review

Balloon kyphoplasty or percutaneous vertebroplasty for osteoporotic vertebral compression fracture? An updated systematic review and meta-analysis

Lin Liang,[a*] Xinlei Chen,[b*] Weimin Jiang,[c] Xuefeng Li,[c] Jie Chen,[c] Lijun Wu,[a] Yangyi Zhu[a]

From the [a]Department of Orthopaedics, Shangyu People's Hospital, Shaoxing, China; [b]Department of Orthopaedics, The Affiliated Hospital of Nantong University, Nantong, China; [c]Department of Orthopaedics, The First Affiliated Hospital of Soochow University, Suzhou, China

Correspondence: Prof. Yangyi Zhu · Department of Orthopaedics, Shangyu People's Hospital, University, No. 899 Pinghai Road, Suzhou 215006, China Shaoxing 312000, China · F: 86057581266120 · boss2014jaing@163.com · ORCID ID: orcid.org/0000-0002-2654-8360.

*Both authors equally contributed to this study.

Ann Saudi Med 2016; 36(3): 165-174

DOI: 10.5144/0256-4947.2016.165

BACKGROUND: Both kyphoplasty (KP) and vertebroplasty (VP) are effective for patients with osteoporotic vertebral compression fracture (OVCF), but which approach might be more effective remains unclear, so we decided to update earlier systematic reviews.
OBJECTIVE: Review and analyze studies published as of August 2015 that compared clinical outcomes and complications of KP versus VP.
DESIGN: Systematic review and meta-analysis.
SEARCH METHOD: Published reports up to August 2015 were found in PubMed, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL).
SELECTION CRITERIA: Randomized controlled trials (RCTs) and prospective and retrospective cohort studies comparing KP and VP in patients with OVCF.
DATA COLLECTION AND ANALYSIS: Two authors independently assessed the studies and extracted data.
RESULTS: Thirty-two studies involving 3274 patients fulfilled the inclusion criteria. There were significant differences between the two groups in short- and long-term postoperative changes in measures of pain intensity and dysfunction (P<.01), in anterior and middle height (P<.01), kyphotic angle (P<.01), and time to injury, but not in posterior height (P=.178). There were no significant differences in the rate of postoperative fractures including adjacent and total fractures, but cement leakage to the intraspinal space was greater in the VP group (P=.035). KP surgery took longer and required a greater volume of injected cement.
CONCLUSIONS: KR resulted in better pain relief, improvements in Oswestry dysfunction and radiographic outcomes with less cement leakage, but further RCTs are needed to verify this conclusion.
LIMITATIONS: Only four RCTs with a certain of risk of bias. Most studies were observational.

The increasing elderly population throughout the globe has brought increasing attention to osteoporosis, the most important cause osteoporotic vertebral compression fractures (OVCF).[1,2] OVCF has a prevalence of more than 30% in the population older than 65 years.[3] OVCF is associated with acute and chronic pain, progressive spinal deformity, a decreased quality of life, impaired physical function and increasing mortality.[4-8]

One method to treat OVCF is conservative nonsurgical management (NSM) which consists of bed rest, use of painkillers, and bracing.[9] However, NSM does not improve vertebral height[10] or reverse kyphotic deformities, and has undesirable effects such as bedsores, bone demineralization and deep vein thrombosis.[11] Since 1987, vertebroplasty (VP) and kyphoplasty (KP) with polymethylmethacrylate (PMMA) augmentation has been increasingly advocated as treatment for

OVCF.[12,13] Both of these minimally invasive techniques increase bone strength and reduce pain. Recently, two randomized controlled trials (RCT) showed that both methods were effective in reducing immediate pain, unlike conservative treatment.[14,15] Several studies have shown that KP achieves better restoration of the kyphotic angle and vertebral height compared with VP[16-18] Furthermore, KP reduced the cement leakage rate compared with VP.[19,20]

The comparative effectiveness and complications of KP and VP have been assessed in a few systematic reviews and meta-analysis, all which pooled randomized contolled trials with observational studies. This systematic review updates previous analyses.[21-25]

PATIENTS AND METHODS

Literature search

We performed a comprehensive systematic computer-based literature search of published reports before August 2015 in PubMed, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL). The reference lists of the selected studies were also searched. The search terms were: "kyphoplasty" or "KP" AND "vertebroplasty" or "VP" AND "vertebral fracture" AND "osteoporotic" or "osteoporosis". We selected randomized controlled trials (RCTs) and prospective and retrospective cohort studies that compared KP with VP with no language restrictions. The protocol was not registered.

Inclusion/Exclusion criteria

The inclusion criteria were that studies be comparative studies (RCTs, prospective and retrospective cohort studies) comparing KP and VP in patients with OVCF. Outcomes had to include the postoperative time to injury, the duration of the operation, pain relief and quality of life, postoperative radiographic data and complications. Studies were excluded from our meta-analysis if they were of vertebral fractures caused by any etiology other than osteoporosis, including neoplastic or invasive, infective and traumatic fracture. Studies involving any type of cement other than PMMA cement were excluded.

Quality assessment and data extraction

RCTs were carefully assessed by two authors (LL and XLC) and any disagreement resolved through discussion. Determination of the risk of bias in the RCTs included the following key domains: adequate sequence generation, allocation concealment, blinding, incomplete outcome data, free from selective reporting, and free from other bias. The prospective and retrospective cohort studies were assessed by the methodological index for non-randomized studies (MINORS), a validated instrument designed to assess the quality of comparative or non-comparative non-RCT studies. LL and XLC independently extracted the data from each article with a standard data extraction form. The data included authors, year of publication, study design, age of population, gender, numbers of vertebral bodies, surgical procedures, duration of follow-up and outcomes parameters. The extracted data were analyzed by YYZ.

Clinical outcomes

Pain intensity and functional disability was measured using the visual analog scale (VAS) and the Oswestry Disability Index (ODI). Radiographic outcomes included the height of the vertebral body (anterior, middle and posterior) and the kyphotic angle. Complication outcomes were cement leakage and new vertebral fracture. Injury time, operation time and the volume of injected cement were also extracted from the reports.

VAS and ODI were extracted and summarized by short-term (less than one week) and long-term (more than six months) follow-up. We defined the short-term period as less than one week and the long-term period as no less than 6 months.[25] If there were several time points in the long-term follow-up, we selected the longest follow-up. We defined the postoperative period as the first day after surgery and improvement as any change between the preoperative and postoperative periods.

Complications

We classified cement leakage as any intraspinal and extraspinal leakage. Intraspinal leakage means that cement leaked into the intraspinal space, including the disc and vertebral body; if cement leaked into an extraspinal space such as the external venous plexus, epidural tissue or spinal canal, we considered that extraspinal leakage. Fractures included re-fracture of the same postoperative vertebral body and fractures of an adjacent vertebral body.

Statistical analysis

We performed all meta-analysis with Stata version 12.0 (StataCorp, College Station, TX). For dichotomous outcomes, the odds ratio (OR) and the 95% confidence interval (95% CI) were assessed. For continuous outcomes, means and standard deviations were pooled to a weighted or standardized mean difference (WMD or SMD), a weighting by the individual variances for each study, and the 95% CI. A probability of $P<.05$ was regarded as statistically significant. Statistical heterogeneity was assessed using Q statistics. Analysis of the outcomes was divided to subgroups according to the time or the region, if possible. For the variables - extraspinal and total leakage, adjacent and total new fracture, posterior height-postoperation, we used a fixed-effects model; for the rest, we used a random-effects model.

RESULTS

Study characteristics

Of 1300 titles and abstracts reviewed preliminarily, 32 met the inclusion criteria for the meta-analysis.[17,26-56] (**Figure 1**). They included 4 RCTs,[27,31,41,53] 14 prospective cohort studies,[17,32,33,36,39,40,41-49,54] and 14 retrospective cohort studies[26,28-30,34,35,37,38,42,50-52,55,56] (**Figures 2 and 3**). There were a total of 3274 patients; 1653 patients underwent the KP surgery and 1621 underwent VP surgery. Individual study sample sizes ranged from 41 to 381 patients. The demographic characteristics of patients are summarized in **Table 1**.

Clinical outcomes

Eighteen studies reported short-term follow-up VAS scores.[17,28,30,31,33,35,36,38-42,47,49-52,55] There was a significant difference between KP and VP (WMD=-0.2, 95% CI=-0.27 to-0.63; *P*<.01). Long-term VAS scores were available from 14 studies.[17,28,30,32,35,36,38,41,45,47,49,51] The pooled result also showed a significant difference between the two groups (WMD=-0.46, 95% CI=-0.57 to -0.36; *P*<.01) (**Figure 4 and Table 2**). Adequate data on short-term ODI scores was present in 7 studies[17,31,35,38,39,47,50] and the difference in overall estimate was statistically significant (WMD-17.56, 95% CI=-18.07 to -17.05; *P*<.01). Eight studies provided long-term ODI data.[17,30,35,36,38-40,47] There was a significant difference between KP and VP (WMD=-2.41, 95% CI= -3.44 to -1.38; *P*<.01) (**Figure 5 and Table 2**).

The dates of injury were available for four trials.[40,41,48,55] The pooled results demonstrated no significant difference between the KP and VP group (WMD=-1.31, 95% CI=-3.37 to 0.75; *P*<.01). Five reports reported the mean and standard deviation for operation time.[27,31,41,43,51] VP required less time for the surgical procedure (WMD=6.58, 95% CI=5.47 to 7.68; *P*<.01) than the KP group (**Table 2**). The reported volume of injected cement analyzed in 12 studies[26,27,38,39,41,44-46,52,53,55,56] was greater in the KP group (WMD=0.51, 95% CI=0.44 to 0.56; *P*<.01) (**Figure 6 and Table 2**).

Radiographic outcome

In the 14 studies that reported the postoperative anterior height of the vertebral body,[17,26,28,30,35,36,41,43,47,48,50-53]

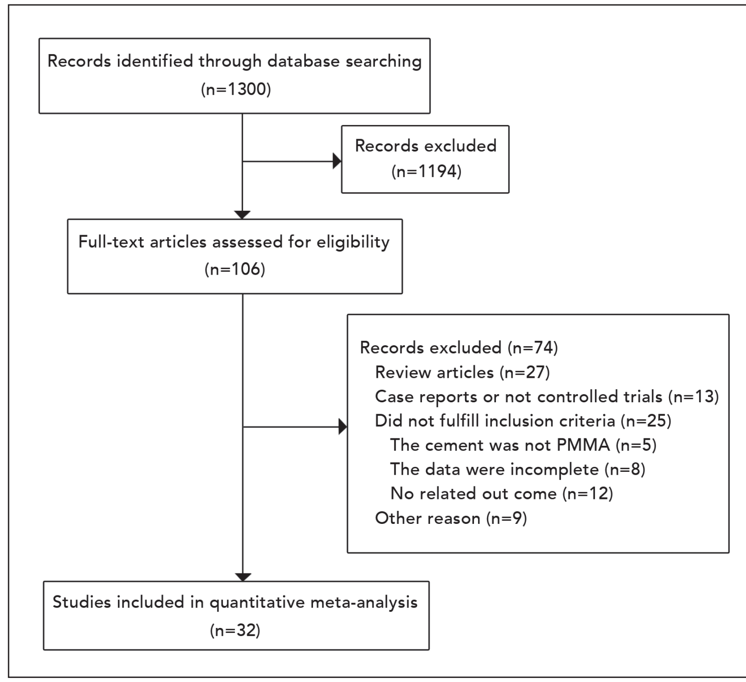

Figure 1. Flow diagram for selection of articles in the meta-analysis..

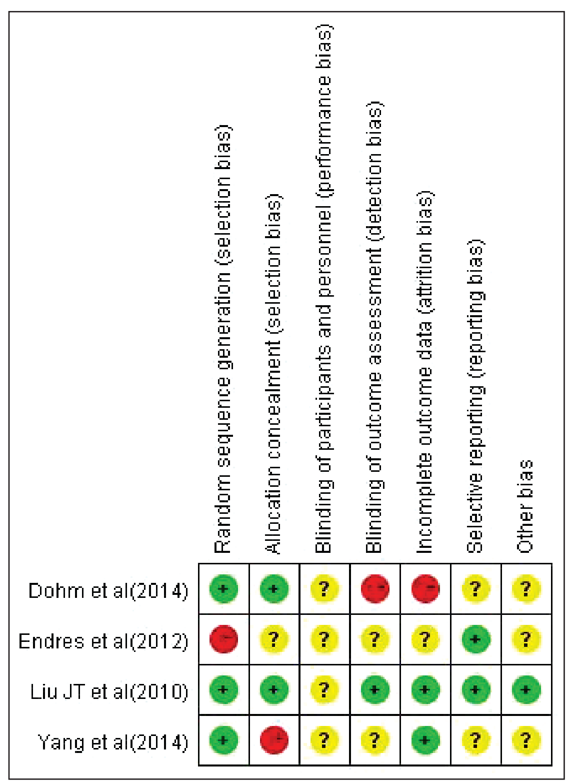

Figure 2. Methodological quality of the randomized controlled trials (n=4) showing risk-of-bias assessment.

Table 1. Patient demographic and study characteristics of the 32 studies in the meta-analysis.

Study	Country	Year	Study design	Patient numbers		Age (years)		Follow-up period (KP/VP) (months)	MINORS scores
				KP	VP	KP	VP		
Bozkurt et al[26]	Turkey	2014	Retrospective	200	96	57.5	57	40	14
Dohm et al[27]	United States	2014	RCT	191	190	75.6		24	-
Dong et al[28]	China	2013	Retrospective	51	35	69.8	70.5	21.3	14
Dong et al[29]	China	2009	Retrospective	20	18	69.5	70.2	3	11
Ee et al[30]	England	2012	Retrospective	97	148	75	77	24	15
Endres et al[31]	Germany	2011	RCT	20	21	63.3	71.3	5.8	-
Figueiredo et al[32]	Brazil	2011	Prospective	22	30	73	77	6	16
Folman et al[33]	Israel	2011	Prospective	31	14	70.7	75.6	12	16
Frankel et al[34]	United States	2007	Retrospective	17	29	70	72	3.5 years	14
Gan et al[35]	China	2014	Retrospective	41	38	69.1	67.1	43.5/41.4	15
Grohs et al[36]	Austria	2005	Prospective	28	23	70	70	24	17
Hiwatashi et al[37]	Japan	2008	Retrospective	40	66	75	77	NR	13
Kong et al[38]	China	2014	Retrospective	29	24	71.9	70.5	12	13
Kumar et al[39]	Canada	2009	Prospective	24	28	73	78	42.3/42.2	17
Li et al[40]	China	2012	Prospective	45	40	68.5	67.1	12	17
Liu JT et al[41]	Taiwan	2009	RCT	50	50	72.3	74.3	>6	-
Liu T et al[42]	China	2013	Retrospective	40	60	68.5	62.5	1 week	13
Lovi et al[43]	Italy	2009	Prospective	36	118	67.6	33m	17	
Movrin et al[44]	Slovenia	2010	Prospective	46	27	67.8	72.9	1 year	16
Omidi-Kashani[45]	Iran	2013	Prospective	29	28	72.1 72.4	6m	13	
Pflugmacher et al[17]	Germany	2005	Prospective	22	20	67	65	12	15
Qian et al[46]	China	2012	Prospective	53	9	66.2	3.9y	16	
Rollinghoff et al[47]	Germany	2009	Prospective	53	51	68.9	1y	17	
Santiago et al[48]	Span	2009	Prospective	30	30	65.9	73	1 year	16
Schofer et al[49]	Germany	2009	Prospective	30	30	72.5	73.8	13.5/13.7	17
Sun et al[50]	China	2010	Retrospective	31	28	74.2	72.3	18	14
Wu et al[51]	China	2014	Retrospective	20	20	65.1	66.3	1 year	15
Yan et al[52]	China	2011	Retrospective	98	94	76.9	77.2	14.3/15.2	14
Yang et al[53]	Korea	2014	RCT	112	109	73.4	73.3	NR	-
Yi et al[54]	China	2014	Prospective	79	90	61.3	49.4m	16	
Yokoyama et al[555]	Japan	2013	Retrospective	38	28	75.5	74	NR	12
Zhang et al[56]	China	2013	Retrospective	30	29	68.7	66.2	25	13

NR = not reported. RCT = randomized controlled trial. Follow-up period is months unless reported otherwise.

The MINORS criteria include the following items: (1) a clearly stated aim; (2) inclusion of consecutive patients; (3) Prospective data collection; (4) endpoints appropriate to the aim of the study; (5) unbiased assessment of the study endpoint; (6) a follow-up period appropriate to the aims of the study; (7) less than 5% loss to follow-up; (8) Prospective calculation of the sample size; (9) an adequate control group; (10) contemporary groups; (11) baseline equivalence of groups; and (12) adequate statistical analysis. The items are scored as follows: 0 (not reported); 1 (reported but inadequate); 2 (reported and adequate). The ideal global score for comparative studies is 24.

Table 2. Meta-analysis of clinical outcomes comparing the KP and VP groups.

Outcomes	No. of studies	No. of patients	Effect estimate (95% CI)	*P*
Visual analog scale				
Short-term	18	1500	-0.2 (-0.27, -0.13)	<.01
Long-term	14	1071	-0.46 (-0.57, -0.36)	<.01
Oswestry Disability Index				
Short-term	7	430	-17.56 (-18.07,-17.05)	<.01
Long-time	8	676	-2.41 (-3.44, -1.38)	<.01
Injury time	4	311	-1.31 (-3.37, 0.75)	<.01
Operation time	5	716	6.58 (5.47, 7.68)	<.01
Volume of injected cement	12	1764	0.51 (0.44, 0.56)	<.01

The effect estimate is weighted mean difference, CI=confidence interval.

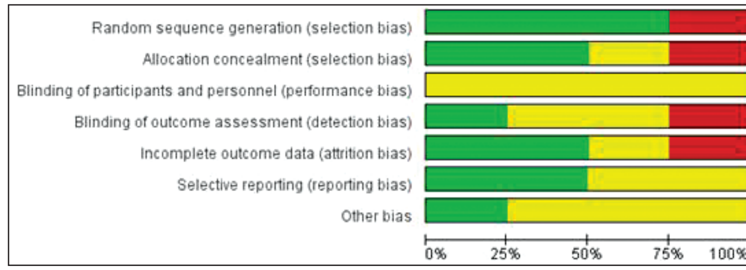

Figure 3. Summarization of risk of bias as percentages for low, unclear and high for the randomized controlled trials (n=4).

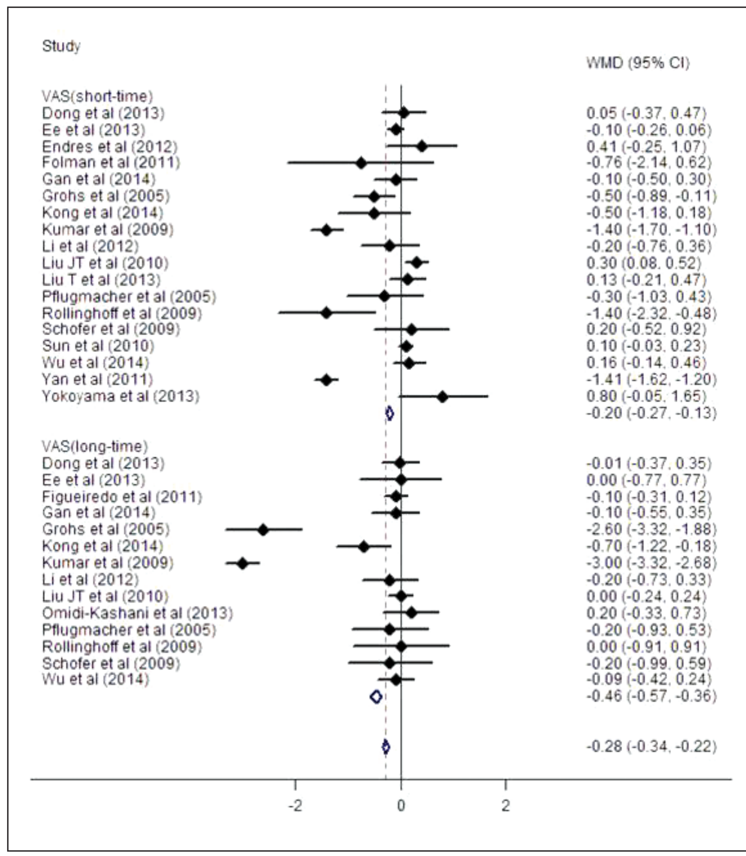

Figure 4. Forest plots for the meta-analysis of the visual analog scale scores.

there was a significant difference in the immediate postoperative follow-up period (WMD=2.55, 95% CI=2.33 to 2.78, *P*<.01), the final follow-up (WMD=2.79, 95% CI=2.39 to 3.19; *P*<.01) and improvement (WMD=5.91, 95% CI=5.19 to 6.64; *P*=<.01) between the KP and VP groups, respectively. Patients who underwent the KP procedure had a better postoperative anterior height of the vertebral body than those who had the VP procedure (**Table 3**).

The pooled measures of middle height included the immediate postoperative follow-up period (WMD=2.44, 95% CI=2.14 to 2.73; *P*<.01) and the final follow-up (WMD=6.92, 95% CI=6.31 to 7.52; *P*<.01) in four[17,35,43,45] and three studies,[17,35,43] respectively. Both showed a significant difference and demonstrated that the KP group had a better result than the VP group for changes in anterior and middle vertebral height, but in three reports there was no significant difference in pooled posterior height between KP and VP[28,43,47] (WMD=0.5, 95% CI=-0.03 to 1.02; *P*=.178/WMD=1.78, 95% CI=1.44 to 2.11; *P*=.033) (**Table 3**).

The kyphotic angle in the immediate postoperative was analyzed in 15 studies.[17,28,33,35,38,40,41,44,47,49-53,56] The kyphotic angle improved more in the KP group than in the VP group (WMD=-2.5, 95% CI=-2.84 to -2.16; *P*<.01). Nine studies[17,28,35,38,40,47,49,51,56] reported the kyphotic angle at the final follow-up (WMD=-1.7, 95%CI=-2.06 to -1.33; *P*<.01) and seven studies[29,30,44,49,52,53,55]

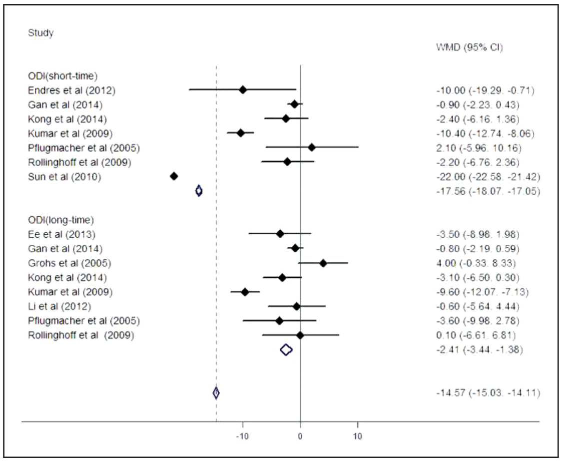

Figure 5. Forest plots for the meta-analysis of the Oswestry Disability Index scores.

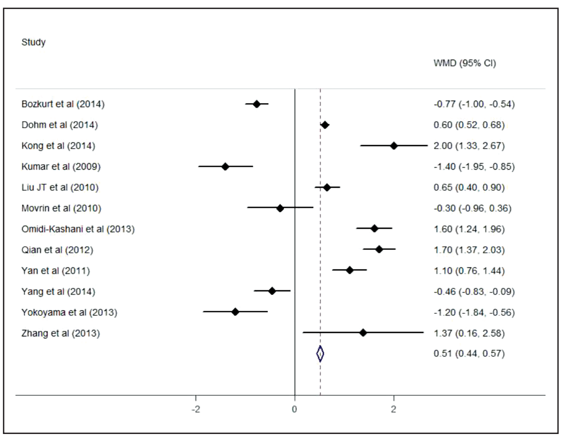

Figure 6. Forest plots for the meta-analysis of the volume of injected cement.

compared the improvement (WMD=4.76, 95%CI=4.19 to 5.32; *P*<.01).With the KP procedure there was more improvement in the kyphotic angle than with the VP procedure (**Figure 7 and Table 3**).

Complications

Cement leakage in the VP group was significantly more frequent than in the KP group in the intraspinal space (OR=0.5, 95% CI=0.3 to 0.85; *P*=.035)[31,32,34,36,37,40,43-45,47,48,52,55] in the extraspinal space (OR=0.36, 95% CI=0.21 to 0.62; *P*=.15)[31,32,34,36,37,40,43,45,47-49,52] and in total leakage (OR=0.53, 95% CI=0.4 to 0.7; *P*=.051) (**Figure 8 and Table 4**).[26,27,30-32,34-36,39,40,40-45,47-53,55,57] Thirteen studies reported complications related to fractures.[26,34-36,39-41,43-45,47,52,54] The pooled analysis showed no significant difference between the KP and VP group (OR=0.94, 95% CI=0.59 to 1.49; *P*=.248). Of these, there were nine reports of adjacent fractures.[26,34,36,39,41,43-45,47] There was no significant difference between the groups (OR=1.41, 95% CI=0.7 to 2.83; *P*=.283) (**Table 4**).

DISCUSSION

Our systematic review and meta-analysis included 4 randomized studies and 28 non-randomized studies that included 1653 patients treated with KP and 1621 patients treated with VP. The main outcome variables were pain intensity and dysfunction measured by VAS and ODI, kyphotic angle, and vertebral height at short-term and long-term follow-ups. Postoperative complications included new vertebral and adjacent fractures, as well as time of injury and duration of surgery.

Treatment of OVCF should lead to a lasting improvement in the pain. More than 90% of pain and dysfunction caused by OVCF can be relieved successfully by KP or VP. Both surgical procedures significantly relieve the pain and improved dysfunction in patients with OVCF. In our analysis, KP was more effective on the VAS and ODI assessments than the VP group. The mechanism of pain reduction reflected in Oswestry score improvements might result from the inhibition and immobility of micro-movements of the fractured vertebral body, as well as the cytotoxic effect of the PMMA cement.[57-59]

We pooled the improvement in kyphotic angle and height, which included the anterior, middle and posterior vertebral body. Improvements in postoperative anterior and middle height were better in the KP group in the immediate postoperative period and at the final follow-up. Improvements in posterior height were similar. One study reported that a reduction in the kyphotic angle depends more on natural healing than surgical treatment.[60] Schofer et al[49] reported a reduction in the kyphotic angle by a mean of 3-6° after the KP procedure compared with a reduction of 1°, suggesting that the balloon-induced restoration had a positive effect.

Total new vertebral fracture did not differ between the KP and VP groups. There was also no difference in the rate of adjacent fractures. Whether bone cement injection causes an increased incidence of new vertebral fractures is an interesting topic of ongoing discussion. Hulme et al[20] showed that the incidence of new vertebral fractures did not increase in osteoporotic patients who had suffered vertebral fractures. New vertebral fractures may relate to the sustained loss of bone mass seen in the osteoporotic population, rather than the surgical procedure itself.

Cement leakage does not usually result in clinical symptoms. In our experience, the high injection pressure and low viscidity of the cement leads to a higher incidence of cement leakage during VP than during KP. The KP procedure creates a hole in which to package

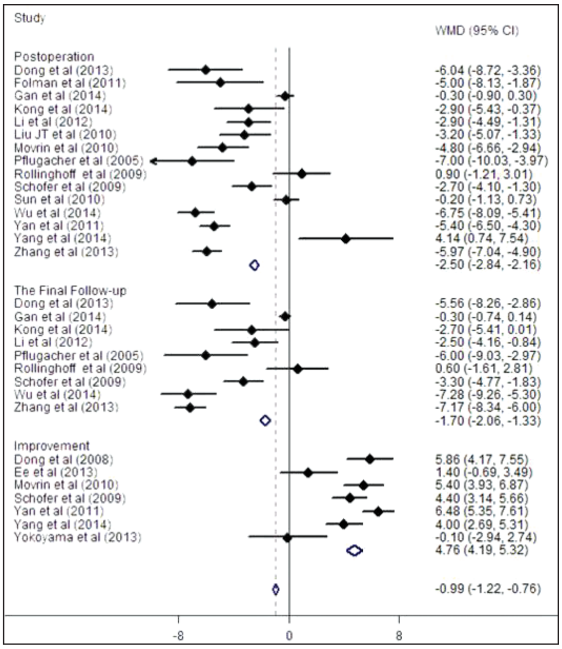

Figure 7. Forest plots for the meta-analysis of the kyphotic angle.

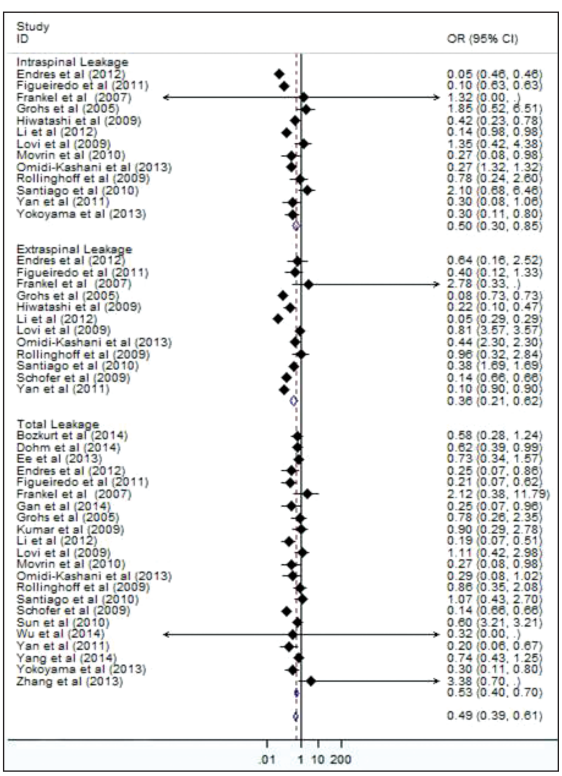

Figure 8. Forest plots for the meta-analysis of leakage.

Table 3. Results of meta-analysis of radiological outcome measures.

Outcomes	No. of studies	No. of patients	Effect estimate (95% CI)	*P*
Anterior height				
Postoperative follow-up	10	1020	2.55 (2.33, 2.78)	<.01
Final follow-up	6	505	2.79 (2.39, 3.19)	<.01
Improvement	4	797	5.91 (5.19, 6.64)	<.01
Middle height				
Postoperative follow-up	4	386	2.44 (2.14, 2.73)	<.01
Final follow-up	3	275	6.92 (6.31, 7.52)	<.01
Posterior height				
Postoperative follow-up	3	344	0.5 (-0.03, 1.02)	.178
Final follow-up	3	344	1.78 (1.44, 2.11)	.033
Kyphotic angle				
Postoperative follow-up	15	1365	-2.5 (-2.84, -2.16)	<.01
Final follow-up	9	641	-1.7 (-2.06, -1.33)	<.01
Improvement	7	916	4.79 (4.19, 5.32)	<.01

Effect estimates are weighted mean difference, CI = confidence interval, postoperative means immediate postoperative follow-up period.

Table 4. Differences in complications between the VP and K groups.

Outcomes	No. of studies	No. of patients	Effect estimate (95% CI)	*P*
Leakage				
Intraspinal	13	1503	0.5 (0.3, 0.85)	.035
Extraspinal	12	1223	0.36 (0.21,0.62)	.15
Total	22	2773	0.53 (0.4, 0.7)	.051
New fractures				
Adjacent	9	1070	1.41 (0.7, 2.83)	.283
Total	13	1628	0.94 (0.59, 1.49)	.248

Effect estimates are weighted mean difference, CI = confidence interval.

the cement with the help of a balloon. The KP group had a lower frequency of leakage than the VP group in our analysis. The intraspinal and extraspinal leakage were greater in the VP group.

An ideal meta-analysis would include only RCTs with little heterogeneity. However, RCTs are rare for surgical procedures. Patients will not usually agree to partake in a randomized surgical option. Every surgeon has his personal specialty and chooses the preferable procedure according to the specific condition. Because of the lack of RCTs, we included prospective and retrospective cohort studies of high quality and designed a baseline form to collect demographic characteristics in a manner that would limit the risk of bias.

In conclusion, we found that the KP procedure was more effective in pain relief, physical functional improvement, improving restoration of vertebral height and kyphotic angle with reduced cement leakage, but the KP surgery took longer and required a greater volume of injected cement. The KP procedure has a higher cost of hospitalization. Additional RCTs are needed to confirm these conclusions and to select the best surgical procedure for patients with OVCF.

Disclosure of conflict of interest
None.

Acknowledgment
This research was funded by the Natural Science Foundation of Jiangsu Province (BK20130274).

REFERENCES

1. Laurent M. Treatment of osteoporotic vertebral fractures. JAMA internal medicine. Apr 2014;174(4):641-642.
2. Wang E, Yi H, Wang M, Huang C. Treatment of osteoporotic vertebral compression fractures with percutaneous kyphoplasty: A report of 196 cases. European Journal of Orthopaedic Surgery and Traumatology. 2013;23(SUPPL. 1):S71-S75.
3. Bonnick SL. Osteoporosis in men and women. Clinical cornerstone. 2006;8(1):28-39.
4. Tang H, Zhao JD, Li Y, et al. Efficacy of percutaneous kyphoplasty in treating osteoporotic multithoracolumbar vertebral compression fractures. Orthopedics. Dec 2010;33(12):885.
5. Lyles KW, Gold DT, Shipp KM, Pieper CF, Martinez S, Mulhausen PL. Association of osteoporotic vertebral compression fractures with impaired functional status. The American journal of medicine. Jun 1993;94(6):595-601.
6. Oleksik A, Lips P, Dawson A, et al. Health-related quality of life in postmenopausal women with low BMD with or without prevalent vertebral fractures. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. Jul 2000;15(7):1384-1392.
7. Cockerill W, Lunt M, Silman AJ, et al. Health-related quality of life and radiographic vertebral fracture. Osteoporosis international: a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. Feb 2004;15(2):113-119.
8. Wang G, Yang H, Pan J. Osteoporotic vertebral compression fractures with osteonecrosis treated by kyphoplasty. Bone. 2010;47:S455-S456.
9. Rapado A. General management of vertebral fractures. Bone. Mar 1996;18(3 Suppl):191S-196S.
10. Convertino VA, Bloomfield SA, Greenleaf JE. An overview of the issues: physiological effects of bed rest and restricted physical activity. Medicine and science in sports and exercise. Feb 1997;29(2):187-190.
11. Takata S, Yasui N. Disuse osteoporosis. The journal of medical investigation : JMI. Aug 2001;48(3-4):147-156.
12. Galibert P, Deramond H, Rosat P, Le Gars D. Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty. Neuro-Chirurgie. 1987;33(2):166-168.
13. Yang HL, Zhao L, Liu J, et al. Changes of pulmonary function for patients with osteoporotic vertebral compression fractures after kyphoplasty. Journal of spinal disorders & techniques. May 2007;20(3):221-225.
14. Wardlaw D, Cummings SR, Van Meirhaeghe J, et al. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. The Lancet. 2009;373(9668):1016-1024.
15. Klazen CA, Lohle PN, de Vries J, et al. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. Lancet. Sep 25 2010;376(9746):1085-1092.
16. Garfin SR, Yuan HA, Reiley MA. New technologies in spine: kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures. Spine. Jul 15 2001;26(14):1511-1515.
17. Pflugmacher R, Kandziora F, Schroder R, et al. Vertebroplasty and kyphoplasty in osteoporotic fractures of vertebral bodies -- a prospective 1-year follow-up analysis. Rofo: progress in the areas of the rontgenstrahlen and medicine[Germen]. Dec 2005;177(12):1670-1676.
18. Grohs JG, Matzner M, Trieb K, Krepler P. Minimal invasive stabilization of osteoporotic vertebral fractures: a prospective nonrandomized comparison of vertebroplasty and balloon kyphoplasty. Journal of spinal disorders & techniques. Jun 2005;18(3):238-242.
19. Bouza C, Lopez T, Magro A, Navalpotro L, Amate JM. Efficacy and safety of balloon kyphoplasty in the treatment of vertebral compression fractures: A systematic review. European Spine Journal. 2006;15(7):1050-1067.
20. Hulme PA, Krebs J, Ferguson SJ, Berlemann U. Vertebroplasty and kyphoplasty: a systematic review of 69 clinical studies. Spine. Aug 1 2006;31(17):1983-2001.
21. Yang H, Liu T, Zhou J, et al. Kyphoplasty versus vertebroplasty for painful osteoporotic vertebral compression fractures-which one is better? A systematic review and meta-analysis. Int J Spine Surg, 2013, 7: e45-57.
22. Ma XL, Xing D, Ma JX, et al. Balloon kyphoplasty versus percutaneous vertebroplasty in treating osteoporotic vertebral compression fracture: grading the evidence through a systematic review and meta-analysis. Eur Spine J, 2012, 21: 1844-1859.
23. Han S, Wan S, Ning L, et al. Percutaneous vertebroplasty versus balloon kyphoplasty for treatment of osteoporotic vertebral compression fracture: a meta-analysis of randomised and non-randomised controlled trials. Int Orthop, 2011, 35: 1349-1358.
24. Lee MJ, Dumonski M, Cahill P, et al. Percutaneous treatment of vertebral compression fractures: a meta-analysis of complications. Spine (Phila Pa 1976), 2009, 34: 1228-1232.
25. Xing D, Ma JX, Ma XL, et al. A meta-analysis of balloon kyphoplasty compared to percutaneous vertebroplasty for treating osteoporotic vertebral compression fractures. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. Jun 2013;20(6):795-803. Need to add up by 4 -- 21+4=25 etc rest of the way up
26. Bozkurt M, Kahilogullari G, Ozdemir M, et al. Comparative analysis of vertebroplasty and kyphoplasty for osteoporotic vertebral compression fractures. Asian spine journal. Feb 2014;8(1):27-34.
27. Dohm M, Black CM, Dacre A, et al. A randomized trial comparing balloon kyphoplasty and vertebroplasty for vertebral compression fractures due to osteoporosis. American Journal of Neuroradiology. 2014;35(12):2227-2236.
28. Dong R, Chen L, Tang T, et al. Pain reduction following vertebroplasty and kyphoplasty. International orthopaedics. 2013;37(1):83-87.
29. Dong R, Chen L, Gu Y, et al. Improvement in respiratory function after vertebroplasty and kyphoplasty. International orthopaedics. Dec 2009;33(6):1689-1694.
30. Ee GWW, Lei J, Guo CM, et al. Comparison of clinical outcomes and radiographic measurements in four different treatment modalities for osteoporotic compression fractures: Retrospective analysis. Journal of Spinal Disorders and Techniques. 2013.
31. Endres S, Badura A. Shield kyphoplasty through a unipedicular approach compared to vertebroplasty and balloon kyphoplasty in osteoporotic thoracolumbar fracture: a prospective randomized study. Orthopaedics & traumatology, surgery & research : OTSR. 2012;98(3):334-340.
32. Figueiredo N, Rotta R, Cavicchioli A, Gonsales D, Casulari LA. Kyphoplasty versus percutaneous vertebroplasty using the traditional and the new side-opening cannula for osteoporotic vertebral fracture. Journal of neurosurgical sciences. Dec 2011;55(4):365-370.
33. Folman Y, Shabat S. A comparison of two new technologies for percutaneous vertebral augmentation: Confidence vertebroplasty vs. sky kyphoplasty. Israel Medical Association Journal. 2011;13(7):394-397.
34. Frankel BM, Monroe T, Wang C. Percutaneous vertebral augmentation: an elevation in adjacent-level fracture risk in kyphoplasty as compared with vertebroplasty. Spine Journal. 2007;7(5):575-582.
35. Gan M, Zou J, Song D, Zhu X, Wang G, Yang H. Is balloon kyphoplasty better than percutaneous vertebroplasty for osteoporotic vertebral biconcave-shaped fractures? Acta radiologica (Stockholm, Sweden: 1987). Oct 2014;55(8):985-991.
36. Grohs JG, Matzner M, Trieb K, Krepler P. Minimal invasive stabilization of osteoporotic vertebral fractures: A prospective nonrondomized comparison of vertebroplasty and balloon kyphoplasty. Journal of Spinal Disorders and Techniques. 2005;18(3):238-242.
37. Hiwatashi A, Westesson PLA, Yoshiura T, et al. Kyphoplasty and vertebroplasty produce the same degree of height restoration. American Journal of Neuroradiology. 2009;30(4):669-673.
38. Kong LD, Wang P, Wang LF, Shen Y, Shang ZK, Meng LC. Comparison of vertebroplasty and kyphoplasty in the treatment of osteoporotic vertebral compression fractures with intravertebral clefts. European Journal of Orthopaedic Surgery and Traumatology. 2014;24(SUPPL.1):S201-S208.
39. Kumar K, Nguyen R, Bishop S. A comparative analysis of the results of vertebroplasty and kyphoplasty in osteoporotic vertebral compression fractures. Neurosurgery. 2010;67(SUPPL. 1):ons171-ons188.
40. Li X, Yang H, Tang T, Qian Z, Chen L, Zhang Z. Comparison of kyphoplasty and vertebroplasty for treatment of painful osteoporotic vertebral compression fractures: twelve-month follow-up in a prospective nonrandomized comparative study. Journal of spinal disorders & techniques. 2012;25(3):142-149.
41. Liu JT, Liao WJ, Tan WC, et al. Balloon kyphoplasty versus vertebroplasty for treatment of osteoporotic vertebral compression fracture: a prospective, comparative, and randomized clinical study. Osteoporosis international: a journal established as result of cooperation between the European Foundation for Osteoporosis and the

National Osteoporosis Foundation of the USA. Feb 2010;21(2):359-364.
42. Liu T, Zhou ZW, Zhou ZX, Xu SW. Percutaneous vertebroplasty versus percutaneous kyphoplasty for the treatment of old vertebral osteoporotic compression fracture. Chinese Journal of Tissue Engineering Research. 2013;17(39):6920-6925.
43. Lovi A, Teli M, Ortolina A, Costa F, Fornari M, Brayda-Bruno M. Vertebroplasty and kyphoplasty: Complementary techniques for the treatment of painful osteoporotic vertebral compression fractures. A prospective non-randomised study on 154 patients. European Spine Journal. 2009;18(SUPPL. 1):S95-S101.
44. Movrin I, Vengust R, Komadina R. Adjacent vertebral fractures after percutaneous vertebral augmentation of osteoporotic vertebral compression fracture: a comparison of balloon kyphoplasty and vertebroplasty. Archives of orthopaedic and trauma surgery. Sep 2010;130(9):1157-1166.
45. Omidi-Kashani F, Samini F, Hasankhani EG, Kachooei AR, Toosi KZ, Golhasani-Keshtan F. Does percutaneous kyphoplasty have better functional outcome than vertebroplasty in single level osteoporotic compression fractures? A comparative prospective study. Journal of osteoporosis. 2013;2013:1-5.
46. Qian J, Yang H, Jing J, et al. The Early Stage Adjacent Disc Degeneration after Percutaneous Vertebroplasty and Kyphoplasty in The Treatment of Osteoporotic VCFs. PLoS ONE. 2012;7(10).
47. Rollinghoff M, Siewe J, Zarghooni K, et al. Effectiveness, security and height restoration on fresh compression fractures a comparative prospective study of vertebroplasty and kyphoplasty. Minimally Invasive Neurosurgery. 2009;52(5-6):233-237.
48. Santiago FR, Abela AP, Alvarez LG, Osuna RM, Garcia Mdel M. Pain and functional outcome after vertebroplasty and kyphoplasty. A comparative study. Eur J Radiol. Aug 2010;75(2):e108-113.
49. Schofer MD, Efe T, Timmesfeld N, Kortmann HR, Quante M. Comparison of kyphoplasty and vertebroplasty in the treatment of fresh vertebral compression fractures. Archives of orthopaedic and trauma surgery. 2009;129(10):1391-1399.
50. Sun ZG, Miao XG, Yuan H, Zhao XB, Wang H, Sun JG. Assessment of percutaneous vertebroplasty and percutaneous kyphoplasty for treatment of senile osteoporotic vertebral compression fractures. Zhongguo gu shang [China] = China journal of orthopaedics and traumatology. 2010;23(10):734-738.
51. Wu Y, Wang F, Zhou JQ, Liu CY, Wu RX. Analysis of clinical effects of percutaneous vertebroplasty and percutaneous kyphoplasty in treating osteoporotic vertebral compression fracture. Zhongguo gu shang [China] = China journal of orthopaedics and traumatology. May 2014;27(5):385-389.
52. Yan D, Duan L, Li J, Soo C, Zhu H, Zhang Z. Comparative study of percutaneous vertebroplasty and kyphoplasty in the treatment of osteoporotic vertebral compression fractures. Archives of orthopaedic and trauma surgery. 2011;131(5):645-650.
53. Yang DH, Cho KH, Chung YS, Kim YR. Effect of vertebroplasty with bone filler device and comparison with balloon kyphoplasty. European Spine Journal. 2014;23(12):2718-2725.
54. Yi X, Lu H, Tian F, et al. Recompression in new levels after percutaneous vertebroplasty and kyphoplasty compared with conservative treatment. Archives of orthopaedic and trauma surgery. 2014;134(1):21-30.
55. Yokoyama K, Kawanishi M, Yamada M, et al. In not only vertebroplasty but also kyphoplasty, the resolution of vertebral deformities depends on vertebral mobility. American Journal of Neuroradiology. 2013;34(7):1474-1478.
56. Zhang C, Zhu K, Zhou J, et al. Influence on adjacent lumbar bone density after strengthening of T12, L1 segment vertebral osteoporotic compression fracture by percutaneous vertebroplasty and percutaneous kyphoplasty. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi [China] = Chinese journal of reparative and reconstructive surgery. Jul 2013;27(7):819-823.
57. Belkoff SM, Mathis JM, Jasper LE, Deramond H. The biomechanics of vertebroplasty. The effect of cement volume on mechanical behavior. Spine. Jul 15 2001;26(14):1537-1541.
58. Belkoff SM, Mathis JM, Jasper LE, Deramond H. An ex vivo biomechanical evaluation of a hydroxyapatite cement for use with vertebroplasty. Spine. Jul 15 2001;26(14):1542-1546.
59. Heini PF, Walchli B, Berlemann U. Percutaneous transpedicular vertebroplasty with PMMA: operative technique and early results. A prospective study for the treatment of osteoporotic compression fractures. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. Oct 2000;9(5):445-450.
60. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA, 3rd, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. Apr 2000;15(4):721-739.