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Original Article

Changes in inflammatory factors in patients with osteoporotic vertebral compression fracture and influences of rehabilitation training on postoperative functional recovery and inflammation

Yehong Li[1], Lin Wang[2]

[1]Department of Spinal Surgery, East Section of Jining No. 1 People's Hospital, Jining, Shandong 272011, P.R. China;
[2]Department of Rehabilitative Medicine, East Section of Jining No. 1 People's Hospital, Jining, Shandong 272011, P.R. China

Abstract

Objective: To observe the changes in inflammatory factors in patients with osteoporotic vertebral compression fracture (OVCF). **Methods:** 40 OVCF patients meeting inclusion criteria were collected, and randomly divided into rehabilitation therapy group (n=20) and traditional therapy group (n=20). 20 normal subjects were collected as control group. Venous blood was collected after admission, and the expression levels of IL-1 and IL-18 were detected via ELISA. Patients in rehabilitation therapy group received rehabilitation training post-operatively, while those in traditional therapy group received conventional therapy. The pain was evaluated using visual analogue scale (VAS) score, and the spinal function was evaluated using Oswestry disability index (ODI) score. The curative effect was evaluated at final follow-up. **Results:** The expression levels of IL-1 and IL-18 of OVCF patients were significantly higher than those in normal subjects ($p<0.01$). The VAS and ODI scores in the rehabilitation therapy group were significantly lower than those in traditional therapy group from the 3rd month after operation ($p<0.05$). The expression levels of IL-1 and IL-18 in the rehabilitation therapy group were obviously lower than those in traditional therapy group from the 3rd month after operation ($p<0.05$). The effective rate in rehabilitation therapy group was higher than that in traditional therapy group. The expression levels of IL-1 and IL-18 in OVCF patients are increased. **Conclusion:** Rehabilitation training is beneficial to functional recovery and reduction of inflammation after OVCF operation.

Keywords: Osteoporotic Vertebral Compression Fracture, Inflammation, Rehabilitation Training

Introduction

Osteoporosis is a systemic disease characterized by decreased bone mass, decline in bone density and quality, increased bone fragility and increased risk of fracture. Osteoporotic fracture is one of the important complications of osteoporosis, and its onset risk continues to be increased, especially that of osteoporotic vertebral compression fracture (OVCF)[1]. Currently, the treatment methods of OVCF mainly include non-surgical treatment and surgical treatment, the former of which is mainly dominated by rehabilitation training, external fixation brace, bed rest, anti-osteoporosis treatment, analgesia, etc., and the latter of which is mainly dominated by percutaneous vertebroplasty (PVP), etc.[2]. The surgery combined with postoperative rehabilitation training is a relatively novel method in the treatment of OVCF at present. Inflammation is one of the important pathological responses after fracture and a kind of defensive response of the body. However, the persistent high expressions of pro-inflammatory factors, interleukin-1 (IL-1) and IL-18, at the fracture site after OVCF are detrimental to damage repair[3]. Therefore, this study aims to investigate the changes in inflammatory factor expressions after OVCF and to explore whether rehabilitation training can promote

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Corresponding author: Lin Wang, Department of Rehabilitative Medicine, East Section of Jining No. 1 People's Hospital, No. 99, Shixian Road, Jining, Shandong 272011, P.R. China
E-mail: w926rc@163.com

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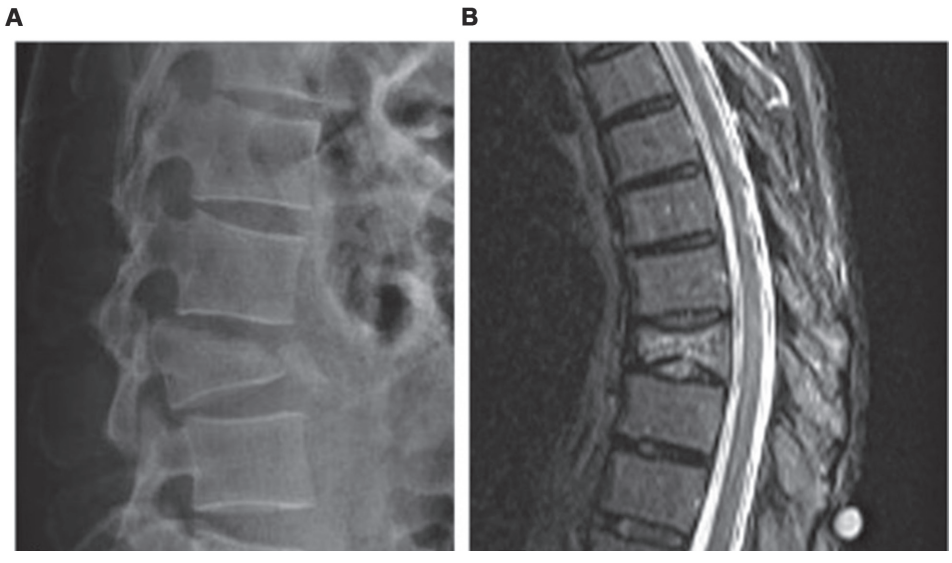

Figure 1. Imaging manifestations of OVCF. Note: A) X-ray film, B) MRI film.

Table I. Diagnostic criteria of nonunion of fracture.

No.	Symptom description
1	Have histories of falling, jolting and other traumas
2	Chest and back pain, pressing pain and percussion pain as main signs
3	X-ray shows decreased and sparse thoracic or (and) lumbar trabecular bone density, and thinner cortex of bone. Fractured vertebra shows tapered morphological changes (Figure 1)
4	No obvious nerve or spinal cord compression symptoms
5	MRI shows fractured vertebra has high signal or spinal edema (Figure 1)

functional recovery through inhibiting inflammatory factor expressions in OVCF patients after operation.

Materials

General materials

A total of 40 OVCF patients admitted into East Section of Jining No. 1 People's Hospital from January 2017 to October 2017 were collected, and were randomly divided into rehabilitation therapy group (n=20) and traditional therapy group (n=20). Another 20 normal subjects were collected as a control group.

Diagnostic criteria

Diagnostic criteria of OVCF are shown in Table I, Figure 1.

Inclusion criteria

Inclusion criteria were: (1) patients who met the above criteria of OVCF, (2) patients aged 18-65, (3) patients who agreed to participate in this study and signed the informed consent, (4) patients with fresh fractures treated in East Section of Jining No. 1 People's Hospital, (5) patients who volunteered to follow doctor's advice, and strictly strictly adhered to treatment.

Exclusion criteria

Exclusion criteria were: (1) patients who did not meet the above inclusion criteria, (2) pregnant or lactating female patients, (3) patients complicated with major internal medicine diseases, such as hypertension, diabetes mellitus or heart disease, (4) patients with a history of serious diseases, such as serious primary disease or mental illness, (5) patients with a history of lumbar fractures, lumbar surgery, bone tumors, bone tuberculosis or other lumbar diseases.

Methods

Surgical methods

OVCF patients received surgical treatment, and the specific method was as follows: After the successful anesthesia, the

fracture site of the patient was positioned under a prone position, disinfected and paved with an aseptic towel. The pedicle of fractured vertebra was positioned using the C-arm scenograph and labeled, and it was expanded using nucleus forceps via percutaneous puncture, followed by hemostasis and injection of the vertebral filler to hold up the collapsed vertebral body. The wound was dressed after operation.

Rehabilitation training

Patients began rehabilitation training from the 3rd day after operation, and the specific method was as follows: First, with the occiput, double elbows and double heels as support points, waist muscle contracted to lift lower back and hip away from the bed for 10 s. The training was performed for 15 times as 1 set, 3 sets each time (once in the morning, afternoon and evening, respectively).

Treatment method in each group

In rehabilitation therapy group, patients received relevant examinations and surgical treatment after admission. After operation, they were given conventional drug therapy. The above rehabilitation training was performed from the 3rd day after operation. Patients were followed up at 1 month, 3 months and 6 months after treatment. The blood was drawn, and the expression levels of inflammatory factors (IL-1 and IL-18) were detected via enzyme-linked immunosorbent assay (ELISA). The visual analogue scale (VAS) score and Oswestry disability index (ODI) score were recorded, and the effective rate was calculated at final follow-up. In traditional therapy group, patients received relevant examinations and surgical treatment after admission. After operation, they were given conventional drug therapy. Patients were followed up at 1 month, 3 months and 6 months after treatment. The blood was drawn, and the expression levels of inflammatory factors (IL-1 and IL-18) were detected via ELISA. The VAS score and ODI score were recorded, and the effective rate was calculated at final follow-up. In control group, the blood was drawn, and the expression levels of inflammatory factors (IL-1 and IL-18) were detected via ELISA.

ELISA

Specific operation steps were as follows: 1) The sample was loaded, 2) the plate was washed, 3) 50 μL distilled water and 50 μL primary antibody working solution in the kit were added into each well (except blank group), and they were mixed evenly in the reaction plate for reaction at 37°C for 20 min, 4) the plate was washed, 5) 100 μL enzyme-labeled antibody working solution in the kit was added to each well, and the reaction plate was placed at 37°C for reaction for 10 min, 6) the plate was washed again, 7) 100 μL substrate working solution in the kit was added into each well, and the reaction plate was placed at 37°C for reaction in a dark place for 15 min, 8) 100 μL stop buffer in the kit was added to each well and mixed evenly, 9) and the optical density value was detected at 450 nm using a microplate reader.

Table II. VAS score.

Point	Description
0 point	No pain
1-3 points	Mild pain
4-6 points	Moderate pain
7-10 points	Severe pain

VAS score

The pain degree of patients was evaluated using the VAS score[4]. A 10 cm-long ruler was used ranging from 0 point (no pain) to 10 points (severe pain), each 1 cm scale represented 1 point of pain degree, and patients selected the corresponding pain scores according to their own pain degrees. Specific scoring criteria are shown in Table II.

ODI score

In this study, the ODI score[5] was used to express the patient's spinal functional recovery after treatment. The higher the ODI score is, the worse the patient's spinal functional recovery will be.

Determination of curative effect

Cured: The pain completely disappears, and the life is normal. Remarkably effective: The pain is significantly relieved, and patients can take care of themselves. Effective: The pain is mildly relieved, and patients need to take painkillers and can partially take care of themselves. Ineffective: The pain is not relieved, and patients need to take painkillers and cannot take care of themselves.

Statistical methods

Statistical Product and Service Solutions (SPSS) 20.0 software was used for statistical analysis. Enumeration data were presented as mean ± standard deviation. *t* test was used for data in line with the normal distribution and homogeneity of variance, corrected *t* test was used for data in line with the normal distribution and heterogeneity of variance, and non-parametric test was used for data in line with the abnormal distribution and homogeneity of variance. Rank sum test was used for ranked data, and chi-square test was used for enumeration data. $p<0.05$ suggested that the difference was statistically significant.

Results

Comparisons of general conditions

A total of 40 OVCF patients meeting criteria were enrolled and divided into rehabilitation therapy group (n=20) and traditional therapy group (n=20). Another 20 subjects were included into control group. Gender and age of patients in

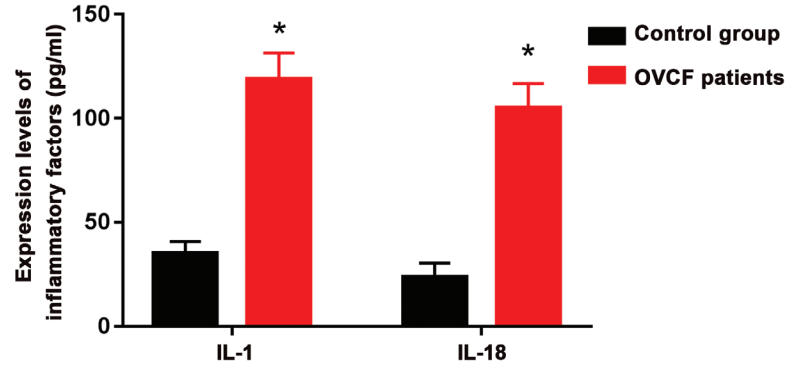

Figure 2. Detection of expression levels of inflammatory factors via ELISA. Note: *p<0.01 vs. normal subjects.

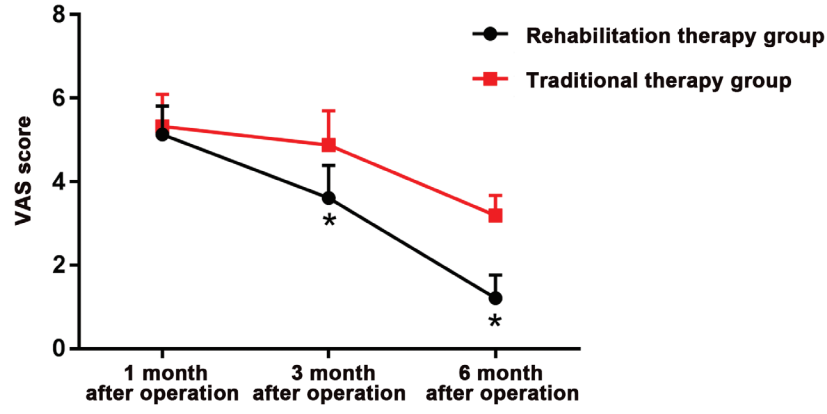

Figure 3. VAS score. Note: *p<0.05 vs. traditional therapy group.

Table III. General conditions in each group.

Group	Male	Female	Average age
Control group	8	12	45.7±10.67
Rehabilitation therapy group	9	11	39.1±12.27
Traditional therapy group	8	12	44.1±11.77

each group are shown in Table III. There were no differences in gender and age among three groups of patients (p>0.05), and data were comparable.

Detection of changes in inflammatory factors in OVCF via ELISA

The expression levels of inflammatory factors (IL-1 and IL-18) in venous blood of OVCF patients were increased and significantly higher than those in control group, and the differences were statistically significant (p<0.05) (Figure 2), suggesting that inflammation occurs in patients after OVCF, and expression levels of inflammatory factors (IL-1 and IL-18) in venous blood are increased.

VAS score

VAS scores in rehabilitation therapy group and traditional therapy group were higher after operation. With the extension of time, VAS scores in rehabilitation therapy group and traditional therapy group were decreased gradually. VAS scores in rehabilitation therapy group were significantly

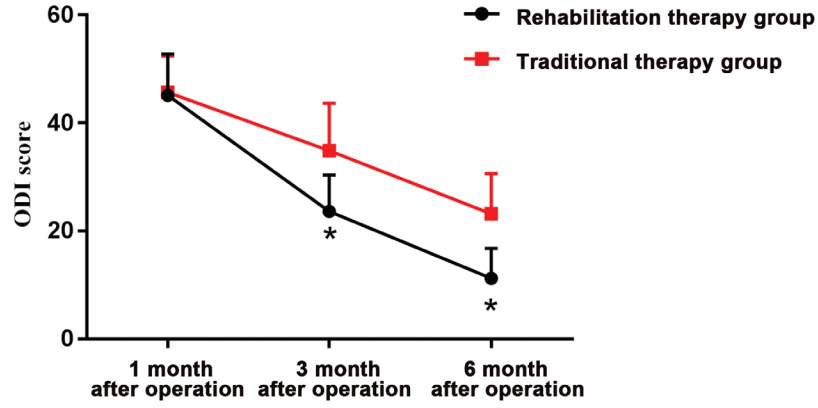

Figure 4. ODI score. Note: *p<0.05 vs. traditional therapy group.

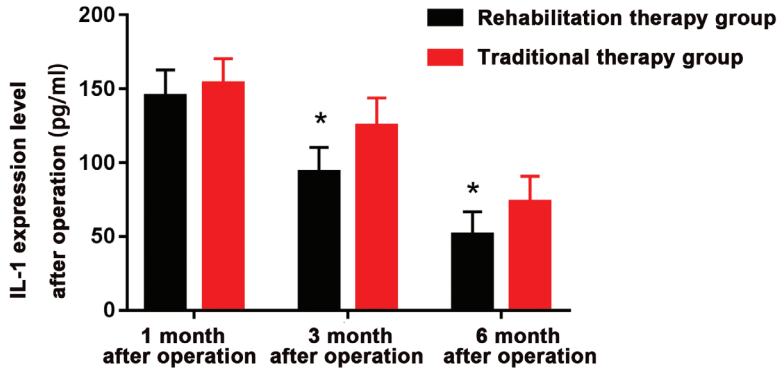

Figure 5. IL-1 expression level after operation. Note: *p<0.05 vs. traditional therapy group.

Table IV. Treatment effect in each group.

	Cured	Remarkably effective	Effective	Ineffective	Remarkably effective rate
Rehabilitation therapy group	6	5	9	0	55%
Traditional therapy group	4	4	12	0	40%

lower than those in traditional therapy group from the 3rd month after operation, and differences were statistically significant (p<0.05) (Figure 3), suggesting that rehabilitation training can better improve the pain in OVCF patients.

ODI score

ODI scores in rehabilitation therapy group and traditional therapy group were higher after operation. With the extension of time, ODI scores in rehabilitation therapy group and traditional therapy group were decreased gradually. ODI scores in rehabilitation therapy group were significantly lower than those in traditional therapy group from the 3rd month after operation, and differences were statistically significant (p<0.05) (Figure 4), suggesting that rehabilitation training can better promote the postoperative spinal functional recovery in OVCF patients.

Treatment effect in each group

In rehabilitation therapy group, 6 cases were cured, 5 cases were remarkably effective, 9 cases were effective and

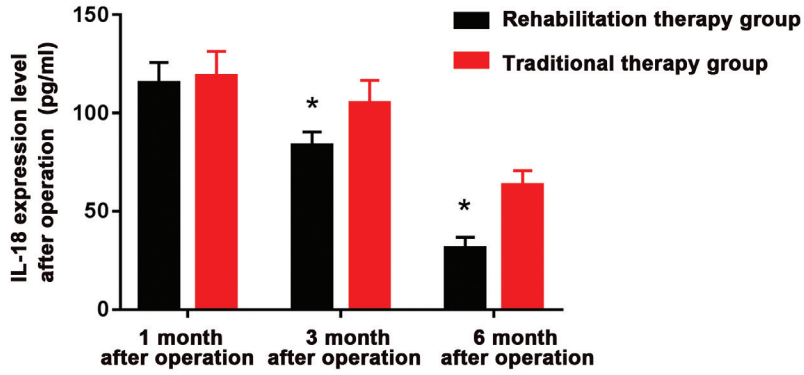

Figure 6. IL-18 expression level after operation. Note: *p<0.05 vs. traditional therapy group.

0 case was ineffective, and the remarkably effective rate was 55%. In traditional therapy group, 4 cases were cured, 4 cases were remarkably effective, 12 cases were effective and 0 case was ineffective, and the remarkably effective rate was 40% (Table IV). The remarkably effective rate in rehabilitation therapy group was higher than that in traditional therapy group, indicating that rehabilitation training can improve the therapeutic effect after OVCF operation.

Effects of rehabilitation training on expressions of inflammatory factors

The expression levels of inflammatory factors (IL-1 and IL-18) were higher in OVCF patients after operation. With the extension of time, the expression levels of inflammatory factors (IL-1 and IL-18) in rehabilitation therapy group and traditional therapy group were decreased gradually. IL-1 and IL-18 expression levels in rehabilitation therapy group were obviously lower than those in traditional treatment group from the 3rd month after operation. Differences were statistically significant compared with those in normal control group (p<0.05) (Figure 5 & 6), indicating that rehabilitation therapy is beneficial to reducing expression levels of inflammatory factors (IL-1 and IL-18) after OVCF operation, and inhibiting inflammation.

Discussion

OVCF is one of the common complications of osteoporosis and one of the common types of osteoporotic fracture[6]. Reduced bone mass and bone structure degeneration caused by osteoporosis result in biomechanical changes in the structural stability of spine, and vertebral compression fracture will be caused under the exogenic action of small trauma, which occurs frequently in thoracolumbar vertebra, most common in T12-L1 vertebral bodies[7]. The pathological response after OVCF is very complicated, and inflammation, as one of the important pathological responses, is one of the important pathological mechanisms leading to chest and back pain after fracture. After OVCF, tissue damage and stress response caused by trauma can increase the inflammatory response. The high-level inflammatory response not only provides the body stress ability, but also inhibits immune function[8,9]. The persistent high-level inflammatory response after fracture can lead to changes in tissue and vascular permeability, as well as obstruction of lymphatic return, eventually causing serious diseases, such as deep venous thrombosis, fat embolism, and pulmonary embolism, and threatening the life[10-12]. Current studies have shown that[13] a large number of inflammatory factors produced by inflammation after OVCF can result in pain symptoms through a series of biochemical reaction infiltration and stimulation of the nerve root. After fracture, various factors, such as local ischemia, mechanical compression, ion imbalance and release of oxygen free radicals, can activate a variety of inflammation-related receptors and pathways in cells, resulting in release of many downstream pro-inflammatory factors, such as IL-1 and IL-18, to the extracellular part, producing inflammation, and leading to pain symptoms[14,15]. These inflammatory factors exert different biochemical effects, and stimulate the nerve root and pain receptors, leading to the nerve root pain, increasing the degree of nerve root pain, and reflecting changes in pain[16]. At the same time, it is not conducive to fracture healing and recovery. IL-1 is an important member of pro-inflammatory factor family, and it is currently known that IL-1 plays a pro-inflammatory role by regulating prostaglandin expression. Animal experiments have confirmed that[17] with the increase of IL-1 expression, the prostaglandin expression level is also increased, and the degree of pain reflex has a positive correlation with IL-1 expression level. Studies have shown that[18] in the rat model of nerve root pain, pain inhibitors significantly reduce the IL-1 expression level in tissues and inhibit the pain. As important pro-inflammatory factors, IL-18 and IL-1 exist extensively in degenerative intervertebral disc tissues and are expressed highly, which are considered as important factors of pain[13,19,20].

At present, surgery is commonly used for the treatment of OVCF. In particular, the bone cement is injected into the

compressed vertebral body in PVP, which can not only hold up the vertebral body and restore its biomechanical stability, but also seal the nerve termination around the compressed vertebral body, and alleviate chest and back pain symptoms, and it is beneficial for patients to get out of bed[21]. Results of this study confirmed that treating OVCF patients with PVP could effectively reduce the expression levels of inflammatory factors (IL-1 and IL-18) in patients, and reduce the VAS score and ODI score of patients, indicating that PVP is beneficial to relieving pain symptoms and improving the spinal function of patients. However, PVP also has shortcomings. For example, injecting the bone cement into the fractured vertebral body can increase the risk of adjacent vertebral fractures, and the long-term curative effect is poor[22,23]. Lumbodorsal muscle functional exercise is simple, easy and economical, and it is an ideal method of rehabilitation training. This method of rehabilitation training promotes regular muscle contraction, produces a certain mechanical stress against vertebral bone, benefits bone formation, reduces bone resorption, and improves osteoporosis state. At the same time, spinal extension exercise in lumbodorsal muscle functional exercise can build up anterior longitudinal ligament and posterior longitudinal ligament, protect the vertebral body, promote vertebral body shape recovery, balance spine stress, and stabilize facet joints. Results of this study suggest that the rehabilitation training of lumbodorsal muscle for 3 months can effectively reduce the expression levels of inflammatory factors (IL-1 and IL-18) in OVCF patients after operation, inhibit inflammation, and improve pain symptoms and spinal function of patients, and it is an ideal auxiliary treatment method after OVCF operation.

Authors' contributions

YL wrote, finalized the manuscript and helped with rehabilitation training. LW collected and analyzed the fundamental data of patients. Both authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the ethics committee of Jining No.1 People's Hospital. Signed written informed consents were obtained from the participating patients and/or guardians.

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