Turk Neurosurg, 2022

Meta-Analysis/Systematic Review

DOI: 10.5137/1019-5149.JTN.37319-21.4

Received: 08.12.2021
Accepted: 08.04.2022

Published Online: 22.08.2022

Cement Leakage in Vertebral Compression Fractures Between Unilateral and Bilateral Percutaneous Vertebral Augmentation: A Meta-Analysis

Xinzhe MA[1]*, Hui SUN[2]*, Shizhao LIU[3], Linchao SANG[1], Kunlong WANG[4], Yue DONG[5], Xiangbei QI[6,7]

[1]The Second Department of Trauma, the Third Hospital of Shijiazhuang, Shijiazhuang, China
[2]Oita University Faculty of Medicine
[3]Hebei Hospital of Traditional Chinese Medicine, Department of Emergency, Shijiazhuang, China
[4]The People Hospital of Gongyi City, Department of Orthopaedic Surgery, Gongyi, China
[5]Baoding First Central Hospital, Department of Orthopedic, Baoding, China
[6]The Third Hospital of Hebei Medical University, Department of Orthopaedic Surgery, Shijiazhuang, China
[7]Tiemenguan District of the Third Hospital of Hebei Medical University, Department of Orthopedics, Shijiazhuang, China

*These authors contributed equally to this work.

Corresponding author: Xiangbei QI ✉ qixiangbei126@126.com

ABSTRACT

AIM: To compare the incidences of cement leakage between unilateral and bilateral percutaneous vertebral augmentation (PVA) in the treatment of osteoporosis vertebral compression fractures, a meta-analysis was performed.

MATERIAL and METHODS: Pertinent studies were identified by a search of the PubMed, Embase, and Web of Science databases up to December 2020. The risk ratio (RR) or weighted mean difference (WMD) was applied to combine the results, and a random-effects or a fixed-effects model was used to pool the results depending on the heterogeneity among studies. Publication bias was estimated using Egger's regression asymmetry test.

RESULTS: A total of 16 trials (including 9 RCTs and 7 cohort studies) met the inclusion criteria and were included in this meta-analysis. The incidences of cement leakage were similar between the bilateral PVA and unilateral PVA groups (RR=0.80, 95%CI: 0.57, 1.11; p=0.182) but unilateral PVA required less cement volume (WMD=−1.34 ml, 95%CI: −1.87, −0.81; p<0.001). Subgroup analysis revealed that the incidence of cement leakage was significantly lower in the unilateral PKP group than in the bilateral PKP group (RR=0.65, 95%CI: 0.44, 0.97; p=0.034).

CONCLUSION: The incidences of cement leakage were similar between unilateral and bilateral PVA, but unilateral PVA required less cement. More large-scale studies are needed to verify our findings.

KEYWORDS: Percutaneous vertebral augmentation, Cement leakage, Meta-analysis, Vertebral compression fractures

ABBREVIATIONS: PVA: Percutaneous vertebral augmentation, **OVCFs:** Osteoporosis vertebral compression fractures, **RR:** Risk ratio, **WMD:** Weighted mean difference, **PVP:** percutaneous vertebroplasty, **PKP:** Percutaneous kyphoplasty

Xinzhe MA : 0000-0002-3631-8534
Hui SUN : 0000-0003-4207-7754
Shizhao LIU : 0000-0002-4893-2339
Linchao SANG : 0000-0002-3110-6268
Kunlong WANG : 0000-0001-9892-6570
Yue DONG : 0000-0002-1158-9194
Xiangbei QI : 0000-0002-0563-370X

INTRODUCTION

Osteoporosis is a systemic disorder characterized by low bone mass, altered bone microarchitecture, and an increased risk of fragility fracture (4). Osteoporosis vertebral compression fractures (OVCFs) are the most common fragility fractures associated with the disorder and affect 25% of postmenopausal women and >200 million individuals worldwide (23). Substantial pain and deformity can result from OVCFs and lead to disabilities and poor quality of life (29).

Current conservative treatments of OVCFs include analgesics, external braces, and physical therapy, but some patients experience severe pain after treatment and may show progressive collapse of the vertebral body and kyphosis with or without neurological deficit (12,30). Percutaneous vertebral augmentation (PVA) methods have been developed to treat OVCF patients and provide better pain relief, functional recovery, and health-related quality of life than provided by conservative or sham treatments (2,27). Moreover, compared with non-surgical treatment, PVA can reduce the risk of mortality in Medicare beneficiaries (18,19).

Among the PVA methods, percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP) are the most commonly used modalities for the treatment of OVCFs. Although PVA is effective for pain relief, it is also associated with complications, including cement leakage, soft-tissue damage, and nerve injury (26,34). Cement leakage during the high-pressure injection is one of the most common complications of PVA. In the standard technique for PVA, a bilateral approach is traditionally used (21,33). Subsequently, a unilateral approach associated with lower operating and radiation exposure times as well as a reduced risk of cement leakage and complications has been advocated (8). Several studies have compared the difference in cement leakage between unilateral and bilateral PVA, but the results have been inconclusive. Therefore, the study aim was to conduct a meta-analysis to determine the differences in cement leakage and cement dosage between unilateral and bilateral PVA.

MATERIAL AND METHODS

Literature Search

The meta-analysis of current relevant literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (32). A comprehensive systematic search of several major electronic databases (e.g., PubMed, Embase, and Web of Science) was conducted before December 2020 and used the following search terms: osteoporotic vertebral compression fractures, OVCFs, vertebral compression fracture, percutaneous vertebroplasty, PVP, percutaneous kyphoplasty, PKP, cement leakage, cement extravasation, unilateral, unipedicular, bilateral, and bipedicular. There was no restriction of language or publication status. Additional relevant articles were obtained by searching the reference lists of the included articles, and the corresponding author was contacted when the necessary data was not reported. This meta-analysis included previously published studies, and no human subjects were involved; therefore, no ethics approval was required.

Inclusion Criteria and Study Selection

The inclusion criteria were as follows: 1) study design: randomized controlled trials (RCTs), cohort, case-control, or comparative studies; 2) population: patients diagnosed with OVCFs; 3) intervention: unilateral PVA; 4) control: bilateral PVA; 5) outcomes: cement leakage or cement volume.

Data Extraction

Two independent investigators used a standard tool to extract the following data from each study: first author's name, year of publication, country, study design, operative methods, number of study patients, baseline patient characteristics (age, sex, race, and number of vertebrae), and outcomes (incidence of cement leakage and cement volume). Disagreements between the investigators were resolved by discussion or decided by a third investigator when necessary.

Quality Assessment of the Included Studies

The method recommended by the Cochrane Collaboration was used to evaluate the risk of bias in each RCT (22) and consisted of the following items: random-sequence generation, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, allocation concealment, selective reporting, and other bias (22). An RCT was considered to be at low risk of bias if all of these key domains were met and considered to be at a high risk of bias if one or more of these key domains were not met; if one or more were unclear, the RCT was classified as having an unclear risk of bias.

The modified Newcastle–Ottawa Scale (NOS) was used to assess the quality of non-RCTs (46). To evaluate study quality, this method comprises three items: patient selection, comparability of the kidney stone group and control group, and outcome assessment (46). The studies were scored from 0 to 9 points, and any study with a total of >5 points was considered to be of high quality (46).

Statistical Analysis

STATA software version 12.0 (Stata Corporation, College Station, TX, USA) was used to perform the meta-analysis. Before the data were synthesized, the Q chi-square test (16) was used to assess the heterogeneity of the studies, with significant heterogeneity indicated by a P-value of <0.10. A random-effects model (DerSimonian–Laird method) (17) was used in the case of significant heterogeneity, otherwise, a fixed-effects model (Mantel–Haenszel method) (31) was used. The pooled estimates from all studies and high-quality articles were calculated and compared to investigate the potential bias introduced by the heterogeneous quality of the included studies. If there was a significant difference in the estimates, outputs derived from the high-quality articles were presented. A subgroup analysis based on the study design and procedure was also performed.

The incidence of cement leakage was expressed as a risk ratio (RR) with 95% confidence intervals (95% CI), and cement

volume was calculated by the weighted mean difference (WMD) with 95% CI. The assessment of publication bias was evaluated using the Egger (20) and Begger (6) tests. p-values of <0.05 were considered to be indicative of statistical significance except where otherwise specified.

RESULTS

Identification of Eligible Studies

The study selection flow diagram is shown in Figure 1. The initial search yielded 786 publications, of which 418 duplicates were excluded. After the title/abstract review, 346 were excluded leaving 22 for full-text information review, of which 6 were excluded because 3 were single-arm trials and 3 did not provide the outcome of our interest. Finally, 16 studies (9-11,13,15,38,42-45,47-49,51,53,54) were included in this meta-analysis.

Characteristics of Eligible Studies

The main characteristics of the included studies published between 2008 and 2020 are presented in Table I. Most studies were conducted in China (9,10,13,42,44,45,47-49,51,53,54) except for one in the USA (38) and one in South Korea (15). Of the 16 studies, 7 were a cohort design (11,15,42,43,45,47,54), and the other 9 were RCTs (9,10,13,38,44,48,49,51,53). The total number of included patients was 1568 (range: 39–309), of which 763 underwent unilateral PVA and 805 underwent bilateral PVA. The clinical characteristics were well balanced for sex, age, fracture location, preoperative Oswestry Disability Index, and visual analog scale. Six of the included studies used PVP as the surgical method (9,44,47,51,53,54), and the other 10 used PKP (10,11,13,15,38,42,43,45,48,49,53).

Quality Assessment

The seven cohort studies were of high quality (Table I) and the details of the bias risk for the nine RCTs are summarized in Figure 2. Among these studies, only one was regarded as having a low risk of bias (44), two had a high risk of bias (13,53), and six had an unclear risk of bias (9,10,38,48,49,51). The two RCTs had a high risk of bias because they did not report the cement volume. All of the studies claimed randomization, but only four trials reported the methods for random-sequence generation or allocation concealment (9,10,44,51); one trial

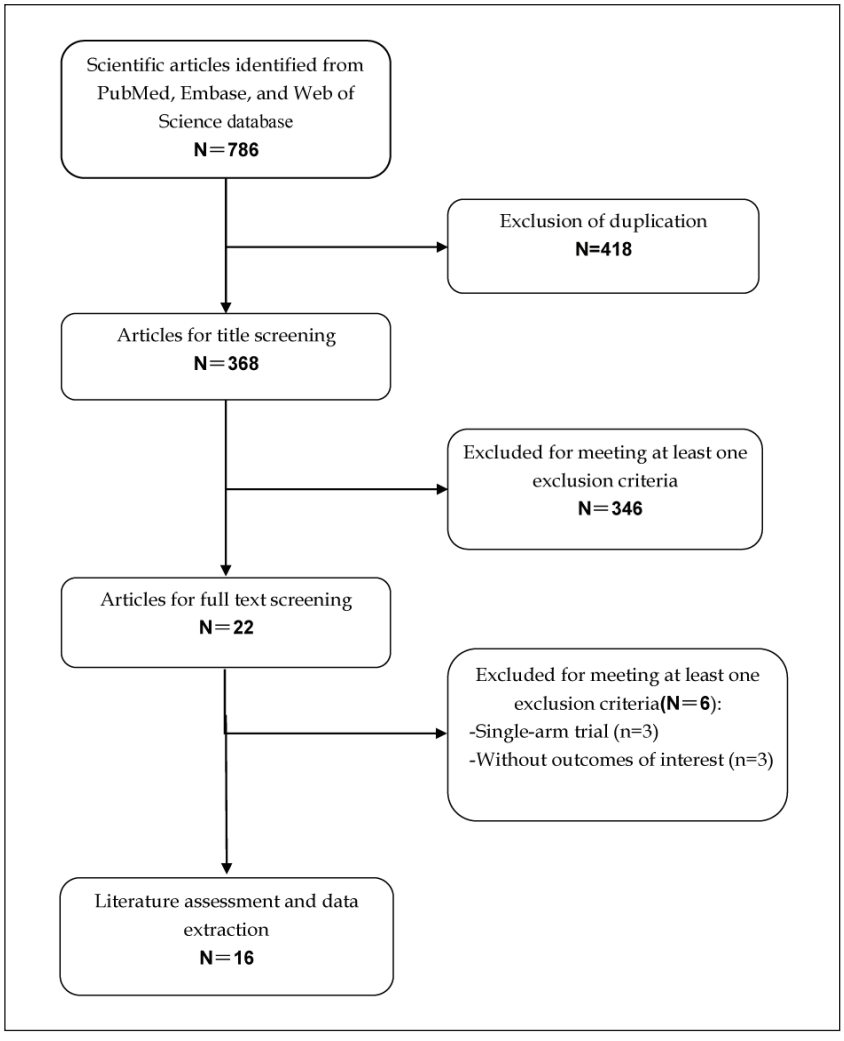

Figure 1: Eligibility of studies for inclusion in meta-analysis.

Table I: Baseline Characteristics of Patients in the Trials Included in the Meta-Analysis

Study	Country	Study design	Treatment regimen	No. of patients	Male/ Female	Age (mean ±SD, y)	NOS score
Zhang et al. 2015 (51)	China	RCT	Unilateral PVP	24	5/19	71.7 ± 7.5	NA
			Bilateral PVP	28	8/18	72.1 ± 6.0	
Zhong et al. 2019 (54)	China	Cohort	Unilateral PVP	29	3/26	70.7 ± 7.5	6
			Bilateral PVP	75	12/63	73.8 ± 8.2	
Chen et al. 2014 (9)	China	RCT	Unilateral PVP	20	NR	69.43 ± 6.25	NA
			Bilateral PVP	19	NR	68.66 ± 8.76	
Chen et al. 2011 (13)	China	RCT	Unilateral PKP	24	4/20	70.4 (52-91)	NA
			Bilateral PKP	25	4/21	72.4 (54-87)	
Wan et al. 2020 (42)	China	Cohort	Unilateral PKP	70	28/42	70.25 ± 7.10	7
			Bilateral PKP	68	22/46	69.82 ± 8.20	
Rebolledo et al. 2013 (38)	USA	RCT	Unilateral PKP	23	4/19	78.7 ± 7.8	NA
			Bilateral PKP	21	2/19	79.3 ± 6.5	
Wang et al. 2012 (43)	China	Cohort	Unilateral PKP	31	13/18	68.3 (59-78)	7
			Bilateral PKP	31	17/14	69.2 (62-79)	
Wang et al. 2019 (44)	China	RCT	Unilateral PVP	151	36/115	68.5 ± 5.23	NA
			Bilateral PVP	140	31/119	69.4 ± 4.35	
Chen et al. 2010 (10)	China	RCT	Unilateral PKP	33	0/33	67.73 ± 7.05	NA
			Bilateral PKP	25	0/25	68.52 ± 7.26	
Yan et al. 2014 (49)	China	RCT	Unilateral PKP	158	46/112	71.9 ± 4.2	NA
			Bilateral PKP	151	43/108	71.1 ± 3.7	
Yan et al. 2016 (48)	China	RCT	Unilateral PKP	55	NR	68.8 (55-74)	NA
			Bilateral PKP	53	NR	68.8 (55-74)	
Zhang et al. 2015 (53)	China	RCT	Unilateral PVP	36	0/36	70.0 ± 2.9	NA
			Bilateral PVP	32	0/32	70.7 ± 2.5	
Xu et al. 2018 (47)	China	Cohort	Unilateral PVP	30	9/21	73.9 ± 10.2	7
			Bilateral PVP	46	6/20	76.4 ± 10.8	
Chung et al. 2008 (15)	South Korea	Cohort	Unilateral PKP	24	2/22	66.8 (57-80)	6
			Bilateral PKP	28	1/27	68.9 (57-83)	
Wang et al. 2015 (43)	China	Cohort	Unilateral PKP	28	11/17	68 ± 7.7	7
			Bilateral PKP	40	16/24	69.6 ± 9.4	
Chen et al. 2011 (11)	China	Cohort	Unilateral PKP	27	0/27	68.37 ± 7.64	6
			Bilateral PKP	23	0/23	69.43 ± 6.22	

SD: *Standard deviation,* ***PVP:*** *Percutaneous vertebroplasty; percutaneous kyphoplasty,* ***RCT:*** *Randomized controlled trial,* ***NA:*** *Not available.*

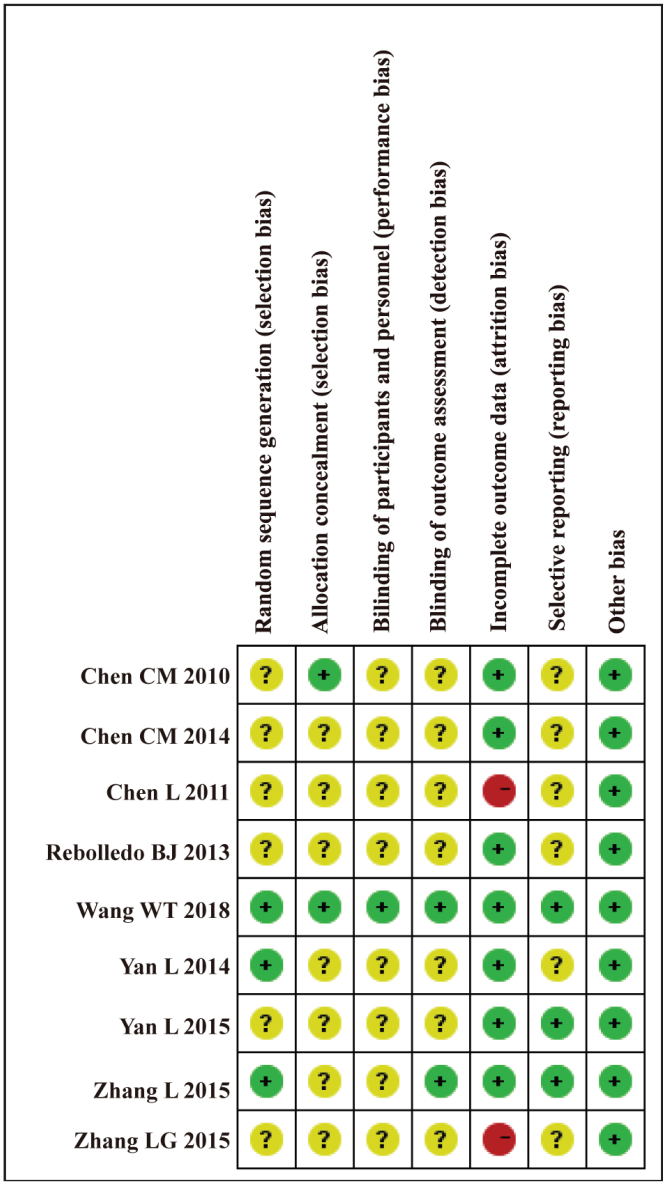

Figure 2: Risk of bias summary.

described the methods of double-blinding (44), and one trial reported the blinding of outcome assessment (51).

Cement Leakage

Fifteen studies reported cement leakage data, with the incidence of cement leakage in the unilateral and bilateral PVA groups of 16.26% and 20.43%, respectively. Pooled estimates showed that the incidences of cement leakage were similar between the unilateral PVA bilateral PVA groups (RR=0.80, 95% CI: 0.57, 1.11; p=0.182) (Figure 3), with non-significant heterogeneity across the included studies (I^2= 44.4%, p=0.033).

Subgroup analysis based on the surgical type suggested that the incidence of cement leakage was significantly lower in the patients who underwent unilateral PKP than bilateral PKP (RR =0.65, 95% CI: 0.44, 0.97; p=0.034) (Figure 3). For patients with PVP, the incidences of cement leakage were similar between the unilateral approach and bilateral approach (RR=0.91, 95% CI: 0.55, 1.52; p=0.719) (Figure 3). Furthermore, the subgroup analysis based on study design showed that patients treated with unilateral PVA had a comparable incidence of cement leakage for both RCT (RR=0.72, 95% CI: 0.48, 1.09; p=0.123) and cohort studies (RR=1.04, 95% CI: 0.53, 2.04; p=0.903) (Figure 4).

Cement dosage

Twelve studies reported cement dosage data. The cement volumes in the unilateral and bilateral PVA groups were 4.3 ± 1.12 ml and 5.65 ± 1.38 ml, respectively. Pooled estimates demonstrated that the cement dosage was significantly lower in the unilateral PVA group than in the bilateral PVA group (WMD = −1.34 ml, 95%CI: −1.87, −0.81; p<0.001) (Figure 5). The subgroup analyses based on surgical type and study design (Figure 5) also indicated that the unilateral approach significantly reduced the cement dosage relative to that for the bilateral approach in both PVP (WMD = −0.86 ml, 95%CI: −1.53, −0.19; p=0.012) and PKP (WMD = −1.83 ml, 95%CI: −2.49, −1.17; p<0.001), as well as in both RCT (WMD = −1.59 ml, 95%CI: −2.44, −0.74; p<0.001) and cohort studies (WMD = −1.15 ml, 95%CI: −1.89, −0.40; p=0.003).

Sensitivity Analysis

The included studies were heterogeneous; therefore, a random-effects model was used to summarize the data, and the pooled estimates from all of the high-quality articles were calculated and compared. The pooled RRs of cement leakage were not significantly different between the studies (RR=0.97, 95% CI: 0.72, 1.30; p=0.821), which confirmed the robustness of the analysis.

Publication bias

The Egger's and Begg's tests were used to assess publication bias and showed that there was no publication bias among the included studies (Egger's test: t=1.74, p=0.105; Begg's test: Z=1.88, p=0.06).

DISCUSSION

Osteoporosis is a prevalent skeletal disorder characterized by loss of bone density and an increased risk of fractures (4). PVA is the optimal treatment for OVCF, providing rapid pain relief and stabilization of the fractured vertebral bodies (3,24) but is associated with cement leakage, the incidence of which ranges from 19% to 65% (36). This meta-analysis found that the incidences of cement leakage in the unilateral and bilateral PVA approaches were 16.26% and 20.43%, respectively, but were not significantly different. In addition, the cement dosage was significantly lower in the unilateral group than in the bilateral group.

Although most patients with cement leakage are clinically asymptomatic, serious complications can occur and are associated with the cement leakage location. These complications include canal stenosis (41), spinal cord compression (25), nerve-root compression (1), cardiopulmonary arrest (7), acute

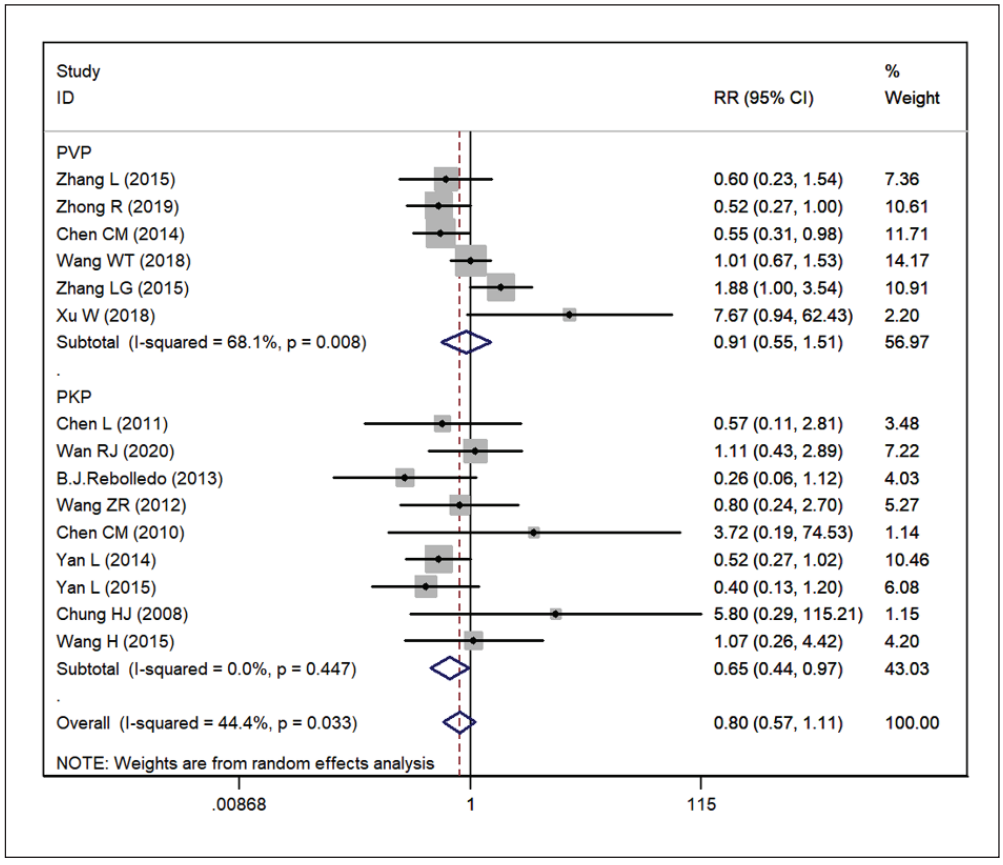

Figure 3: Forest plot showing the subgroup analysis based on surgical type between unilateral and bilateral PVA in cement leakage.

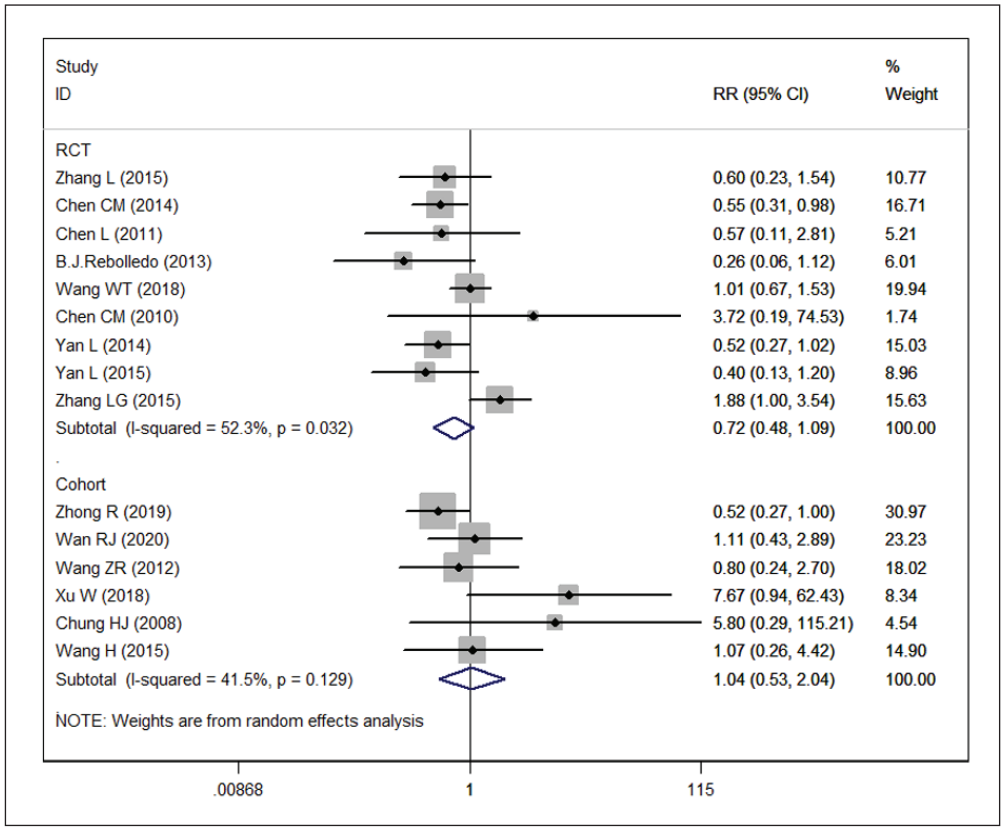

Figure 4: Forest plot showing the subgroup analysis based on study design between unilateral and bilateral PVA in cement leakage.

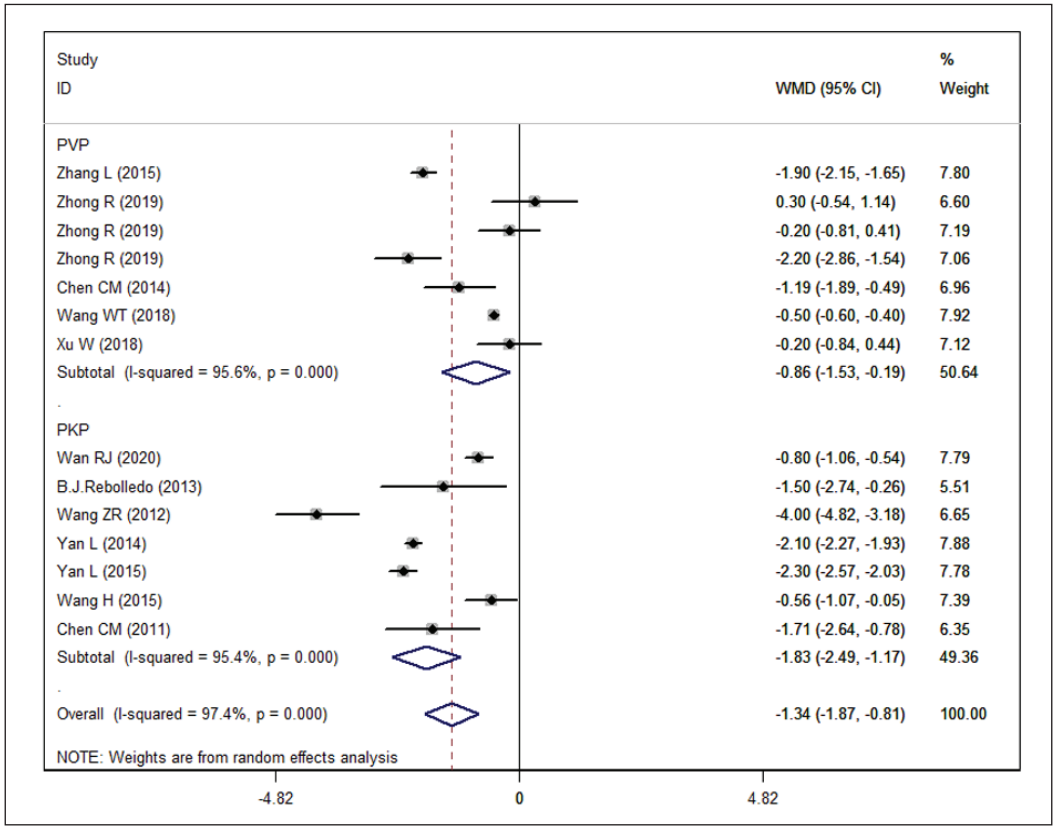

Figure 5: Forest plot showing the subgroup analysis based on surgical type between unilateral and bilateral PVA in cement dosage.

kidney injury (3), paradoxical embolism through a patent foramen ovale (39), arterial embolization (50), and cement pulmonary embolism (37). Three factors might affect the cement flow into and out of the vertebral body, including bone fracture severity grade, cement properties, and bone-cement volume (51). Although fracture morphology is impossible to control, the latter two factors may be manipulated to ultimately reduce the complication rate.

The viscosity of bone cement used in PVP can affect the outcome. Increased viscosity improves the circularity of the cement cloud and reduces the spreading distance (3,5); therefore, PVP with high-viscosity cement provides several advantages, especially a decreased cement leakage rate and improved clinical safety (3). Some studies have reported that bilateral PVA is superior to unilateral PVA for pain relief because of the symmetrical distribution of bone cement in the vertebral body (28). However, the risk of bone-cement leakage in bilateral PVA is theoretically twice that in unilateral PVA (52). Moreover, the operative time, X-ray exposure, and medical costs are also reduced in unilateral PVA (9,40).

Despite numerous studies comparing the safety between unilateral and bilateral PVA, there is no consensus on whether or not the bilateral approach reduces the risk of cement leakage relative to that of the unilateral approach. Recently, Chen et al. (14) performed a meta-analysis of six RCTs that compared the incidence of cement leakage between unilateral and bilateral PVA in treating OVCFs and concluded that the unilateral approach reduces the incidence of cement leakage in PVA (RR=0.50, 95% CI:0.35, 0.72; p=0.0002) (14), a finding in contrast to that of the present meta-analysis.

Our study had the following advantages. First, based on a previous meta-analysis, we included an additional 10 studies, including 3 RCTs and 7 cohort studies. The sample size in the present meta-analysis was 1568 versus 491 in the previous meta-analysis, which enhanced the statistical power for exploring the differences between the two approaches. Second, our results were obtained from RCTs and cohort studies, and the subgroup analysis showed that the study design did not change the overall estimate, indicating the reliability and robustness of our results. Moreover, we also performed sensitivity analysis by pooling the data from high-quality studies, and the result was in agreement with the results synthesized from all of the studies, demonstrating that the results of this meta-analysis were convincing.

The incidences of cement leakage were similar between unilateral PVA and bilateral PVA but not in the subgroup of patients who underwent PKP. Compared with the patients treated with the bilateral approach, those who underwent unilateral PKP had a significantly lower incidence of cement leakage (RR = 0.65, 95% CI: 0.44, 0.97; p=0.034). The finding of similar incidences of cement leakage between the two approaches was consistent with the finding from a prospective study of 382 patients (44) in which the cement leakage rates were similar between patients who underwent unilateral PKP (36/151, 23.85%) and patients who underwent bilateral PKP (33/140, 23.6%), indicating that the bilateral approach did

not increase the risk of cement leakage. However, in another prospective RCT, Rebolledo et al. reported that the incidence of cement leakage was significantly higher for bilateral PKP than for unilateral PKP (38). In that study, fractured vertebrae with asymptomatic cement leakage occurred in nine patients, including two in the unilateral group (2/23, 8.70%) and seven in the bilateral group (7/21, 33.33%) (38) (p=0.009). The authors attributed this result to the high rate of patients lost to follow-up, which was because the kyphoplasty patients did not return for follow-up unless they developed a complication or further symptoms (35).

Regarding the cement dosage, our meta-analysis showed that the cement dosage was significantly lower for unilateral PVA than for bilateral PVA, and difference remained significant in all of the subgroup analyses. Wang et al. compared the outcomes of unilateral and bilateral PKP in 62 patients and found that the cement volume was much lower in the unilateral approach (3.5 ± 1.2 ml) than in the unilateral approach (7.5 ± 2.0 ml) (45). Similarly, Chen et al. conducted a prospective RCT including 39 patients with 44 severe OVCFs and reported that the average amount of cement injected into one vertebra was significantly less in the unilateral group (3.17 ± 1.24 ml) than in the bilateral group (4.36 ± 1.14 ml) (9).

There were several potential limitations in this study. First, this meta-analysis included nine RCTs and seven cohort studies, and some of the included studies had relatively small sample sizes (N<50). Although most of the included studies were regarded as high quality, the pooled estimate might have been overestimated since the studies with a small sample size were more susceptible to overestimating the treatment effect. Second, gray literature is an important source of information for review syntheses because there is a greater tendency to report negative results honestly. Although no gray literature was searched in this study, the results of the sensitivity analysis and publication bias reflected the stability of the synthesis; thus, the synthesized results of 16 trials should be reliable as a reference for further research. Third, heterogeneity was identified among the included studies, which is unsurprising considering the differences in study designs, treatment regimens, and durations of follow-up across the included studies. To explore the potential sources of heterogeneity, we performed a subgroup analysis and a sensitivity analysis, but neither changed the overall study results, indicating the reliability and robustness of the results obtained.

CONCLUSION

Unilateral PVA was found to have a cement leakage rate similar to that of bilateral PVA but required less injected cement. Considering the potential limitations of this meta-analysis, more large-scale, well-designed RCTs are needed to verify our findings.

AUTHORSHIP CONTRIBUTION

Study conception and design: XM, HS

Data collection: XQ

Analysis and interpretation of results: SL, LS, KW, YD

Draft manuscript preparation: XM, HS

Critical revision of the article: XQ

Other (study supervision, fundings, materials, etc...): XQ

All authors (XM, HS, SL, LS, KW, YD, XQ) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Alvarez L, Pérez-Higueras A, Quiñones D, Calvo E, Rossi RE: Vertebroplasty in the treatment of vertebral tumors: postprocedural outcome and quality of life. Eur Spine J 12:356-360, 2003
2. Anderson PA, Froyshteter AB, Tontz WL Jr: Meta-analysis of vertebral augmentation compared with conservative treatment for osteoporotic spinal fractures. J Bone Miner Res 28:372-382, 2013
3. Anselmetti GC, Zoarski G, Manca A, Masala S, Eminefendic H, Russo F, Regge D: Percutaneous vertebroplasty and bone cement leakage: Clinical experience with a new high-viscosity bone cement and delivery system for vertebral augmentation in benign and malignant compression fractures. Cardiovasc Intervent Radiol 31:937-947, 2008
4. Appelman-Dijkstra NM, Papapoulos SE: Novel approaches to the treatment of osteoporosis. Best Pract Res Clin Endocrinol Metab 28:843-857, 2014
5. Baroud G, Crookshank M, Bohner M: High-viscosity cement significantly enhances uniformity of cement filling in vertebroplasty: An experimental model and study on cement leakage. Spine 31:2562-2568, 2006
6. Begg CB, Mazumdar M: Operating characteristics of a rank correlation test for publication bias. Biometrics 50:1088-1101, 1994
7. Braiteh F, Row M: Right ventricular acrylic cement embolism: Late complication of percutaneous vertebroplasty. Heart 95(4):275, 2009
8. Chang WS, Lee SH, Choi WG, Choi G, Jo BJ: Unipedicular vertebroplasty for osteoporotic compression fracture using an individualized needle insertion angle. Clin J Pain 23:767-773, 2007
9. Chen C, Bian J, Zhang W, Zhang W, Zhao C, Wei H: Unilateral versus bilateral vertebroplasty for severe osteoporotic vertebral compression fractures. J Spinal Disord Tech 27(8):E301-304, 2014
10. Chen CM, Chen L, Gu Y, Xu Y, Liu Y, Bai XL, Zhu XS, Yang HL: Kyphoplasty for chronic painful osteoporotic vertebral compression fractures via unipedicular versus bipedicular approachment: A comparative study in early stage. Injury 41:356-359, 2010
11. Chen CM, Wei H, Zhang W, Gu Y, Tang G, Dong R, Xu Y, Chen L: Comparative study of kyphoplasty for chronic painful osteoporotic vertebral compression fractures via unipedicular versus bipedicular approach. J Spinal Disord Tech 24:E62-65, 2011

12. Chen D, An ZQ, Song S, Tang JF, Qin H: Percutaneous vertebroplasty compared with conservative treatment in patients with chronic painful osteoporotic spinal fractures. J Clin Neurosci 21:473-477, 2014
13. Chen L, Yang H, Tang T: Unilateral versus bilateral balloon kyphoplasty for multilevel osteoporotic vertebral compression fractures: A prospective study. Spine 36:534-540, 2011
14. Chen W, Xie W, Xiao Z, Chen H, Jin D, Ding J: Incidence of cement leakage between unilateral and bilateral percutaneous vertebral augmentation for osteoporotic vertebral compression fractures: A meta-analysis of randomized controlled trials. World Neurosurg 122:342-348, 2019
15. Chung HJ, Chung KJ, Yoon HS, Kwon IH: Comparative study of balloon kyphoplasty with unilateral versus bilateral approach in osteoporotic vertebral compression fractures. Int Orthop 32:817-820, 2008
16. Cochran WG: The combination of estimates from different experiments. Biometrics 10(1):101, 1954
17. DerSimonian R, Laird N: Meta-analysis in clinical trials. Control Clin Trials 7(3):177-188, 1986
18. Edidin AA, Ong KL, Lau E, Kurtz SM: Mortality risk for operated and nonoperated vertebral fracture patients in the medicare population. J Bone Miner Res 26(7):1617-1626, 2011
19. Edidin AA, Ong KL, Lau E, Kurtz SM: Morbidity and mortality after vertebral fractures: Comparison of vertebral augmentation and nonoperative management in the medicare population. Spine 40(15):1228-1241, 2015
20. Egger M, Davey Smith G, Schneider M, Minder C: Bias in meta-analysis detected by a simple, graphical test. BMJ 315:629-634, 1997
21. Georgy BA: Clinical experience with high-viscosity cements for percutaneous vertebral body augmentation: Occurrence, degree, and location of cement leakage compared with kyphoplasty. Am J Neuroradiol 31:504-508, 2010
22. Higgins JPT, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JAC: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 343:d5928, 2011
23. Johnell O, Kanis JA: An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int 17:1726-1733, 2006
24. Kim JH, Yoo SH, Kim JH: Long-term follow-up of percutaneous vertebroplasty in osteoporotic compression fracture: Minimum of 5 years follow-up. Asian Spine J 6(1):6-14, 2012
25. Lai PL, Tai CL, Chen LH, Nien NY: Cement leakage causes potential thermal injury in vertebroplasty. BMC Musculoskelet Disord 12:116, 2011
26. Lee MJ, Dumonski M, Cahill P, Stanley T, Park D, Singh K: Percutaneous treatment of vertebral compression fractures: A meta-analysis of complications. Spine 34:1228-1232, 2009
27. Li L, Ren J, Liu J, Wang H, Wang X, Liu Z, Sun T: Results of vertebral augmentation treatment for patients of painful osteoporotic vertebral compression fractures: A meta-analysis of eight randomized controlled trials. PloS One 10(9):e0138126, 2015
28. Liebschner MA, Rosenberg WS, Keaveny TM: Effects of bone cement volume and distribution on vertebral stiffness after vertebroplasty. Spine 26:1547-1554, 2001
29. Lindsay R, Silverman SL, Cooper C, Hanley DA, Barton I, Broy SB, Licata A, Benhamou L, Geusens P, Flowers K, Stracke H, Seeman E: Risk of new vertebral fracture in the year following a fracture. JAMA 285:320-323, 2001
30. Liu J, Li X, Tang D, Cui X, Li X, Yao M, Yu P, Qian X, Wang Y, Jiang H: Comparing pain reduction following vertebroplasty and conservative treatment for osteoporotic vertebral compression fractures: A meta-analysis of randomized controlled trials. Pain Physician 16:455-464, 2013
31. Mantel N, Haenszel W: Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 22:719-748, 1959
32. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. BMJ 339:b2535, 2009
33. Nieuwenhuijse MJ, Muijs SPJ, van Erkel AR, Dijkstra SPD: A clinical comparative study on low versus medium viscosity polymethylmetacrylate bone cement in percutaneous vertebroplasty: Viscosity associated with cement leakage. Spine 35:E1037-1044, 2010
34. Nieuwenhuijse MJ, Van Erkel AR, Sander Dijkstra PD: Cement leakage in percutaneous vertebroplasty for osteoporotic vertebral compression fractures: Identification of risk factors. Spine J 11:839-848, 2011
35. Papadopoulos EC, Edobor-Osula F, Gardner MJ, Shindle MK, Lane JM: Unipedicular balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures: Early results. J Spinal Disord Tech 21:589-596, 2008
36. Phillips FM: Minimally invasive treatments of osteoporotic vertebral compression fractures. Spine 28:S45-53, 2003
37. Rahimi B, Boroofeh B, Dinparastisaleh R, Nazifi H: Cement pulmonary embolism after percutaneous vertebroplasty in a patient with cushing's syndrome: A case report. Respir Med Case Rep 25:78-85, 2018
38. Rebolledo BJ, Gladnick BP, Unnanuntana A, Nguyen JT, Kepler CK, Lane JM: Comparison of unipedicular and bipedicular balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures: A prospective randomised study. Bone Joint J 95-b:401-406, 2013
39. Scroop R, Eskridge J, Britz GW: Paradoxical cerebral arterial embolization of cement during intraoperative vertebroplasty: Case report. AJNR Am J Neuroradiol 23:868-870, 2002
40. Sun H, Li C: Comparison of unilateral and bilateral percutaneous vertebroplasty for osteoporotic vertebral compression fractures: A systematic review and meta-analysis. J Orthop Surg Res 11:156, 2016
41. Teng MMH, Cheng H, Ho DMT, Chang CY: Intraspinal leakage of bone cement after vertebroplasty: A report of 3 cases. AJNR Am J Neuroradiol 27:224-229, 2006
42. Wan R, Liu S: Efficacy and safety of unilateral and bilateral percutaneous balloon kyphoplasty for AOspineA3/A4 osteoporotic thoracolumbar burst fractures. Medicine 99:e21276, 2020

43. Wang H, Sun Z, Wang Z, Jiang W: Single-balloon versus double-balloon bipedicular kyphoplasty for osteoporotic vertebral compression fractures. J Clin Neurosci 22:680-684, 2015
44. Wang W, Duan K, Ma M, Jiang Y, Liu T, Liu J, Hao D: Can an unipedicular approach replace bipedicular percutaneous vertebroplasty for osteoporotic vertebral compression fracture? J Back Musculoskelet Rehabil 32:261-267, 2019
45. Wang Z, Wang G, Yang H: Comparison of unilateral versus bilateral balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. J Clin Neuroscience 19:723-726, 2012
46. Wells GA, Shea B, O'connell D, Peterson J, Welch V, Losos M, Tugwell P: The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. 3rd Symposium on Systematic Reviews: Beyond the Basics, 2000
47. Xu W, Wang S, Chen C, Li Y, Ji Y, Zhu X, Li Z: Correlation analysis between the magnetic resonance imaging characteristics of osteoporotic vertebral compression fractures and the efficacy of percutaneous vertebroplasty: A prospective cohort study. BMC Musculoskelet Disord 19:114, 2018
48. Yan L, He B, Guo H, Liu T, Hao D: The prospective self-controlled study of unilateral transverse process-pedicle and bilateral puncture techniques in percutaneous kyphoplasty. Osteoporos Int 27:1849-1855, 2016
49. Yan L, Jiang R, He B, Liu T, Hao D: A comparison between unilateral transverse process-pedicle and bilateral puncture techniques in percutaneous kyphoplasty. Spine 39:B19-26, 2014
50. Yazbeck PG, Al Rouhban RB, Slaba SG, Kreichati GE, Kharrat KE: Anterior spinal artery syndrome after percutaneous vertebroplasty. Spine J 11:e5-8, 2011
51. Zhang L, Liu Z, Wang J, Feng X, Yang J, Tao Y, Zhang S: Unipedicular versus bipedicular percutaneous vertebroplasty for osteoporotic vertebral compression fractures: A prospective randomized study. BMC Musculoskelet Disord 16:145, 2015
52. Zhang L, Wang J, Feng X, Tao Y, Yang J, Wang Y, Zhang S, Cai J, Huang J: A comparison of high viscosity bone cement and low viscosity bone cement vertebroplasty for severe osteoporotic vertebral compression fractures. Clin Neurol Neurosurg 129:10-16, 2015
53. Zhang LG, Gu X, Zhang HL, Zhang QG, Cai XB, Tao K: Unilateral or bilateral percutaneous vertebroplasty for acute osteoporotic vertebral fracture: A prospective study. J Spinal Disord Tech 28:E85-88, 2015
54. Zhong R, Liu J, Wang R, Liu Y, Chen B, Jiang W, Mao K, Tang P: Unilateral curved versus bipedicular vertebroplasty in the treatment of osteoporotic vertebral compression fractures. BMC Surg 19:193, 2019