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Cross-sectional Study

Post-kyphoplasty secondary vertebral compression fractures in Vietnamese patients: A single-center prospective cross-sectional study

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ABSTRACT

Background: Despite its well-known effectiveness in vertebral compression fractures (VCFs), kyphoplasty could also bring the risk of developing subsequent VCFs post-augmentation, especially at adjacent vertebrae, which has been rarely reported in Asian countries.

Methods: In this cross-sectional study, we performed cement augmentation on 69 vertebrae in 65 patients at the Spine Surgery Department, Viet Duc University Hospital, from June 2019 to November 2020. Cement augmentation was performed on 69 vertebrae in 65 patients. They then were followed and assessed for subsequent VCFs every 3, 6, 9 months after surgery.

Results: 69 vertebrae in 65 patients were treated by kyphoplasty, 2 patients had 2 vertebrae treated and only one patient had 3 vertebrae injected. The average age recorded was 72 ± 8 years old. The average amount of cement injected was 5.4 ± 1.4 ml per vertebrae. At the end of the study, 63 patients did not develop subsequent VCFs. Two patients (3.07%) had new VCFs post-augmentation within the first two-month period post-injection. Age, gender, history of steroid injection and number of vertebrae treated with kyphoplasty showed no significant difference between the two groups.

Conclusions: Kyphoplasty is an effective pain-reliving treatment for patients with osteoporotic VCFs and would pose no threats to subsequent VCFs. For patients developing abnormal acute pain within the period of two months, further examinations and MRI scan should be performed to detect subsequent VCFs in time.

1. Introduction

Osteoporotic vertebral compression fractures (VCFs) is a common pathology in older patients and has been becoming more prevalent recently. The number of this condition in America is estimated approximately 700 000 cases every year [1], which is more than double the number of femoral neck fractures cases. Among such cases, about a third is patients with VCFs experiencing persistent back pain at the point of injury, thus impeding daily activities and negatively affecting their quality of life.

In term of treatment, in the past, patients could only cope with VCFs-related back pain using long-term pain-relieving drug treatment, back braces, or immobilization on bed. Recently, in accordance with technological advances, kyphoplasty has become more common in pain-reliving treatment for osteoporotic VCFs.

Despite its well-known reported effectiveness, kyphoplasty also brings the risk of developing subsequent VCFs post-augmentation, especially at adjacent vertebrae. Previous published research on spinal biomechanics reported very contradicting results. Some studies revealed the treated vertebrae did not put further stress onto adjacent vertebrae, while others proved that the adjacent VCFs risk associated with the straining of cement-augmented vertebrae, which affected the surrounding structural flexibility. These results make kyphoplasty a controversial method for osteoporotic VCFs around the world.

In Vietnam, kyphoplasty has been applied with good results but had yet to see any report on secondary VCFs after cement augmentation. The aim of this research was to assess the rate of subsequent VCFs in Vietnamese patients who already had kyphoplasty and to initially investigate contributing risk factors in those patients.

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2. Materials and methods

This study has been reported in line with the STROCSS criteria [2] and has been registered at the Research Registry with the Unique Identifying Number: researchregistry7846.

* **Methodology and sample size:** The study was carried out prospectively, at the Spine Surgery Department, Institute of Orthopedic and Trauma, from May 2019 to November 2020. Cement augmentation was performed on 69 vertebrae in 65 patients. The study excluded patients having multiple myeloma, metabolic skeletal disorders, or patients who could not participate in long-term observation. All patients were carefully examined, X-ray scanned in supine and lateral position of the lumbar spine, MRI scanned, and their bone density measured prior to cement augmentation to diagnose osteoporotic VCFs.

Additional periodic examinations were carried out for the patients' post-treatment every 3, 6, 9 months. X-ray and MRI scans were also performed in cases of possible secondary VCFs. Risk factors attributable to subsequent VCFs were examined for each patient: age, gender, history of chronic steroid use, levels of treated vertebra and number of treated vertebrae.

* **Secondary Vertebral Compression fractures:** Diagnosis of subsequent VCFs after kyphoplasty was based on changes in the medical imaging results regarding adjacent and remote vertebrae. Adjacent VCFs was diagnosed when VCFs occurred directly above or below the cement treated vertebra. On the other hand, remote VCFs could be observed when VCFs occurred in a vertebra at least one normal segment distance (either in the superior or inferior direction). Locked vertebra was defined as the normal vertebra in the middle position of two cement-augmented segments.

One patient was diagnosed with symptomatic secondary VCFs when all four symptoms were presented: 1) The patient had complaint of increasing acute pain after kyphoplasty treatment, 2) The patient could identify the pain location in accordance with the point of injury observed from radiographs, 3) Lateral X-ray result detected fractures in newly treated vertebrae in comparison to X-ray result prior to cement injection, 4) MRI result detected edema in the corresponding vertebral segment.

* **Vertebrae Augmentation techniques:** All patients underwent vertebrae augmentation by kyphoplasty in one or more vertebrae, by bilateral-*trans*-pedicle needle-putting, under the guidance of C-arm. Two balloons after being inserted into the collapsed vertebra will be slowly inflated until they almost reach the upper and lower endplate of the vertebrae, or the maximum inflation pressure is 300 PSI. The cement is then injected into the newly created void, until it almost reaches the posterior two-thirds of the posterior vertebral wall, under the guidance of the C-arm. Depending on the size of the collapsed vertebra, the maximum amount of cement injected can range from 1.5 to 8 ml per vertebra.
* **Data analysis:** The patient having subsequent VCFs group was compared with the primary VCFs group by using T test and Fisher test. Attributable factors were compared: age, gender, demographic history, corticoid usage history, and number of vertebrae treated. *P*-value of less than 0.05 was considered significant.

3. Results

A total of 69 vertebrae in 65 patients were treated by kyphoplasty. 62 out of 65 patients had cement injected into 1 vertebra, while 2 patients had 2 vertebrae treated and only one patient had 3 vertebrae injected. The study observed 57 female and 8 male patients. The average age recorded was 72 ± 8 years old. The average amount of cement injected was 5.4 ± 1.4 ml per vertebrae.

At the end of the research, 63 patients did not develop subsequent VCFs. Two patients (3.07%) had new VCFs post-augmentation within the first two-months period post-injection: The first patient was injected 4,2 ml cement and the second patient was injected 4,7 ml cement. One patient with subsequent VCFs had the second kyphoplasty treatment, showing very effective pain-relieving result (see Fig. 1), the other VCFs patient refused the second augmentation and choosing conservative treatment instead. Acute pain for less than two months (47.5 days) was found in two patients having secondary VCFs.

Information on risk factors attributable to VCFs was illustrated in Table 1. In regard of age factor, the study found no significant difference between patients having secondary VCFs and patients without VCFs ($p = 0.184$). Two other factors, gender and history of steroid injection, were analyzed with Chi – square test in which both factors showed no significant difference between the two groups ($p = 0.3058$ and $p = 0.4784$ respectively).

Table 2 demonstrated association between the number of vertebrae augmented and the number of patients with subsequent VCFs. The number of vertebrae treated was found to have no significant association with the proportion of patients having subsequent VCFs, according to results of Chi-square test ($p > 0.05$). There were two patients with subsequent VCF, which had cement injected into 1 vertebra and such fractures were adjacent to their previously treated vertebrae. Patients with more vertebrae injected posing no risk of the subsequent complication in our study. In other words, patients with multiple vertebrae treated did not have a higher risk of subsequent VCFs. Overall; vertebrae augmentation did increase the risk of developing subsequent VCFs.

4. Discussion

The World Health Organization (WHO) defined: Osteoporosis is a disorder of the skeletal, characterized by lost in skeletal density and strength; and increase in fractures risks. The natural progression of osteoporotic VCFs was not thoroughly understood. A known research involving 2725 women with an average age of 74 [1], the rate of primary VCFs was 6.6%, but the rate of secondary VCFS was 19% in the following year. Approximately only 5% of female patients with untreated primary VCFs developed subsequent VCFs with clinical symptoms after one year. Among those secondary VCFs patients, only 23% of them experienced clinical symptoms and seek medical intervention. Meanwhile, other researchers revealed the statistically significant difference between the rate of secondary VCFs due to natural osteoporosis (19%) and due to primary kyphoplasty within the first 60 days (21%).

What could be the causes of subsequent VCFs in patients? One of the reasons, as already mentioned in previous researches, is natural aging. Natural VCFs could decrease the vertebral body's height and cause kyphotic spine. The body weight would then be pushed forward, increasing the momentum and stress on the anterior wall of the fractured vertebrae's body and other adjacent segments. In case of osteoporosis on the whole vertebral column, the heavier stress pushed on adjacent vertebrae could increase the risk of adjacent and remote subsequent VCFs. Primary VCFs could later be the cause of subsequent VCFs. The question to be raised following such basis was: After undergoing kyphoplasty, could osteoporotic patients have a higher risk of developing secondary VCFs? There were some explanations for VCFs adjacent to the cement augmented segments. Theoretically the cement section could change the degradation of the adjacent skeletal structure, thus the treated vertebral segment would be considerably stiffer than surrounding vertebrae [3]. Baroud and colleagues [4] carried out their cadaveric biomechanical research about the stress of the augmented vertebra upon the adjacent segments. The research verified that the treated vertebra acted as a rigid upright pillar, thus limiting the physiologically shock absorption function of the vertebral pedicles. This reaction resulted in a load shift onto adjacent intervertebral discs (up to 19%) and vertebrae.

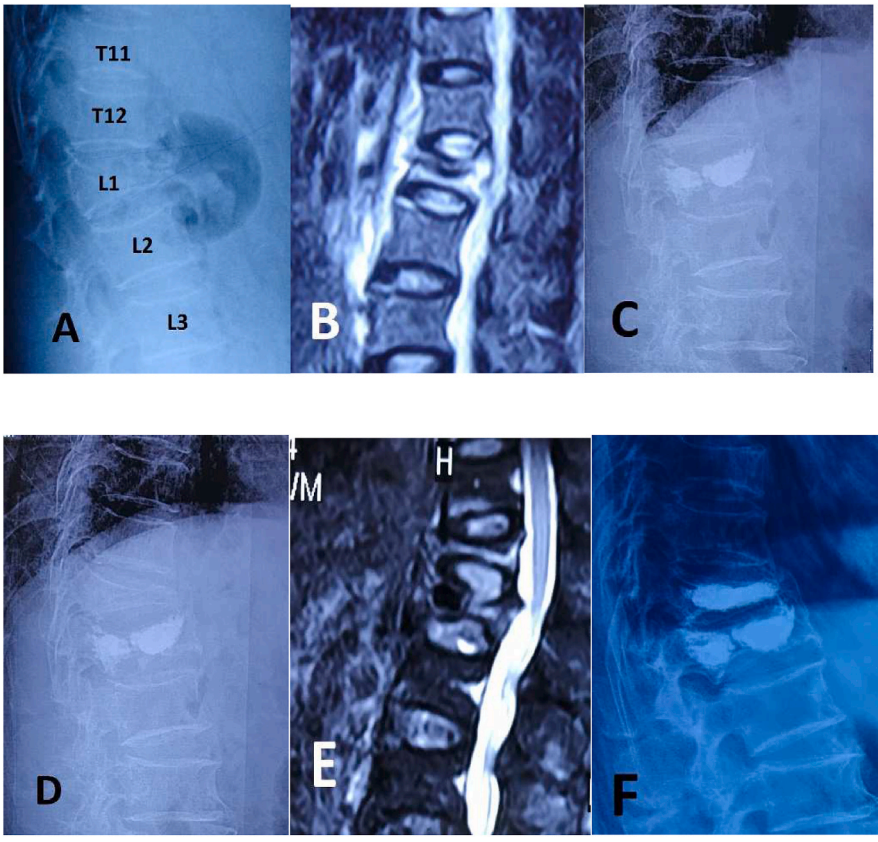

Fig. 1. Female patient, 89 years of age, with back pain for two weeks without any history of injury. X-rays results detected fractures at L1, along with MRI results showing edema (A), (B). The patient had her vertebrae augmented by kyphoplasty with effective pain-reliving result (C). Eight weeks later, the patient experienced intensive acute back pain. X-rays scans showed fractures at T12 and MRI revealed edema at corresponding vertebra (E), (F). The patient underwent the second kyphoplasty procedure with very effective pain-reliving result (G), (H).

Table 1
Association of subsequent VCF patients with contributing risk factors.

	Without subsequent VCFs (n = 63)	With subsequent VCFs (n = 2)	Total (n = 65)	P value
Age	72 ± 10	71 ± 6	72 ± 8	0.1874 T test
Male	8	0	8	0.3058
Female	55	2	57	X^2
Used Steroid	3	0	3	0.4784 X^2

Table 2
Association between number of patients with secondary VCFs and number of vertebrae treated per patient.

Subsequent VCFs	Number of vertebrae treated with kyphoplasty			Total
	1	2	3	
Yes	2	0	0	2
No	60	2	1	63
Total	62	2	1	65

The author hypothesized the load shift mechanism increased risk of subsequent VCFs post-treatment.

Contradicting researchers such as Daniel Cher [5] mentioned the advantages of kyphoplasty were the vertebral height reconstruction by inflating two balloons. The height restoration could reduce the forward momentum and hence lighten the load on adjacent vertebrae. Theoretically, such adjustment of the vertebral height along with restoration of the kyphosis curve angle could reduce risk of secondary VCFs. The author also stated that the opinion of post-kyphoplasty secondary VCFs risk arose from the concept of skeletal augmentation surgery, vertebral fixation raised the treated vertebral segment's stiffness, therefore increased the load and degradation on adjacent intervertebral discs. However, the emphasis was that the role of intervertebral discs should be clearly understood. One mechanical unit of the vertebral column included two vertebrae and one intervertebral disc. The unit together formed the three springs structure (Fig. 2). In the mentioned unit, the weakest spring was the lumbar disc (0.5–2.5 MPa), also much weaker than vertebral body stiffness (~100 MPa). Even in the case of osteoporosis and degraded disc, the vertebrae were still much stiffer comparing to intervertebral discs. Fig. 2 (A, B) validated that two hard springs (two vertebrae) would not shift under heavy load, instead the stress would be

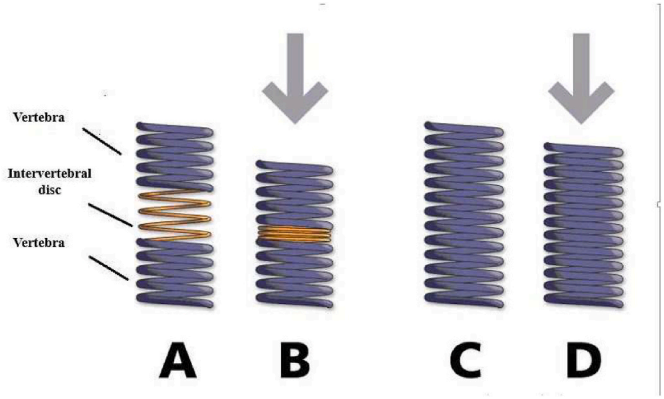

Fig. 2. A. Functional units illustrated as two coiled springs. The two vertebrae were two stiffer coiled while the intervertebral disc being the softer part. **B.** The similar unit when compressed. The softer disc was compressed at a higher rate than the two stronger coils. **C.** Still the same vertebral unit after treatment. At this stage all three springs had similar stiffness as the intervertebral disc was augmented. **D.** The treated vertebral unit when compressed. The compression load was distributed evenly across all three sub-units and also across adjacent units.

shifted to the softer spring (disc). Even when the vertebrae were injected, the load would still be shifted to the intervertebral disc and not the skeleton. On the other hand, in treated vertebral units, the load would be distributed across the whole spine. In such cases the intervertebral discs were already replaced (5–10 times stiffer) as in Fig. 2 (C, D). This increase in stiffness explained the degeneration occurred adjacently to treated segment. Therefore, the biomechanical researches on subsequent VCFs after cement injection were still controversial. We could not conclude that secondary VCFs were a result of kyphoplasty or natural osteoporosis. Meanwhile, to further investigate this association, the patient should be assessed through the multi-relationships of various known risk factors such as age, gender, osteoporosis level, past steroid usage, number of injected vertebrae …

In our study there were only two patients experiencing secondary VCFs after cement injection (3.07%). One patient proceeded to receive the second kyphoplasty with very positive result. This ratio was significantly lower than the 19% rate of subsequent VCFs due to natural osteoporosis and lower than in other previous studies. In all possibilities, our research results could be influenced by other relating factors.

Both patients with subsequent VCFs were females with no history of steroid usage. However, James S.H. [6]. recorded in his research 35 cases of subsequent VCFs, in which 17 cases (48.6%) were found to have past usage of steroid, out of 115 patients undergoing kyphoplasty. The mentioned author emphasized steroid as a new risk factor for VCFs. Steroid could inhibit osteogenesis, decrease calcium accumulation inside vertebral bodies or reduce osteocytes count. The different results of the two researches could be explained by our low number of involved patients or the many differences of the two countries regarding the diagnosis systems, pathology structures, local habit and culture concerning drug usage.

William F.L. [7]. detected, while performing kyphoplasty on 94 patients, that the rate of subsequent VCFs was higher among patients with multiple cement-injected vertebrae when compared with patients with only one treated vertebrae ($p < 0.005$). According to the afore author, when multiple vertebrae were treated with cement injection, the stiffness of the vertebral unit increased on a longer segment, hence the weight load was distributed even more onto the other adjacent segments, increasing the risk of secondary VCFs. In regards of our research, both subsequent VCFs patients only had cement injection on one preceding level. With such humble result, we could not verify the association published by above-mentioned author. Averagely we injected 5.4 $\pm$ 1.4 ml cement. Eun-Su Moon [8] injected an average of 4.3 ml per vertebra for 111 patients and this author noticed a higher rate of subsequent VCFs in patients with respectively higher amount of cement injection.

Our research population had two subsequent VCFs patients, who were diagnosed within the first two-month period post-injection, and both cases were adjacent VCFs without any sign of remote fractures. Similarly, David F [9] performed kyphoplasty for 38 cases and detected most secondary VCFs patients were presented with adjacent fractures within the first two-month post-treatment. Outside of the two-months period, subsequent VCFs patients were less often recorded and many of such were remote fractures [1]. Therefore, patients who experienced sudden onset of pain within the first two-month post-injection should be further examined and MRI scanned to detect possible subsequent VCFs.

The advantages in our study was the prospective methodology, the patients were observed in appropriate time length (9 months for secondary VCFs), all patients had their operations done and monitored in the Spine Surgery Department. The research, therefore, assured the continuality on a planned schedule.

On the other hand, certain shortcomings were to be taken into account. Firstly, our patients count was small, making the subsequent VCF rate significantly lower when comparing to other existing publications. This also affected the results in which we could not identify the association between secondary VCFs and other related risk factors such as the amount of cement injected, numbers of injected vertebrae, history of potent steroid usage. Secondly, two third of subsequent VCFs patients were without clinical symptoms and thus may be excluded from further examination to identify asymptomatic subsequent VCFs.

In the future, further research and development of cement material with better biomechanically characteristics would help reduce the risk of subsequent VCFs. Meanwhile, health promotion for patients about the importance of post-surgery osteoporosis treatment and the strict compliance with osteoporosis treatment regimen will help reduce secondary VCFs risks.

5. Conclusion

Kyphoplasty is an effective pain-reliving treatment for patients with osteoporotic VCFs and would pose no threats to subsequent VCFs. For patients developing abnormal acute pain within the period of two months, further examinations and MRI scan should be performed to detect subsequent VCFs in time. Further studies are needed to determine if secondary VCFs was the consequence of kyphoplasty or a natural progression of osteoporosis.

6. Provenance and peer review

Not commissioned, externally peer-reviewed.

Conflicts of interest

The authors have no conflicts of interest to declare.

Sources of funding

This is a non-funded study.

Ethical approval

This study was approved by Ethics Committee at Viet Duc hospital with Decision number 1421/QĐ-VĐ. Participants were explained sufficiently about the study and asked for their consent by documents.

Consent

Written informed consent was obtained from the patients for publication of this study and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

HMD: creating study concept and design and writing the paper, LHN: data collection, data analysis, writing the paper, TTD: data analysis, data interpretation, HTND: design, writing and proofreading the paper.

Registration of research studies

1. Name of the registry: Research Registry
2. Unique Identifying number or registration ID: researchregistry7846
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://researchregistry.knack.com/research-registry#home/registrationdetails/6268b47ed7c2200020d349cf/

Guarantor

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.

org/10.1016/j.amsu.2022.103756.

References

[1] R. Lindsay, et al., Risk of new vertebral fracture in the year following a fracture, JAMA 285 (3) (2001) 320–323.
[2] G. Mathew, et al., Strocss 2021: strengthening the reporting of cohort, cross-sectional and case-control studies in surgery, International Journal of Surgery Open 37 (2021), 100430.
[3] R. Pflugmacher, R.-J. Schroeder, C. Klostermann, Incidence of adjacent vertebral fractures in patients treated with balloon kyphoplasty: two years' prospective follow-up, Acta Radiol. 47 (8) (2006) 830–840.
[4] G. Baroud, et al., Load shift of the intervertebral disc after a vertebroplasty: a finite-element study, Eur. Spine J. 12 (4) (2003) 421–426.
[5] e.a. Daniel Cher, Risk of subsequent vertebral body compression fractures after balloon kyphoplasty, Kyphon Broch (2006) 1–16.
[6] J.S. Harrop, et al., Primary and secondary osteoporosis' incidence of subsequent vertebral compression fractures after kyphoplasty, Spine 29 (19) (2004) 2120–2125.
[7] W.F. Lavelle, R. Cheney, Recurrent fracture after vertebral kyphoplasty, Spine J. 6 (5) (2006) 488–493.
[8] E.-S. Moon, et al., The incidence of new vertebral compression fractures in women after kyphoplasty and factors involved, Yonsei Med. J. 48 (4) (2007) 645–652.
[9] D. Fribourg, et al., Incidence of subsequent vertebral fracture after kyphoplasty, Spine 29 (20) (2004) 2270–2276.