (stronger) structure.

3. Hip (femoral neck) BMD was obtained by DXA prior to and 6 months after surgery.
4. Patients were evaluated for the presence or absence of PJK at each follow-up visit. PJK was defined as a proximal junctional angle greater than 10° and at least 10° greater than the corresponding preoperative measurement; both criteria had to be present [12]. Using our Boachie-Yagi modified PJK/PJF classification system, PJKs were categorized as follows: grade A, a proximal junctional increase of 10°–19°; grade B, a proximal junctional increase of 20°–29°; and grade C, a proximal junctional increase of 30° or greater. Three types of PJK were also defined: PJK resulting from disc and ligamentous failure (type 1), from bone failure (type 2), or from implant/bone interface failure (type 3) [16].

Blood and urine samples

Blood and urine samples were taken just before and 6 months after surgery and used to measure the levels of serum intact procollagen type I N propeptide (PINP) and urinary N-terminal cross-linking telopeptide of type I collagen corrected for creatinine (NTX-I; a biochemical marker of bone resorption), respectively.

Clinical outcomes

Patient outcome parameters were evaluated prior to and 2 years after surgery using the Scoliosis Research Society Patient Questionnaire (SRS22r) and the Oswestry Disability Index (ODI) [22, 23]. Completed questionnaires were available for 26 of the 33 control patients and for 40 of the 43 patients in the TP group.

Statistical analysis

Continuous variables were analyzed by the Mann–Whitney U test; a p value less than 0.05 with a confidence interval of 95 % was considered statistically significant. All analyses were performed using the Statistical Package for the Social Sciences (SPSS version 21.0 IBM Corp., Armonk, NY).

Results

Baseline patient characterization

The control group and TP group before surgery did not differ significantly in gender, age, baseline hip BMD, fusion level, LIV level distribution, or clinical outcome parameters (Table 1). The hip BMD was 0.721 g/cm^2 in the TP group and 0.759 g/cm^2 in the control group; the T-score was −1.1 in the TP group and −0.9 in the control group.

Radiographic comparisons

There were no significant differences in the baseline or 2-year postoperative sagittal alignment between the TP and control groups. Two years after surgery, both groups showed significant improvements in sagittal alignment, including lumbar lordosis, pelvic incidence–lumbar lordosis, pelvic tilt, and C7 sagittal vertical axis (Table 2).

Clinical outcomes

All of the patients were successfully followed for 2 years after surgery. There were no significant differences in the 2-year postoperative clinical outcomes between the TP and control groups, with both groups showing significant improvements in clinical outcomes, including SRS22r and ODI scores, at the 2-year follow-up (Table 3).

Hip BMD and PJK/PJF incidence

At the 2-year follow-up, the hip BMD had increased significantly (6.7 %) from baseline in the TP group but was unchanged in the control group (Table 3). There was no significant difference in the overall incidence of PJK between the TP group (9.3 %) and control group (18.2 %) at the 2-year follow-up (Table 3); however, the incidence of PJK/PJF type 2 in the TP group was 2/43 (4.6 %), which was significantly lower than in the control group (5/33, 15.2 %; $p = 0.02$) (Table 3). The two groups did not differ significantly in the proximal junction angle at baseline, immediately after surgery, or at the 2-year follow-up (Table 4).

Table 1 Baseline characteristics of patient cohort

	TP group	Control group	*p* value
No. of patients	43	33	
Follow-up (months)	27.9 ± 3.9	43.6 ± 4.9	0.02*
Age (years)	68.6 ± 6.9	66.7 ± 6.9	0.39
Hip BMD (g/cm^2)	0.721 ± 0.119	0.759 ± 0.209	0.47
T-score	−1.1 ± 0.4	−0.9 ± 1.2	0.69
Level involved	9.1 ± 1.1	9.1 ± 1.3	0.88
LIV (pelvis)	34/43 (78 %)	22/33 (67 %)	0.13
ODI (%)	56.4 ± 12.9	59.9 ± 11.3	0.35
SRS22r total	2.51 ± 0.47	2.34 ± 0.34	0.56
SRS22r function	2.84 ± 0.45	2.79 ± 0.43	0.88
SRS22r pain	2.51 ± 0.66	2.53 ± 0.49	0.78

Means and SDs

BMD bone mineral density, *LIV* lowest instrumented vertebra, *ODI* Oswestry Disability Index, *SRS22r* Scoliosis Research Society Patient Questionnaire 22r

*Statistically significant

Table 3 Two-year postoperative summary of patient cohort

	TP group	Control group	*p* value
Hip BMD (g/cm^2)	0.771 ± 0.219	0.729 ± 0.107	0.11
%change	6.7 ± 4.9	−1.4 ± 4.2	0.05*
No. of PJK	4/43 (9.3 %)	6/33 (18.2 %)	0.23
No. of PJ fracture	2/43 (4.6 %)	5/33 (15.2 %)	0.01 *
ODI (%)	25.8 ± 11.9	29.9 ± 12.8	0.13
SRS22r total	3.59 ± 0.51	3.34 ± 0.39	0.54
SRS22r function	3.77 ± 0.52	3.57 ± 0.49	0.52
SRS22r pain	3.88 ± 0.51	3.68 ± 0.41	0.70

Means and SDs

PJK proximal junction kyphosis, *PJ* proximal joint, *ODI* Oswestry Disability Index, *SRS22r* Scoliosis Research Society 22-r

*Statistically significant

Complications of TP therapy

Of the 43 patients in the TP group, three (7 %) discontinued TP therapy due to complications. Of these, two had nausea and headaches, and one had a nonspecific elevation of blood C-reactive protein (CRP). All of the complications were resolved by discontinuing TP therapy. No data was used from the three patients that discontinued the TP therapy

Serum P1NP and urinary NTX-I

In the TP group, the PINP concentration increased to a level significantly greater than baseline by 1 month after starting TP treatment and then continued to increase, remaining significantly elevated 6 months after starting treatment ($p < 0.019$). The NTX-I level in the TP group was not elevated after 1 month of TP therapy but was significantly elevated after 3 months (Fig. 1).

MDCT data analysis

In the TP group 6 months after beginning TP therapy, the volumetric BMD at U1V+1 had increased from 326 to 366 mg/cm^3 (14 %, $p = 0.0038$), and the BMC had increased from 553 to 622 mg (16 %, $p = 0.0060$). The bone volume/tissue volume ratio also increased significantly, from 46 to 54 % ($p = 0.008$). Two years after beginning TP therapy, the trabecular bone thickness had increased 14 % (619.4 to 699.4 μm, $p = 0.012$), the trabecular number had increased 5 % (0.74 to 0.77, $p = 0.043$), and trabecular bone space had decreased 17 % (745.1 to 608.0 μm, $p = 0.010$). Significant improvements were also noted in the trabecular bone pattern factor (0.38 to −0.080, $p = 0.006$), the SMI (0.82 to 0.43, $p = 0.004$) (Table 5), the bone marrow space star volume (16.97 to 10.17 mm^3, $p = 0.022$), and the trabecular star volume (32.7 to 46.17 mm^3, $p = 0.014$).

Table 2 Preoperative and 2-year postoperative radiographic parameters

	Preoperative			Postoperative		
	TP group	Control group	*p* value	TP group	Control group	*p* value
Cobb angle (°)	37.4 ± 14.4	33.2 ± 14.4	0.81	10.9 ± 6.6	11.3 ± 7.4	0.89
TK (°)	18.9 ± 14.1	17.2 ± 13.2	0.81	24.1 ± 8.4	21.1 ± 9.2	0.77
LL (°)	−14.1 ± 10.1	−15.3 ± 8.5	0.52	−36.9 ± 4.9	−31.9 ± 3.5	0.52
SS (°)	9.2 ± 11.6	8.3 ± 8.1	0.97	30.2 ± 6.5	28.3 ± 5.1	0.67
PI (°)	47.4 ± 10.3	45.8 ± 8.5	0.52	47.4 ± 10.3	45.8 ± 8.5	0.52
PT (°)	24.8 ± 9.5	29.4 ± 9.5	0.37	17.1 ± 5.5	19.4 ± 4.5	0.37
C7SVA (cm)	11.1 ± 2.9	10.5 ± 3.9	0.81	4.6 ± 3.3	5.4 ± 3.1	0.81

Means and SDs

TK thoracic kyphosis, *LL* lumbar lordosis, *PI* pelvic incidence, *PT* pelvic tilt, *C7SVA* C7 sagittal vertical axis

Table 4 Changes in proximal junctional angle after surgery for ASD

PJK (°)	Total	TP group	Control group	*p* value
Preoperative	4.3 ± 6.3	4.0 ± 4.1	4.7 ± 7.3	0.29
Immediate post-op	9.6 ± 6.6	8.9 ± 4.4	10.7 ± 8.1	0.43
2-year post-op	15.3 ± 5.9	13.2 ± 5.2	17.9 ± 7.1	0.09
Δ1 PJK	5.7 ± 6.4	4.3 ± 5.5	7.2 ± 5.2	0.23
Δ2 PJK	10.9 ± 7.9	9.2 ± 7.7	13.2 ± 6.2	0.21

Means and SDs

Δ1 PJK the change in PJ angle from prior to surgery to 2 years after, *Δ2 PJK* the change in PJ angle from just after surgery to 2 years after

Discussion

We previously reported that the incidence of PJK among patients who were surgically treated for ASD was 22 % [14]. Kim et al. found a 39 % prevalence of PJK during the long-term follow-up of patients who underwent long posterior spinal fusion to correct ASD [5]. PJK that requires surgery, called PJF, causes devastating complications such as paralysis, intolerable pain, and severe kyphosis, particularly in the elderly. Considering the severity of these complications, it is vital to find ways to prevent PJF.

PJK is a multifactorial phenomenon. Several recent studies have reported potential risk factors for developing PJK after long instrumented spinal fusion in adolescents and adults with scoliosis [5, 7, 18]. These risk factors include an older age at the time of surgery, posterior spinal fusion, combined antero-posterior spinal fusion, a preoperative proximal junctional angle of more than 5° at one level cephalad to the UIV, fusion to the sacrum, a preexisting low BMD, and surgical correction of the thoracic kyphosis by more than 50 % [5–7, 14, 15, 19]. Although there are many confounding factors, poor bone strength is thought to be an essential risk factor for developing PJK. Bone strength may be the most important factor for tolerating the postoperative increase in junctional stress concentration [4, 5, 7, 16, 20]. The incidence of PJK after surgery for pediatric spine deformity is significantly lower than that after surgery for ASD (an incidence of 20–40 %), indicating the importance of vertebral bone strength in this phenomenon [1, 5, 6, 14, 19].

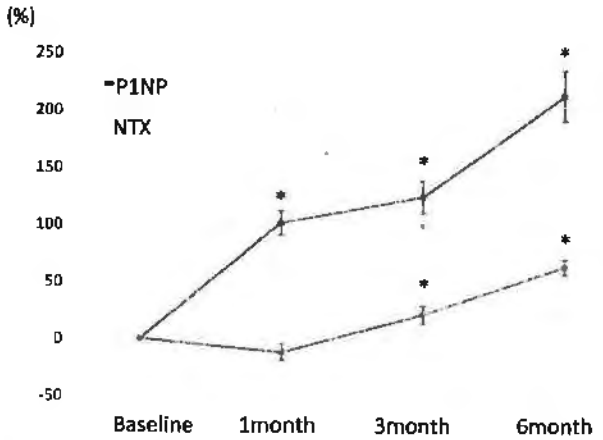

Fig. 1 Changes in serum PINP and urine NTX-1 concentrations after beginning of TP treatment. *Bars* represent standard error of the means

In the present study, although the overall incidence of PJK was not significantly lower in the TP group than in the control group, the incidence of PJK type 2 was significantly lower in the TP group. Our findings indicate that rather than decreasing the incidence of PJK, prophylactic TP therapy addressed preexisting bone weakness in the UIV+1 vertebra, thereby reducing the vertebral fractures following corrective surgery for ASD. Preliminary results have been reported for various trials aimed at reducing the incidence of PJK; the proposed methods include using a hook construct at the proximal level, performing vertebroplasty for the UIV+1 vertebra, and extending the proximal extent of the fusion [31, 32]. The present study clearly showed that TP therapy decreased the incidence of PJK type 2, since the sample population, the baseline demographic and radiographic data, the surgical procedure, and the surgeon were all the same between the TP and control groups. Moreover, to avoid surgeon bias, all of the data were analyzed in a blinded manner by a radiologist who works at another institution and had no other involvement with the study.

A discrepancy between bone strength and BMD determined by DXA is widely recognized [26, 30]. Eckstein et al. reported that the bone strength at clinically relevant sites within an individual exhibits substantial heterogeneity and thus is best predicted from site-specific bone densitometry [30]. The rationale for imaging the bone's macrostructure and microstructure is to obtain information beyond the BMD, to improve fracture-risk prediction, define the skeletal response to therapy, and assess biomechanical relationships. In this study, we evaluated the bone quality in ASD patients who underwent surgical treatment, who had osteopenia or osteoporosis, and who had received TP therapy, by measuring the trabecular microstructure using in vivo MDCT images. We found that TP therapy actually improved the bone quality of the UIV+1 vertebra.

We analyzed the volumetric BMD, BMC, and fine bone structure in the UIV+1 vertebra, and found significant increases in the volumetric BMD (327 to 365 g/cm^3) and BMC (553 to 622 g) after TP therapy, indicating that prophylactic TP therapy actually increased the bone density in the UIV+1 vertebra. We observed significant improvements in the bone volume/tissue volume ratio (from 46 to 54 %), the trabecular thickness (619 to 699 μm), the trabecular number (0.74 to 0.77), and the SMI (0.82 to 0.43). The SMI is used to evaluate whether trabecular bone is rod-like or plate-like; a smaller value indicates a more plate-like structure [32, 33]. We also noted significant improvements in the bone-marrow space star volume (16.97 to 10.17 mm^3) and trabecular star volume (32.74 to 46.17 mm^3). Previous reports indicated that

Table 5 Changes in bone characteristics after TP treatment

	BV (mm^3)	BS (mm^2)	BV/TV (%)	TB.Th (μm)	TB.N (1/mm)	TB.Sp (μm)	TBPf (1/mm)	SMI	V*m.space (mm^3)	V* tr (mm^3)
Pre-op	2466.4 ± 657.2	7965.2 ± 1620.3	46.1 ± 9.9	619.4 ± 90.4	0.74 ± 0.07	745.1 ± 188.5	0.38 ± 0.55	**0.82 ± 0.43**	16.9 ± 10.5	32.7 ± 17.2
Post-op	2868.3 ± 632.6	8307.1 ± 1653.8	53.8 ± 10.8	699.4 ± 116.3	0.77 ± 0.05	607.9 ± 158.5	−0.08 ± 0.62	0.43 ± 0.54	10.2 ± 6.8	46.2 ± 22.8
%change	20.4	4.5	20.4	14.6	4.5	−17.2	−98.1	−40.6	−33.9	53.5
p value	0.011*	0.048*	0.008*	0.012*	0.043*	0.010*	0.006*	0.004*	0.022*	0.014*

Means and SDs

BV bone volume, *BS* bone surface, *BV/TV* bone volume/tissue volume, *TB.Th* trabecular (Tb) thickness, *TB.N* TB number, *TB.Sp* Tb separation, *TBPf* Tb bone pattern factor (ΔBS/ΔBV), *SMI* structure model index, *V*m. space* bone marrow space star volume, and *V* tr* TB star volume

*Statistically significant

the bone marrow and trabecular star spaces can provide an unbiased estimation of the absolute mean size of the marrow space and thus give an indirect estimate of the connectivity of the trabecular bone structure [23, 34, 35]. We also noted a significant improvement in the trabecular bone pattern factor (0.38 to −0.080). The trabecular bone pattern factor quantitatively describes the ratio of inter-trabecular connectivity, as reported by Hahn et al. [36], and the value is positive for concave structures and negative for convex ones. The negative value seen in the TP group indicated that the trabecular bone of the UIV+1 vertebra had a honeycomb structure [22, 34]. Good bone quality is reflected in a higher ratio of bone volume to tissue volume, a higher trabecular thickness, a smaller trabecular space, a trabecular bone pattern factor less than 0, and a lower SMI [33–35, 37–39]. Our results showed that prophylactic TP therapy significantly improved not only the volumetric BMD but also the microstructure of the bone, thus strengthening the UIV+1 vertebra.

As surrogate monitors of TP therapy, we investigated the serum PINP and urine NTX-I concentrations. The PINP concentration in the TP group increased rapidly to a level significantly above baseline and then continued to rise, remaining significantly above the baseline at 6 months after the beginning of treatment. The NTX-I level was not elevated after 1 month of TP therapy but was elevated after 3 months. These changes in serum PINP and urine NTX-I concentration are consistent with TP's anabolic mechanism of action, as reported previously [22]. Krege et al. examined the use of PINP as a biological response marker during TP therapy, by reviewing the results of clinical trials [22]. They found that PINP increased consistently within 3 months of initiating TP, to levels significantly greater than the baseline or placebo-treated group levels [22]. They further showed that increases in PINP during TP therapy correlated well with increases in skeletal activity as assessed by radioisotope bone scans and quantitative bone histomorphometry parameters. Krege et al. also reported that patients who experience a significant increase in PINP after initiating TP therapy may receive an earlier confirmation of the anabolic effect. The elevation of serum PINP in the present study strongly indicated that the PT therapy had an anabolic effect in our patient population.

This study has some limitations. First, it had a relatively small sample size. However, we consider our data to be important, as we found statistically significant differences in the bone quality of the UIV+1 vertebra for each microstructural parameter and a significant decrease in the incidence of PJK type 2 in the TP group. Second, the study was not prospectively randomized, and the control group used in the present study was a historical control. The surgeries for the control group were performed in 2010–2012 and for the TP group were performed in 2012–2014. However, all of the surgeries were performed by the senior author using the same intraoperative procedures, which might have reduced the effect of

surgical selection bias. A larger-sample, prospectively randomized series of studies will be necessary to elucidate the prophylactic effect and cost–benefit ratio of TP therapy for patients with a preexisting low BMD who undergo long instrumented fusion for spinal deformity.

Third, we did not evaluate the accuracy of the MDCT data. However, Baum et al. reported that, with regard to the trabecular microstructure and bone quality in vertebral bone, there is no difference between MDCT data and high-resolution pQCT [40]. Therefore, we strongly believe that MDCT is a useful tool for evaluating the trabecular microstructure of the thoracic vertebrae. Based on our clinical results and microstructure analysis, we recommend using TP to prevent PJK type 2 in patients who have been surgically treated for ASD and who have a preexisting low BMD.

Conclusion

Prophylactic TP treatment decreased the incidence of PJK type 2 in patients who underwent surgical treatment for ASD. TP therapy improved the volumetric BMD, fine bone structure, and bone strength. Larger-sample series studies will be necessary to elucidate the prophylactic effect and cost-benefit ratio of TP therapy for patients with a preexisting low BMD who undergo long instrumented fusion for spinal deformity.

Compliance with ethical standards This study was approved by the appropriate institutional review board.

Conflicts of interest None.

References

1. Kim YJ, Lenke LG, Bridwell KH et al (2007) Proximal junctional kyphosis in adolescent idiopathic scoliosis after 3 different types of posterior segmental spinal instrumentation and fusions: incidence and risk factor analysis of 410 cases. Spine (Phila Pa 1976) 32:2731–8
2. Lee GA, Betz RR, Clements DH 3rd et al (1999) Proximal kyphosis after posterior spinal fusion in patients with idiopathic scoliosis. Spine (Phila Pa 1976) 24:795–9
3. DeWald CJ, Stanley T (2006) Instrumentation-related complications of multilevel fusions for adult spinal deformity patients over age 65: surgical considerations and treatment options in patients with poor bone quality. Spine (Phila Pa 1976) 31:S144–51
4. Hart RA, Prendergast MA, Roberts WG et al (2008) Proximal junctional acute collapse cranial to multi-level lumbar fusion: a cost analysis of prophylactic vertebral augmentation. Spine J 8:875–81
5. Kim YJ, Bridwell KH, Lenke LG et al (2008) Proximal junctional kyphosis in adult spinal deformity after segmental posterior spinal instrumentation and fusion: minimum five-year follow-up. Spine (Phila Pa 1976) 33:2179–84
6. Kim YJ, Bridwell KH, Lenke LG et al (2005) Proximal junctional kyphosis in adolescent idiopathic scoliosis following segmental posterior spinal instrumentation and fusion: minimum 5-year follow-up. Spine (Phila Pa 1976) 30:2045–50
7. Yang SH, Chen PQ (2003) Proximal kyphosis after short posterior fusion for thoracolumbar scoliosis. Clin Orthop Relat Res 152–8.
8. Helgeson MD, Shah SA, Newton PO et al (2010) Evaluation of proximal junctional kyphosis in adolescent idiopathic scoliosis following pedicle screw, hook, or hybrid instrumentation. Spine (Phila Pa 1976) 35:177–81
9. Hollenbeck SM, Glattes RC, Asher MA et al (2008) The prevalence of increased proximal junctional flexion following posterior instrumentation and arthrodesis for adolescent idiopathic scoliosis. Spine (Phila Pa 1976) 33:1675–81
10. Watanabe K, Lenke LG, Bridwell KH et al (2010) Proximal junctional vertebral fracture in adults after spinal deformity surgery using pedicle screw constructs: analysis of morphological features. Spine (Phila Pa 1976) 35:138–45
11. Lowe TG, Kasten MD (1994) An analysis of sagittal curves and balance after Cotrel-Dubousset instrumentation for kyphosis secondary to Scheuermann's disease. A review of 32 patients. Spine (Phila Pa 1976) 19:1680–5
12. Glattes RC, Bridwell KH, Lenke LG et al (2005) Proximal junctional kyphosis in adult spinal deformity following long instrumented posterior spinal fusion: incidence, outcomes, and risk factor analysis. Spine (Phila Pa 1976) 30:1643–9
13. Good CR, Lenke LG, Bridwell KH et al (2010) Can posterior-only surgery provide similar radiographic and clinical results as combined anterior (thoracotomy/thoracoabdominal)/posterior approaches for adult scoliosis? Spine (Phila Pa 1976) 35:210–8
14. Yagi M, King A, Boachie-Adjei O (2011) Incidence, risk factors and classification of proximal junctional kyphosis: surgical outcomes review of adult idiopathic scoliosis. Spine (Phila Pa 1976) 36(1):60–8
15. Yagi M, King AB, Boachie-Adjei O (2012) Incidence, risk factors, and natural course of proximal junctional kyphosis: surgical outcomes review of adult idiopathic scoliosis. Minimum 5 years of follow-up. Spine (Phila Pa 1976) 37(17):1479–89
16. Yagi M, Rahm M, Gaines R et al (2014) Characterization and surgical outcomes of proximal junctional failure (PJF) in surgically treated adult spine deformity patients. Spine (Phila Pa 1976) 39:E607–14
17. Yagi M, Hosogane N, Okada E et al (2014) Factors affecting the post operative progression of thoracic kyphosis in surgically treated adult patient with lumbar degenerative scoliosis. Spine (Phila Pa 1976) 39: E521–8
18. Yagi M, Patel R, Lawhorne TW et al (2013) Adult thoracolumbar and lumbar scoliosis treated with long vertebral fusion to the sacropelvis: a comparison between new hybrid selective spinal fusion versus anterior-posterior spinal instrumentation. The Spine J 14:637–45
19. Yagi M, Cunningham E, King A et al (2013) Long term clinical and radiographic outcomes of pedicle subtraction osteotomy for fixed sagittal imbalance: does level of proximal fusion affect the outcome?—minimum 5years follow-up. Spine Deformity 1:123–31
20. Yagi M, King AB, Boachie-Adjei O (2011) Characterization of osteopenia/osteoporosis in adult scoliosis: does bone density affect surgical outcome? Spine (Phila Pa 1976) 36(20):1652–7
21. Muneroto M, Kido A, Sakamoto Y et al (2016) Analysis of trabecular bone microstructure in osteoporotic femoral heads in human patients: in vivo study using multidetector row computed tomography. BMC Musculoskelet Disord 17(1):13
22. Krege J, Lane N, Harris J et al (2014) PINP as a biological response marker during teriparatide treatment for osteoporosis. Osteoporos Int 25(9):2159–2171
23. Croucher P, Garrahan N, Compston J (1996) Assessment of cancellous bone structure: comparison of strut analysis, trabecular bone pattern factor, and marrow space star volume. J Bone Miner Res 11(7):955–61
24. Yakacki CM, Poukalova M, Guldberg RE et al (2010) The effect of the trabecular microstructure on the pullout strength of suture anchors. J Biomech 43(10):1953–9