Archives of Osteoporosis (2021) 16: 180
https://doi.org/10.1007/s11657-021-00922-9

ORIGINAL ARTICLE

Do sandwich vertebral bodies increase the risk of post-augmentation fractures? A retrospective cohort study

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Received: 25 October 2020 / Accepted: 10 March 2021 / Published online: 1 December 2021

Abstract

Summary Until now, there have been only a few retrospective studies that focused on the outcomes of sandwich vertebral bodies (SVBs). This is a long-term retrospective cohort study to investigate the SVBs. We found that although patients with SVBs had a relatively high risk of developing new fractures after VA, the incidence rate of new fractures was not significantly different from that of the control group. However, the statistical power of this study was very limited. Therefore, and because the refracture rate in these patients is substantial, routine long-term monitoring of patients after VA for osteoporosis is strongly recommended.

Background Sandwich vertebral bodies (SVBs) are intact unaugmented vertebral bodies between two previously augmented vertebrae. Until recently, only a few studies have reported the outcomes and strategies for SVBs. This retrospective cohort study aimed to describe the clinical features and incidence of new fractures in patients with SVBs.

Methods The clinical data were collected from 179 patients with 237 symptomatic osteoporotic vertebral compression fractures who underwent vertebral augmentation (VA). Among them, 23 patients with 24 levels of SVBs were included. Spinal radiographs (X-ray and CT) of all patients were evaluated prior to surgery 1 day after primary VA and during follow-up.

Results All patients successfully underwent PKP with an average follow-up period of 21.48 months. Asymptomatic cement leakage occurred in four patients (17.4%), and eight patients (34.8%) developed new fractures following primary PKP, including four sandwich, six adjacent, four remote vertebral fractures, and one re-collapse of cemented vertebrae. The incidence of new fractures in the SVB and control groups was 16.7% (4/24) and 13.0% (6/46), respectively, but there was no significant difference.

Conclusions Although patients with SVBs had a relatively high risk of developing new fractures after VA, the incidence rate of new fractures was not significantly different from that of the control group. However, the statistical power of this study was very limited. Therefore, and because the refracture rate in these patients is substantial, routine long-term monitoring of patients after VA for osteoporosis is strongly recommended.

Keywords Sandwich vertebral bodies · Vertebra augmentation · Osteoporosis vertebral compression fractures · New fractures

Introduction

The U.S. National Institutes of Health in 2001 defined osteoporosis as a "skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture" [1]. As the proportion of elderly persons in the global population has increased rapidly in the past several decades, the incidence of osteoporosis continues to rise; as a result, osteoporotic fracture is becoming an increasing burden on health care worldwide. Osteoporotic vertebral compression fractures (OVCFs) are the most common types of osteoporotic fracture globally, accounting for approximately 1.4 million cases annually, which results in increased morbidity, mortality, and health care-related costs [2–4].

The majority of OVCFs are asymptomatic or only associated with mild pain. However, some OVCFs could result in severe back pain resistant to regular conservative treatment and increase the risk of age-adjusted mortality [4]. Vertebral augmentation (VA) could obtain satisfactory clinical results for symptomatic OVCFs. The result of a recent randomized control trial favored VA over conservative treatment for

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patients with symptomatic OVCFs, as VA can alleviate back pain and stabilize the fractured vertebral body [5].

Despite the favorable clinical outcome of VA in patients with symptomatic OVCFs, previous studies reported that the incidence of developing new OVCFs at adjacent segments following VA was approximately 6.3% to 47.5% [6–9]. There is a great deal of debate on whether the high incidence of new adjacent segment vertebral fractures was associated with VA, as this technique increased the stiffness and strength of the augment segment, causing shift load distribution on adjacent vertebral bodies [10–12]. A sandwich vertebral body (SVB) was defined as an intact unaugmented vertebral body between two previously augmented vertebrae. With double-load shift, increased stiffness and strength at the adjacent segment, and preexisting severe osteoporosis, the SVB may increase the risk of developing new vertebral fractures.

Until now, only a few studies have reported the outcomes of and treatment strategies for SVBs [13–16]. Thus, we retrospectively analyzed data of 179 patients who received percutaneous kyphoplasty (PKP) for OVCFs in our institution. The purpose of this study was to describe the clinical feature and incidence of new fractures of SVBs.

Methods

Patient population

Between October 2017 and June 2019, 179 patients with 237 symptomatic OVCFs who underwent VA were enrolled in the study. All patients were treated at the Department of Orthopedics of the Beijing Chao-yang Hospital, Capital Medical University of China.

The inclusion criteria were (1) patients with fresh OVCFs confirmed by pre-operative spinal radiograph, computed tomography (CT), and magnetic resonance imaging (MRI) with the presence of bone marrow edema at the fat-suppression sequences; (2) patients with acute back pain (visual analog scale (VAS) of more than 6 points) resistant to conservative treatment for at least 2 weeks; (3) patients who cannot bear the adverse effect of medicine; (4) treatment of PKP alone; and (5) regular follow-ups after discharge.

Patients with symptoms of neurological function impairment and those with CT and MRI revealing other causes of vertebral compression fractures (VCFs), including spinal malignant lesions, spinal metastatic diseases, and infectious spinal diseases, were excluded from this study.

SVB was defined as an intact unaugmented vertebral body between two previously augmented vertebrae. Among the 179 patients included in the study, there were 23 patients with a total of 24 levels of SVBs. Patients with an intact vertebra between two augmented vertebrae were classified into the sandwich vertebral bodies group (SVG) ($n = 24$), and an intact vertebra adjacent to the augmented vertebrae were classified into the adjacent vertebral bodies group (AVG) ($n = 46$) (Fig. 1). The incidence of developing new fractures between the two groups was investigated. The diagnosis of new OVCFs at the SVB level was confirmed using MRI, which showed increased signal intensity on fat-suppression sequences, indicating acute bone marrow edema. Clinical data of the two groups were also retrospectively collected. The baseline features and surgical information, such as sex, age at the time of surgery, bone mineral density (BMD), SVB segment, surgery segment, volume of injected cement, and intra- or post-operative complications of the patients were collected prior to surgery and during follow-up. Clinical questionnaires were completed and collected through the outpatient service or by telephone. After kyphoplasty, all patients were told to wear the lumbar or thoracic-lumbar brace for at least 1 month and take anti-osteoporotic medicine for as long as possible. The conventional use of anti-osteoporotic medicine including three types: (1) calcium, 1000 to 1200 mg per day; (2) bisphosphonates (alendronate), 5 mg per day; (3) vitamin D, 800 to 1000 IU per day.

This study was approved by the local Ethics Committee of Beijing Chao-Yang Hospital, Capital Medical University of

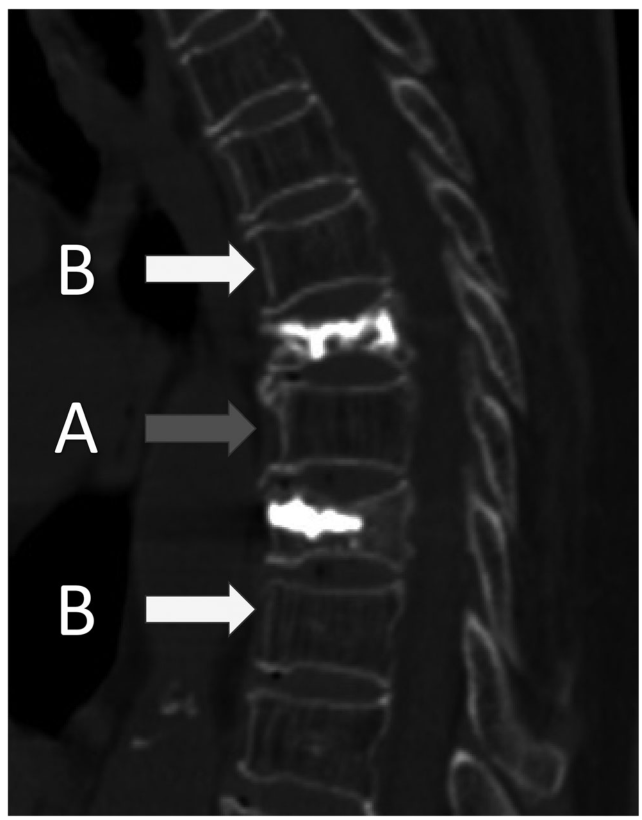

Fig. 1 An intact vertebra between two augmented vertebrae were classified into SVB group (grey arrow, A), and the intact vertebrae adjacent to augmented vertebrae were classified into control group (white arrows, B)

China. Written informed consent was obtained from all enrolled patients.

Operative techniques

All patients underwent unilateral PKP procedures by a senior spine surgeon. Initially, patients were placed in the prone position on a Jackson table, and spinal anterior-posterior and lateral plane radiographs were obtained using a C-arm angiographic unit to determine the entry point. After disinfection, the surgical area was draped in a sterile manner. Local anesthesia (1% lidocaine) was administered using unilateral needles inserted toward the pedicle. Next, the spinal needle was removed, and a small skin incision was introduced at the entry point. A tapered tube was then inserted along the guidewire, which targeted the midline of the vertebral body by the transpedicular approach. Then, kyphoplasty was performed using an expansible balloon to restore the height of the vertebral body. Finally, high barium content acrylic resin cement (Mendec Spine) was carefully injected under fluorescence. After the cement was satisfactorily distributed, the working tubes were removed, and the incision was covered with surgical dressing.

Radiographic evaluation

X-ray of all patients was evaluated prior to surgery, 1 day after the primary PKP, and during follow-up (1, 3, 12 months post-operation). CT was evaluated prior to surgery, 1 day after the primary PKP, and 1 month post-operation. The anterior vertebral height, posterior vertebral height, and angle of local kyphosis in the SVG and AVG were measured after primary PKP (Fig. 2). The angle of local kyphosis was defined as the angle between the superior endplate and the inferior endplate of the vertebra.

Data analysis

Patient data were analyzed using SPSS software (version 19.0, SPSS Inc., Chicago, IL, USA). The mean ± standard deviation (SD) was used to express continuous variables. To analyze categorical variables, the chi-square analyses and Fisher's exact tests were employed. A p-value less than 0.05 was considered statistically significant. Statistical power for this study was performed by PASS 15, and the test statistic used is the Z-test with unpooled variance. The significance level of the test is 0.0500.

Results

Demographics and surgical data

One hundred and seventy-nine patients who underwent VA for symptomatic OVCFs and who met the inclusion criteria were initially enrolled. Among them, 23 patients (9 male patients, 14 female patients, mean age at surgery was 74.38 years) with 24 SVBs and 46 segments adjacent to an augmented vertebra were enrolled. The demographics and surgical data of the enrolled patients' groups are shown in Table 1.

All patients successfully underwent PKP with an average follow-up period of 21.48 months. The VAS score of back pain was significantly decreased from the pre-operative average of 6.81 to 2.08 at 24 h, 1.42 at 1 month, and 1.18 at 12 months post-operation. The ODI scores improved from the pre-operative average of 68.69 to 27.03 1 month post-operatively (Table 2). The average cement injection volume was 3.65 ± 1.059 (ml) per vertebral body.

Asymptomatic cement leakage occurred in four patients (17.4%), and eight patients (34.8%) developed new fractures following primary PKP, including four sandwich vertebral fractures (Figs. 2, 3, 4), six adjacent vertebral fractures (Figs. 5–7), four remote vertebral fractures, and one re-collapse of the cemented vertebrae. Among the eight patients with new vertebral fractures, seven underwent secondary VA due to severe back pain; the remaining patient received comprehensive conservative treatments because the clinical symptoms were not severe. Other complications included surgical site infections, symptomatic cement leakage, and nerve root injuries (Table 1).

The incidence of new fractures in the SVG and AVG was 16.7% (4/24) and 13.0% (6/46), respectively. The difference in the incidence of new fractures was not statistically significant (p = 0.727). Also, no statistically significant differences

Fig. 2 Patient A, a 55-year-old female patients complained of severe back pain after fell down. Spine X-ray and MRI showed T12 and L2 fresh fractures. The patient received VA at T12 and L2

Table 1 Clinical features of the patients (± SD)

Clinical features	
Variation	Value
No. of cases	23
Baseline date	
Male	N = 9 (39.1%)
Female	N = 14 (60.9%)
Age	74.38 ± 11.569
BMD of lumbar spine (*T*-value)	− 2.73 ± 1.214
BMI	23.86 ± 3.837
Following-up period(months)	21.48 ± 5.74
Surgical procedure	
Duration of operation per vertebral (minutes)	21.315 ± 7.259
Cement volume (ml)	3.65 ± 1.059
Complications	
New fracture	*N* = 8 (34.8%)
New sandwich vertebrae fracture	4
New adjacent vertebrae fracture	6
New remote vertebrae fracture	4
Re-collapse of cemented vertebrae	1
Cement leakage	*N* = 4 (17.4%)

in baseline and radiological parameters were found between the two groups (Table 3). However, due the low occurrence rate of SVB and new fracture and small simple size, the result of statistical power calculation showed that this study only achieved 10.793% power to detect a difference between the groups, which was weak and underpower.

Discussion

With an aging worldwide population, the proportion of elderly suffering from osteoporosis continue to rise, and OVCF has become one of the major diseases affecting the quality of life among the elderly [2, 3]. VA has gained popularity among spine surgeons and patients due to its short duration of operation, short hospitalization time, limited tissue damage, and significant analgesic effect. Despite the clinical advantages and favorable clinical outcomes of VA, previous studies reported that the incidence of developing new fracture ranged from 6.3 to 47.5% [6–9]. New vertebral fractures after VA include SVB fractures, adjacent vertebral fractures, re-collapse of the cemented vertebrae, and remote vertebral fractures. It should be emphasized that despite relatively high new fracture rate in our study (8/23, 34.8% per patient), the incidence of SVBs fractures was as low as 16.7%. We presume that several possible mechanisms may have contributed to this phenomenon.

Studies have investigated possible risk factors for developing new fractures following VA, the hypotheses of which include change in biomechanical characteristics, cement leakage into the intravertebral disc, vertebral height restoration, and preexisting severe osteoporosis [17, 18]. Researchers believe that SVBs bear extra pressure from the superior and inferior augmented vertebrae. However, no conclusions have been achieved; the precise relationship between VA and high fracture rates of vertebral bodies adjacent to the augmented vertebrae remains controversial. Several hypotheses are mentioned in previous studies. According to a few human cadaver studies, VA may increase the stiffness and strength of the augmented vertebrae leading to a shift load distribution on adjacent unaugmented vertebral bodies; as a result, there is an increased pressure on adjacent endplate and disc of the unaugmented vertebral body [19, 20]. On the other hand, Rohlmann et al. reported that the change in pressure on adjacent unaugmented vertebrae caused by biomechanical characteristics was almost negligible [12]. In our study, there were seven patients who underwent secondary VA due to new OVCFs. Before VA, they underwent a second BMD test by dual energy X-ray examination. Compared to the initial BMD result, the *T*-value in the augmented vertebrae was significantly increased, indicating that there were remarkable improvements in the stiffness and strength of the augmented vertebrae. Whether the difference in stiffness and strength was sufficient to result in new vertebrae factures is doubtful; according to the results of this study, the incidence of new fractures in the SVG and AVG were 16.7% (4/24) and 13.0% (6/46), respectively, without a significant statistical difference.

Another possible mechanism that may contribute to the high incidence of developing new fracture in our study was preexisting severe osteoporosis in these patients. The mean pre-operative *T*-value of BMD was − 2.73 ± 1.214 in our study. Osteoporosis compromised bone strength, predisposing these patients to an increased, relatively equal risk of developing vertebral fracture at SVBs and adjacent vertebrae. Another study reported that the presence of more than two preexisting VCFs was an independent risk factor for the development of new VCFs [17].

Table 2 Comparison of VAS and ODI scores of patients with lower back pain pre- and post-operation (x̄ ± SD)

	VAS score	*P*-value
Pre-operation	6.81 ± 0.680	
Post-operation (24 h)	1.81 ± 0.873	< 0.001
Post-operation (1 m)	1.52 ± 0.602	< 0.001
Post-operation (12 m)	1.38 ± 0.500	< 0.001
	ODI score	*P*-value
Pre-operation	75.06 ± 6.859	
Post-operation (1 m)	21.62 ± 7.864	< 0.001

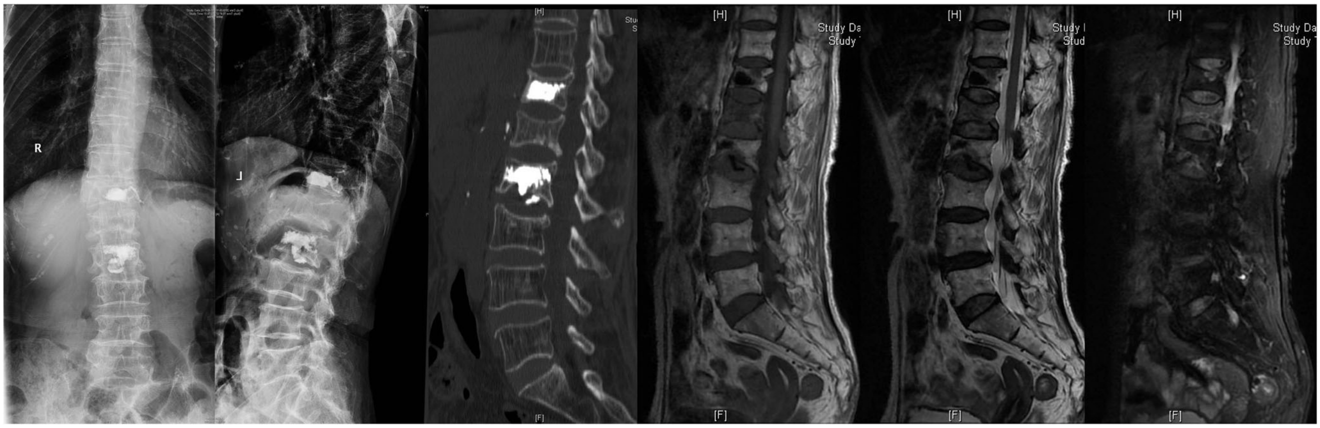

Fig. 3 Three months later, patient A complained of severe back pain again without obvious incentive. Spine X-ray and MRI showed L1 fracture

Until recently, only a few articles focused on the prognosis and new fracture rate of SVBs [13–16]. In 2006, Komemushi et al. [16] showed that SVBs were not significant risk factors in developing new fractures. Another study investigated the rate of adjacent level fractures after sandwiching compared with conservative treatment. The author concluded although SVBs were subjected to double-load shifts, the sandwich vertebra was not prone to structural failure [14]. A retrospective study in 2018, which aimed to determine the incidence of adjacent level new fractures in a sandwich constellation compared with two-level percutaneous vertebroplasty, showed that sandwich constellations were prone to refractures after prophylactic vertebroplasty (PVP) [13]. However, it classified both one and two untreated vertebrae between two cemented vertebrae as SVBs, which may affect the accuracy of the conclusion. It also reported that single-level sandwich constellations were uncommon (7.7% incidence rate). Application of a prophylactic PVP with resorbable bone cement was introduced by Jia et al. [15], which could reportedly decrease the rate of new fractures of sandwich vertebrae. However, given the relatively low rate of new fractures at single SVB segments, the necessity of performing prophylactic PVP is controversial.

The incidence of new fractures in SVG and AVG groups were 16.7% (4/24) and 13.0% (6/46), respectively, without a significant statistical difference, indicating that the double-load shift on SVBs was not associated with increased risk of developing new fractures. However, the statistical power of this study was very limited. Therefore, and because the refracture rate in these patients is substantial, routine long-term monitoring of patients after VA for osteoporosis is strongly recommended [14].

Limitation

Until now, there have been only a few retrospective studies that focused on the future outcomes of SVBs with different academic tendencies [13–16].

This is a long-term retrospective cohort study to investigate the possible mechanisms and incidence of new fractures in patients with SVBs. However, this is a single-center study with a relatively small sample size. Due to the low occurrence rate of SVB and new fracture and small simple size, the result of statistical power calculation showed that this study only achieved 10.793% power to detect a difference between the groups. Thus, the

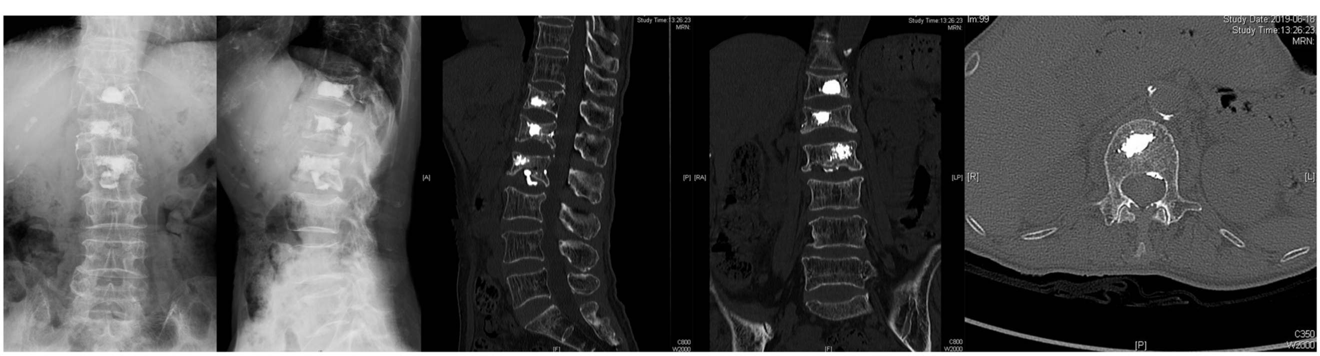

Fig. 4 Patient A received secondary VA at L1; post-operative spine X-ray and CT showed the satisfactory distribution of cement

Table 3 Comparison of the baseline and radiological parameters between SVG and AVG

	SVG	AVG	*P*-value
No. of cases	24	46	
New fracture	4 (16.7%)	6 (13.0%)	0.727
No. of thoracic lumbar junction segment (%)	11 (45.8%)	19 (41.3%)	0.801
Anterior vertebral height	21.40 ± 4.534	22.19 ± 4.113	0.464
Posterior vertebral height	24.98 ± 4.790	26.67 ± 4.007	0.126
Angle of local kyphosis	10.90 ± 7.015	8.41 ± 7.308	0.161

conclusion was underpower. Not all patients received MRI during the follow-up, only those with decrease of anterior vertebral height (more than 1/4) or complained of severe low back pain received spine MRI during the follow-up. There is a possibility that we missed asymptomatic fractures without anterior vertebral height change. Hence, a prospective study with large sample is warranted to investigate the risk factors and possible mechanism using the Cox multivariate regression analysis and Kaplan-Meier survival analysis.

Conclusions

In our study, patients with SVBs have a relatively high risk of developing new fracture after vertebral augmentation compared with previous studies. But, there was no significant statistical difference in the incidence of developing new fracture between the SVG and AVG groups. However, the statistical power of this study was very limited. Therefore, and because the refracture rate in these patients is substantial, routine long-term monitoring of patients after VA for osteoporosis is strongly recommended.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11657-021-00922-9.

Declarations

Conflict of interest None.

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