Systematic Review and Meta-Analysis

Medicine®

OPEN

Therapeutic effect of kyphoplasty and balloon vertebroplasty on osteoporotic vertebral compression fracture

A systematic review and meta-analysis of randomized controlled trials

Yi Zhu, PhD, MD[a,b], Jie Cheng, PhD, MD[c], Jichao Yin, MS[d], Zhijie Zhang, PhD[e], Chunlong Liu, MS[f], Dingjun Hao, MD[a,*]

Abstract

Introduction: This study aimed to assess the treatment effects of kyphoplasty (KP) compared with percutaneous vertebroplasty (VP) in patients with osteoporotic vertebral compression fracture, based on evidence from randomized controlled trials (RCTs).

Methods: The electronic databases PubMed (from 1966), EmBase (from 1974), and Cochrane Library (including Cochrane Central Register of Controlled Trials and Cochrane Reviews) were searched systematically to identify relevant studies published up to August 31, 2019. Meta-analyses were conducted for subjective pain as measured using visual analogue scale (VAS), disability function as measured by Oswestry disability index (ODI), and cement leakage. For VAS and ODI, mean change from the baseline and standard deviation were used; for cement leakage, numbers of events and patients in each group were used. The random-effects model was applied to summarize the effects across trials.

Results: Previous reviews and meta-analysis included non-RCTs, which brought (for those studies) a higher risk of bias. Therefore, 6 RCTs involving 1077 patients were included in the meta-analysis. No between-group difference was found. The weighted mean difference was −0.19 (95% confidence interval [CI], −0.39–0.01; $P = .057$) for VAS and −3.51 (95% CI, −8.70–1.67; $P = .184$) for ODI. However, KP had numerically lower rates of cement leakage across trials in a consistent fashion (relative risk, 0.83; 95% CI, 0.74–0.94; $P = .004$).

Conclusions: Both KP and VP had clinically meaningful beneficial effects on pain and disability, and the effects were stable and similar. KP had significantly fewer cement leakages.

Abbreviations: CI = confidence interval, KP = kyphoplasty, ODI = Oswestry disability index, OVCF = osteoporotic vertebral compression fracture, RCTs = randomized controlled trials, RR = relative risk, SD = standard deviation, VAS = visual analogue scale, VCFs = vertebral compression fractures, VP = vertebroplasty, WMD = weighted mean difference.

Keywords: kyphoplasty, osteoporotic vertebral compression fracture, Oswestry disability index, vertebroplasty, visual analogue scale

1. Introduction

Osteoporosis is a bone disorder characterized by a low bone density that leads to fragile bones and higher fracture risks. The most frequent osteoporotic fracture is osteoporotic vertebral compression fracture (OVCF). Vertebral fracture is one of the major healthcare problems all over the world due to their high incidence, adverse consequences on the health-related quality of

Editor: Yan Li.

YZ and JC contributed equally to this work.

The study was supported by the China Postdoctoral Science Foundation (2016M602847) and the Natural Science Foundation of Shanxi Province (20168291).

The authors have no conflicts of interest to disclose.

[a] Department of Spine Surgery, Honghui Hospital, Xi'an Jiaotong University, Xi'an, [b] Department of Musculoskeletal Pain Rehabilitation, The Fifth Affiliated Hospital of Zhengzhou University, Zhengzhou, [c] The Second Clinical College, Nanjing University of Chinese Medicine, Nanjing, [d] Department of Orthopaedics and Traumatology, Xi'an Hospital of Traditional Chinese Medicine, Xi'an, [e] Rehabilitation Therapy Center, Henan Province Orthopedic Hospital, Luoyang, [f] Clinical Medical College of Acupuncture, Moxibustion and Rehabilitation, Guangzhou University of Chinese Medicine, Guangzhou, China.

[*] Correspondence: Dingjun Hao, Department of Spine Surgery, Honghui Hospital, Xi'an Jiaotong University, Xi'an 710054, China (e-mail: haodingjun@126.com).

How to cite this article: Zhu Y, Cheng J, Yin J, Zhang Z, Liu C, Hao D. Therapeutic effect of kyphoplasty and balloon vertebroplasty on osteoporotic vertebral compression fracture. Medicine 2019;98:45(e17810).

Received: 6 December 2018 / Received in final form: 19 September 2019 / Accepted: 7 October 2019

http://dx.doi.org/10.1097/MD.0000000000017810

life of the patients, and huge expenses.[1,2] Patients with osteoporosis are subject to multiple incidences of fractures during lifetime, and the risk increases with age. The age-standardized incidence of vertebral fracture was 12.1/1000 person–years in women and 6.8/1000 person–years in men aged more than 50 years in Europe.[3] The consequences of OVCF can be burdensome to patients and healthcare system if left untreated. The physical symptoms of vertebral compression fractures (VCFs) include chronic back pain, severe vertebral deformity, and disability.[4] The disability caused by VCFs, in turn, adds to healthcare budgets and social security cost by increasing the use of long-term care facilities, hospitalization, and vertebral augmentation procedures.[5] VCFs also have a negative impact on mental health. Prolonged VCFs may cause anxiety and depression and impair social functions of patients.[6]

Different treatment approaches for improving pain control, preventing deterioration and deformity, and treating underlying osteoporosis are currently available. The conventional treatments include medications, bed rest, and bracing. However, they are only partially effective for people suffering from OVCFs.[4] On the contrary, previous studies have found that conservative treatments often fail to improve pain and mobility.[7] Minimally invasive approaches have been gradually adopted in recent years.[8–10] Percutaneous vertebroplasty (VP) is regarded as an effective and safe treatment for OVCFs. In this procedure, bone cement is injected through the pedicle into a collapsed and porotic vertebral body.[11–13] As a modification of VP, balloon kyphoplasty (KP) was developed to reduce vertebral deformity, pain, and disability by inserting balloons into the vertebral body and then fixing the fracture fragments through polymethylmethacrylate injection.[14] Currently, both techniques are widely used clinically as major noninvasive treatments to OVCF. Both are shown to be more effective in providing pain relief and improving daily function and quality of life compared with conservative therapy.[15] However, the optimal treatment is still controversial.

Previously, systematic reviews and meta-analyses were conducted to tackle this question, but no conclusive agreement was reached due to the following limitations: insufficient number of randomized controlled trials (RCTs), lack of conformity in the duration of follow-up, and heterogeneity mainly among observational studies due to bias.[15–17] Thus, this systematic review and meta-analysis was conducted to overcome the aforementioned limitations by focusing on RCTs and subgrouping outcomes to compare the effects of KP and VP on patients with OVCF depending on the timing of measurement.

2. Methods

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement issued in 2009.[18] The meta-analysis based on public literature is not applicable for ethical approval

2.1. Literature search

A systematic search was performed to identify relevant studies published up to August 31, 2019, using electronic databases PubMed (from 1966), EmBase (from 1974), and Cochrane Library (including Cochrane Central Register of Controlled Trials and Cochrane Reviews). The following key words were used: vertebroplasty, kyphoplasty, compression, fracture, fractures, osteoporotic, and osteoporosis.

2.2. Study selection

Because previous reviews and meta-analysis have included studies with homogeneous methods and high risk of bias, the aim of this study was to draw conclusions from homogeneous studies of the highest available quality. The inclusion criteria for this systematic review were as follows: RCTs on humans; publication in the English or Chinese language; study population with OVCFs; and randomization to VP and KP. The exclusion criteria were as follows: observational study design or interventional study without randomization; inclusion of patients with fractures related to indications other than OVCFs, such as fractures related to cancer; and no explicit comparison between KP and VP. Only RCTs were included to avoid biases common in observational studies. The patient population included only those with OVCFs who underwent VP or KP. If the study included patients with diverse indications, patients with OVCFs were assessed and reported as a subgroup separately to be considered for inclusion. The interventions of interest were KP and VP. Comparisons between 2 interventions were explicitly made. If more than 2 interventions were investigated, only the results on the 2 relevant groups were included. The study outcomes focused on measuring pain, quality of life, or new fractures.

Two reviewers screened the studies to determine eligibility for inclusion. Studies were included when both agreed; in case of any disagreement, a third reviewer made the final decision. The screening included 2 stages. First, all titles and abstracts were reviewed against inclusion and exclusion criteria. In case information was inadequate to make a decision, the full text was retrieved to further examine the eligibility of the study. Systematic reviews that shared the scope similar to this review were also identified during screening, and their reference lists were scanned and added to the screening data set.

2.3. Data extraction and quality assessment

For all included studies, information on study characteristics and outcomes was extracted into summary tables. Specifically, author name, year, sample sizes, patient demographics, pain scores, disability index, and cement leakages were extracted.

The reviewer assessed the methodological quality of the included studies according to the Jadad score. Studies were evaluated in terms of the following 3 key methodological features for an overall score of 0 to 5: randomization, masking, and accountability of all patients; a higher score meant higher quality.[19] The Cochrane risk-of-bias tool provided a detailed assessment of each aspect of the study design and reporting.[20] A graph was plotted using Review Manager 5.3 (version 5.3; The Nordic Cochrane Centre, Copenhagen, Denmark, The Cochrane Collaboration, 2014).

2.4. Statistical methods

The commonly reported outcomes were the visual analogue scale (VAS), the Oswestry disability index (ODI), and cement leakage. The pain was assessed using VAS or pain score with a scale of either 0 to 10 or 0 to 100 after 3 days, 1 month, 3 months, 6 months, 12 months, and 60 months. The mean and standard deviation for each group were extracted, and scores on a scale of 0 to 100 were standardized to 0 to 10 by dividing the mean and standard deviation by 10. The level of disability was measured using ODI after 3 days, 3 months, and 12 months. The mean and standard deviation for each group were extracted and then

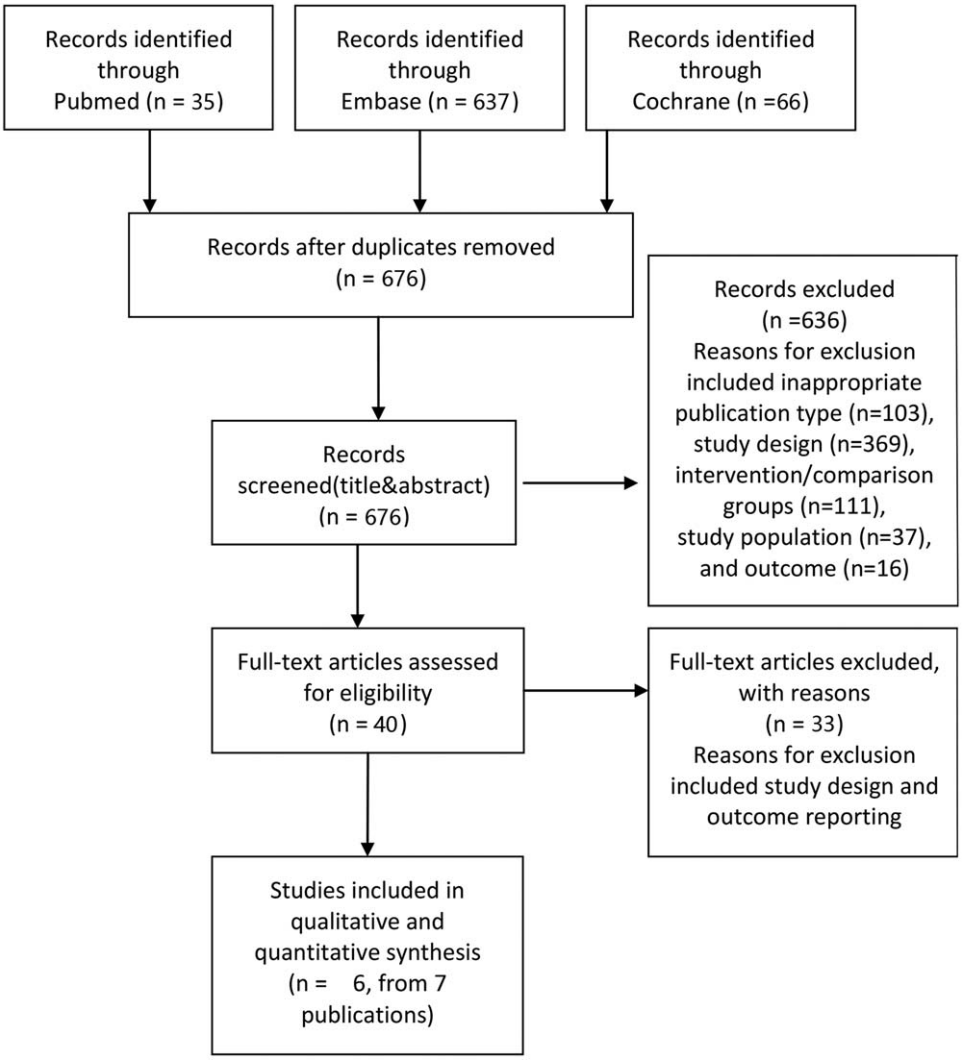

Figure 1. Flowchart of study selection and inclusion process.

meta-analyzed. For the main analysis, only the final endpoint (the one with the longest follow-up) from each trial was included. Meta-analyses for pain scores, ODI, and cement leakage were conducted to quantitatively summarize the evidence. For continuous outcomes, weighted mean difference (WMD) and 95% confidence intervals (CIs) were presented. For dichotomous outcomes, risk ratio and 95% CI were presented. The selection between the random-effects model and the fixed-effects model was based on the measure of heterogeneity (the random-effects model was used when the I^2 value was ≥50%; otherwise, the fixed-effects model was used).[21] A sensitivity analysis was conducted to evaluate whether outcome measurement instruments and potential publication bias had impacts on the effect estimate. The sensitivity analysis for measurement instruments included pain scores other than the most reported VAS, and the standardized mean difference was estimated to take into account different measurement scales.[20] Funnel plots were generated, and Egger and Begg tests were conducted to detect publication bias.[22,23] The significance level for all tests was set at 0.05. All the analyses were conducted in Stata 13.1 (StataCorp 2013, TX).

3. Results

3.1. Study and patient characteristics

Figure 1 is a flowchart of studies screened and reviewed. A total of 676 studies were identified from the search after duplicates excluded. The exclusion was based on the following criteria: publication types, including letters, reviews, case reports, opinions, book chapters, and protocols (n=103); non-RCT study design (n=369); interventions not of interest or no comparison between KP and VP (n=111); study population, including patients with cancer and trauma (n=37); and nonclinical outcomes such as cost or mechanical properties of cement (n=16). Previous meta-analyses included studies with homogeneous methods and high risk of bias. Therefore, this study aimed to draw conclusions from homogeneous studies of the highest available quality.[15–17] Eventually, 6 RCTs reported by 7 studies[24–30] were included based on the inclusion criteria. The most common reasons for exclusion were non-RCT study design and inappropriate comparison groups. Detailed patient characteristics at baseline in each study are shown in Table 1.

Table 1

Basic characteristics of eligible studies.

References	Country	Race	Sample size		Mean age (year)		Gender (M/F)		KP group	VP group	Follow-up (month)	Main outcomes
			KP	VP	KP	VP	KP	VP				
[26]	Germany	Caucasian	20	21	63 (range: 53–77)	71 (range: 63–77)	6/14	8/13	Balloon kyphoplasty was also performed using a unipedicular approach with a unilateral working cannula. A drill passing through the cannula created a tract for the 20-mm balloon to be inserted into the center of the vertebral body. Cement was injected as described for vertebroplasty. Injection was given usually about 14 min after start of mixing	Vertebroplasty was performed through a unipedicular transpedicular approach with 1 13-gauge bone biopsy needle placed in the anterior third of the vertebral body. Liquid and powder polymethylmethacrylate were mixed to toothpaste consistency. Under biplane fluoroscopic guidance, the cement was injected through the needle until the vertebral body was filled in the posterior 25% or until there was leakage	6	VAS ODI cement leakage
[28]	USA	Caucasian	191	190	75.6 (entire sample)		77.4% women (baseline)		KP was performed using a bilateral approach. Details not provided	VP was performed according to local practices. Details not provided	24	Back pain score ODI cement leakage
[29]	Taiwan	East Asian	50	50	72 (SD: 8)	74 (SD: 6)	11/39	12/38	The surgical procedures involved intravenous general anesthesia + 2% xylocaine injected locally. Under X-ray guidance, 2 small incisions were made and a probe was placed into the vertebral space at the fracture site. The bone was drilled, and a balloon was inserted on each side. The balloons were then inflated with contrast medium, expanded to the desired height, and removed. The spaces created by the balloons were then filled with PMMA to bind the fracture	Same anesthetic protocol as KP. A special bone biopsy needle was passed percutaneously and slowly through each side of the pedicle into the vertebral body. The bone filler PMMA was prepared and mixed with both an antibiotic (gentamicin), to reduce the risk of infection, and a powder containing barium, allowing X-ray visualization. An optimal amount of bone filler was injected into the vertebral body via the needles on both sides. All procedures were performed under a mobile C-arm X-ray	60	VAS
[27]	USA	Caucasian	59	56	75 (SD: 10)	76 (SD: 10)	21/38	13/43	Both vertebral augmentation procedures were performed according to standard practice based on each practitioner's preference. The approach, device, and cement used for the procedure were at the operators' discretion		12	Pain score

(*continued*)

Table 1

(continued).

References	Country	Race	Sample size		Mean age (year)		Gender (M/F)		KP group	VP group	Follow-up (month)	Main outcomes
			KP	VP	KP	VP	KP	VP				
[25]	China	East Asian	30	30	70 (SD: 7)	70 (SD: 9)	7/23	5/25	Balloon kyphoplasty was also performed using a unipedicular approach with a unilateral working cannula. A drill passing through the cannula created a tract for the balloon to be inserted into the center of the vertebral body. Cement was injected through the needle until the vertebral body was filled or until leakage occurred	Vertebroplasty was performed using a unipedicular transpedicular approach. Once the needle was in place, polymethylmethacrylate was injected through the needle until the vertebral body was filled or until leakage occurred	0.1	VAS ODI cement leakage
[24]	China	East Asian	40	40	66 (SD: 2)	66 (SD: 2)	10/30	13/27	Same aesthetic and needle placement method was used as VP. Once the needle was placed, the bone was drilled to 2–3 mm and a balloon was inserted. The balloons were then inflated with contrast medium under X-ray guidance, expanded to the desired height, and removed. The spaces created by the balloons were then filled with PMMA to bind the fracture	Vertebroplasty was performed using a unipedicular transpedicular approach with 1 bone biopsy needle placed in the anterior third of the vertebral body. Polymethylmethacrylate cement was mixed according to the manufacturer's instructions. Under X-ray guidance, the cement was injected through the needle until the vertebral body was filled or until leakage occurred	12	VAS ODI cement leakage

KP = Kyphoplasty, NR = not reported, ODI = Oswestry disability index, SD = standard deviation, VAS = visual analogue scale, VP = vertebroplasty.

Table 2

Methodological quality of studies included in the meta-analysis.

	Randomization			Blinding			An account of all patients		
References	Appropriate (2)	Unclear (1)	Not appropriate (0)	Appropriate (2)	Unclear (1)	Not appropriate (0)	Described (1)	Not described (0)	Total
[26]		√				√	√		2
[28]	√					√	√		3
[29,30]		√				√	√		2
[25]		√			√		√		3
[24]	√					√	√		3
[27]	√			√			√		5

Sample sizes of the included studies ranged from 41 to 381. The total number of patients was 1077. The Jadad score for most trials was 2 (n = 2)[26,29] or 3 (n = 3),[24,25,28] except 1 trial with a score of 5.[27] This indicated poor to moderate quality of the trials in general. The details on Jadad scores are presented in Table 2. Quality assessment using the Cochrane risk-of-bias tool is presented in Figure 2. Common issues included unclear or high risks in randomization and patient and investigator blinding. All

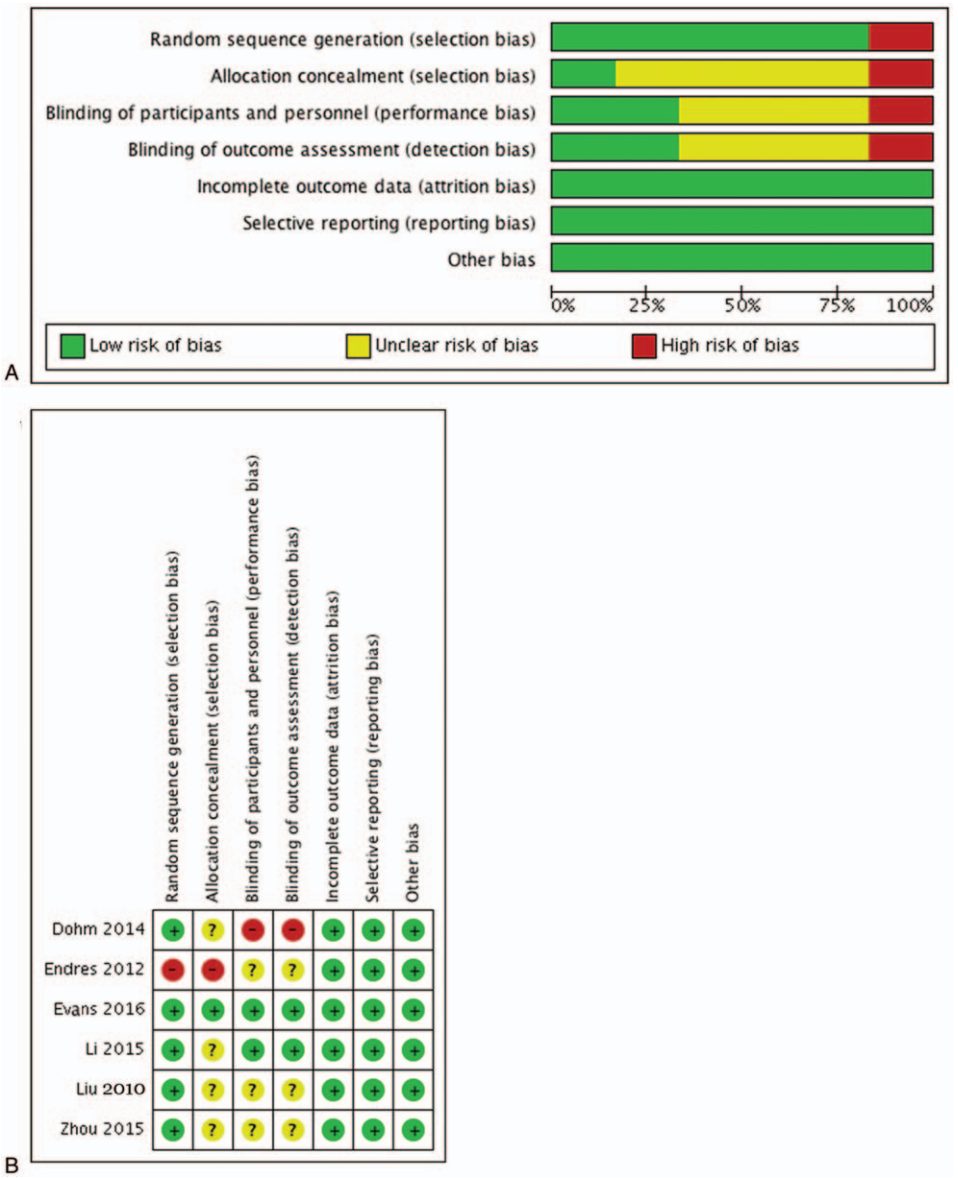

Figure 2. (A and B) Cochrane risk-of-bias evaluations.

Table 3

The results of therapeutic effect of kyphoplasty and vertebroplasty on osteoporotic vertebral compression fracture in the meta-analysis.

	N*	WMD/RR (95%CI)	I^2†	P†
Pain	4	−0.19 (−0.39, 0.01)	34.5%	.057
ODI	4	−3.51 (−8.70, 1.67)	83.5%	.184
Cement leakage	4	0.83 (0.74, 0.94)	23.8%	.004

Random-effects model was used when *P* value for heterogeneity test <.05 or I^2 ≧50%; otherwise, fixed-effects model was used.

WMD = weighted mean difference; RR = relative risk.

* Number of studies.

† *P* value of Q test for heterogeneity.

the trials measured and reported on pain, while 4 out of 6 reported on ODI or the incidence of cement leakage. All the patients had OVCFs confirmed radiologically. After randomization, patients in the intervention groups were balanced in terms of demographics and clinical manifestation. The results of therapeutic effect of KP and VP on patients with OVCF in the meta-analysis are shown in Table 3.

3.2. Clinical outcomes

3.2.1. Pain. Four[24–26,29] of the 6 trials measured subjective pain using the VAS score on a scale of either 0 to 10 or 0 to 100. The other 2[27,28] measured pain scores and a pain intensity numeric rating scale were not included in the main analysis but tested in a sensitivity analysis. The between-group difference in effect was estimated using a meta-analysis (Fig. 3). The final endpoints with the longest length of follow-up from each of the 5 trials were included in the meta-analysis. The overall WMD was not statistically significant (WMD −0.19; 95% CI, −0.39–0.01; $P = .057$). The I^2 value attributed 34.5% variation in WMD to heterogeneity; therefore, a fixed-effects model was applied.

One trial (Liu 2015) included a long-term follow-up after 5 years. The authors claimed no between-group difference without reporting the numeric values. Therefore, the data were not used in the meta-analysis, and the 6-month endpoint was used instead (Liu 2009).

3.2.2. Oswestry disability index. Four[24–26,28] of 6 trials measured the perceived level of disability using the ODI on a scale of 0 to 100. A lower score represented a lower level of disability. The final endpoints from 4 trials were included in the meta-analysis. The overall WMD was not statistically significant (WMD −3.51; 95% CI, −8.70–1.67; $P = .184$). The I^2 value attributed 83.5% variation in WMD to heterogeneity (Fig. 4); therefore, a random-effects model was used.

3.2.3. Cement leakage. Four[24–26,28] trials measured the rate of cement leakage right after surgery, all showing a nonstatistically

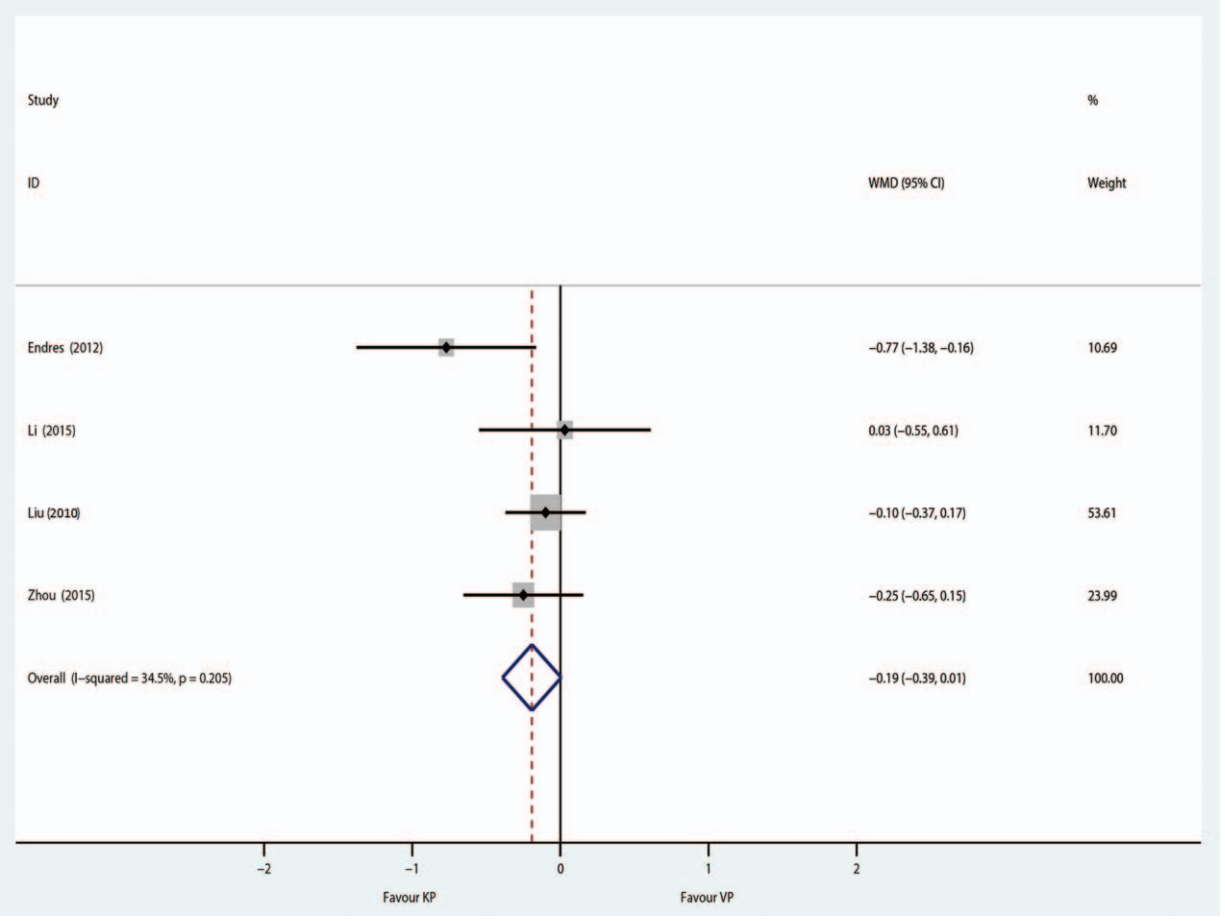

Figure 3. Forest plot showing the WMD estimates for VAS. KP = kyphoplasty, VAS = visual analogue scale, VP = vertebroplasty, WMD = weighted mean difference.

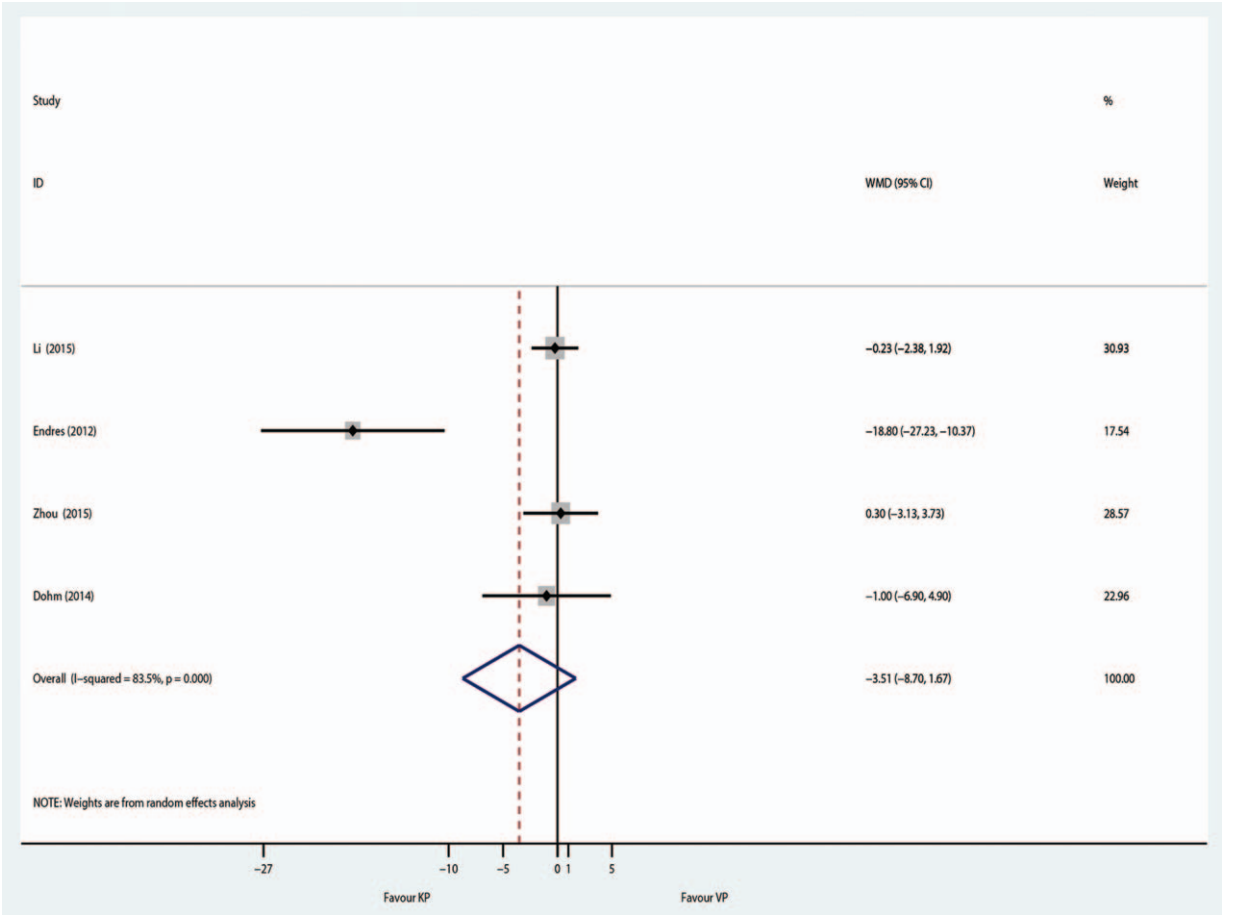

Figure 4. Forest plot showing the WMD estimates for ODI. KP = kyphoplasty, ODI = Oswestry disability index, VP = vertebroplasty, WMD = weighted mean difference.

significantly lower rate with KP. A meta-analysis estimated a borderline statistically significant risk ratio of 0.83 (95% CI, 0.74–0.94; $P = .004$), suggesting a lower risk of leakage with KP (Fig. 5). The I^2 value attributed 23.8% variation to heterogeneity; therefore, a fixed-effects model was used.

3.3. Sensitivity analysis

The 2 trials that measured pain using a pain score instead of VAS were combined with the other 4 in a sensitivity analysis. The overall mean difference remained nonstatistically significant, with a mean of −0.05 (95% CI, −0.19–0.10; $P = .534$; Fig. 6). The I^2 value was 49.3%, so a fixed-effects model was used.

3.4. Publication bias

The review of the funnel plots could not rule out the potential publication bias for VAS, ODI, and cement leakage (Figs. 7–9). The Egger and Begg tests showed no evidence of publication bias for VAS ($P = .480$ and .308, respectively), ODI ($P = .265$ and .089, respectively), and cement leakage ($P = .087$ and .734, respectively).

4. Discussion

A meta-analysis of RCTs showed that both KP and VP had statistically significant and clinically meaningful beneficial effects on pain and disability. KP and VP demonstrated similar treatment effects on pain and disability in patients with OVCF. KP had a lower cement leakage compared with VP. This most-updated systematic review and meta-analysis focused on examining the treatment effects of KP and VP in patients with OVCFs based on evidence from RCTs and specifically stratified on the duration of follow-up. Previous meta-analyses, including observational studies of varied and insufficient quality, have drawn conflicting and ambiguous conclusions. Most studies indicated no differential effects but heterogeneity among individual studies.[16,17] Some have pointed out the need for more RCTs to be conducted and included in the meta-analysis.[15] Recently, Li et al [25] tried to demonstrate that the bone-filling mesh container with polymethylmethyl acrylic bone cement for treatment of OVCFs can have a significant result in relieving the pain, lifting the injured vertebral height, and the correction of kyphosis, which can also reduce the leakage rate of bone cement. In addition, Evans et al [27] suggested that VP could be considered as the surgical procedure of choice, apart from mostly asymptomatic cement leakage. However, the results were still unclear and even controversial. Therefore, this comprehensive meta-analysis was conducted to clarify the treatment effects of KP compared with VP in patients with OVCF, based on evidence from RCTs.

This meta-analysis aimed to fill the evidence gap by focusing on RCTs and including trials published recently. The results showed

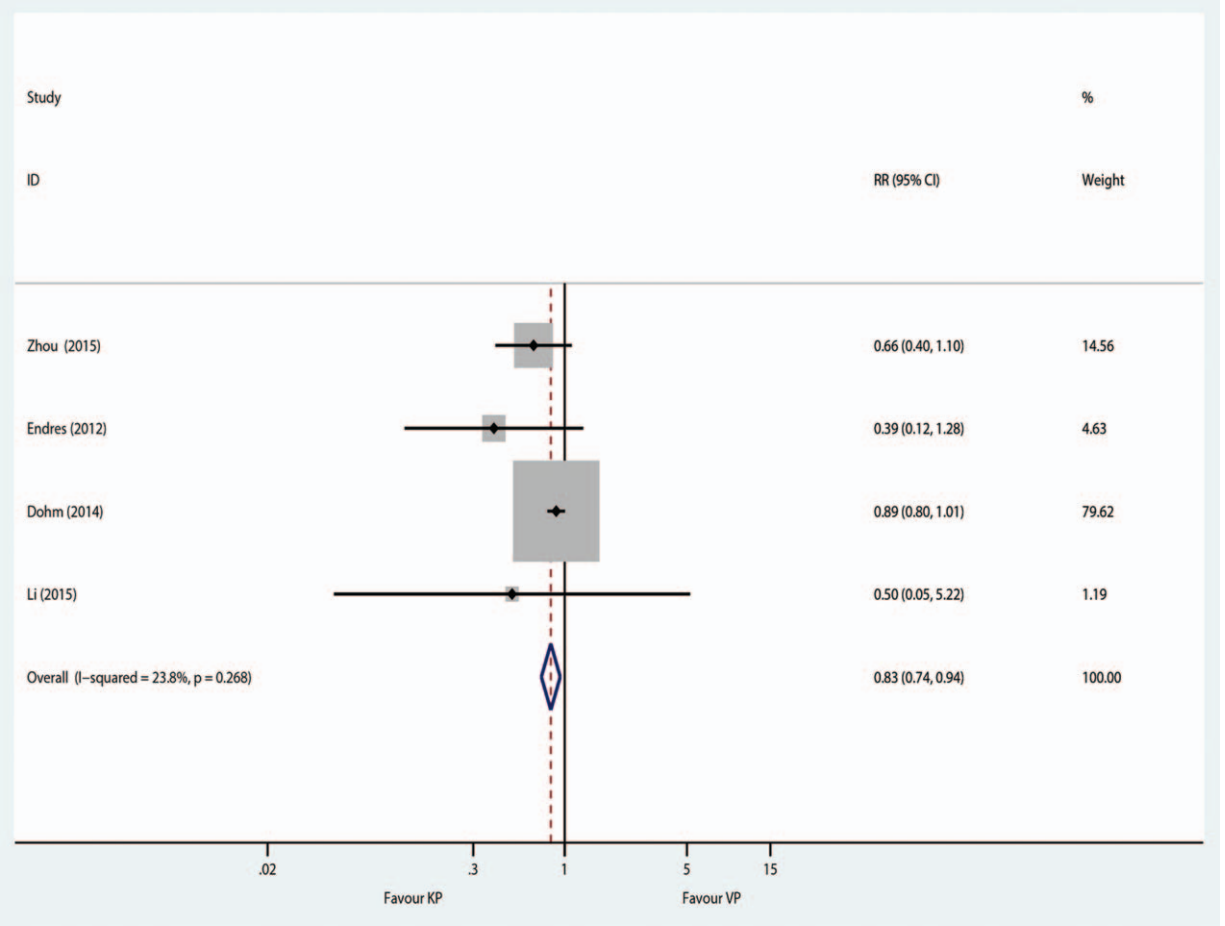

Figure 5. Forest plot showing the risk ratio estimates for cement leakage. CI = confidence interval, KP = kyphoplasty, RR = relative risk, VP = vertebroplasty.

that KP and VP both significantly improved pain and disability and had a comparable impact on VAS and ODI. In addition, it also demonstrated that the effects of these 2 procedures were generally consistent among trials and durations of the follow-up. With the source of evidence restricted to RCTs of moderate to high quality, measured and unmeasured confounding factors common in observational studies were minimized. Thus, the results were more consistent among trials. The data were meta-analyzed with the duration of follow-up well controlled in RCTs. The study also found a statistically significant lower rate of cement leakage with KP compared with VP. The mechanism underlying this difference was that KP involved an inflatable bone filling into the vertebral body to form a cavity, consequently contributing to decreased cement extravasation and lower pressure.[31]

The evidence suggested a moderate to high heterogeneity for the pain and disability outcomes and a small heterogeneity for the cement leakage outcome. Moderate heterogeneity in VAS has been found across trials because although VAS is a valid tool to measure pain at 1 time point, it may not behave linearly and its responsiveness may vary according to the type of pain.[32,33] Therefore, the interpretation of raw change in VAS may be heterogeneous among studies. However, this hypothesis could not be tested in the present study due to the lack of access to patient-level data. On the contrary, little variation in cement leakage rates was anticipated because the detection technique was quite standardized, which was a computed tomography scan immediately after the procedure; also, a binary outcome was determined regardless of the volume of the leakage. It was not clear why much greater heterogeneity was observed for the ODI outcome compared with the other 2 outcomes. However, 1 possibility was that the timing of final endpoint varied greatly among the 4 trials, ranging from 3 days after the procedure to 2 years later. It is possible that the effect size changes with time, which should be further explored in the future. Also noteworthy is the fact that although most researchers agreed that it was appropriate to treat ODI as a continuum having a linear correlation with a disability, the changes should be compared without considering the starting point.[34] Little and MacDonald[35] suggested that the change should be expressed as a percentage of the original score. This argument might provide another explanation for the observed heterogeneity in ODI because of the variation observed in the baseline ODI (ranging from 60–75). Further validation of the methodology is needed to explain this phenomenon.

The strengths of this systematic review and meta-analysis included relatively homogenous studies due to RCT design, ability to conduct a meta-analysis on multiple follow-up durations, and focus on clinically relevant outcome measures. However, including solely RCTs is not without limitations. Some

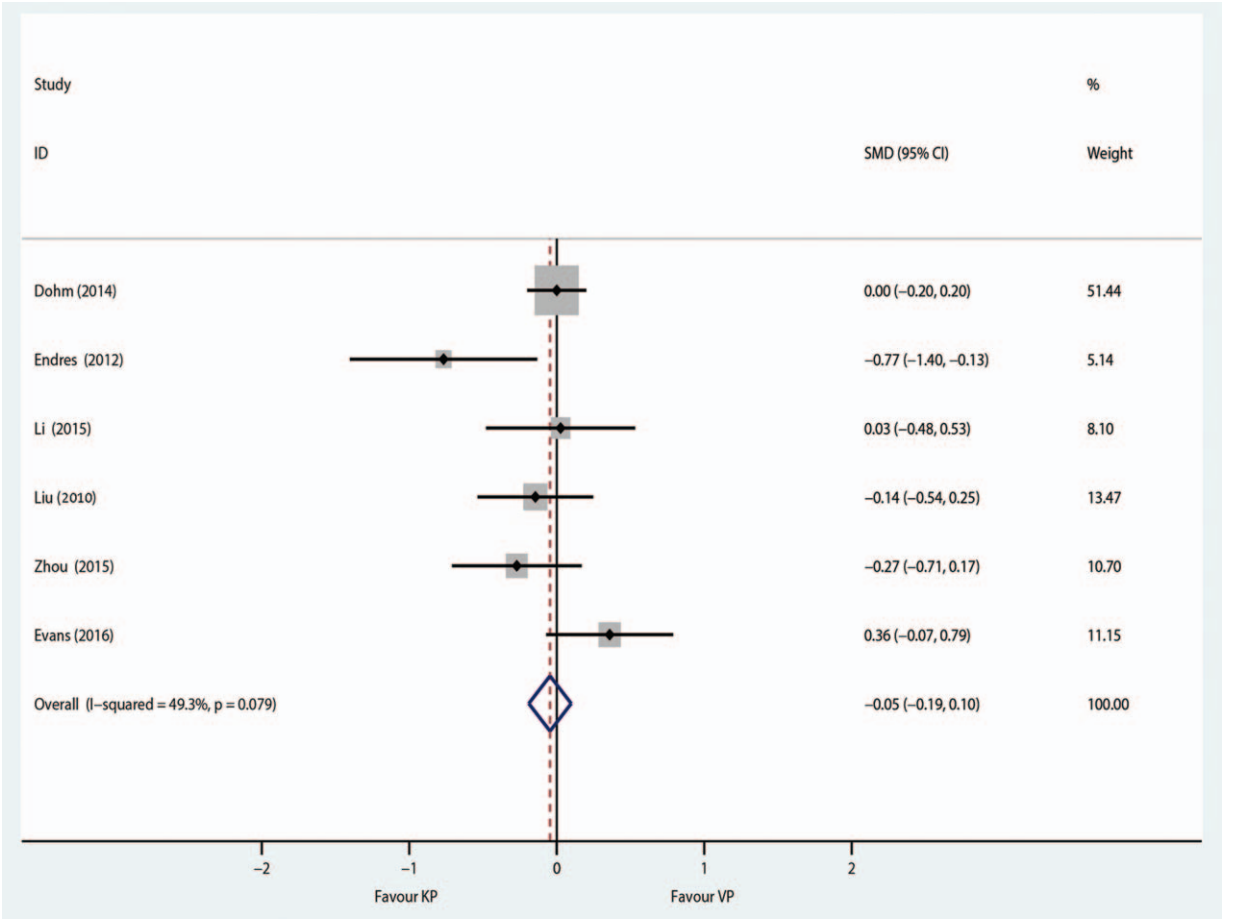

Figure 6. Sensitivity analysis of the standardized mean difference estimates for pain. CI = confidence interval, KP = kyphoplasty, VP = vertebroplasty.

important and meaningful outcomes more often measured in liberal settings, such as cohort studies, are not easily measured in a controlled environment in RCTs. For example, quality of life was measured only in 1 trial using SF-36 and EQ-5D, and thus no meta-analysis could be conducted. Some outcomes that required a longer follow-up were not often measured in RCTs either. One example was the incidence of new fractures, which was also measured in only 1 trial, showing similar rates with both interventions. It would be interesting to examine cumulative evidence from more trials on this critical endpoint. Some evidence on other clinical measurements was not summarized in this review due to the lack of uniformity in the measures and the fact

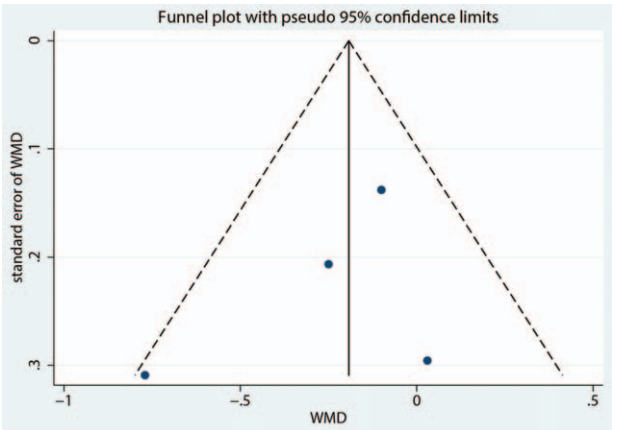

Figure 7. Funnel plot for publication bias test of VAS outcome. VAS = visual analogue scale, WMD = weighted mean difference.

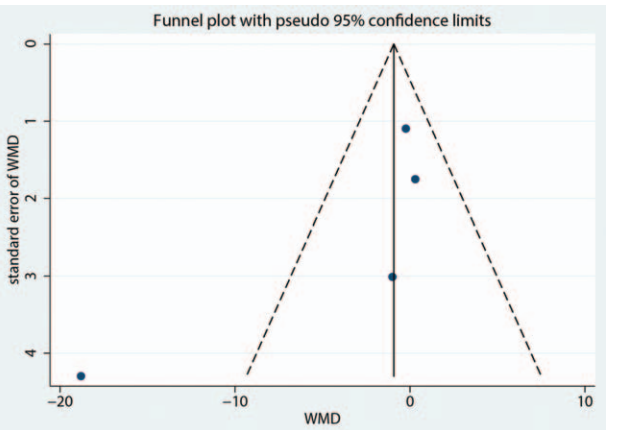

Figure 8. Funnel plot for publication bias test of ODI outcome. ODI = Oswestry disability index, WMD = weighted mean difference

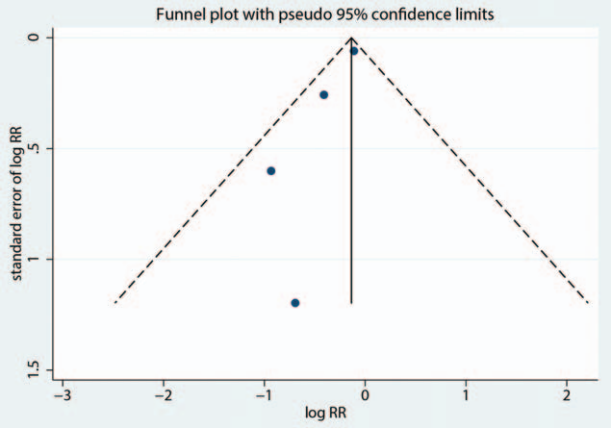

Figure 9. Funnel plot for publication bias test of cement leakage outcome. RR = relative risk.

that they were intermediate outcomes. For example, the regaining of vertebral height would be of less clinical relevance without improvement in function. The measure of height restoration was highly attributable to patient's position, which varied from site to site, or even patient to patient.[16] As a result, it was believed that this review should prioritize examining the most critical and reliable outcomes. In addition, useful data on the associations among the kind of cement (high or low viscosity), the rates of complications (pulmonary cement embolisms, neurological, restoration of segmental kyphosis), and the risk of osteoporotic vertebral fractures could not be obtained from the included studies.

In summary, this systematic review and meta-analysis provided the most up-to-date evidence on the comparative effect of KP and VP on pain, ODI, and cement leakage. However, more high-quality data are still needed to validate the findings. As more RCTs are conducted and published and the existing ones provide long-term follow-up results, a switch from systematic reviews of observational studies to RCTs and examining a detailed list of outcome measures are expected.

5. Conclusions

Evidence from RCTs showed that both KP and VP had statistically significant and clinically meaningful beneficial effects on pain and disability that was stable over time up to 5 years. KP and VP demonstrated similar treatment effects on pain and disability in patients with OVCF. KP probably had a lower cement leakage compared with VP. These conclusions suggested that KP avoided potential risk of cement leakage and exerted treatment effects comparable with those of VP. However, the results of this study need further validation through large-scale RCTs due to the limitation regarding the quantity and quality of the included trials.

Author contributions

Conceptualization: Dingjun Hao.
Investigation: Yi Zhu, Jie Cheng, Jichao Yin, Zhijie Zhang, Chunlong Liu.
Methodology: Yi Zhu, Jie Cheng, Jichao Yin, Zhijie Zhang, Chunlong Liu.
Writing – original draft: Yi Zhu, Jie Cheng.
Writing – review & editing: Dingjun Hao.

References

[1] Ettinger B, Black DM, Nevitt MC, et al. Contribution of vertebral deformities to chronic back pain and disability. The Study of Osteoporotic Fractures Research Group. J Bone Miner Res 1992;7: 449–56.
[2] Lips P, Cooper C, Agnusdei D, et al. Quality of life in patients with vertebral fractures: validation of the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO). Working Party for Quality of Life of the European Foundation for Osteoporosis. Osteoporos Int 1999;10:150–60.
[3] Felsenberg D, Silman AJ, Lunt M, et al. EPOSIncidence of vertebral fracture in Europe: Results From the European Prospective Osteoporosis Study (EPOS). J Bone Miner Res 2002;17:716–24.
[4] 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:e46323.
[5] Lad SP, Patil CG, Lad EM, Boakye M. Trends in pathological vertebral fractures in the United States: 1993 to 2004. J Neurosurg Spine 2007;7:305–10.
[6] Kumar K, Nguyen R, Bishop S. A comparative analysis of the results of vertebroplasty and kyphoplasty in osteoporotic vertebral compression fractures. Neurosurgery 2010;67(3 Suppl Operative):ons171–88.
[7] Hallberg I, Rosenqvist AM, Kartous L, et al. Health-related quality of life after osteoporotic fractures. Osteoporos Int 2004;15:834–41.
[8] Robinson Y, Heyde CE, Forsth P, Olerud C. Kyphoplasty in osteoporotic vertebral compression fractures: guidelines and technical considerations. J Orthop Surg Res 2011;6:43.
[9] Rho YJ, Choe WJ, Chun YI. Risk factors predicting the new symptomatic vertebral compression fractures after percutaneous vertebroplasty or kyphoplasty. Eur Spine J 2012;21:905–11.
[10] 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;35:1349–58.
[11] 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 2010;376:1085–92.
[12] Wilson DJ. Vertebroplasty for vertebral fracture. BMJ 2011;343:d3470.
[13] Saliou G, Kocheida el M, Lehmann P, et al. Percutaneous vertebroplasty for pain management in malignant fractures of the spine with epidural involvement. Radiology 2010;254:882–90.
[14] Burton AW, Mendoza T, Gebhardt R, et al. Vertebral compression fracture treatment with vertebroplasty and kyphoplasty: experience in 407 patients with 1,156 fractures in a tertiary cancer center. Pain Med 2011;12:1750–7.
[15] Zhao S, Xu CY, Zhu AR, et al. Comparison of the efficacy and safety of 3 treatments for patients with osteoporotic vertebral compression fractures: a network meta-analysis. Medicine 2017;96:e7328.
[16] 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;21:1844–59.
[17] Zhao DH, Chen K, Zhu J, et al. Postoperative functional evaluation of percutaneous vertebroplasty compared with percutaneous kyphoplasty for vertebral compression fractures. Am J Ther 2016;23:e1381–90.
[18] Moher D, Liberati A, Tetzlaff J, et al. PRISMA GroupPreferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006–12.
[19] Appendix: Jadad Scale for Reporting Randomized Controlled Trials. *Evidence-based Obstetric Anesthesia*: Blackwell Publishing Ltd; 2007:237-238
[20] Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. 2011;The Cochrane Collaboration,
[21] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58.
[22] Song F, Gilbody S. Bias in meta-analysis detected by a simple, graphical test. Increase in studies of publication bias coincided with increasing use of meta-analysis. BMJ 1998;316:471.

[23] Peters JL, Sutton AJ, Jones DR, et al. Comparison of two methods to detect publication bias in meta-analysis. JAMA 2006;295:676–80.
[24] Zhou W. Percutaneous vertebroplasty with high-viscosity bone cement for treatment of severe osteoporotic thoracolumbar vertebral compression fractures. Chin J Tissue Eng Res 2015;19:7534–8.
[25] Li DH, Liu XW, Peng XT, et al. Bone filling mesh container for treatment of vertebral compression fractures can reduce the leakage of bone cement. Chin J Tissue Eng Res 2015;19:358–63.
[26] Endres S, Badura A. Shield kyphoplasty through a unipedicular approach compared to vertebroplasty and balloon kyphoplasty in osteoporotic thoracolumbar fracture: a prospective randomized study. Orthop Traumatol Surg Res 2012;98:334–40.
[27] Evans A, Kip K, Brinjikji W, et al. Randomized controlled trial of vertebroplasty versus kyphoplasty in the treatment of vertebral compression fractures. J Neurointerv Surg 2016;8:756–63.
[28] Dohm M, Black C, Dacre A, et al. A randomized trial comparing balloon kyphoplasty and vertebroplasty for vertebral compression fractures due to osteoporosis. AJNR Am J Neuroradiol 2014;35: 2227–36.
[29] Liu J, Liao W, Tan W, et al. Balloon kyphoplasty versus vertebroplasty for treatment of osteoporotic vertebral compression fracture: a prospective, comparative, and randomized clinical study. Osteoporos Int 2010;21:359–64.
[30] Liu J, Li C, Chang C, Liao WJ. Long-term follow-up study of osteoporotic vertebral compression fracture treated using balloon kyphoplasty and vertebroplasty. J Neurosurg Spine 2015;23:94–8.
[31] Xiao H, Yang J, Feng X, et al. Comparing complications of vertebroplasty and kyphoplasty for treating osteoporotic vertebral compression fractures: a meta-analysis of the randomized and non-randomized controlled studies. Eur J Orthop Surg Traumatol 2015;25 (Suppl 1):S77–85.
[32] Thomee R, Grimby G, Wright BD, Linacre JM. Rasch analysis of visual analog scale measurements before and after treatment of Patellofemoral Pain Syndrome in women. Scand J Rehabil Med 1995;27:145–51.
[33] Kersten P, White PJ, Tennant A. Is the pain visual analogue scale linear and responsive to change? An exploration using Rasch analysis. PLoS One 2014;9:e99485.
[34] Fairbank JC, Pynsent PB. The Oswestry disability index. Spine (Phila Pa 1976) 2000;25:2940–52.
[35] Little DG, MacDonald D. The use of the percentage change in Oswestry disability index score as an outcome measure in lumbar spinal surgery. Spine (Phila Pa 1976) 1994;19:2139–43.