EFFECT OF PKP ON SERUM SOST IN PATIENTS WITH VERTEBRAL COMPRESSION FRACTURES

EFEITO DE PKP EM SOST SORO EM PACIENTES COM FRATURAS DE COMPRESSÃO VERTEBRAL

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ABSTRACT

Objective: This study sought to determine serum sclerostin (SOST) expression in patients with osteoporotic thoracolumbar vertebral compression fractures before and after percutaneous kyphoplasty (PKP). Methods: Serum SOST levels were quantified with a sandwich enzyme-linked immunosorbent assay (ELISA) preoperatively and six months postoperatively. Anterior vertebral height, kyphotic angles, and Visual Analog Scale (VAS) scores were also recorded. Results: Serum SOST was highly expressed in patients and remained negatively correlated with bone mineral density (BMD). Vertebral heights, local kyphotic angles, and VAS scores were all significantly improved after PKP. However, serum SOST was positively correlated with BMD six months after surgery. Conclusion: PKP was an effective treatment strategy for osteoporotic thoracolumbar vertebral compression fractures, improving BMD and decreasing serum SOST levels.

Keywords: Bone Density. Kyphoplasty. Osteoporosis.

INTRODUCTION

Osteoporosis is a common skeletal disease characterized by low bone mass, impaired bone mechanical functions, and increased bone fragility. It has become a major cause of disability and death among older adults, leading to an increased fracture risk.1 Vertebral fracture is the most common outcome of osteoporosis, especially osteoporotic vertebral compression fractures (OVCF), which frequently occur at the thoracolumbar segment.2 Patients with that type of fracture usually suffer from low back and lumbosacral pain that is aggravated by activities. We believe osteoporotic fracture is traditionally treated with bed rest and analgesics. However, long-term bed rest might result in potential complications such as pulmonary infection, atelectasis, thrombosis, and pulmonary embolism.3 Open surgery and minimally invasive procedures have been developed to treat such fractures. Percutaneous kyphoplasty (PKP) involves filling the vertebral body with bone cement to improve the mechanical integrity of the fractured vertebra.4 The study was conducted at Ningbo Women and Children’s Hospital.

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invasive surgery are well documented alternative methods for the operative treatment of OVCF. Open surgeries, such as laminectomy and internal fixation, are appropriate for patients who present signs of neurological deficits, or those with space-occupying lesions in spinal canal and spinal cord compression, based on nerve computed tomography (CT) and magnetic resonance imaging (MRI) scans. However, open surgery entails two major disadvantages: greater blood loss and high failure rate."}

"Sclerostin (SOST) is an important osteocyte-derived glycoprotein that functions as a negative regulator of bone formation by inhibiting Wnt/β-catenin signaling to promote osteogenic differentiation. SOST-KO mice showed to enhance bone defects healing and highly expressed serum SOST is associated with fracture healing. SOST functions as a therapeutic target for treating osteoporotic fractures. However, the influence of PKP treatment on SOST expression remained unclear. Considering that, this study sought to analyze the serum SOST expression among patients with osteoporotic thoracolumbar vertebral compression fractures and their response to PKP treatment.

MATERIALS AND METHODS

| Chart 1. Highlights. |
|----------------------|
| Serum SOST was highly expressed in patients with osteoporotic thoracolumbar vertebral compression fractures. |
| Vertebral heights, Cobb’s angles, and VAS scores were significantly improved after PKP |
| Postoperative SOST was positively correlated with BMD during 6 months follow-up |

Study population

From January 2017 to June 2018, 150 patients with osteoporotic fractures examined by computed tomography (CT) or magnetic resonance imaging (MRI) of the thoracolumbar spine were evaluated. Of these, sixty cases of thoracolumbar vertebral compression fractures were included in the study. Patients with severe heart and lung disease and coagulation disorders were excluded. Our study group included 33 women and 27 men with body mass index (BMI) ranging from 22 to 28 kg/m². Average age at surgery was 69 years (range: 44 to 78 years) and average duration of symptoms was eight weeks (range: 2 to 24 weeks). Sixty gender- and age-matched individuals with normal bone mineral density (BMD), confirmed by physical examination during the same period, composed the control group. A written informed consent form was obtained from each participant. All experimental protocols for this study were approved by the Ethics Committee of Ningbo Women and Children's Hospital.

Surgical procedure

Percutaneous kyphoplasty (PKP) was performed under general anesthesia in prone position, as previously described. Bone marrow biopsy needle was percutaneously inserted under C-arm fluoroscopy guidance (BAITENG Medical, Shanghai, China) into the fractured vertebra body through pedicle. Then a balloon was inserted into the vertebra to restore vertebral body height and create a cavity for bone cement injection. Bone cement introducer was removed after the cement was well diffused. The same surgeons performed all operations, and no bone cement leakage and balloon rupture occurred during operation.

Enzyme-linked immunosorbent assay

Fasting blood samples containing anticoagulant were collected from patients with thoracolumbar vertebral compression fractures and healthy volunteers and centrifuged at 3000 rpm for twenty minutes. Serum specimens were then stored at -80 °C until analysis. Serum sclerostin (SOST) protein levels in serum were measured using the Human SOST ELISA kit (Boster, Wuhan, China), according to manufacturer’s instruction.

Clinical and radiographic examinations

Values of bone mineral density (BMD), visual analogue scale (VAS), anterior vertebral body height of the fractured level (AVHF), and Cobb’s angle were investigated to evaluate improvement in patients’ pain and outcomes. BMD was measured by dual energy X-ray absorptiometry using the QDR-2000 (Hologic Inc., Waltham, MA, USA). Clinical evaluation of pain employed the VAS score, ranging from 0 (no pain) to 10 (severe pain). X-ray examination was obtained preoperatively and one-week postoperatively. Cobb’s angle was measured between the superior vertebral endplate, one level above the treated vertebra, and the inferior vertebral body endplate, one level below the treated vertebra. Anterior height was determined by measuring the length between the superior endplate most antero-superior point and the inferior endplate most antero-inferior point of the fractured vertebra body.

Statistical analysis

Data were expressed as mean ± standard deviation (SD) and analyzed using SPSS version 22.0 (SPSS, Chicago, IL, USA). Statistical differences were assessed using two-sided Student’s t test or analysis of variance, and p value < 0.05 was considered significantly different. Spearman’s rank correlation coefficient was used to analyze the correlation between serum SOST and BMD.

RESULTS

SOST and BMD association in patients with osteoporotic thoracolumbar vertebral compression fractures

Patients with osteoporotic thoracolumbar vertebral compression fractures showed higher serum SOST (Figure 1A, p < 0.05) and lower BMD (Figure 1B, p < 0.05) than healthy controls. We found a significant negative correlation between serum SOST and BMD, according to Spearman’s correlation coefficient (Figure 1C, r = 0.5345, p < 0.001).
Pre- and postoperative outcomes comparisons

All patients underwent successful surgery. Mean operative time was seventy minutes (range 45–120 minutes). Intraoperative blood loss ranged from 8 to 14 mL, with an average of 10 mL. All patients were able to get out of bed within 3 to 5 days after surgery. Forty-six cases reported complete pain relief, 12 partial relief, and two no relief; complete remission rate was 96.60%. Patients developed no complications such as constipation, pneumonia, and lower extremities deep venous thrombosis.

As presented in Table 1, the average preoperative pain based on VAS was 7.24 (SD = 0.29) and the average postoperative VAS was 2.24 (SD = 0.14), suggesting pain relief one week after PKP. We also observed postoperative improvement in the anterior vertebral height and a significant decrease in the average vertebral Cobb’s angle when compared to with preoperative values (all, p < 0.05).

Postoperative SOST expression in patients and its correlation with BMD

To better understand the efficacy of PKP for treating thoracolumbar vertebral compression fractures and its effect on SOST expression, we compared serum SOST levels and BMD before and after surgery. Figure 2 shows that serum SOST was markedly downregulated (Figure 2A) while BMD shows an upward trend (Figure 2B) at one, three and six months postoperatively in comparison to preoperative values (all, p < 0.05). We found a positive correlation between serum SOST level and BMD within six-month postoperative (Table 2, p < 0.05).

Table 1. Pre- and postoperative Visual Analogue Scale, anterior vertebral height, and Cobb’s angle.

| Group       | VAS    | anterior vertebral height (mm) | Cobb’s angle (°) |
|-------------|--------|--------------------------------|-----------------|
| preoperative| 7.24 ± 0.29 | 18.47 ± 0.82                  | 23.72 ± 1.15    |
| postoperative| 2.24 ± 0.14* | 24.38 ± 1.62*                 | 8.84 ± 1.42*    |

VAS: Visual Analog Scale.

Table 2. Correlation between serum sclerostin and postoperative bone mineral density.

|                  | r      | P      |
|------------------|--------|--------|
| one month        | 0.269  | 0.037  |
| three months     | 0.621  | 0.000  |
| six months       | 0.629  | 0.000  |
DISCUSSION
Osteoporosis vertebral compression fracture (OVCF), a common complication of osteoporosis, may lead to severe lower back pain, limited movement, and spinal and kyphotic deformity. Bone remodeling mainly relies on the activity of two major cell types – bone-forming osteoblasts and bone-resorbing osteoclasts. Recently, accumulating evidence strongly implied that Wnt/β-catenin signaling plays an important role in controlling bone mass, increasing proliferation and differentiation of osteoblastic precursor cells and improving bone mineral density (BMD). In mammalian cells, Serum sclerostin (SOST) inhibits Wnt signaling by binding to Wnt receptors extracellular domain. Thus, SOST is increasingly recognized as a vital negative regulator of bone formation. SOST deficiency-induced diseases in humans are characterized by increased bone mass. Gaudio and colleagues found high SOST serum levels expression in patients with immobilization-induced bone loss. According to Shen et al., anti-SOST is a potential therapy for osteoporosis. In our study, SOST serum levels were significantly higher in patients with osteoporotic thoracolumbar vertebral compression fractures when compared with healthy controls. More importantly, serum SOST was negatively correlated with BMD.

With the continuous socioeconomic development and the improvement in medical technology, several surgical methods are used for treating thoracolumbar fractures. Percutaneous kyphoplasty (PKP) is a minimally invasive, safe, and effective treatment for OVCF that can effectively and quickly relieve pain, improve functional capacity, reduce the incidence of complications, increase vertebral strength, avoid postoperative vertebral height loss, and prevent secondary fractures. Sun et al. reported low-viscosity for PKP results in the restoration of middle vertebral height for treating OVCF. Zhao et al. found PKP to be associated with a significantly longer operation time and a lower risk of cement leakage. In our study, all patients showed significant improvement in VAS score, anterior vertebral height, and Cobb’s angle within one week after operation compared with values before operation. PKP surgery also resulted in serum SOST downregulation and BMD increase at 6-month follow-up. SOST was positively correlated with BMD after PKP treatment.

CONCLUSION
In conclusion, PKP treatment may not only restore compressed vertebral body height and correct kyphosis, but also reduce SOST expression to achieve an effective treatment of patients with osteoporotic thoracolumbar vertebral compression fractures.

AUTHORS’ CONTRIBUTIONS: Each author contributed individually and significantly to the development of this article. EW: designed the study; JL: designed the study; GX: conducted the experiments and analyzed the data; XW: conducted the experiments and analyzed the data; MC: conducted most of the experiments and wrote the manuscript.

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