MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2018; 24: 50-57
DOI: 10.12659/MSM.905729

Received: 2017.06.11
Accepted: 2017.07.17
Published: 2018.01.03

Impact of Magnetic Resonance Imaging on Treatment-Related Decision Making for Osteoporotic Vertebral Compression Fracture: A Prospective Randomized Trial

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AEF **Cong Jin**
BC **Guojian Xu**
BD **Dong Weng**
BC **Minghua Xie**
AG **Yu Qian**

Department of Orthopedics, Shaoxing People's Hospital, Shaoxing, Zhejiang, P.R. China

Corresponding Author: Yu Qian, e-mail: qianyuspine@163.com
Source of support: This study was supported by National Natural Science Foundation of China (No. 81572126)

Background: The aim of this study was to analyze the impact and usefulness of characteristic signal change of a linear black signal on magnetic resonance imaging (MRI) on treatment-related decision making.

Material/Methods: Forty-one patients with a linear black signal on MRI were enrolled in this prospective study. They were randomly divided into the percutaneous kyphoplasty (PKP) group (n=24) and the conservative treatment group (n=17). Clinical measures, including visual analog scale (VAS) and short-form 36 (SF-36) questionnaire, were analyzed. Radiographic measures, including anterior vertebral body height, kyphosis angle and rate of bone-union, were evaluated.

Results: VAS scores were significantly lower in the PKP group than in the conservative treatment group post-treatment and at one-year follow-up. After one year of treatment, the values for physical functioning, physical health, and body pain were significantly higher in the PKP group than in the conservative treatment group ($p<0.05$). The PKP group had a significantly higher anterior vertebral body height, rate of bone-union, and lower kyphosis angle than the conservative treatment group at one-year follow-up ($p<0.05$).

Conclusions: In patients with a linear black signal detected on MRI, the first-choice treatment should be PKP rather than conservative treatment.

MeSH Keywords: **Fractures, Compression • Magnetic Resonance Imaging • Osteoporotic Fractures**

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/905729

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

Vertebral compression fractures (VCF) are the most common fractures in osteoporotic patients, followed by hip, wrist, or ankle fractures [1–3]. The incidence of osteoporotic vertebral compression fractures (OVCF) in women older than 50 years is more than 1 in 100 per year [3]. Approximately 25% of women older than 70 years and more than half the women older than 80 years have at least one OVCF [3,4]. As a result of OVCF, patients experience severe chronic pain, kyphosis, compromised mobility, pulmonary function reduction, and high mortality; therefore, it is necessary to adopt appropriate treatment modalities for OVCF [5,6].

Percutaneous kyphoplasty (PKP) was first developed by Reiley et al. in 1998 and it became the mainstream treatment for OVCF [7]. In PKP, the morphology of the collapsed vertebral body was restored with inflated balloon catheters, and the vertebral body was stabilized with a cement injection [8]. Numerous reports have demonstrated that the advantages of PKP in comparison to conservative management have been well established in terms of pain reduction and functional outcome; however, some authors were also concerned about the complications associated with PKP, including cement extravasations and adjacent vertebral fractures [9-11]. Moreover, some reports showed that PKP and conservative treatment have equivalent efficacies, as seen at long-term follow-up [12,13]. Therefore, the methods used for the treatment of OVCF are still controversial.

Magnetic resonance imaging (MRI) and particularly the short tau inversion recovery (STIR) sequence are very sensitive tools for detecting vertebral edema as a result of fresh fractures or micro-fractures [14]. In recent years, some authors have drawn our attention towards the use of MRI for differential diagnosis and predictive prognosis of VCF. For instance, Ogura et al. reported that STIR images were useful for differential diagnosis between malignant and benign VCFs [15]. Additionally, some studies suggested that characteristic signal changes on STIR images were effective in predicting subsequent pseudarthrosis resulting from OVCF and subsequent vertebral collapse after percutaneous vertebroplasty [16,17]. To our knowledge, the relationship between treatment outcomes and MRI findings regarding OVCF has not been previously reported. We conducted a prospective clinical study with a series of consecutive patients with OVCF admitted to our hospital. The aim of this study was to analyze the impact and usefulness of characteristic signal change of a linear black signal on MRI on treatment-related decision making.

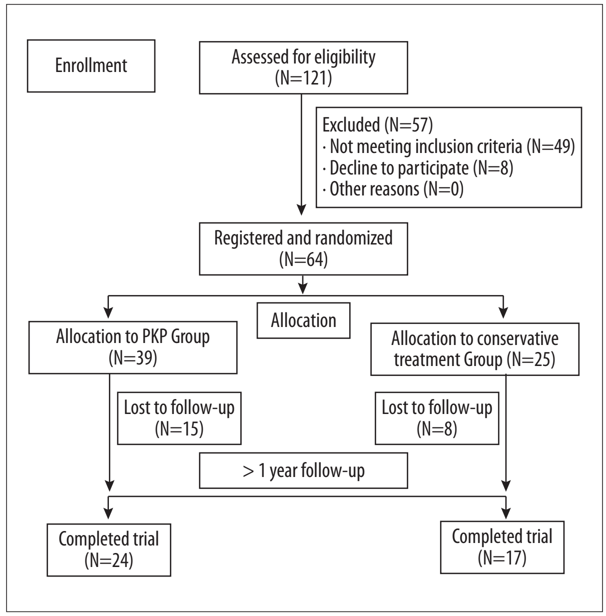

Figure 1. Flow chart showing the categorization of patients into different groups.

Material and Methods

Study design

We conducted a single-center prospective randomized trial at the Shaoxing People's Hospital. The study was designed to compare the clinical and radiographic outcomes between PKP and conservative treatments for treating OVCF with linear black signal on STIR images. Ethical approval was obtained from the Medical Ethics Committee of Shaoxing People's Hospital (No. 2014021). The study was initiated on October 1, 2014 and completed on March 30, 2017.

Patient selection

Our inclusion criteria for this project were as follows: single level thoracolumbar osteoporotic vertebral fracture in patients older than 60 years, concordance of local pain and injured vertebra during clinical examination, and linear black signal detection on STIR image. Exclusion criteria included multilevel compression fractures, secondary osteoporosis (inflammation, endocrine disorders, and corticosteroids), burst fractures, radicular syndrome, primary bone tumors, and spinal metastases. After obtaining signed informed consent from patients before enrollment, patients were randomly divided into the PKP group and conservative treatment groups by the table of random numbers. The flow chart for categorization of patients into groups is shown in Figure 1. Forty-one patients were available for analysis: 24 patients were treated with PKP and 17 patients were treated with conservative therapy.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

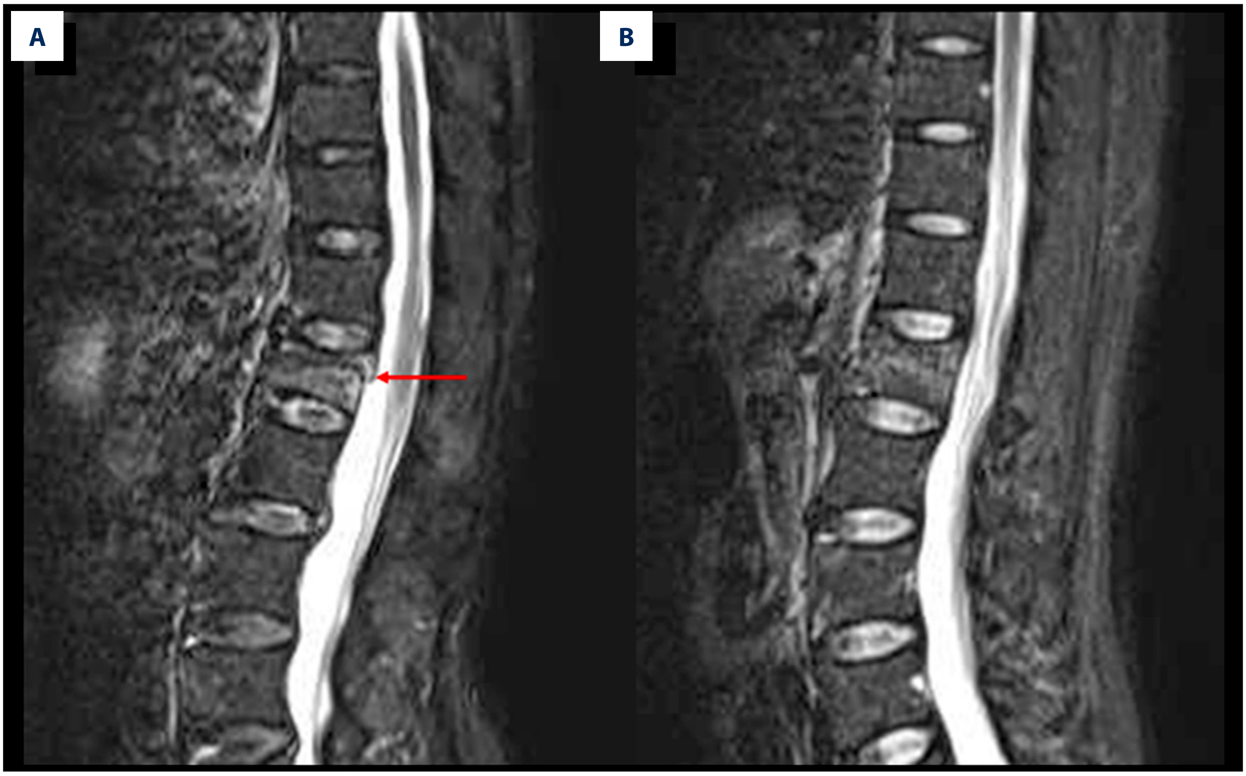

Figure 2. (**A**) Typical linear black signal on STIR sequence. (**B**) Non-linear black signal on STIR sequence.

MRI signal changes

Conventional vertebral column MRI examinations were performed in all patients, using a 3.0 Tesla MRI apparatus (Siemens Magnetom Symphony Quantum, Erlangen, Germany) with a spine coil. Routine sequences studied in patients with trauma consisted of T1-weighted spin echo (SE), T2-weighted SE sagittal, T2-weighted SE axial, and STIR sagittal sections. All MRI examinations were performed within one week after trauma. According to a previous study, the linear black signal change was defined as a linear black signal area of more than half the length of the fractured vertebral body on STIR image [17] (Figure 2).

Conservative therapy

Patients who refused PKP received systematic bed rest, back brace treatment, and analgesic therapy (i.e., celecoxib 200 mg, orally twice daily) for two weeks. Anti-osteoporosis treatment was administered to patients in the conservative treatment group for 12 months, which included 200 IU calcitonin, nasally administered daily (Novartis Pharma S.A.S. France), 0.25 µg calcitriol orally, administered daily, and 600 mg calcium carbonate, orally administered daily.

Percutaneous kyphoplasty (PKP)

The surgeries were performed by two surgeons. Under local anesthesia, the patient was positioned prone on a radiolucent table. A small skin puncture was made approximately 2.5 cm off the midline. With simultaneous viewing of anteroposterior and lateral projections of the spine by C-arm fluoroscopy, a transpedicular entry point into the vertebral body was identified. An 11-gauge needle was placed with the tip lateral to the pedicle projection in the anteroposterior view and parallel to the superior endplate in the lateral view. The working channel, which extends to the junction of the anterior and middle third of the vertebral body, was created. An inflatable balloon was inserted unilaterally into the fractured vertebral body through the working channel and gradually inflated to create a vertebral cavity. Under fluoroscopic guidance, the operator controlled the volume of the balloon to restore the damaged vertebral body until adequate kyphosis angle reduction was obtained. Thereafter, the balloons were deflated and removed; the void was filled with the polymethyl methacrylate (PMMA) cement. Patients could move freely 24 hours postoperatively and they also received anti-osteoporosis treatment for 12 months.

Outcome measures

Demographic data, including age, sex, fracture location, bone mineral density, and follow-up time were recorded. Two

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 1. Summary of patients' demographics data.

Variable	PKP group	Conservative treatment group	P
Number	24	17	
Age	75.8±7.8	72.1±8.0	0.147
Female/Male	18/6	12/5	0.753
Damaged vertebrae			
Thoracic vertebrae	11	7	0.767
Lumbar vertebrae	13	10	
Bone mineral density	−2.9±0.4	−3.0±0.3	0.126
Follow-up time	19.4±4.7	18.1±5.0	0.347

independent senior radiologists evaluated the radiographic outcomes, and clinical follow-up examinations of the patients were independently performed by an orthopedic specialist.

Clinical outcomes were evaluated by the visual analog scale (VAS) and the short-form 36 (SF-36) questionnaire [18]. VAS was used to record patients' daily pain scores during the pre-treatment and follow-up periods (post-treatment, one week, three months, six months, and one year). Eight dimensionality concepts were measured and analyzed according to the physical and mental health based on the SF-36, including physical functioning (PF), role limitations due to physical health (RP), bodily pain (BP), role limitations due to emotional problems (RE), social functioning (SF), general health perceptions (GH), general mental health (MH), and vitality (VT) [18]. The questionnaires were completed one year after therapy.

The anterior vertebral body height (AH) and the kyphosis angle were measured on radiographs preoperatively, postoperatively, and after one-year follow-up. The AH was defined as the percentage of the intact anterior height of the fractured vertebrae compared to the caudal vertebral body. The kyphosis angle was measured as the angle between the inferior endplate of the intact vertebra above and the superior endplate of the intact vertebra below. Additionally, nonunion of the fractured vertebrae was defined as the occurrence of an intravertebral vacuum cleft or change of vertebral height between standing and supine positions on lateral radiographs after at least one-year follow-up [19].

Statistical analyses

Data are expressed in terms of mean ± standard deviation. We compared VAS, SF-36 dimensions, anterior vertebral height, and kyphosis angle between the PKP and conservative treatment groups using the Student's *t* test. The Pearson χ^2 test was conducted to compare the rate of bone-union between the PKP and conservative treatment groups. Statistical analyses were conducted using SPSS 19.0 for Windows, and the level of significance was set at $p<0.05$.

Results

Demographic data

Forty-one patients who had follow-up for at least one year were enrolled in this study. Patients were randomly divided into the PKP group (n=24) and the conservative treatment group (n=17). The summary of patient demographics is shown in Table 1. There were no statistically significant differences between the PKP group and the conservative treatment group in terms of age, sex, location of damaged vertebrae, bone mineral density, and follow-up time.

VAS

VAS scores were lower in the PKP group than in the conservative treatment group at the one-year follow-up. The VAS score in the PKP group improved from 7.54±1.25 (pre-treatment) to 1.95 ± 1.00 (post-treatment) with a significant difference. The VAS score was significantly lower in the PKP group than in the conservative treatment group post-treatment (1.95±1.00 versus 7.64±1.00; p=0.000). One week after treatment, the VAS score was 1.70 ± 1.04 in the PKP group and 7.12±1.11 in the conservative treatment group (p=0.000). Moreover, the VAS score in the PKP group was 0.92±0.83, which was also significantly lower than 3.47±2.40 in the conservative treatment group three months post-treatment (p=0.000). One year after treatment, the VAS score was 0.46±0.66 in the PKP group and 2.29±2.89 in the conservative treatment group (p=0.019; Figure 3).

SF-36 dimensions

One year after treatment, the PF value in the PKP group was 78.1±11.5, which was significantly higher than 64.5 ± 20.3 in

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

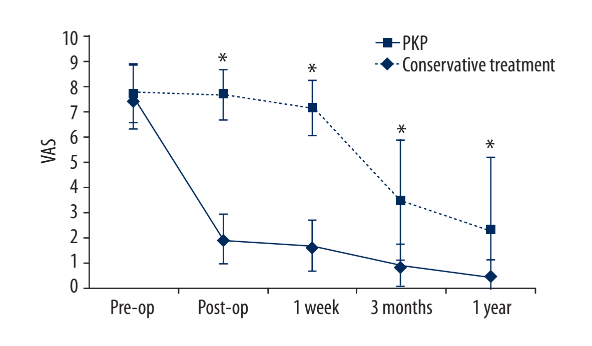

Figure 3. VAS scores of the two groups at pre-treatment and at one-year follow-up. * *p*<0.05 when compared to the conservative treatment group. VAS – visual analogue scale.

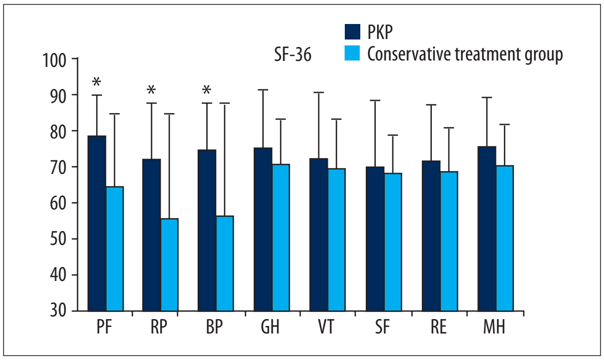

Figure 4. SF-36 questionnaire dimensions for the two groups at one-year follow-up. * *p*<0.05 when compared to the conservative treatment group.

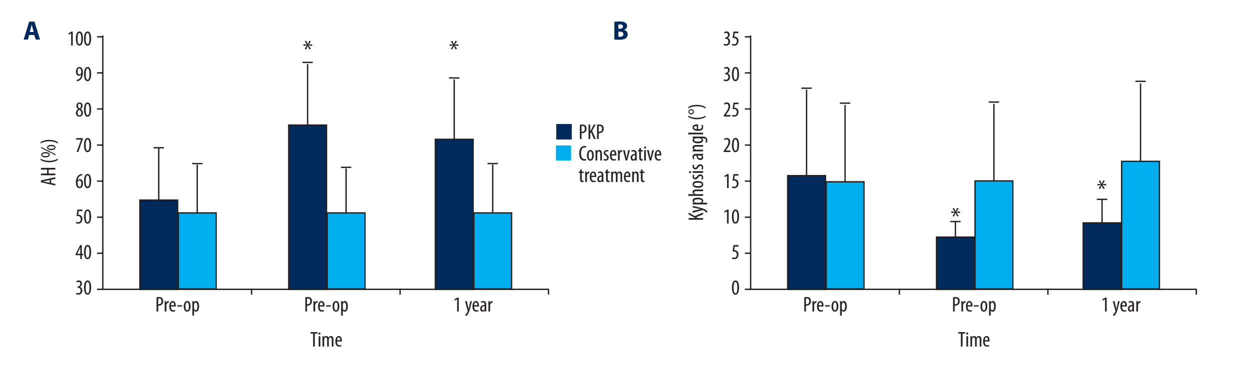

Figure 5. (**A**) AH in the two groups at pre-treatment and at one-year follow-up. (**B**) Kyphosis angle in the two groups at pre-treatment and at one-year follow-up. * *p*<0.05 when compared to the conservative treatment group.

the conservative treatment group (*p*=0.020). The RP value of the PKP group was significantly higher than that of the conservative treatment group (72.0±15.1 versus 55.6±28.8; *p*=0.043). The BP value was 74.5±13.3 in the PKP group and 56.2±30.9 in the conservative treatment group (*p*=0.032). There were no statistically significant differences between the PKP group and the conservative treatment group in terms of GH, VT, SF, RE, and MH values (Figure 4).

Radiographic data

The AH in the PKP group was significantly improved from 54.58±14.78 (pre-treatment) to 75.66±17.15 (post-treatment). Post-treatment, the AH in the PKP group was 75.66±17.15, which was significantly higher than 51.08±13.16 in the conservative treatment group (*p*=0.000). The AH of the PKP group was significantly higher than that of the conservative treatment group, one year after treatment (71.22±17.72 versus 51.22±14.18; *p*=0.000) (Figure 5A).

The kyphosis angle in the PKP group also significantly improved from 15.78±12.46 (pre-treatment) to 6.89±2.01

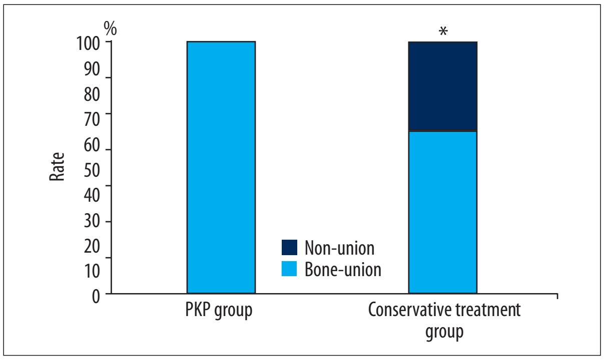

Figure 6. Rate of bone-union in the two groups, one-year after treatment. * *p*<0.05 when compared to the PKP group.

(post-treatment). Post-treatment, the kyphosis angle was 6.89±2.01 in the PKP group and 14.88±11.10 in the conservative treatment group (*p*=0.000). The kyphosis angle in the PKP group was 8.68±3.50, which was also significantly lower than 17.55±11.56 in the conservative treatment group, one year after treatment (*p*=0.000; Figure 5B).

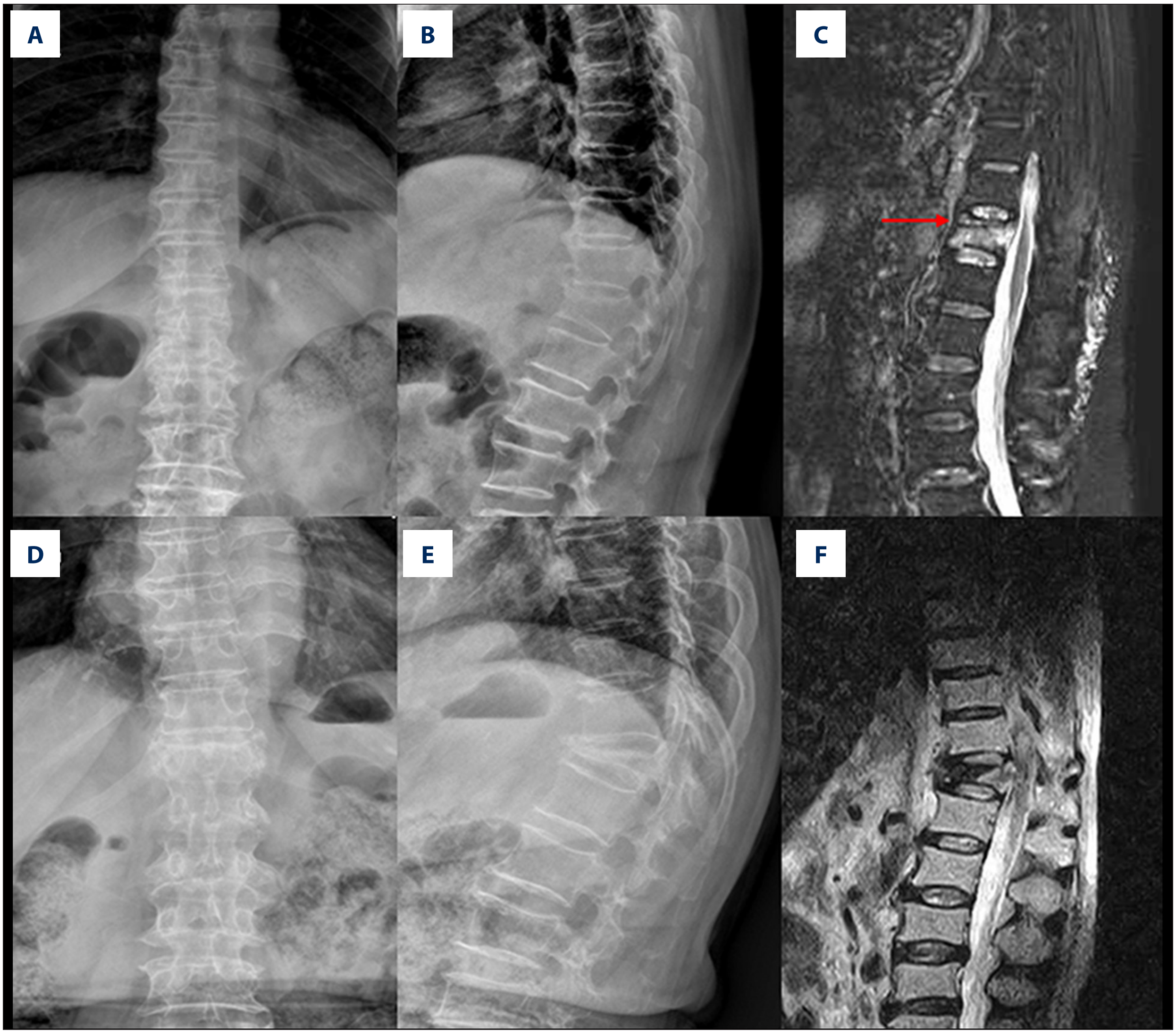

Figure 7. A 72-year-old female patient had a L1 osteoporotic vertebral compression fracture as a result of a fall. (**A, B**) X-ray showed L1 vertebral compression fracture. (**C**) A linear black signal was detected on MRI STIR sequence (red arrow). (**D, E**) At one-year follow-up, significant collapse of the L1 vertebral body could be seen on the anteroposterior and lateral views. (**F**) The L1 vertebral segment was collapsed, and intravertebral vacuum cleft was seen on MRI T2 sequence at one-year follow-up.

Rate of bone-union

Twenty-four patients in the PKP group and 17 patients in the conservative treatment group achieved 24 (100%) and 11 (64.7%) bone-unions, respectively, with a significant difference ($p<0.05$) (Figures 6–8).

Discussion

PKP evolved from the technique of vertebroplasty, which represents the percutaneous injection of PMMA bone cement into a damaged vertebral body [14]. Galibert et al. first used this method to treat vertebral angioma [20]. As soon as the pain relieving potential of this technique was detected, it was applied to the treatment of OVCF. Studies have indicated that PKP successfully reduces pain, substantially restores the morphology of the vertebrae, and significantly improves the quality of life [21,22]. Conservative treatment for pain caused by OVCF includes analgesic medication, bed rest, and back braces. Some reports indicated that these therapies do not address spinal deformities. Pain and disability may be prolonged while the fractured vertebral body heals; however, some reports showed that conservative treatment and PKP have equivalent efficacies at long-term follow-up [12,13]. The controversies regarding the treatment for OVCF still exist. We found that some MRI characteristic signal changes could aid in deciding the most appropriate treatment for OVCF. A prospective clinical study

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

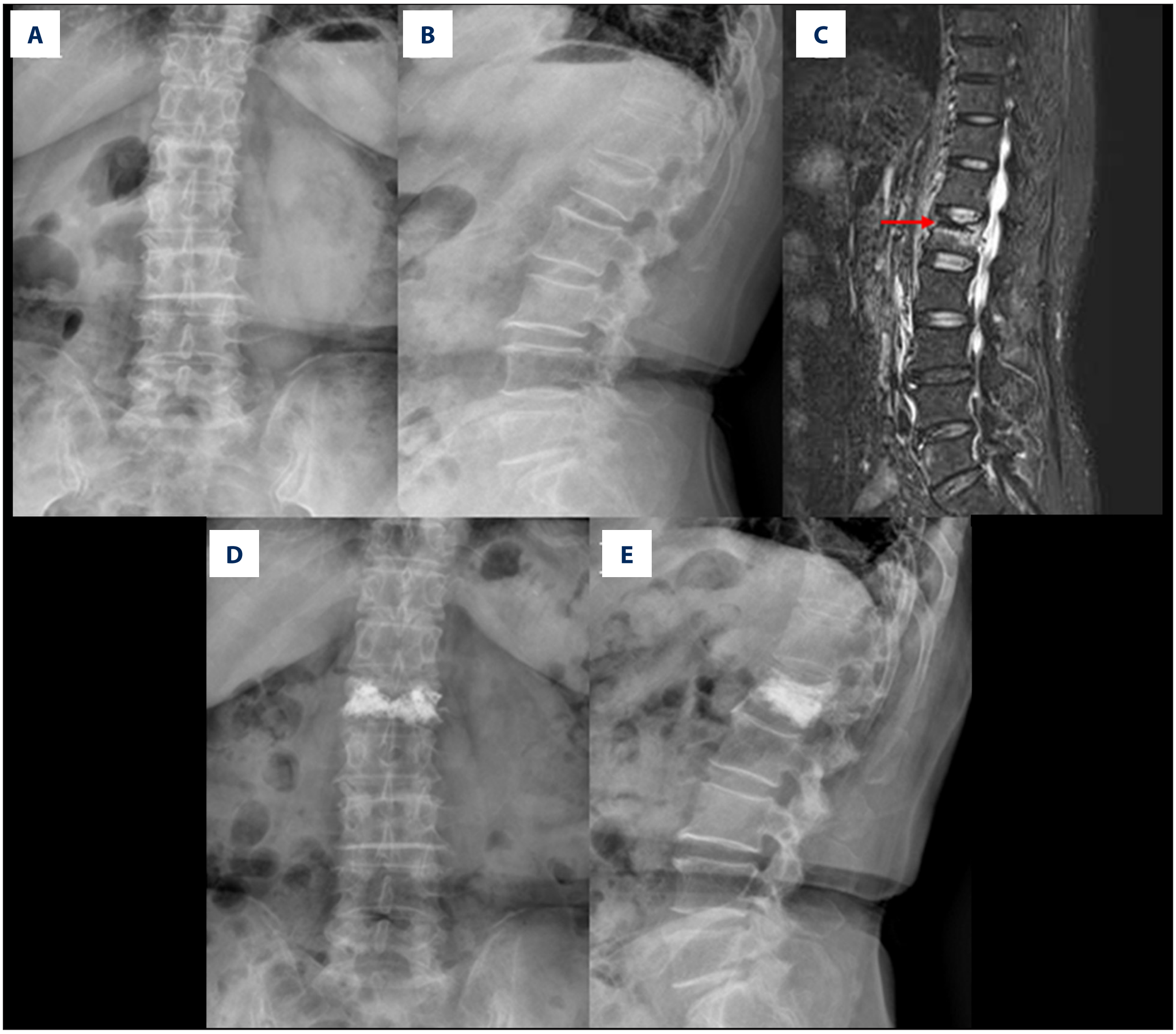

Figure 8. A 67-year-old female patient had a L1 osteoporotic vertebral compression fracture as a result of a fall. (**A, B**) X ray showed L1 vertebral compression fracture. (**C**) A linear black signal was detected on MRI STIR sequence (red arrow). (**D, E**) At one-year follow-up, bone-union was achieved after PKP. Anteroposterior and lateral radiographs showed no decrease in anterior vertebral height and no increase in kyphosis angle after a follow-up of one year.

was conducted to analyze the relationship between treatment outcomes and MRI findings for OVCF.

In our study, for patients with linear black signal changes, the VAS pain scores were significantly lower in the PKP group than in the conservative treatment group at the one-year follow-up. The PF, RP, and BP values in the PKP group were significantly higher than those in the conservative treatment group; there were significant differences observed. The PKP group had a significantly higher bone-union rate than the conservative treatment group. Therefore, PKP is superior to conservative treatment with regard to short-term and long-term pain relief, functional outcome, vertebral restoration, and bone-union. The first-choice treatment for patients with a linear black signal change should be PKP rather than conservative treatment.

The typical MRI findings in an acute vertebral compression fracture are hypointensity on T1-weighted images, hyperintensity or heterogeneous intensity on T2-weighted images, and hyperintensity on fat-suppressed T2-weighted images or on short-inversion time-inversion recovery images [23–25]. Characteristic signal changes on a STIR image, such as a linear black signal, have been previously reported by Hirotsugu et al. [17]. They also reported that the linear black signal area was a significant predictor of nonunion in OVCF. However, the histopathological findings correlated to this characteristic signal change have not been reported by previous studies [17]. We proposed that linear black signal area is an early post-traumatic avascular necrosis of the vertebral body, which may finally lead to nonunion of OVCF. Initial trauma may cause predominately trabecular microfractures in the linear black signal area, resulting in structural disruptions and microhemorrhages. These changes in the spongiosa lead to early osteonecrosis in the linear black signal area. Furthermore, because of impaired healing, a vicious circle develops, the trabecular fractures progress resulting in instability and vertebral body collapse, and then nonunion. However, in the PKP procedure, the stability of vertebral body is achieved, which could prevent progressive collapse and nonunion of vertebrae. In the further studies, biopsies could be used to show pathological change in the linear black signal area, and the relationship between the linear black signal change and the vertebral nonunion on MRI images should be verified in long-term follow-up.

There were several limitations to this study. First, it was conducted at a single center and the sample size was small. Therefore, future multi-center studies with larger patient numbers are necessary. Second, we only included patients whose date of fracture could be identified by the onset of pain or a specific injury. The enrolled patients underwent MRI to identify acute osteoporotic vertebral fractures within one week after trauma. Patients with a fracture age greater than one week were not included in this study.

Conclusions

PKP is superior to conservative treatment in patients showing a linear black signal change with regard to pain relief, functional outcome, vertebral restoration, and bone-union, as seen at short-term and long-term follow-up. If linear black signal change was detected, the first-choice treatment for the patients should be PKP rather than conservative treatment.

Conflicts of interest

None.

References:

1. Suzuki N, Ogikubo O, Hansson T: Previous vertebral compression fractures add to the deterioration of the disability and quality of life after an acute compression fracture. Eur Spine J, 2010; 19: 567–74
2. Qasem KM, Suzuki A, Yamada K et al: Discriminating imaging findings of acute osteoporotic vertebral fracture: A prospective multicenter cohort study. J Orthop Surg Res, 2014; 9: 96
3. Goldstein CL, Chutkan NB, Choma TJ, Orr RD: Management of the elderly with vertebral compression fractures. Neurosurgery, 2015; 77: 33–45
4. Yimin Y, Zhiwei R, Wei M, Jha R: Current status of percutaneous vertebroplasty and percutaneous kyphoplasty – a review. Med Sci Monit, 2013; 19: 826–36
5. Balkarli H, Kilic M, Balkarli A, Erdogan M et al: An evaluation of the functional and radiological results of percutaneous vertebroplasty versus conservative treatment for acute symptomatic osteoporotic spinal fractures. Injury, 2016; 47: 865–71
6. Yang EZ, Xu JG, Huang GZ et al: Percutaneous vertebroplasty versus conservative treatment in aged patients with acute osteoporotic vertebral compression fractures: A prospective randomized controlled clinical study. Spine (Phila Pa 1976), 2016; 41: 653–60
7. Chandra RV, Yoo AJ, Hirsch JA: Vertebral augmentation: Update on safety, efficacy, cost effectiveness and increased survival? Pain Physician, 2013; 16: 309–20
8. Yuan WH, Hsu HC, Lai KL: Vertebroplasty and balloon kyphoplasty versus conservative treatment for osteoporotic vertebral compression fractures: A meta-analysis. Medicine (Baltimore), 2016; 95: e4491
9. Wardlaw D, Cummings SR, Van Meirhaeghe J et al: Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): A randomised controlled trial. Lancet, 2009; 373: 1016–24
10. Taylor RS, Taylor RJ, Fritzell P: Balloon kyphoplasty and vertebroplasty for vertebral compression fractures: A comparative systematic review of efficacy and safety. Spine (Phila Pa 1976), 2006; 31: 2747–55
11. Phillips FM, Ho E, Campbell-Hupp M et al: Early radiographic and clinical results of balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. Spine (Phila Pa 1976), 2003; 28: 2260–65
12. Tang H, Zhao J, Hao C: Osteoporotic vertebral compression fractures: Surgery versus non-operative management. J Int Med Res, 2011; 39: 1438–47
13. Berenson J, Pflugmacher R, Jarzem P et al: Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: A multicentre, randomised controlled trial. Lancet Oncol, 2011; 12: 225–35
14. Spiegl UJ, Beisse R, Hauck S et al: Value of MRI imaging prior to a kyphoplasty for osteoporotic insufficiency fractures. Eur Spine J, 2009; 18: 1287–92
15. Ogura A, Hayakawa K, Maeda F et al: Differential diagnosis of vertebral compression fracture using in-phase/opposed-phase and short TI inversion recovery imaging. Acta Radiol, 2012; 53: 450–55
16. Lin WC, Lu CH, Chen HL et al: The impact of preoperative magnetic resonance images on outcome of cemented vertebrae. Eur Spine J, 2010; 19: 1899–906
17. Omi H, Yokoyama T, Ono A et al: Can MRI predict subsequent pseudarthrosis resulting from osteoporotic thoracolumbar vertebral fractures? Eur Spine J, 2014; 23: 2705–10
18. Ruta D, Garratt A, Abdalla M et al: The SF 36 health survey questionnaire. A valid measure of health status. BMJ, 1993; 307: 448–49
19. Hashidate H, Kamimura M, Nakagawa H et al: Pseudoarthrosis of vertebral fracture: Radiographic and characteristic clinical features and natural history. J Orthop Sci, 2006; 11: 28–33
20. Galibert P, Deramond H, Rosat P, Le Gars D: [Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty.] Neurochirurgie, 1987; 33: 166–68 in French]
21. Andrei D, Popa I, Brad S et al: The variability of vertebral body volume and pain associated with osteoporotic vertebral fractures: Conservative treatment versus percutaneous transpedicular vertebroplasty. Int Orthop, 2017; 41: 963–68
22. Clark W, Bird P, Gonski P et al: Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): A multicentre, randomised, double-blind, placebo-controlled trial. Lancet, 2016; 388: 1408–16
23. Abdel-Wanis, ME, Solyman MT, Hasan NM: Sensitivity, specificity and accuracy of magnetic resonance imaging for differentiating vertebral compression fractures caused by malignancy, osteoporosis, and infections. J Orthop Surg (Hong Kong), 2011; 19: 145–50
24. Yuh WT, Mayr NA, Petropoulou K, Beall DP: MR fluid sign in osteoporotic vertebral fracture. Radiology, 2003; 227: 905
25. Tan DY, Tsou IY, Chee TS: Differentiation of malignant vertebral collapse from osteoporotic and other benign causes using magnetic resonance imaging. Ann Acad Med Singapore, 2002; 31: 8–14

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]