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Original Article

Intravertebral clefts in osteoporotic compression fractures of the spine: incidence, characteristics, and therapeutic efficacy

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Abstract: Objective: To determine the pathogenesis and characteristics and to assess the long-term effectiveness of polymethylmethacry late (PMMA) vertebroplasty treatment in patients with intravertebral cleft (IVC) in osteoporotic compression fractures. Methods: A retrospective analysis of radiological and clinical parameters was performed on 388 patients who underwent percutaneous vertebroplasty or kyphoplasty to treat osteoporotic compression fractures from January 2010 to October 2012. IVC sign was observed in the MRI of 47 patients. Postoperative follow-ups were conducted for at least 2 years after surgery. Results: IVC incidence was associated with older age and lower bone mineral density. Other baseline measurements, such as preoperative visual analogue scale and Oswestry Disability Index (ODI), showed no significant difference between IVC and non-IVC fracture patients. Vertebral height and kyphotic angle were corrected after percutaneous vertebroplasty or kyphoplasty with no significant difference in outcome between the two procedures. Restored vertebral height collapsed and the kyphotic angle became aggravated during the 2 years following surgery in patients with IVC. Similarly, initial improvements in visual analogue scale and ODI decreased over time. Non-IVC patients' had a slight recurrence of compression and kyphosis that began to normalize after 1 year. Visual analogue scale and ODI at 2 years' post-surgery was also significantly lower in non-IVC than IVC patients. Conclusion: Polymethylmethacrylate vertebroplasty treatment of osteoporotic compression fractures is initially effective for patients with signs of IVC, but compression and kyphosis gradually reoccur. Therefore, we strongly recommend strict observation and follow-up after vertebroplasty.

Keywords: Avascular osteonecrosis, osteoporosis, spinal fracture, vertebroplasty, intravertebral vacuum cleft

Introduction

Osteoporosis is the most common metabolic bone disorder and the leading cause of vertebral compression fractures in China. Over one-third of patients will experience chronic pain associated with osteoporosis vertebral compression fractures. These fractures can be debilitating, leading to spinal deformity and associated gait and balance impairments [1, 2], reduced lung function [3], increased subsequent fracture risk [6], and increased mortality [4, 5].

Appearance of the intravertebral vacuum cleft (IVC) is common in these patients and has received much attention in recent reports [6-8]. In flexion and extension lateral films, the sign of IVC is characterized as dynamic instability or pseudoarthrosis [14, 15]. Patients with IVC sign complained of severe pain, especially when they changed positions, and did not respond to conservative therapies. Thus, surgical intervention was recommended [16].

IVC is considered to be a sign of avascular necrosis of the vertebral body, also known as Kummell's disease [9]; however, recent studies have questioned this association. Young et al. reported that IVC sign is probably not pathognomonic of Kummell's disease [10]. Hasegawa et al. described IVC as a fibrocartilaginous tissue lined pseudarthrosis with significant motion [11]; they also observed joint fluid in IVC in the operating field. In other reports, characteristic magnetic resonance imaging of osteonecrotic vertebral fractures showed a collection of intravertebral fluid or the presence of conjunction with air [12, 13].

The purpose of this study is to determine the incidence and characteristics of IVC sign in osteoporotic compression, and to assess the radiological and clinical outcomes of patients who underwent percutaneous kyphoplasty (PKP) or percutaneous vertebroplasty (PVP) to treat osteoporotic vertebral compression fractures with and without IVC.

Materials and methods

This is a retrospective study of clinical and radiological parameters and analysis of characteristics of IVC sign. From January 2010 to October 2012, 426 patients with osteoporotic compression fractures were treated by percutaneous kyphoplasty (PKP) or percutaneous vertebroplasty (PVP) with PMMA. We included only patients who had a single-level osteoporotic vertebral compression fracture and had been followed up for more than 2 years. We excluded patients with clinical history of bone metabolic disorders or malignancies. A total of 388 levels in 388 patients were enrolled in our study. The average age of the patients was 72.3 years (range 61-93 years). 297 patients were female and 91 were male.

Before vertebroplasty, we took x-rays, measured bone mineral density, and performed MRI to define acute osteoporotic compression fractures. Among these patients, 47 were diagnosed as acute osteoporotic compression fractures with IVC, (36 females and 9 males, age range 61 to 93 years (mean, 75.3 years). The affected vertebra was T11 in 8 patients, T12 in 12 patients, L1 in 16 patients, L2 in 8 patients, L3 in 2 patients, and L4 in 1 patient (**Table 1**). The remaining patients (341) were diagnosed with acute osteoporotic compression fractures without IVC (261 females and 80 males, age range 61 to 91 years (mean, 71.2 years). The affected vertebra was T6 in 2 patients, T7 in 4 patients, T8 in 3 patients, T9 in 7 patients, T10 in 11 patients, T11 in 18 patients, T12 in 78 patients, L1 in 86 patients, L2 in 39 patients, L3 in 9 patients, L4 in 3 patients, and L5 in 1 patient (**Table 1**).

We performed a PVP or PVP after postural reduction of the compressed vertebral body [17] using a transpedicular approach (bipedicular needle insertion). PVP was carried out on 39 patients with IVC and 148 patients without IVC, while PKP was used on 8 patients with IVC and 113 patients without IVC.

Analysis of radiological parameters

We retrospectively reviewed preoperative radiological images to evaluate the presence of IVC sign in the vertebral body, which was defined as the collection of intravertebral fluid or the presence of conjunction with air as seen via MRI. An MRI finding of intravertebral fluid was defined as an area of hypointensity on T1-weighted images and hyperintensity on T2-weighted images, and intravertebral air was defined as an area of hypointensity or a signal intensity void on T1- and T2-weighted images [18, 19].

Radiological parameters, such as the compression ratio and kyphotic angle, were also reviewed from follow-up plain radiographs immediately after the vertebroplasty and postoperatively at 1 year and 2 or more years (the final follow-up period). The anterior and posterior heights of the fractured vertebral body with or without IVC were assessed to calculate the compression ratio (anterior/posterior height, anterior/posterior ratio) before and after the vertebroplasty. The kyphotic angle was measured using the Picture Archiving and Communication System and related computer software (PiViewSTAR 5.0, INFINITT, Seoul, Korea) in the department of radiology. We determined the angle between the lower end plate of the upper vertebral body and the lower end plate of the affected vertebral body.

For all patients, we calculated the degree of the progression of compression of the cemented vertebral bodies, which is the compression ratio difference between the immediate post-vertebroplasty measurement and the follow-up period measurements. The difference between compression ratios measured at 1 year after vertebroplasty and at the final follow-up were also calculated.

Analysis of clinical parameters

We retrospectively reviewed several preoperative clinical parameters, including age, sex, bone mineral density, visual analogue scale (VAS) score of the back, and Oswestry Disability Index (ODI). Preoperative and postoperative (1 day, 1 year, and 2 years or more) VAS score of the back and ODI were compared.

Table 1. Baseline characteristics of patients in this study

Characteristic parameters	IVC group	Non-IVC group	
Number of patients (%)	47 (12.11)	341 (87.89)	388
Age in years[a]	75.27 ± 15.72*	73.21 ± 9.32*	72.32 ± 12.93
Number of females (%)	36 (76.61)	261 (76.52)	297 (76.5)
Fracture location (#)	T11 (8); T12 (12); L1 (16); L2 (8); L3 (2); L4 (1)	T6 (2); T7 (4); T8 (3); T9 (7); T10 (11); T11 (18); T12 (78); L1 (86); L2 (39); L3 (9); L4 (3); L5 (1)	
BMD T-score[a]	-4.34 ± 0.72^	-3.26 ± 1.57^	-3.62 ± 1.74
Visual analogue scale on back[a]	8.44 ± 1.21*	7.89 ± 1.07*	8.02 ±1.93
ODI[a]	84.77 ± 6.44*	80.18 ± 7.12*	82.36 ± 6.93
Surgical procedure (#)	PVP (26); PKP (21)	PVP (148); PKP (113)	
Local kyphotic angle (PVP)[a]	12.97 ± 4.07*	12.68 ± 3.08*	12.93 ± 4.15
Local kyphotic angle (PKP)[a]	13.17 ± 4.89*	13.06 ± 5.18*	13.09 ± 4.93

BMD: bone mineral density. ODI: Oswestry Disability Index. PVP: percutaneous vertebroplasty. PKP: percutaneous kyphoplasty. [a], Shown as mean ± standard deviation. *p>0.05 for the comparison between the two groups; ^P<0.01 for the comparison between the two groups. SPSS 12.0 for Windows (SPSS, Chicago, IL).

Table 2. Comparison of bone mineral density scores (BMD) between three age groups

	Group A	Group B	Group C	Total
Age in years	61-70 (n=3)	71-80 (n=17)	81-93 (n=27)	
BMD T-score[a]	-2.66 ± 0.71*	-3.45 ± 0.92*	-4.72 ± 0.59*	-3.52 ± 0.92

BMD: bone mineral density. [a], Shown as mean ± standard deviation. *P<0.01, comparison between the groups.

Table 3. Clinical and radiological measurements before and after treatment of IVC

	Preoperative	Immediate post-op	1 year post-op	2 year post-op
Visual analog scale	8.44 ± 1.21	1.89 ± 1.09*	2.29 ± 1.03	3.07 ± 1.57*
ODI	84.77 ± 6.44	27.9 ± 7.3*	32.9 ± 8.7	40.4 ± 8.9*
Compression ratio	0.51 ± 0.17	0.72 ± 0.18*	0.59 ± 0.13	0.49 ± 0.15*
Kyphotic angle	13.06 ± 4.16	8.01 ± 3.11*	11.79 ± 4.22	13.15 ± 6.02*

ODI: Oswestry disability index. *P<0.05 compared to the preoperative measurements. All values are mean standard deviation. Post-op: Postvertebroplasty.

Table 4. Clinical and radiological measurements before and after treatment of non-IVC

	Preoperative	Immediate post-op	1 year post-op	2 year post-op
Visual analog scale	7.89 ± 1.07	1.59 ± 1.31*	1.89 ± 1.13	2.01 ± 1.27*
ODI	80.18 ± 7.12	26.7 ± 4.3*	29.8 ± 4.6	30.5 ± 4.9*
Compression ratio	0.53 ± 0.19	0.80 ± 0.16*	0.76 ± 0.15	0.71 ± 0.17*
Kyphotic angle	12.98 ± 3.59	7.11 ± 3.61*	8.69 ± 4.12	8.97 ± 5.21*

ODI: Oswestry Disability Index. *p<0.05 compared to the preoperative measurement. All values are shown as mean ± standard deviation.

Statistical analysis

SPSS 12.0 for Windows (SPSS, Chicago, IL) was used for all statistical analysis. A *p*-value of less than 0.05, calculated by either the Fisher exact test or Mann-Whitney U test, was considered significant.

Results

A total of 388 levels in 388 patients who had osteoporotic compression fractures were treated by PKP or PVP with PMMA. Majority of the patients were women (297 women and 91 men), the average age of the patients was 72.3 ± 12.9 and the mean follow-up period was 24.1 ± 6.5 months (24-49 months). Of the 388 patients, only 47 had IVC (12.1% incidence). The treated vertebrae, with IVC, ranged from T11 to L4 and the treated vertebrae, without IVC, ranged from T6 to L5 (**Table 1**). No significant differences in sex, VAS, ODI, or local kyphotic angle were observed between IVC and non-IVC groups. However, bone mineral density (BMD) in the IVC group was significantly lower than in the non-IVC group (**Table 1**). When all patients were grouped by age, the mean BMD T-score decreased with increasing age (**Table 2**). In addition, BMD was significantly lower in the IVC group; this observation was not biased by age since there was no significant difference in mean age between IVC and non-IVC groups (**Table 1**).

The mean corrected kyphotic angle and restored compression ratio of fractured vertebrae before and after vertebroplasty were 5.07° ± 2.98° and 0.23 ± 0.37, respectively. No significant differences for the baseline of these two measurements existed between the IVC and non-IVC groups (**Table 1**). Vertebral height and kyphotic angle were significantly corrected after vertebroplasty in both groups (P<0.05); however, we observed collapse of vertebral height in the IVC group, but not in the non-IVC group, within 2 years after surgery (**Tables 3** and **4**). The difference between the kyphotic angle of the treated vertebrae with and without IVC, after 2 years, was statistically significant (P<0.05, **Table 5**). Progression of the recompression of the cemented vertebral bodies in IVC patients was confirmed by analysis of plain x-ray films from serial follow-ups (**Figure 1**). The immediate postoperative mean compression ratio in the IVC group was 0.72 ± 0.18 and decreased to 0.59 ± 0.13 at 1 year following vertebroplasty. Furthermore, the mean postoperative compression ratio continued to decrease to 0.49

Table 5. Comparison of pre and post-op measurements of vertebrae with or without IVC

	Preoperative	Immediate post-op	1 year post-op	≥2 year post-op
Visual analogue scale on back with IVC	8.44 ± 1.21	1.89 ± 1.09#	2.29 ± 1.03	3.07 ± 1.57*
Visual analogue scale on back without IVC	7.89 ± 1.07	1.59 ± 1.31#	1.89 ± 1.13	2.01 ± 1.27*
ODI with IVC	84.77 ± 6.44	27.9 ± 7.3#	32.9 ± 8.7	40.4 ± 8.9*
ODI without IVC	80.18 ± 7.12	26.7 ± 4.3#	29.8 ± 4.6	30.5 ± 4.9*
Compression ratio (IVC)	0.51 ± 0.17	0.72 ± 0.18#	0.59 ± 0.13	0.49 ± 0.15*
Compression ratio (non-IVC)	0.53 ± 0.19	0.8 ± 0.16#	0.76 ± 0.15	0.71 ± 0.17*
Kyphotic angle with IVC	13.06 ± 4.16	8.01 ± 3.11#	11.79 ± 4.22	13.15 ± 6.02*
Kyphotic angle without IVC	12.98 ± 3.59	7.11 ± 3.61#	8.69 ± 4.12	8.97 ± 5.21*

ODI: Oswestry Disability Index. All values are shown as mean ± standard deviation. *P<0.05, #P>0.05. Post-op: Postvertebroplasty.

± 0.15 at 2 years after the vertebroplasty (P<0.05, **Table 3**). The kyphotic angle was also found to be more significant at the >2 year follow-up. The immediate postoperative mean kyphotic angle was 8.01 ± 3.11°, and it increased to 11.79 ± 4.22° by 1 year following the vertebroplasty. The postoperative mean kyphotic angle continued to increase to 13.15 ± 6.02° at 2 years after the vertebroplasty (P<0.05, **Table 3**).

The mean VAS score decreased significantly following the initial surgery in both IVC and non-IVC groups. The mean preoperative VAS score in the IVC group and non-IVC group were 8.44 ± 1.21 and 7.89 ± 1.07, and on postoperative day 1 it dropped to 1.89 ± 1.09 and 1.59 ± 1.31, respectively (P<0.05, **Tables 3** and **4**). Postoperative follow-up showed the mean VAS scores at 1 and 2 years after surgery were still lower than preoperative measurements, for both groups. While the immediate and >2 year postoperative mean VAS scores did not significantly change in the non-IVC group, there was a significant increase after 2 years for the IVC group (**Tables 3** and **4**). The 2-year postoperative VAS scores of the IVC and non-IVC groups were significantly different when compared to each other (P<0.05, **Table 5**).

The mean preoperative ODI in the IVC and non-IVC groups were, 84.77 ± 6.44 and 80.18 ± 7.12, 27.9 ± 7.3 and 26.7 ± 4.3 on postoperative day 1, and 40.4 ± 8.9 and 30.5 ± 4.9 at the final follow-up appointment, respectively. Although the mean ODI was significantly decreased following vertebroplasty in the IVC group, it showed gradual increase for at least 2 years after vertebroplasty (P<0.05, **Table 3**). In contrast, the postoperative mean ODI of the non-IVC group at >2 years was not significantly different from day 1 following vertebroplasty (P>0.05, **Table 4**). A comparison of the >2 year postoperative ODI of IVC and non-IVC patients showed a statistically significant difference (P<0.05, **Table 5**).

None of the patients presented with symptoms of neurological complications.

Discussion

We evaluated PVP and PKP surgery for the treatment of osteoporotic compression fractures in patients with and without IVC. Most of the enrolled patients reported satisfactory pain relief and good restoration of the compressed vertebral body immediately after surgery. PVP and PKP corrected kyphotic angulation with similar efficacy for patients with and without IVC. However, collapse of the augmented vertebral body and kyphosis progressed continuously in IVC patients during the 2 years following PVP or PKP surgery. As collapse and kyphosis were aggravated over time, patients again complained of back pain. Intravertebral instability is considered to be the predominant cause of collapse and kyphosis following surgical treatment.

Osteoporotic vertebral compression fractures instigate an active remodeling of the vertebral body. In some areas, significant amounts of new hypertrophic trabecular bone restore the structural integrity of the vertebral body, while in other areas, necrotic fragments of bone, cartilage, and intervertebral disc contents are sequestrated in a nonreactive vascular fibrous

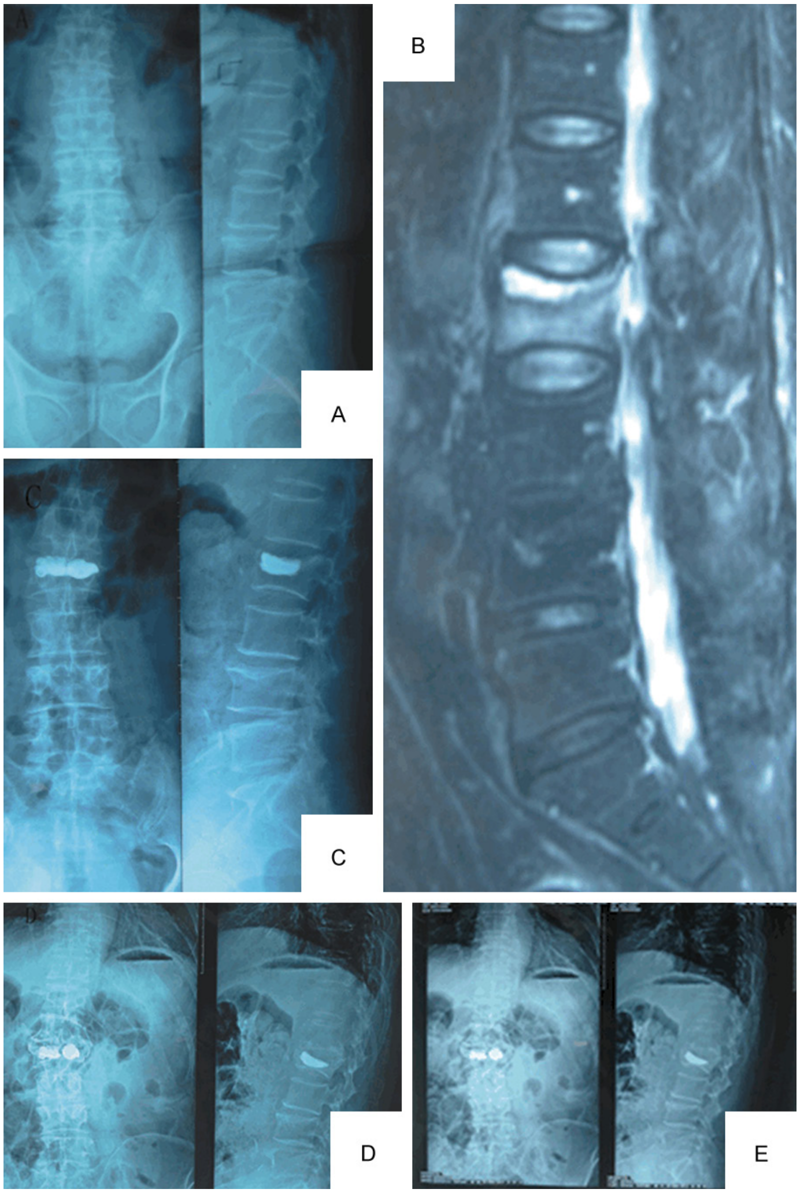

Figure 1. Radiological studies of an 82-year-old male with an L2 compression fracture. (A) Preoperative plain x-ray image showing L2 compression fracture with an air cleft. (B) MRI of a typical IVC sign and upper end-plate disruption. Hyper-intensity is seen on this fat-suppressed T2-weighted image. (C) Immediate postoperative plain x-ray radiographs showing well-deposited polymethylmethacrylate cement and reexpansion of compressed vertebral body. Recollapse and bone resorption developed in the vertebral body 1 year (D) and 2 years (E) after vertebroplasty.

stroma [20]. Benedek and Nicholas have reported several factors that are associated with failure of the bone healing process, including impairment of the vertebral blood supply, cartilaginous (Schmorl) nodes, and normal stress placed on a weakened vertebra [21]. Dupuy et al., observed necrotic cancellous bone, hyaline cartilage with fractured callus, and fluid collections in IVCs during CT-guided biopsies and suggested that these findings were associated with underlying avascular necrosis [22]. Although intravertebral cleft is highly suggestive of osteonecrosis, the pathogenesis of IVC is unclear. Maldague et al., first associated avascular necrosis with signs of IVC [23]. Anatomical studies support the relationship between IVC and avascular necrosis. The vasculature of thoracic and lumbar vertebral bodies arises from paired segmental arteries. Posterior central branches to the dorsum of the body supply two adjacent vertebral bodies, while anterior central branches to the ventral side of the body supply one vertebral body. The blood supply of the vertebral ventral zone from the short branch of the early anterior central branches, which creates a higher risk of vascular insufficiency for the vertebral ventral zone. The weak blood supply of the vertebral ventral zone was also demonstrated by Ratcliffe [24].

IVC is also associated with Kümmell's disease, which was first described by Dr. Hermann Kümmell [25]. The disease is initially asymptomatic for weeks to months with delayed post-traumatic osteonecrosis, which frequently leads to osteoporotic spine fractures [26]. Young et al., recently reported, however, that IVC sign is not pathognomonic of Kummell's disease, but rather highly suggestive of it [10]. This is because IVC is found in various other spinal diseases, including infection, prolonged use of steroids, diabetes, and malignancy [27]. The symptoms of some

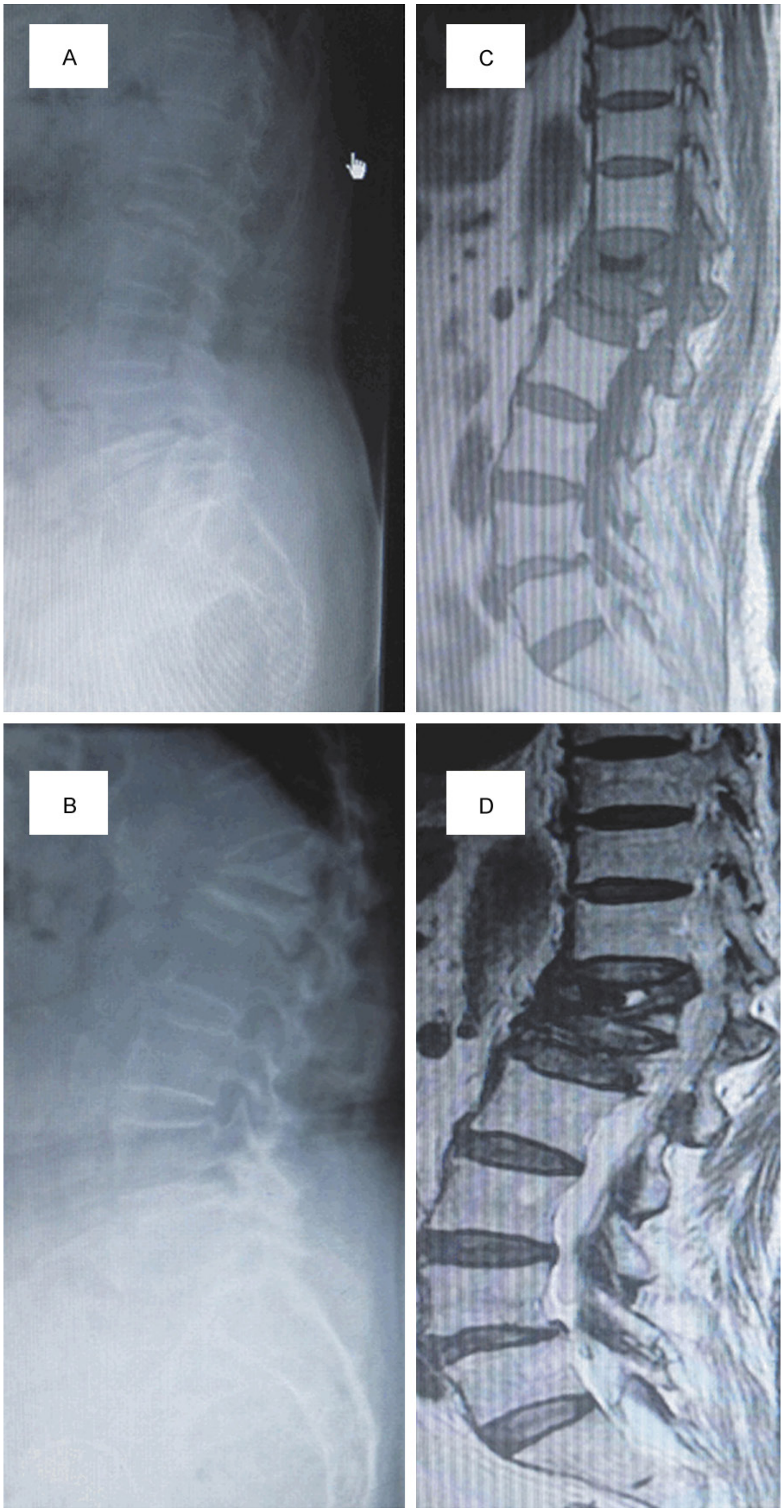

Figure 2. Radiological studies of an 85-year-old woman with an L1, T12 compression fracture. A. Lateral plain x-ray image after initial injury. The patient had severe back pain and did not respond to conservative treatments such as bed rest, medication and orthosis. B. Radiograph depicting bone resorption and collapse of the vertebra 3 months after injury in L1 and T12. C and D. Typical IVC signs in MRI of L1 and T12. Hypo-intensity (vacuum cleft and intravertebral fluid) is seen in the T1-weighted image, and hyper-intensity (intravertebral fluid) and hypo-intensity (vacuum cleft) is visible in the T2-weighted image.

patients with IVC are very similar to Kümmell's disease, thus it is reasonable for some clinicians to regard the sign of IVC as "Kümmell's sign", and diagnose some OVCFs patients with IVC as Kümmell's disease.

IVC is common in patients with osteoporotic vertebral compression fractures [28] and has dynamic mobility indicating instability within the fracture [14]. In our study, of the 388 patients, 47 had IVC and 341 did not. The incidence of IVC was 12.1%, and was associated with age and bone density. Patients with IVC usually had lower BMD and were older. BMD in the IVC group was significantly lower than the BMD in the non-IVC group. BMD decreased with increasing age, and this trend was statistically significant between all groups ($P<0.05$, **Table 2**). Since patients with IVC usually display lower BMD and higher age, resorption and collapse of vertebral bone often appear (**Figure 2**); thus, they should be treated actively.

Patients with IVC usually have severe back pain and do not respond to conservative treatments such as bed rest, medication, and orthosis. Surgical intervention is recommended [16] with PKP or PVP as the cardinal therapeutic option [29, 30]. In our study, the vertebral height and kyphotic angle were significantly corrected following PVP or PKP with no statistically significant difference between the two treatments. The restored vertebral height collapsed ($P<0.05$), and the kyphotic angle became aggravated (P<0.05) in patients with IVC during the 2 years following surgery. Visual analogue scale and ODI were significantly decreased at postoperative day 1, and significantly increased at 2 years post vertebroplasty in patients with IVC. Visual analogue scale and ODI in patients with IVC were significantly higher than in patients without IVC during the 2 years of postoperative follow-up. Percutaneous vertebroplasty and percutaneous kyphoplasty are effective and safe interventions providing clinically meaningful improvement in the treatment of osteoporotic vertebral compression fractures. However, as our results show, there are long-term problems with PKP or PVP treatment of intravertebral clefts in osteoporotic compression.

Conclusion

According to our results, in cases of osteoporotic vertebral compression fractures with IVC that manifest as an intravertebral vacuum phenomenon, pseudoarthrosis, or intravertebral fluid collection, polymethylmethacrylate vertebroplasty treatment may not provide stabilization for an extended period of time. Following vertebroplasty, the compression and kyphosis of osteoporotic vertebral compression fractures with IVC progressed continuously for 2 years or longer. Therefore, we strongly recommend rigorous observation and extended follow-up for patients who have undergone vertebroplasty to treat osteoporotic vertebral compression fractures with IVC. Furthermore, optimal surgical intervention should be performed if any symptoms of neurological complications appear following vertebroplasty.

Disclosure of conflict of interest

None.

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