

# Unilateral versus bilateral percutaneous kyphoplasty for osteoporotic vertebral compression fractures

## A meta-analysis

Wenli Chang, MD<sup>a</sup>, Xinyan Zhang, MD<sup>b</sup>, Ning Jiao, MD<sup>c</sup>, Peizhi Yuwen, MD<sup>a</sup>, Yanbin Zhu, MD<sup>a</sup>, Fei Zhang, MD<sup>a</sup>, Wei Chen, MD<sup>a,\*</sup>

### Abstract

**Background:** The debate on the efficacy of unilateral percutaneous kyphoplasty (UPKP) and bilateral percutaneous kyphoplasty (BPKP) for the treatment of osteoporotic vertebral compression fractures (OVCFs) is ongoing.

This meta-analysis aimed to evaluate the clinical results of UPKP and BPKP in the treatment of OVCFs.

**Methods:** Web of Science, PubMed, Embase, and the Chinese Biomedical Database publication databases were searched using a date range of January 2008 to November 2016, for studies comparing UPKP and BPKP for the treatment of OVCFs. The clinical effectiveness was assessed by comparing perioperative outcomes (surgery time, the volume of injected cement, X-ray exposure time, and kyphotic angle reduction), clinical outcomes (visual analogue scale [VAS] for pain relief and Oswestry Disability Index [ODI] for quality of life), and surgery-related complications (cement leakage and adjacent vertebral fractures). Data were analyzed using Stata/SE11.0 software.

**Results:** Fourteen trials with 1194 patients were retrieved. The pooled results showed significant differences in surgery time (weighted mean difference [WMD]  $-21.44$ , 95% confidence interval [CI]  $[-23.57$  to  $-19.30]$ ;  $P < .001$ ); volume of injected cement [WMD  $-1.90$ , 95% CI  $[-2.26$  to  $-1.54]$ ;  $P < .001$ ]; and X-ray exposure time (WMD  $-13.66$ , 95%CI  $[-19.59$  to  $-7.72]$ ;  $P < .001$ ) between UPKP and BPKP treatments. However, the pooled results showed no significant differences in kyphotic angle reduction, VAS in the short-term, VAS in the long-term, ODI, cement leakage, or adjacent vertebral fractures between the 2 surgical procedures. Following a subgroup analysis, the results based on randomized controlled trials (RCTs) indicated that there were significant differences in surgery time (WMD  $-24.65$ , 95%CI  $[-26.53$  to  $-22.77]$ ;  $P < .001$ ) and the volume of injected cement (WMD  $-1.66$ , 95%CI  $[-1.97$  to  $-1.36]$ ;  $P < .001$ ) between UPKP and BPKP treatment procedures, respectively. The results based on RCTs indicated that there were no significant differences, either in kyphotic angle reduction or in X-ray exposure time, between the 2 surgical procedures.

**Conclusions:** Compared to BPKP procedures, UPKP procedures may achieve similar clinical results in the treatment of OVCFs when assessed in terms of the pain relief, improvements in life quality, and surgery-related complications. However, UPKP procedures had a shorter operation time and volume of injected cement compared with BPKP procedures. Additional high quality and multicenter RCTs are needed to provide further robust evidence.

**Abbreviations:** BPKP = bilateral percutaneous kyphoplasty, CS = cohort study, ODI = Oswestry Disability Index, OVCF = osteoporotic vertebral compression fracture, RCT = randomized controlled trial, RR = risk ratio, UPKP = unilateral percutaneous kyphoplasty, VAS = visual analogue scale, WMD = weighted mean difference.

**Keywords:** bilateral percutaneous kyphoplasty, meta-analysis, osteoporotic vertebral compression fractures, unilateral percutaneous kyphoplasty

Editor: Kenneth Casey.

WC, XZ, and NJ contributed equally to this work.

The authors have no funding and conflicts of interest to disclose.

<sup>a</sup> Department of Orthopaedic Surgery, <sup>b</sup> Department of Radiology, <sup>c</sup> Department of Pharmacy, the Third Hospital of Hebei Medical University, Shijiazhuang, P.R. China.

\* Correspondence: Wei Chen, Department of Orthopaedic Surgery, the Third Hospital of Hebei Medical University, No. 139 Ziqiang Road, Qiaoxi District, Shijiazhuang 050051, P.R. China (e-mail: drchenwei1@163.com).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Medicine (2017) 96:17(e6738)

Received: 24 December 2016 / Received in final form: 24 February 2017 /

Accepted: 26 March 2017

<http://dx.doi.org/10.1097/MD.0000000000006738>

## 1. Introduction

Vertebral compression fractures are the most common fractures that occur in patients with osteoporosis, affecting approximately 20% of individuals older than 70 years.<sup>[1]</sup> Osteoporotic vertebral compression fractures (OVCFs), especially those that are not treated properly, can lead to deformity, disability, and poor quality of life. Traditionally, patients with OVCFs have been treated with bed rest, physical therapy, analgesics, and the use of an external brace, options that all often have limited effectiveness, especially in elderly patients who have an increased risk of pneumonia, decubitus ulcers, and venous thromboembolism.<sup>[2]</sup> Furthermore, some patients who do not respond to these conservative treatments turn to surgical treatment, which is typically reserved for OVCFs coupled with neurological deficits or spinal instabilities.<sup>[3]</sup> Vertebroplasty and balloon kyphoplasty are 2 treatments that were developed for the management of

symptomatic OVCFs. Both percutaneous vertebroplasty and balloon kyphoplasty can increase bone strength as well as alleviate the pain caused by OVCFs. However, Buchbinder et al performed 2 multicenter, randomized, double-blind, placebo-controlled trials and found no beneficial effect of vertebroplasty compared with a sham procedure in patients with painful osteoporotic vertebral fractures at 1 week or at 1, 3, 6, 12, or 24 months after treatment.<sup>[4,5]</sup> Because meta-analysis can offer the highest level of scientific evidence about the efficacy of an intervention based on the principles of evidence-based medicine, in 2015, Buchbinder et al included 11 randomized controlled trials (RCTs) and 1 quasi-RCT conducted in various countries in another study.<sup>[6–8]</sup> This review did not support a role for vertebroplasty in the treatment of osteoporotic vertebral fractures in routine practice. In addition, this procedure was indicated to be incapable of restoring the initial height of the vertebral body.<sup>[9]</sup>

Conversely, height deformity can be corrected by percutaneous balloon kyphoplasty. Specifically, percutaneous balloon kyphoplasty was initially introduced for tumoral and osteoporotic lesions, and the procedure was later adapted for the management of vertebral fractures.<sup>[10]</sup> In balloon kyphoplasty, an inflatable bone tamp is used to raise the vertebral body height followed by injection of polymethyl methacrylate for mechanical stabilization.<sup>[11]</sup> Wang et al<sup>[12]</sup> determined that kyphoplasty was a safe and effective surgical procedure in treating OVCFs and offered a less injected cement volume, better short-term pain relief, better improvement of short- and long-term kyphotic angle, and a lower cement leakage rate. This technique consists of unilateral percutaneous kyphoplasty (UPKP) and bilateral percutaneous kyphoplasty (BPKP) procedures.

In recent years, some meta-analyses have been conducted to evaluate the advantages and disadvantages of the use of UPKP and BPKP in treating OVCFs.<sup>[13–16]</sup> However, although the 2 latest meta-analyses have updated results from the previous reviews, they did not investigate the potential heterogeneity in the sources through either sensitivity analysis or subgroup analysis, which may weaken the reliability of the pooled results, especially if there was large heterogeneity.<sup>[13,14]</sup> There have been additional studies since those reviews were conducted that may further enrich the final results, however. Therefore, this study is intended to evaluate the clinical results of UPKP and BPKP for the treatment of OVCFs according to the following aspects: perioperative outcomes (surgery time, the volume of injected cement, X-ray exposure time, and kyphotic angle reduction); clinical outcomes (visual analogue scale [VAS] for pain relief and Oswestry Disability Index [ODI] for quality of life); and complications (cement leakage and adjacent vertebral fractures).

## 2. Methods

### 2.1. Ethical review

No ethical approval and patient informed consent are required in this article, because all analyses were based on previous published studies.

### 2.2. Search strategy

A search was conducted in Web of Science, PubMed, Embase, and the Chinese Biomedical Database publication databases for all comparative studies published from January 2008 to November 2016 that compared the use of UPKP and BPKP for the treatment of OVCFs. The search terms used included

“osteoporotic vertebral compression fractures,” “unilateral balloon kyphoplasty,” “unipedicular balloon kyphoplasty,” “bipedicular balloon kyphoplasty,” “bilateral balloon kyphoplasty,” “bilateral approach,” and “unilateral approach.”

### 2.3. Eligibility criteria

Studies that met the following criteria were included: patients had primary OVCFs; the treatment interventions used were either UPKP or BPKP; the study made comparisons between UPKP and BPKP; outcomes were reported for at least one of the following factors: surgery time, the volume of injected cement, X-ray exposure time, kyphotic angle reduction, cement leakage, adjacent vertebral fracture, VAS, or ODI; and the study was an RCT or cohort study (CS). Studies were excluded if the study was a duplicate publication, a review, or case report; the study enrolled patients with traumatic fractures, infections, or secondary osteoporosis, such as corticosteroids or endocrine disorders; or the study did not report on the outcomes that were the focus of our meta-analysis.

### 2.4. Data extraction and quality assessment

Two investigators independently collected data from the included studies. Any disagreements were resolved by discussion, or in some cases, a 3rd investigator resolved the conflict. General data from the studies, including first author, year of publication, study design, the number of patients, mean age of the patients (in years), sex ratio (M/F), follow-up (in months), and other outcomes of interest were collected. The assessment of study quality was based on the classic Newcastle Ottawa Scale. Newcastle Ottawa Scale scores ranged from 0 to 9 points, with higher scores indicating better quality.

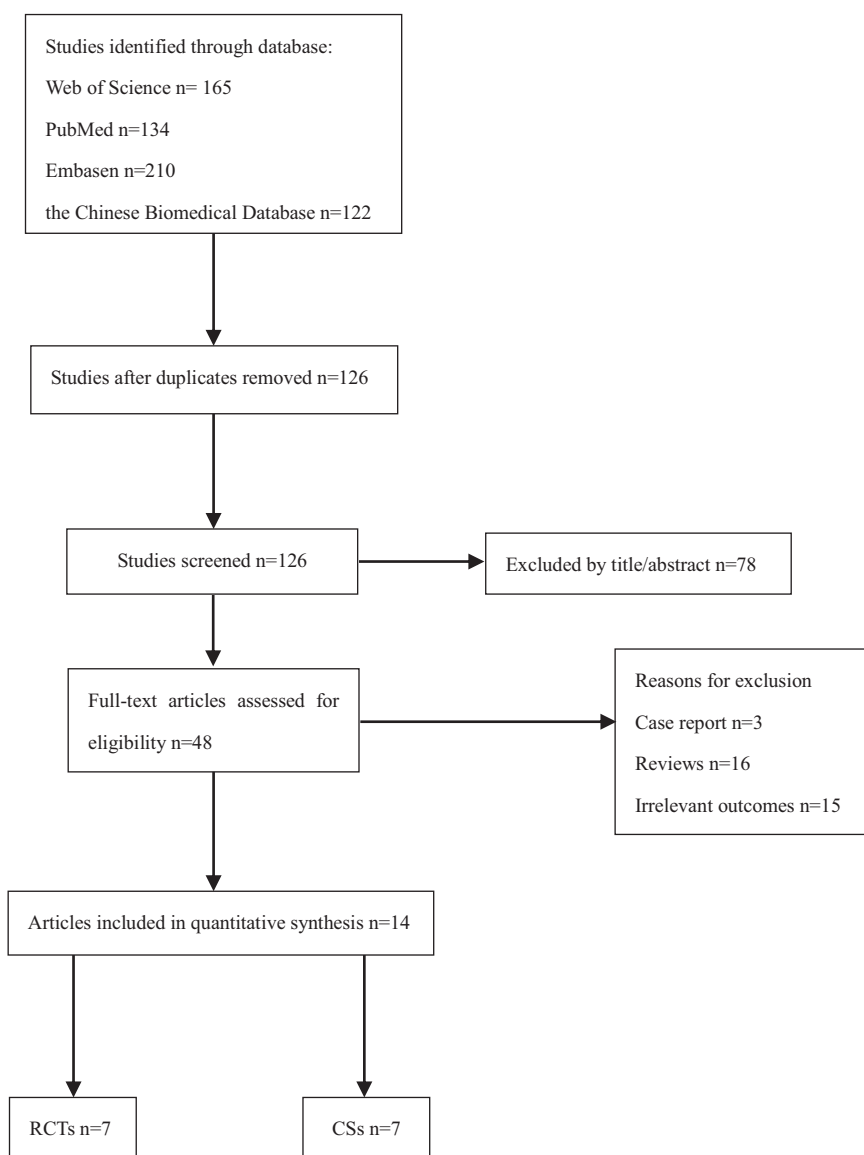
### 2.5. Statistical analyses

All statistical analyses were conducted using Stata/SE11.0 software (Stata Corporation, College Station, TX). For continuous outcomes, weighted mean difference (WMD) and the 95% confidence interval (CI) were calculated. Risk ratio (RR) and the 95% CI were calculated for dichotomous outcomes. Heterogeneity among studies was assessed using  $I^2$  statistics with judging values  $<50\%$  (or  $P > .10$ ) indicating acceptable heterogeneity, and values  $>50\%$  (or  $P < .10$ ) indicating substantial heterogeneity. In the absence of significant heterogeneity, a fixed-effects model was used. Otherwise, a random-effects model was used. For outcome measures, a  $P$  value  $< .05$  was considered statistically significant. Sensitivity analysis was performed using the “metaninf” command in the Stata/SE 11.0 software. A subgroup analysis was then used to determine the potential source of heterogeneity. In cases in which the data had a large sample size ( $>10$ ), a funnel plot analysis was applied to determine publication bias.

## 3. Results

### 3.1. Search results and study description

In total, 631 potential studies in the Web of Science (165), PubMed (134), Embase (210), and the Chinese Biomedical Database (122) publication databases were reviewed. A flow diagram of the article selection process is shown in Fig. 1. Fourteen trials with a total of 1194 patients were retrieved, with the number of patients receiving UPKP and BPKP treatments



**Figure 1.** Flow diagram of article selection process.

measuring at 602 and 592, respectively. Descriptions of the basic characteristics of all studies included in this study are listed in Table 1.<sup>[28,18,20,23,26,17,19,27,25,24,22,21]</sup>

### 3.2. Outcome measures and data on perioperative aspects

Eleven studies provided data for operation times (Fig. 2).<sup>[11,17-26]</sup> There was high evidence of heterogeneity ( $I^2=67.7\%$ ) across these studies. The pooled data indicated significant differences in surgery time (WMD  $-21.44$ , 95% CI  $[-23.57$  to  $-19.30]$ ;  $P<.001$ ) between UPKP and BPKP. Following subgroup analysis, the results based on the RCTs revealed significant differences in surgery time (WMD  $-24.65$ , 95% CI  $[-26.53$  to  $-22.77]$ ;  $P<.001$ ) between the 2 surgical procedures without heterogeneity ( $I^2=0\%$ ) noted between the 2 approaches. The results based on CSs revealed significant differences in surgery time (WMD  $-19.24$ , 95% CI  $[-21.17$  to  $-17.31]$ ;  $P<.001$ ) between the 2 surgical procedures, with

significant heterogeneity ( $I^2=50.3\%$ ) between the 2 approaches observed (Table 2).

Ten studies reported on the volume of injected cement (Fig. 3).<sup>[11,17,19-27]</sup> High heterogeneity ( $I^2=84.9\%$ ) across the studies was observed. The pooled results revealed significant differences in the volume of injected cement (WMD  $-1.90$ , 95% CI  $[-2.26$  to  $-1.54]$ ;  $P<.001$ ) between the UPKP and BPKP procedures. After a subgroup analysis, the results based on RCTs indicated significant differences in the volume of injected cement (WMD  $-1.66$ , 95% CI  $[-1.97$  to  $-1.36]$ ;  $P<.001$ ) between the 2 surgical procedures, with no heterogeneity observed ( $I^2=0\%$ ) between the 2 approaches. Results based on CSs revealed significant differences in the volume of injected cement (WMD  $-2.16$ , 95% CI  $[-2.69$  to  $-1.63]$ ;  $P<.001$ ) between the 2 surgical procedures, and substantial heterogeneity ( $I^2=92.6\%$ ) between the 2 approaches was observed (Table 2).

X-ray exposure time were provided in 5 studies (Fig. 4).<sup>[17,23-25,27]</sup> Heterogeneity across the studies was 97.3%; therefore, a random-effects model was used.

**Table 1**

**Basic characteristics of included 14 studies.**

Number	First author, year	Study design	No of patient		Mean age, y		Sex ratio (M/F)		Follow-up, mo		Outcome of interest	NOS
			UPKP	BPKP	UPKP	BPKP	UPKP	BPKP	UPKP	BPKP		
1	Chung, 2008 <sup>[28]</sup>	RCT	24	28	66.80	68.90	2/22	1/27	17.8	16.6	Cement leakage, kyphotic angle reduction	6
2	Song, 2009 <sup>[9]</sup>	CS	15	30	63.60	69.57	6/9	10/20	NR	NR	Kyphotic angle reduction	5
3	Chen CM, 2010 <sup>[18]</sup>	RCT	33	25	67.73±7.05	68.52±7.26	0/33	0/25	0.5	0.5	Surgery time, cement leakage, ODI	7
4	Chen CM, 2011 <sup>[20]</sup>	RCT	27	23	68.37	69.43	NR	NR	24.0	24.0	Surgery time, the volume of injected cement, cement leakage, adjacent vertebral fractures	7
5	Chen L, 2011 <sup>[11]</sup>	RCT	24	25	70.40	72.40	4/20	4/21	33.5	35.2	Surgery time, the volume of injected cement, cement leakage, Kyphotic angle reduction, adjacent vertebral fractures	6
6	Li 2012 <sup>[23]</sup>	CS	50	41	70.80	73.10	6/44	4/37	36.0	36.0	Surgery time, the volume of injected cement, VAS	6
7	Zou 2012 <sup>[26]</sup>	CS	61	56	67.9±7.10	67.4±7.50	29/88		17.0	17.0	Surgery time, the volume of injected cement, VAS, ODI	6
8	Wang, 2012 <sup>[17]</sup>	CS	31	31	68.30	69.20	13/18	17/14	16.7±2.5	15.9±3.2	Surgery time, the volume of injected cement, cement leakage	5
9	Rebolledo, 2013 <sup>[19]</sup>	RCT	23	21	78.70	79.30	4/19	2/19	12.0	12.0	Surgery time, the volume of injected cement, cement leakage, Kyphotic angle reduction	8
10	He 2014 <sup>[27]</sup>	CS	46	50	70.20	71.30	14/32	16/34	34.6	34.6	VAS	6
11	Li 2014 <sup>[25]</sup>	RCT	38	37	71.13±8.71	67.65±6.30	13/25	10/27	24.0	24.0	Surgery time, the volume of injected cement, cement leakage, adjacent vertebral fractures	7
12	Liu 2014 <sup>[24]</sup>	RCT	38*	40	71.20±5.60	71.90±6.40	15/25	16/24	24	24	Surgery time, the volume of injected cement, cement leakage, adjacent vertebral fractures, VAS	7
13	Zhu 2014 <sup>[22]</sup>	CS	34	34	73.70±5.60	75.80±6.00	10/24	13/21	76.2±2.9	17.1±3.7	Surgery time, the volume of injected cement, VAS	6
14	Yan, 2014 <sup>[21]</sup>	CS	158	151	71.90	71.10	NR	NR	12.0	12.0	Surgery time, the volume of injected cement, cement leakage, Kyphotic angle reduction, adjacent vertebral fractures, VAS	5

BPKP = bilateral percutaneous kyphoplasty, CS = cohort study, NOS = Newcastle Ottawa Scale, NR = not reported, ODI = Oswestry Disability Index, RCT = randomized controlled trial, UPKP = unilateral percutaneous kyphoplasty, VAS = visual analogue scale.  
 \* Due to the failure of cement injection, 2 cases in this study dropped out.

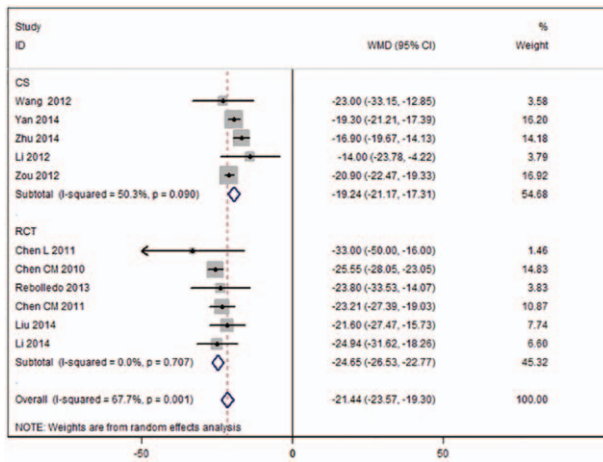


Figure 2. Forest plot of surgery time.

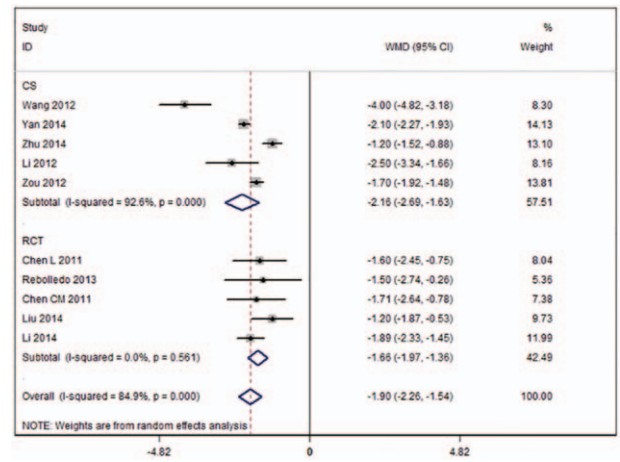


Figure 3. Forest plot of the volume of injected cement.

Meta-analysis results demonstrated significant differences in X-ray exposure time (WMD -13.66, 95% CI [-19.59 to -7.72];  $P < .001$ ) between the 2 surgical procedures. Following subgroup analysis, the identified results based on RCTs indicated that there were significant differences in X-ray exposure time (WMD -17.05, 95%CI [-34.29 to 0.19];  $P < .001$ ) between the UPKP and BPKP procedures, while the results based on CSs indicated that there were no significant differences in X-ray exposure time (WMD -10.43, 95%CI [-16.13 to -4.72];  $P = .053$ ) between the 2 surgical procedures. The heterogeneity across the studies after subgroup analysis was more than 96.1% for both the RCTs and CSs (Table 2).

Kyphotic angle reduction was provided in 4 studies (Fig. 5).<sup>[9,11,19,21]</sup> Heterogeneity across these studies was 85.3%, so a random-effects model was used. Meta-analysis results demonstrated that there were no differences in kyphotic angle reduction (WMD 1.19, 95%CI [-1.38 to 3.76];  $P = .365$ )

between the 2 surgical procedures. Following subgroup analysis, the results based on RCTs indicated that there were no significant differences in kyphotic angle reduction (WMD 0.02, 95% CI [-1.94 to 1.97];  $P = .987$ ) between the UPKP and BPKP procedures without heterogeneity ( $I^2 = 0%$ ) across the 2 approaches. The results based on the CSs indicated that there were no significant differences in kyphotic angle reduction (WMD 2.16, 95%CI [-1.38 to 5.70];  $P = .053$ ) between the 2 surgical procedures. The heterogeneity across the studies was 88.6% (Table 2).

### 3.3. Clinical outcomes

Four studies included in this meta-analysis reported VAS in the short-term (ie, a maximum of 1 month of follow-up) (Fig. 6).<sup>[23,24,26,27]</sup> No heterogeneity across these studies was observed ( $I^2 = 0%$ ), and no statistically significant differences in

**Table 2**  
Meta-analysis of all outcomes and subgroup analysis for significant outcomes with the heterogeneity.

Outcomes of interest	Study design	No of studies	$I^2$ , %	WMD or RR (95%CI)	P	
Perioperative outcomes						
	Surgery time	RCT + CS	11	67.7	-21.44 (-23.57 to -19.30)	.001*
		RCT	6	0	-24.65 (-26.53 to -22.77)	.001*
The volume of injected cement						
		CS	5	50.3	-19.24 (-21.17 to -17.31)	.001*
		RCT + CS	10	84.9	-1.90 (-2.26 to -1.54)	.001*
X-ray exposure time						
		RCT	5	0	-1.66 (-1.97 to -1.36)	.001*
		CS	5	92.6	-2.16 (-2.69 to -1.63)	.001*
Kyphotic angle reduction						
		RCT + CS	4	85.3	1.19 (-1.38 to 3.76)	.365
		RCT	2	0	0.02 (-1.94 to 1.97)	.987
Clinical outcomes						
		CS	2	88.6	2.16 (-1.38 to 5.70)	.223
	VAS in the short-term	RCT + CS	4	0	-0.06 (-0.32 to 0.20)	.638
VAS in the long-term	RCT + CS	5	0	0.07 (-0.09 to 0.22)	.390	
ODI	RCT + CS	2	0	-0.95 (-2.72 to 0.81)	.290	
Surgery-related complications						
	Cement leakage	RCT + CS	10	0	0.71 (0.50 to 1.02)	.062
Adjacent vertebral fracture	RCT + CS	5	0	0.73 (0.38 to 1.40)	.341	

$I^2$ , heterogeneity statistic. \* $P < .001$ . CI = confidence interval, CS = cohort study, ODI = Oswestry Disability Index, RCT = randomized controlled trial, RR = risk ratio, VAS = visual analogue scale, WMD = weighted mean difference.



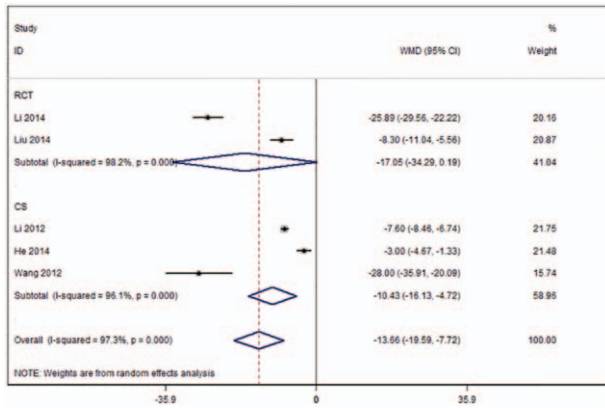


Figure 4. Forest plot of X-ray exposure time.

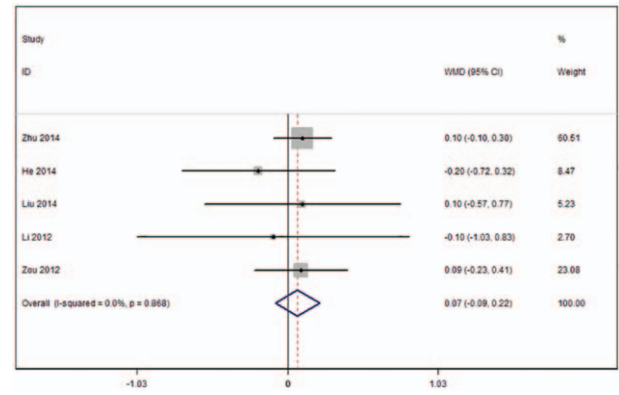


Figure 7. Forest plot of visual analogue scale (VAS) in the long-term ( $\geq 1$  year follow-up).

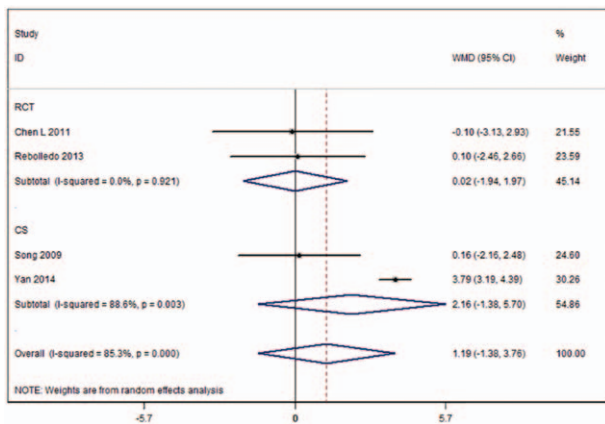


Figure 5. Forest plot of the volume for kyphotic angle reduction.

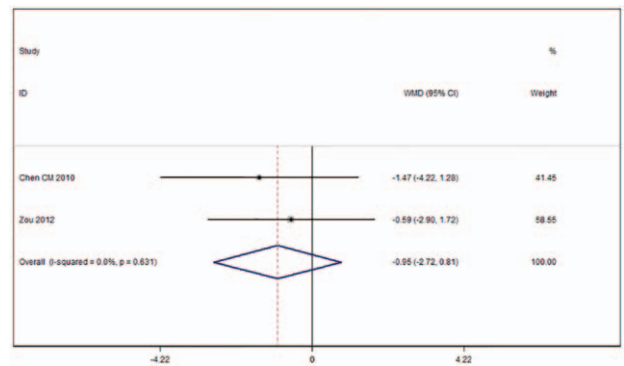


Figure 8. Forest plot of Oswestry Disability Index (ODI).

VAS after either form of kyphoplasty were found (WMD  $-0.06$ , 95% CI  $[-0.32$  to  $0.20]$ ;  $P = .638$ ).

Five studies were included in this meta-analysis that reported VAS for follow-up periods  $\geq 1$  year (Fig. 7).<sup>[22–24,26,27]</sup> No heterogeneity across these studies was observed ( $I^2 = 0\%$ ) and the pooled results showed no significant differences in VAS for at least 1 year of follow-up (WMD  $0.07$ , 95% CI  $[-0.09$  to  $0.22]$ ;  $P = .390$ ) between the 2 surgical procedures.

Regarding ODI, 2 studies met the eligibility criteria for consideration (Fig. 8).<sup>[18,26]</sup> There was no heterogeneity across these studies ( $I^2 = 0\%$ ). The ODI for UPKP was similar to that for BPKP (WMD  $-0.95$ , 95% CI  $[-2.72$  to  $0.81]$ ;  $P = .290$ ).

### 3.4. Surgery-related complications

Ten studies reported occurrences of cement leakage in the 2 procedure groups, with a heterogeneity test showing relatively low statistically significant heterogeneity between the groups ( $I^2 = 0\%$ ) (Fig. 9).<sup>[11,17–21,24–26,28]</sup> Meta-analysis results indicated

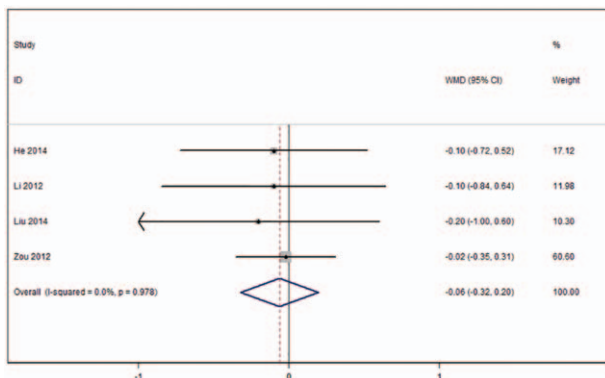


Figure 6. Forest plot of visual analogue scale (VAS) in the short-term ( $\leq 1$  month follow-up).

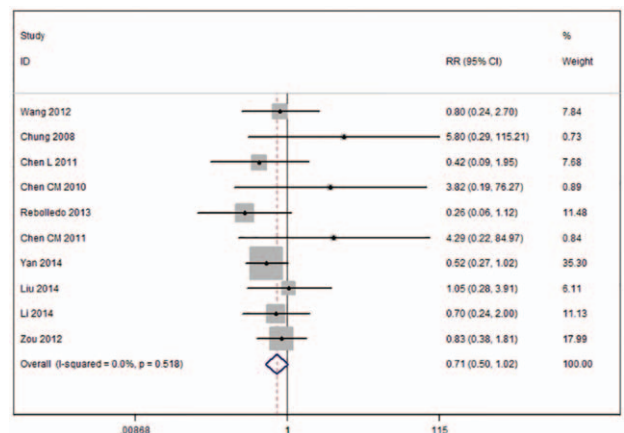


Figure 9. Forest plot for volume of cement leakage.

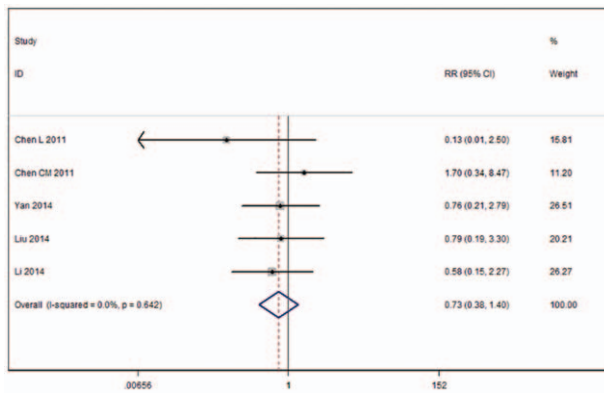


Figure 10. Forest plot for adjacent vertebral fractures.

that there was no significant difference in occurrence of cement leakage between the 2 groups (RR 0.71, 95%CI [0.50–1.02];  $P=0.062$ ).

Five of the included studies reported occurrences of adjacent vertebral fractures (Fig. 10).<sup>[11,20,21,24,25]</sup> No statistically significant heterogeneity was found between the 2 groups ( $I^2=0\%$ ), and a fixed-effects model was applied for meta-analysis. The number of adjacent vertebral fractures among patients receiving UPKP was not higher than among those receiving BPKP (RR 0.73, 95% CI [0.38–1.40];  $P=.341$ ).

### 3.5. Sensitivity analysis

Sensitivity analysis was performed using the “metaninf” command in Stata/SE 11.0 software. Any single elimination of these studies did not have an influence on the overall outcomes that were assessed.

### 3.6. Publication bias

Due to the large sample size ( $\geq 10$ ) in this meta-analysis, the outcomes that were pooled, such as surgery time and the volume of injected cement, were applicable for funnel plot analysis (Figs. 11 and 12). The funnel plots not only showed asymmetry but also had 2 outliers.

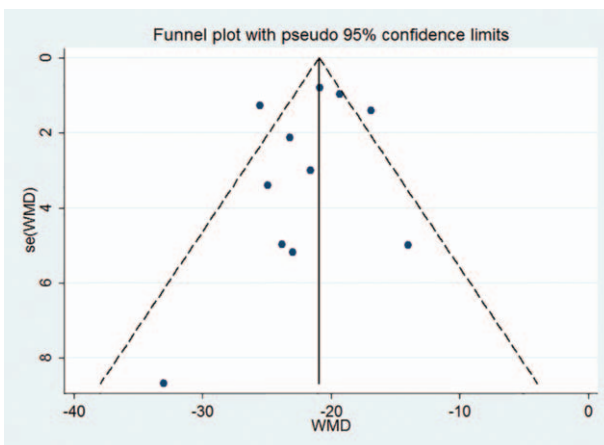


Figure 11. Funnel plot for surgery time.

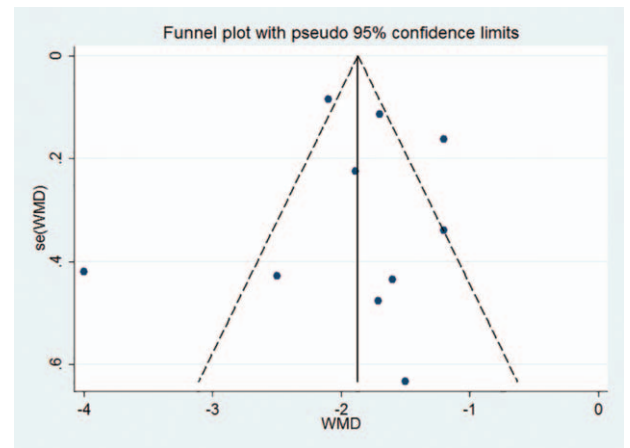


Figure 12. Funnel plot for the volume of injected cement.

## 4. Discussion

Kyphoplasty is an effective and safe treatment choice for the management of OVCFs in the elderly, and involves realigning the spinal column and restoring the compressed vertebral body height.<sup>[29]</sup> Specific kyphoplasty treatment options include UPKP and BPKP. Nevertheless, the optimal surgical procedure for OVCFs is still being debated. The objective of our study was to gather as much data as possible to ascertain which procedure (ie, UPKP or BPKP) is superior. Overall, we included 14 studies with 1194 patients in our study. Our meta-analysis found that UPKP was associated with shorter surgery time and lower volumes of injected cement. However, there were no significant differences in VAS, ODI, X-ray exposure time, kyphotic angle reduction, cement leakage, or adjacent vertebral fracture between the 2 surgical procedures.

Compared to UPKP, BPKP theoretically required twice as much cement injection volume, which yielded stronger stability for the vertebral body. Moreover, the stabilization of the vertebral body was probably beneficial to pain relief.<sup>[30,31]</sup> Therefore, we concluded that the BPKP procedure can produce more satisfactory pain relief and a more significant improvement in quality of life in patients with OVCFs. Both VAS for pain relief and ODI for life quality improvement were used to assess the clinical outcomes of the 2 surgical procedures. However, although we divided the final follow-up times into short-term ( $\leq 1$ -month follow-up) and long-term ( $\geq 1$ -year follow-up) groups, our pooled results did not indicate an advantage of the BPKP procedure over UPKP in terms of either the short-term VAS or the long-term VAS without heterogeneity across the studies. This result was also confirmed in another study by Chen et al<sup>[20]</sup> that reported that both VAS and ODI for BPKP were similar to that for UPKP.

This study demonstrated that patients undergoing UPKP procedures needed less surgery time, less injected cement, and had lower radiation exposure time compared to those undergoing BPKP. However, there was great heterogeneity between the 2 procedures. To investigate potential sources of heterogeneity, we conducted a sensitivity analysis and found that the single elimination of these studies did not have an influence on the pooled outcomes that were assessed. However, when a subgroup analysis was conducted according to the type of studies that were included, we found that the heterogeneity between the 2 groups

disappeared after the removal of the CSs. Based on that analysis, we inferred that the heterogeneity across the 2 procedures in surgery time and the volume of injected cement primarily arose from the presence of the CSs. Nevertheless, the results identified after subgroup analysis demonstrated that the UPKP group had no differences in X-ray exposure time as compared with the BPKP group, which contrasted the result that we obtained before subgroup analysis. Moreover, substantial heterogeneity across all of the studies still existed. Based on our statistical analysis, the potential heterogeneity may not be due to the study design, but could be attributed to the presence of 2 of the RCTs that were included. Thus, we should be very careful in interpreting the meta-analysis results, especially the results that are based on a relatively small number of studies. Finally, we believed that our results were reliable, except for X-ray exposure time. Compared to BPKP procedures, patients undergoing UPKP required less surgery time and less injected cement.

With regard to the type of vertebral body fracture, there were 7 studies reporting anterior wedging, 6 reporting centrally scalloping, and 1 reporting posterior wedging, respectively.<sup>[11,17,22,24–27]</sup> Because the original studies evaluated did not regard the type of fracture as a confounding factor affecting the efficacy of surgery, therefore, we could not perform the necessary meta-analysis and thus, were not able to determine whether the type of fracture was one of the factors affecting the efficacy of kyphoplasty.

In this study, we did not perform a meta-analysis reporting compressed vertebral body height and its restoration. Due to different definitions of compressed vertebral body height in the included RCTs, we were unable to gather comparable data to evaluate compressed vertebral body height. Khurjekar et al<sup>[32]</sup> and Muto et al<sup>[33]</sup> reported that kyphotic angle reduction may be a more important measure than the restoration of compressed vertebral body height in kyphoplasty. The results demonstrated the UPKP group had no more kyphotic angle reduction than as compared with the BPKP group. However, it is worth noting that the heterogeneity across the studies was 85.3%. Although Feng et al<sup>[13]</sup> also performed a meta-analysis for kyphotic angle reduction with 85% heterogeneity, they did not explore the potential sources of heterogeneity further. Unlike the study by Feng et al, we conducted a subgroup analysis for kyphotic angle reduction and found that the heterogeneity across the studies was 0% after the CSs were removed. Thus, we believed that the heterogeneity was due to CSs. Overall, there were no differences in kyphotic angle reduction and no heterogeneity between the 2 procedures was indicated.

A concern about using cement to treat OVCFs was cement leakage. It was reported that cement leakage through the posterior cortex or the pedicle after removal of the trocar may result in paraparesis.<sup>[34,35]</sup> The cement injection volume has a positive correlation with cement leakage.<sup>[36]</sup> In fact, 2 mL of polymethyl methacrylate cement has been shown to have enough power to restore the strength of a compressed vertebral body.<sup>[37]</sup> Too much cement, however, is a substantial risk factor for cement leakage.<sup>[16]</sup> In a BPKP procedure, cement is injected through 2 pedicles, which requires twice the volume of cement used in a UPKP procedure. The cemented vertebrae that result can change the biomechanics of the spine and subsequently increase the incidence of new adjacent vertebral fractures.<sup>[38]</sup> Accordingly, we predicted that patients who had undergone BPKP would have higher incidences of cement leakage and adjacent vertebral fractures as compared to patients who had undergone UPKP. However, our results did not support this hypothesis. We may

have ignored possible risk factors, such as injection pressure. Robinson et al<sup>[39]</sup> compared balloon pressure in fresh fractures and in partially healed compression fractures and found that patients with fresh fractures needed more pressure. Excessive pressure on a partially healed compression fracture was more likely to lead to cement leakage. As such, surgeons should pay close attention to the relationship between the treatment time for the fracture and the pressure of the injected cement.

In terms of surgery time and the volume of injected cement, the funnel plots not only showed asymmetry but also 2 outliers. This publication bias was likely due to the low quality of some of the studies that were included. Additionally, many of the selected studies were conducted in Asia, which may also have resulted in a degree of selection bias.

## 5. Limitations

This study has some limitations. First, low-quality studies that were included might have weakened the strength of our analysis. Second, the type of bone cement was not all described in the selected articles, and we did not analyze this factor at this time. Third, the time from fracture to treatment ranged from less than 1 week to more than 6 months, which may have had an impact on surgical effectiveness.<sup>[18,20,25]</sup> However, no useful data could be collected and analyzed for the determination of the impact of this factor. Therefore, this study does not report the timing from the presumed onset of the fracture to the treatment on the clinical outcomes. Fourth, the loss of vertebral height assessing the degree of the vertebral body compression was not stated, since the RCTs included in our meta-analysis applied different definitions of compressed vertebral body. It is desirable to have uniform standards for the measurement of vertebral height changes in future RCTs.

## 6. Conclusion

Compared to BPKP, UPKP can achieve similar clinical results for the treatment of OVCFs when assessed in terms of pain relief, improvement of life quality, and presence and significance of surgery-related complications. However, the UPKP procedures evaluated had shorter operation time and a lower volume of injected cement compared to the BPKP procedures. Additional high quality and multicenter RCTs are needed to provide further robust evidence for consideration.

## References

- [1] Cohen LD. Fractures of the osteoporotic spine. *Orthop Clin North Am* 1990;21:143–50.
- [2] Klotzbuecher CM, Ross PD, Landsman PB, et al. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner Res* 2000;15:721–39.
- [3] Phillips FM. Minimally invasive treatments of osteoporotic vertebral compression fractures. *Spine* 2003;28(15 Suppl):S45–53.
- [4] Kroon F, Staples M, Ebeling PR, et al. Two-year results of a randomized placebo-controlled trial of vertebroplasty for acute osteoporotic vertebral fractures. *J Bone Miner Res* 2014;29:1346–55.
- [5] Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med* 2009;361:557–68.
- [6] Guyatt GH. Evidence-based management of patients with osteoporosis. *J Clin Densitom* 1998;1:395–402.
- [7] Guyatt GH, Sinclair J, Cook DJ, et al. Users' guides to the medical literature: XVI. How to use a treatment recommendation. Evidence-Based Medicine Working Group and the Cochrane Applicability Methods Working Group. *JAMA* 1999;281:1836–43.



- [8] Buchbinder R, Golmohammadi K, Johnston RV, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. *Cochrane Library* 2015;DOI: 10.1002/14651858.CD006349.pub2.
- [9] Song BK, Eun JP, Oh YM. Clinical and radiological comparison of unipedicular versus bipedicular balloon kyphoplasty for the treatment of vertebral compression fractures. *Osteoporos Int* 2009;20:1717–23.
- [10] Hoffmann RT, Jakobs TF, Wallnofer A, et al. Percutaneous vertebroplasty (pv): indications, contraindications, and technique. *Radiologe* 2003;43:709–17.
- [11] Chen L, Yang H, Tang T. Unilateral versus bilateral balloon kyphoplasty for multilevel osteoporotic vertebral compression fractures: a prospective study. *Spine* 2011;36:534–40.
- [12] Wang H, Sribastav SS, Ye F, et al. Comparison of percutaneous vertebroplasty and balloon kyphoplasty for the treatment of single level vertebral compression fractures: a meta-analysis of the literature. *Pain Physician* 2015;18:209–22.
- [13] Feng H, Huang P, Zhang X, et al. Unilateral versus bilateral percutaneous kyphoplasty for osteoporotic vertebral compression fractures: a systematic review and meta-analysis of RCTs. *J Orthop Res* 2015;33:1713–23.
- [14] Chen H, Tang P, Zhao Y, et al. Unilateral versus bilateral balloon kyphoplasty in the treatment of osteoporotic vertebral compression fractures. *Orthopedics* 2014;37:e828–35.
- [15] Huang Z, Wan S, Ning L, et al. Is unilateral kyphoplasty as effective and safe as bilateral kyphoplasties for osteoporotic vertebral compression fractures? A meta-analysis. *Clin Orthop Relat Res* 2014;472:2833–42.
- [16] Yang LY, Wang XL, Zhou L, et al. A systematic review and meta-analysis of randomized controlled trials of unilateral versus bilateral kyphoplasty for osteoporotic vertebral compression fractures. *Pain Physician* 2013;16:277–90.
- [17] Wang Z, Wang G, Yang H. Comparison of unilateral versus bilateral balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. *J Clin Neurosci* 2012;19:723–6.
- [18] Chen C, Chen L, Gu Y, et al. Kyphoplasty for chronic painful osteoporotic vertebral compression fractures via unipedicular versus bipedicular approach: a comparative study in early stage. *Injury* 2010;41:356–9.
- [19] Rebolledo BJ, Gladnick BP, Unnanuntana A, et al. Comparison of unipedicular and bipedicular balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. *Bone Joint J* 2013;95:401–6.
- [20] Chen C, Wei H, Zhang W, et al. Comparative study of kyphoplasty for chronic painful osteoporotic vertebral compression fractures via unipedicular versus bipedicular approach. *J Spinal Disord Tech* 2011;24:E62–5.
- [21] Yan L, Jiang R, He B, et al. A comparison between unilateral transverse process-pedicle and bilateral puncture techniques in percutaneous kyphoplasty. *Spine* 2014;39(26 Spec No.):B19–26.
- [22] Zhu Y, Zhang N, Ren W. Unilateral versus bilateral percutaneous kyphoplasty for osteoporotic vertebral compression fractures. *Chin J Gen Pract* 2014;12:1941–4.
- [23] Li Q, Li M, Zheng C. Unilateral versus bilateral percutaneous kyphoplasty for the treatment of osteoporotic compression fracture: a prospective case control study. *Med J Wuhan Univ* 2012;33:567–70.
- [24] Liu X, Wang X, Zuo C, et al. The randomized controlled study of unilateral versus bilateral percutaneous kyphoplasty for the treatment of elderly osteoporotic vertebral compression fractures. *J Cervicodyn Lumbodyn* 2014;35:266–70.
- [25] Li L, Wang M, Ma H, et al. Comparison of unilateral and bilateral penetrating kyphoplasty for osteoporotic centrum compression fractures. *Orthop J China* 2014;22:678–82.
- [26] Zou D, Zhou D, Zhang K, et al. Treatment of thoracolumbar osteoporotic vertebral compression fractures by unilateral or bilateral percutaneous kyphoplasty. *Orthop J China* 2012;20:108–11.
- [27] He C, Yang A. Effects of unipedicular versus bipedicular kyphoplasty for treatment of osteoporosis vertebral compression fractures. *Chin J Bone Joint Injury* 2014;29:227–9.
- [28] Chung HJ, Chung KJ, Yoon HS, et al. Comparative study of balloon kyphoplasty with unilateral versus bilateral approach in osteoporotic vertebral compression fractures. *Int Orthop* 2008;32:817–20.
- [29] Garfin SR, Yuan HA, Reiley MA. New technologies in spine: kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures. *Spine* 2001;26:1511–5.
- [30] Deramond H, Depriester C, Toussaint P, et al. Percutaneous vertebroplasty. *Semin Musculoskelet Radiol* 1997;1:285–96.
- [31] Lemke DM, Haccinbey L. Metastatic compression fractures – vertebroplasty for pain control. *J Neurosci Nurs* 2003;35:50–5.
- [32] Khurjekar K, Shyam AK, Sancheti PK, et al. Correlation of kyphosis and wedge angles with outcome after percutaneous vertebroplasty: a prospective cohort study. *J Orthop Surg* 2011;19:35–40.
- [33] Muto M, Marcia S, Guarnieri G, et al. Assisted techniques for vertebral cementoplasty: why should we do it? *Eur J Radiol* 2014;84:783–8.
- [34] Ohba T, Ebata S, Clinton D, et al. Instability of treated vertebrae after balloon kyphoplasty causing paraparesis in osteoporotic vertebral compression fracture: a report of two cases. *Eur Spine J* 2013;22:341–5.
- [35] 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 Neuro-radiol* 2010;31:504–8.
- [36] Phillips FM, Todd WF, Lieberman I, et al. An in vivo comparison of the potential for extravertebral cement leak after vertebroplasty and kyphoplasty. *Spine* 2002;27:2173–8.
- [37] Belkoff SM, Mathis JM, Jasper LE, et al. The biomechanics of vertebroplasty. The effect of cement volume on mechanical behavior. *Spine* 2001;26:1537–41.
- [38] Tanigawa N, Komemushi A, Kariya S, et al. Relationship between cement distribution pattern and new compression fracture after percutaneous vertebroplasty. *Am J Roentgenol* 2007;189:348–52.
- [39] Robinson Y, Heyde CE, Forsth P, et al. Kyphoplasty in osteoporotic vertebral compression fractures – guidelines and technical considerations. *J Orthop Surg Res* 2011;6:1–8.