

Balloon kyphoplasty versus percutaneous vertebroplasty for treatment of osteoporotic vertebral compression fractures (OVCFs)

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Abstract

Summary The study investigated whether kyphoplasty (KP) was superior to vertebroplasty (VP) in treating patients with osteoporotic vertebral compression fractures (OVCFs). KP may be superior to VP for treating patients with OVCFs based on long-term VAS and ODI but not short-term VAS. Further large-scale trials are needed to verify these findings due to potential risk of selection bias.

Introduction This study aimed to assess whether KP was superior to VP in treating patients with OVCFs.

Methods The Medline, Embase, and Cochrane databases and references within articles and proceedings of major meetings were systematically searched. Eligible studies included patients with OVCFs who received either KP or VP. Standard mean differences (SMDs) and relative risks (RRs) were used as measures of efficacy and safety in a random-effects model.

Results Eleven studies enrolling 869 patients with OVCFs were identified as eligible for final analysis. Compared with VP, KP was associated with significant improvements in long-term (SMD, -0.70 ; 95 % confidence interval [CI]: -1.30 , -0.10 ; $P=0.023$) visual analog scale (VAS); short-term (SMD, -1.50 ; 95 % CI: -2.94 , -0.07 ; $P=0.040$) and long-term (SMD, -1.03 ; 95 % CI: -1.88 , -0.18 ; $P=0.017$) Oswestry Disability Indexes (ODIs); short-term (SMD, -0.74 ; 95 % CI: -1.42 , -0.06 ; $P=0.032$) and long-term (SMD, -0.71 ; 95 % CI: -1.19 , -0.23 ; $P=0.004$) kyphosis angles; and vertebral body height (SMD, 1.56 ; 95 % CI: 0.62 , 2.49 ; $P=0.001$) and anterior vertebral body height

(SMD, 3.04 ; 95 % CI: 0.53 , 5.56 ; $P=0.018$). KP was also associated with a significantly longer operation time (SMD, 0.73 ; 95 % CI: 0.26 , 1.19 ; $P=0.002$) and a lower risk of cement extravasation (RR, 0.68 ; 95 % CI: 0.48 , 0.96 ; $P=0.030$) compared with VP. No significant differences were found in the short-term VAS, posterior vertebral body height, and adjacent-level fractures.

Conclusion Acknowledging some risk of selection bias, KP displayed a significantly better performance compared with VP only in one of the two primary endpoints, that is, for ODI but not for short-term VAS. Further randomized studies are required to confirm these results.

Keywords Kyphoplasty · Meta-analysis · Osteoporotic vertebral compression fractures · Vertebroplasty

Introduction

Osteoporosis is a systemic bone disorder characterized by reduced bone mass and degradation of skeletal microarchitecture, with a consequent higher risk of bone fracture [1]. Osteoporosis is one of the most noticeable causes of vertebral compression fractures (VCFs) [2–4]. VCFs usually occur following a break in any of the spinal column vertebrae, especially the collapse of the front of the vertebral body [2]. Osteoporotic vertebral compression fractures (OVCFs) constitute a major health problem due to their impact on health-related quality of life and high treatment costs [5–8]. It is therefore necessary to develop more effective therapies for patients with OVCFs.

The treatment goals are to restore mobility, reduce pain, and avoid new fractures [9–12]. Noninvasive interventions include bed rest, painkillers, and back braces to alleviate symptoms and strengthen the spine [13, 14]. Hormone

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replacement treatments, lifestyle modulation, and various pharmacologic agents are also used for managing OVCFs [15, 16]. Compared with these noninvasive treatments, Boonen et al. and Taylor et al. indicated that kyphoplasty (KP) and vertebroplasty (VP) greatly relieved pain, restored vertebral body height, improved physical function, lowered disability, and enhanced quality of life [17, 18]. Currently, invasive strategies for decompression and/or fusion are used for treating patients with OVCFs. VP and KP are minimally invasive surgical procedures involving the injection of a cement-like material into the vertebral body to support and stabilize the fracture or collapsed bone [19, 20]. Previous trials and studies suggested that KP and VP not only reduced pain and improved mobility but also restored vertebral height [2, 21, 22]. Therefore, VP and KP are recommended for treating patients with unhealed OVCFs regardless of pain management with the level of fracture-related pain confirmed clinically [12]. However, the relative efficacy of the two interventions in treating OVCFs still needs to be investigated.

Several recent trials have evaluated KP versus VP for treating patients with OVCFs. A systematic review and meta-analysis of pooled data were conducted to assess the superiority of KP over VP in treating patients with OVCFs.

Methods

Data sources, search strategy, and selection criteria

This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement issued in 2009 (Checklist S1) [23].

The electronic databases and other sources were comprehensively searched to include all the studies related to the effectiveness of VP and KP as interventions for OVCFs. The electronic databases, such as Medline, Embase, and the Cochrane library, including the Cochrane database of systematic reviews, were searched using the following key words: “vertebroplasty,” “kyphoplasty,” and “osteoporosis vertebral compression fracture.” The databases for abstracts of reviews and health technology assessment were used to search unpublished studies. Manual searches of reference lists from the relevant original and review articles were also conducted to identify additional eligible studies.

The inclusion criteria were studies reporting people with painful OVCFs, patients undergoing percutaneous vertebroplasty or percutaneous balloon kyphoplasty, KP versus VP, and outcome measures. The primary outcomes included visual analog scale (VAS) and Oswestry Disability Index (ODI), and the secondary outcomes included kyphosis angle, vertebral body height, operation time, incidence of cement leakage, and adjacent-level fractures.

Studies that reported data involving animal experiments and comparison of VP and KP with optimal pain medication were excluded. To facilitate the comparison, short-term outcomes were defined as those involving testing up to 4 weeks, while long-term outcomes included data exceeding 6 months.

A two-stage process was introduced to select eligible studies based on the aforementioned eligibility criteria [12]. Studies selected via systematic identification were evaluated for consistency through title, abstract, and full text, and those that failed to meet the inclusion criteria were rejected. For the articles with abstract only, attempts were made to contact the corresponding author in an effort to obtain the full text. Two independent reviewers were involved in this selection process: one checked title, abstract, and full text for inclusion, and the other performed a screening of 10 % of included references, which were selected by the previous reviewer. No discrepancies were found when the kappa coefficient was used to assess the inter-rater reliability.

Data collection and quality assessment

Two reviewers independently extracted data from eligible studies using a standardized data extraction table. Any disagreement was settled by discussion or by a third reviewer in the absence of a consensus. The following items were extracted: study country, study design, baseline characteristics, interventions, number of vertebral bodies, volume of cement injected, follow-up and loss to follow-up, and outcomes of interest. Bias of individual studies was examined by two reviewers independently, according to the *Cochrane Handbook for Systematic Reviews of Interventions* version 5.1. [24]. The bias of selection, performance, detection, attrition, reporting, and others was assessed during this process.

Statistical analysis

Standard mean differences (SMDs) or relative risks (RRs) with 95 % confidence intervals (CIs) were calculated using the outcomes extracted from each study before data pooling. RRs with 95 % CIs were used to estimate the safety of KP versus VP in terms of cement leakage and adjacent-level fractures. SMDs with 95 % CI were used to estimate the efficacy of KP versus VP on VAS, ODI, kyphosis angle, vertebral body height, and operation time [25]. Heterogeneity among trials was investigated using the Q statistic. *P* values less than 0.10 were indicative of significant heterogeneity [26]. A sensitivity analysis was also conducted to assess the impact of individual trials that contributed higher heterogeneity to the results of the meta-analysis [27]. The Egger [28] and Begg [29] tests were used to statistically evaluate publication bias. All reported *P* values were two sided, and *P* values <0.05 were considered statistically significant for all included studies.

Statistical analyses were performed using STATA software version 10.0 (Stata Corporation, TX, USA).

Results

Literature search

A total of 1588 potentially relevant references were identified after the systematic search of electronic databases, professional journals, and other sources. After reviewing the title or abstract, only 131 articles were selected for full-text review. However, 107 studies were discarded at the stage of full-text review. Among the remaining 24 citations, 11 studies [5, 30–39] were finally identified and included for analyzing the efficacy and safety of VP and KP. The other studies were excluded for the following reasons: conference abstracts without full text, incomparable data, systematic reviews, ongoing trials, and duplication. The results of the study selection process are shown in Fig. 1.

Study characteristics

The characteristics of all included studies are listed in Table 1. One randomized controlled trial (RCT) [5] and 10 prospective comparative studies [30–39], with a total of 458 patients in the KP group and 411 cases in the VP group, were included in the final meta-analysis. The sample sizes of each study varied, ranging from 45 to 154 OVCFs. One study [37] did not report the long-term VAS of pain, and three [31, 32, 39] of the 11 articles did not show data highlighting short-term pain relief. Data outlining new anterior vertebral body height were reported in four studies [5, 31, 33, 39], while those dealing with new postoperative kyphosis angle were also reported in five studies [5, 33, 34, 37, 39]. The strategy of measuring new postoperative kyphosis angle was only reported in the study by Dong et al. [39]. Folman et al. only included patients with OVCFs with a collapse of the vertebral height more than 15 % and a VAS ≥ 5 [37]. Three studies included patients with OVCFs having clearly defined fracture type or fresh fractures [5, 33, 34].

Quality assessment of included studies

The bias within the selected studies was assessed, and the results are presented in Fig. 2a. Of the 11 eligible studies, only one [5] was described as a randomized clinical trial, indicating a higher risk of selection bias. Three [5, 33, 36] out of the 11 citations claimed low risk of selection bias regarding allocation concealment, and the remainder were associated with elevated or unclear risk. None of the studies reported blinding of participants and personnel, and an incomplete outcome resulted in unclear bias of performance and attrition. All the articles reported data selectively, which indicated a low risk of

reporting bias. As illustrated in Fig. 2b, low risk of bias with 100 % existed only in selective reporting, and high risk of bias mainly occurred in selection bias.

Visual analog scale

As VAS was used to indicate pain relief in different groups, the data were pooled for analysis. The VAS was classified into short and long term according to the duration of follow-up. A total of six and eight studies reported short-term and long-term VASs, respectively. In the meta-analysis of the short-term VAS scores, a random-effects model was used to assess the efficacy of KP versus VP. The pooled data showed the absence of significant differences between KP and VP treatment in short-term VAS (SMD, -0.28 ; 95 % CI: $-0.98, 0.42$; $P=0.434$; Fig. 3a). In contrast, KP was associated with a lower long-term VAS (SMD, -0.70 ; 95 % CI: $-1.30, -0.10$; $P=0.023$; Fig. 3b) when compared with VP.

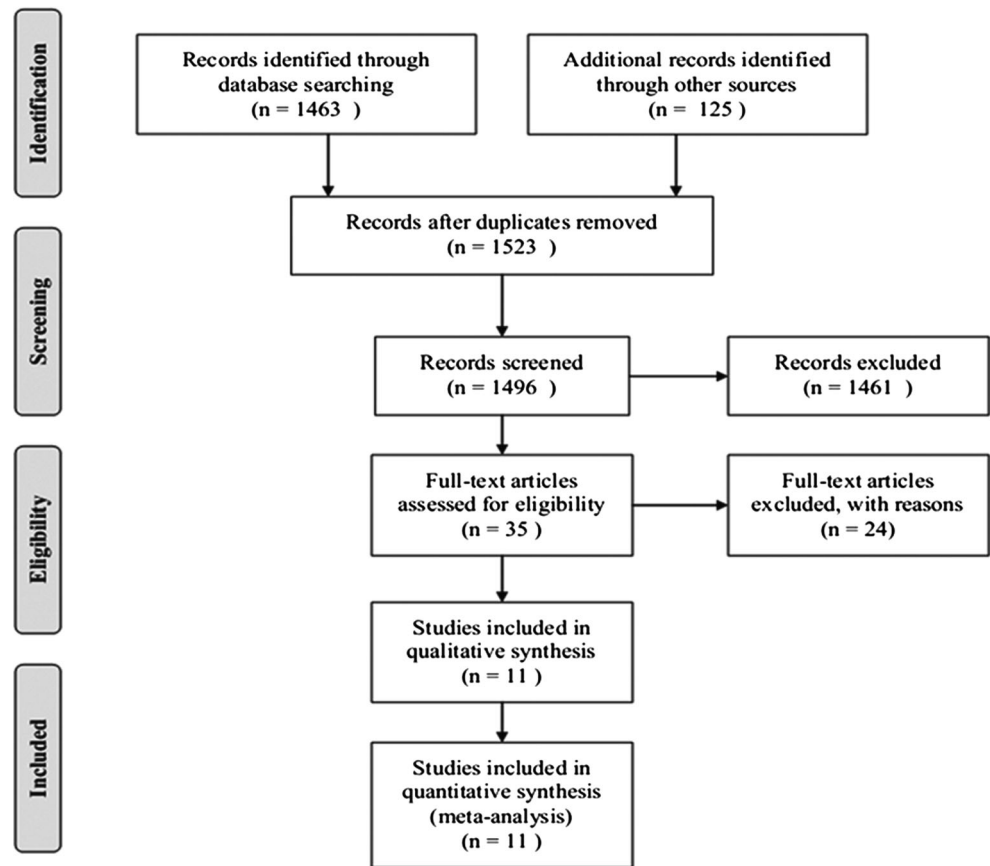
Significant publication bias in short-term and long-term VASs was also tested and the results of the Begg and Egger tests proved the absence of significant bias ($P>0.05$). The sensitivity analysis indicated the lack of significant impact on the final pooled result following the exclusion of any of the eligible studies in either a short-term or a long-term analysis.

Oswestry Disability Index

ODI was used to indicate the functional improvement in patients treated with either KP or VP. Three studies were involved in analyzing short-term ODI, and four articles provided data for long-term ODI analysis. As shown in Fig. 4, the pooled SMD showed that KP was associated with significant improvement in short-term (SMD, -1.50 ; 95 % CI: $-2.94, -0.07$; $P=0.040$) and long-term (SMD, -1.03 ; 95 % CI: $-1.88, -0.18$; $P=0.012$) ODI when compared with VP.

Kyphosis angle and vertebral body height

Four trials were involved in analyzing short-term kyphosis angle, and five articles provided data for long-term kyphosis angle. Figure 5 illustrates significant improvements in short-term (SMD, -0.74 ; 95 % CI: $-1.42, -0.06$; $P=0.032$) and long-term (SMD, -0.71 ; 95 % CI: $-1.19, -0.23$; $P=0.004$) kyphosis angles. Further, KP was associated with significant improvement in vertebral body height (SMD, 1.56 ; 95 % CI: $0.62, 2.49$; $P=0.001$) and anterior vertebral body height (SMD, 3.04 ; 95 % CI: $0.53, 5.56$; $P=0.018$), whereas KP had a minimal effect on posterior vertebral body height (SMD, 0.23 ; 95 % CI: $-0.06, 0.52$; $P=0.113$; Fig. 5). The sensitivity analysis showed that the reliance of the pooled short-term result was relatively low. Exclusion of any study published by Schofer [34], Movrin [36], and Dong [39] led to

Fig. 1 Summary of study selection and exclusion

a similar effect on the restoration of kyphotic angle between the VP and KP groups.

Operation time

Data from the two studies were used to assess the impact of VP versus KP on operation time (Fig. 6a). The pooled analysis showed that KP was associated with longer operation time when compared with VP (SMD, 0.73; 95 % CI: 0.26, 1.19; $P=0.002$).

Complications

The comprehensive search identified seven studies that described the incidence of cement leakage and adjacent fractures after KP or VP. Overall, the data relevant to cement leakage were pooled, and KP intervention was found to be superior to VP with a lower risk of cement leakage (RR, 0.68; 95 % CI: 0.48, 0.96; $P=0.030$; Fig. 6b). The test of publication bias revealed no significant bias ($P>0.05$). The sensitivity analysis established that the studies of Schofer [34] and Movrin [36] were the main sources of heterogeneity. These two articles significantly influenced the final result of comparison of the occurrence of cement leakage between the KP and VP groups.

Seven studies discussed adjacent fractures, and the meta-analysis indicated the absence of significant differences in the risk of adjacent vertebral body fractures between the VP and KP groups (RR, 1.25; 95 % CI: 0.54, 2.86; $P=0.600$; Fig. 6c). No significant publication bias was observed. In addition, the sensitivity analysis suggested no significant variation in RR attributable to heterogeneity.

Discussion

Summary of evidence

Previous studies suggested that both KP and VP exhibit significant improvements in health-related quality of life, pain control, and restoration of functional ability, when compared with optimal pain medication. Indeed, in a recently released guidance, KP and VP were recommended as options for treating selected patients with OVCFs [12]. However, little evidence exists supporting the recommendation for KP or VP. The present meta-analysis demonstrated that KP and VP offered similar benefits in terms of short-term pain relief and incidence of adjacent fractures. KP was also found to be a better option compared with VP for improving long-term

Table 1 Study characteristics

Study	Country	Study design	Patient numbers		Age (years)		Gender (M/F)		No. of vertebral bodies		Volume of cement injected (cm ³)		Follow-up (mo)	Lost to follow-up
			KP	VP	KP	VP	KP	VP	KP	VP	KP	VP		
Dong 2012	China	Prospective comparative study	51	35	69.8 (60–80)	70.5 (62–81)	34/52	57	37	NR	NR	21.3 (7–36)	NR	
Folman 2011	Israel	Prospective comparative study	31	14	70.71 ± 13.4	75.57 ± 7.3	9/22	5/9	31	14	NR	NR	12	NR
Kumar 2010	Canada	Prospective comparative study	24	28	73 (52–89)	78 (57–94)	7/17	9/19	39	56	1.8 (0.75–5.0)	3.2 (1.0–7.0)	42.3 for KP; 42.2 for VP	6
Movrin 2010	Slovenia	Prospective comparative study	46	27	67.8 ± 5.4	72.9 ± 5.6	10/36	5/22	51	32	5.5 ± 1.1	5.8 ± 1.7	12	NR
Liu 2010	China	Randomized controlled trial	50	50	72.3 ± 7.6	74.3 ± 6.4	11/39	12/38	50	50	5.56 ± 0.62	4.91 ± 0.65	6	NR
Santiago 2010	Spain	Prospective comparative study	30	30	65.9 ± 1.9	73 ± 1.5	9/21	5/25	42	69	NR	NR	12	NR
Rollinghoff 2009	Germany	Prospective comparative study	53	51	68.9 ± 10.4		17/73	53	51	NR	NR	NR	12	10
Schofer 2009	Germany	Prospective comparative study	30	30	72.5 ± 5.7	73.8 ± 6.4	8/22	6/24	30	30	4.9 ± 1.2	3.9 ± 1.5	13.5 for KP; 13.7 for VP	11
Lovi 2009	Italy	Prospective comparative study	36	118	67.6 (53–95)		56/98	47	152	3.2	2.5	33	10	
Zhou 2008	China	Prospective comparative study	42	56	64 (31–74)	62 (28–73)	17/25	21/35	42	56	NR	NR	12	NR
Grohs 2005	Australia	Prospective comparative study	28	23	70 (65–74)		7/21	5/18	35	29	NR	NR	24	NR

KP kyphoplasty, VP vertebroplasty, M male, F female, mo month, NR not reported

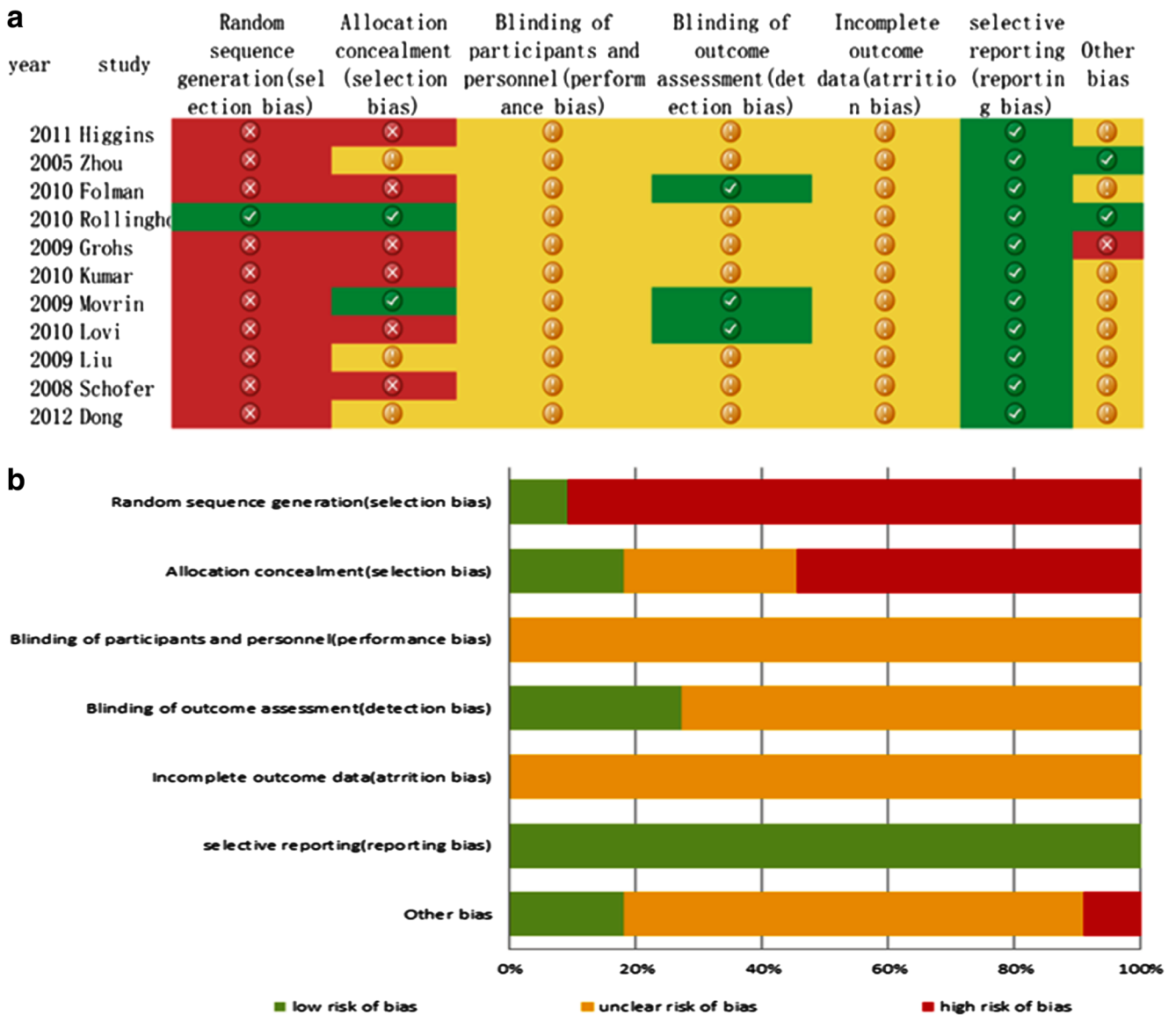


Fig. 2 Assessment of bias in included studies (a) and percentage of evaluated bias among all included studies (b)

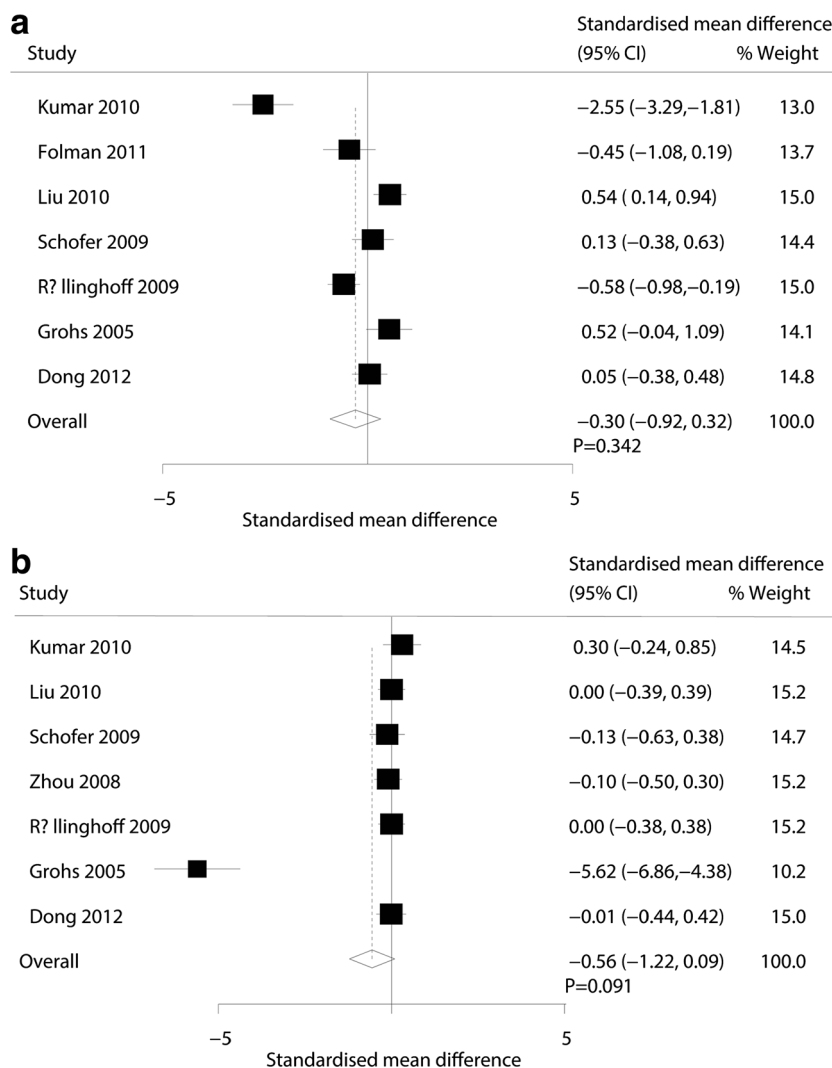
VAS, ODI, vertebral body height, and kyphosis angle, with a significantly lower risk of cement leakage.

The methodological evaluation of each included study was limited by selection, allocation, performance, and detection bias. The present meta-analysis included only one RCT, and the remaining 10 studies were prospective comparative studies. None of the included studies provide clear methods of blinding, suggesting detection and performance bias. Although all the studies were associated with a low risk of reporting bias, the other bias contributed to heterogeneity in every study. Ultimately, considering the unsatisfactory quality of the included studies, recommendations were provided with caution for treating patients with OVCFs.

The previous works reviewed in this study revealed that vertebral augmentation techniques provided immediate pain

relief and improved function in patients with OVCFs [40–43]. Furthermore, no significant differences were observed in the incidence of secondary fractures between vertebral augmentation techniques and conservative treatment for patients with OVCFs [44]. Traditionally, bed rest, optimal pain medication, and other noninvasive interventions were used to treat OVCFs. In recent years, several studies [4, 7] comparing VP with optimal pain therapy reported that pain was measured using VAS, with significant improvements in short-term and medium-term pain relief after VP treatment. The FREE study [7] compared KP with a nonoperative therapy and used SF-36 to assess changes in pain from baseline to post-KP. The FREE study indicated that the participants undergoing KP improved more than those undergoing traditional therapy after 12 months of follow-up. However, two RCTs [44, 45] reported that when compared with operative placebo in blinding, VP

Fig. 3 Forest plot and pooled data showing the standard mean difference (SMD) in the VAS scores in KP and VP interventions (**a** short-term, **b** long-term)



failed to show superior efficacy in controlling pain. When compared with VP, KP had no significant impact on short-term VAS and resulted in significant improvements in long-term pain relief. These results were consistent with those of Liu et al. [5], who used a randomized controlled design to demonstrate that VAS pain scores did not differ significantly between the treatment groups after 6 months of follow-up.

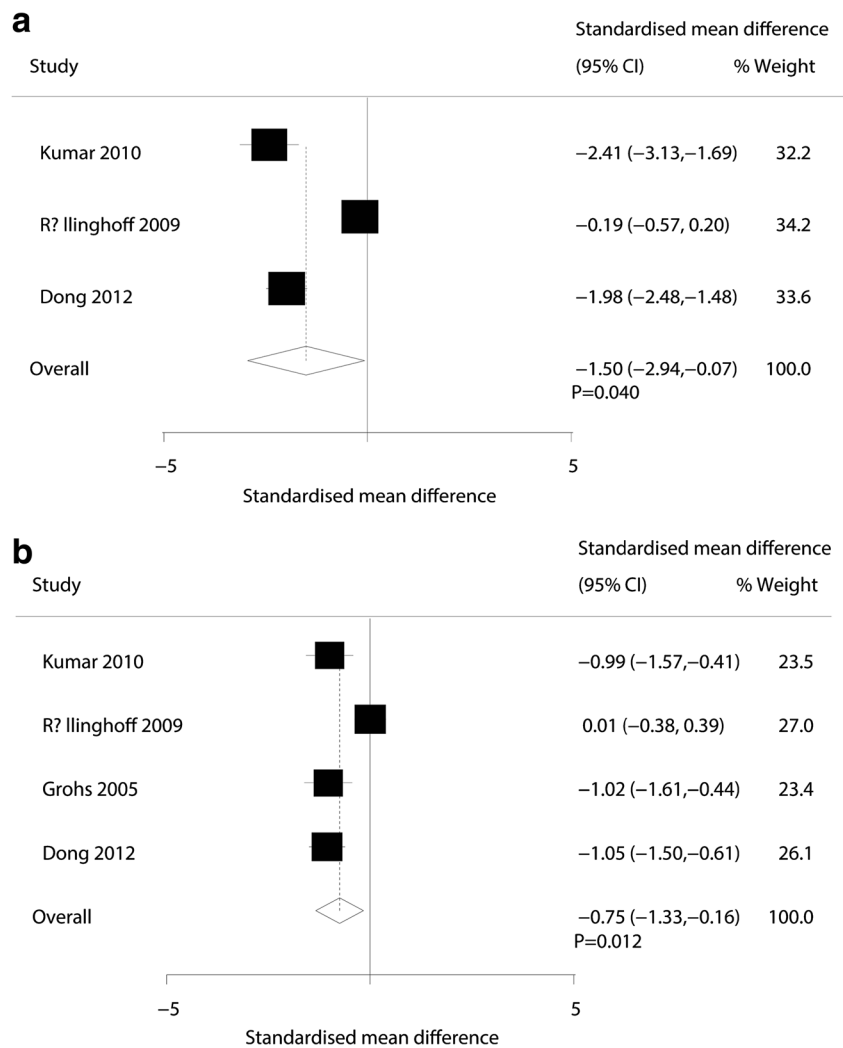
ODI scores serve as indicators of quality of life. A review [2] showed that KP and VP were associated with better functionality, based on improved ODI scores. In the present analysis, significant differences were found in short-term and long-term improvement of ODIs between the KP and VP groups, contrary to the results of other meta-analyses [46, 47]. The findings of the present study were consistent with those of Kumar et al. [35], which indicated that KP showed 10 % greater improvement, and at the last follow-up, the patients who received KP continued to show greater improvements in disability compared with the VP group. However, these conclusions might be untenable due to smaller sample

sizes. The present results provide a synthetic and comprehensive review.

The pooled analysis of data suggested that KP was more effective in restoring vertebral body height and kyphosis angle compared with VP. However, some studies suggested that improvements in vertebral body height were not correlated with better clinical outcomes in either KP or VP [33, 34]. In analyzing the kyphosis angle in short-term and long-term studies, KP showed convincing improvement in restoring the kyphosis angle. However, different methods of measuring postoperative kyphosis angle, different duration of follow-up, and individual conditions may reduce the reliability of these results.

KP and VP were invasive procedures with treatment-associated complications such as cement leakage. Compared with KP, VP was associated with a higher risk of cement leakage, which increased the risk of pulmonary embolism, myelopathy, or radiculopathy [48–50]. The creation of balloon cavity and the use of more viscous cement account for the

Fig. 4 Improving quality of life by directly pooling ODI data (**a** short-term, **b** long-term): KP versus VP



major differences between VP and KP [50]. In VP, the materials injected into the gaps of fractures were less viscous, enabling it to easily flow through gaps in the fractured vertebral body. In addition, the trabecular bone influenced the leakage of cement in the cortex [50]. The fracture patterns of the endplates and anterior or posterior walls were additional factors affecting the incidence of cement leakage in both the KP and VP groups. In previous studies, the prevalence of cement leakage was found to be incidental. However, these incidental events were attended to as the leaks caused transient or continuous pain or spinal cord compression if the leakage volume was large [50–52].

Adjacent-level fracture was another complication. No significant differences in adjacent-level fractures were found between KP and VP due to the lower risk of cement leakage and other improvements with KP [53]. Patients with a history of vertebral body fractures had a higher risk of developing new vertebral fractures than patients who never experienced a fracture [54, 55]. Studies that focused on the risk of newly diagnosed fractures in patients with OVCFs following VP or KP

[55] suggest that the risk of vertebral body fracture increased following KP. However, this study had several limitations, and additional studies are needed to resolve this issue.

Limitations

Similar to other meta-analyses, the limitations of the present study were as follows. First, the poor quality of included studies hampered the quality of work. Lack of randomization, blinding, and other methodological parameters were the most obvious limitations associated with selection bias, reporting bias, performance bias, and detection bias, resulting in the overestimation or underestimation of treatment effects. Second, the methods using for measuring pain and other

Fig. 5 Comparison of KP and VP in improving kyphotic angle, vertebral body height, anterior vertebral body height, and posterior vertebral body height (**a** short-term kyphotic angle, **b** long-term kyphotic angle, **c** vertebral body height, **d** anterior vertebral body height, **e** posterior vertebral body height)

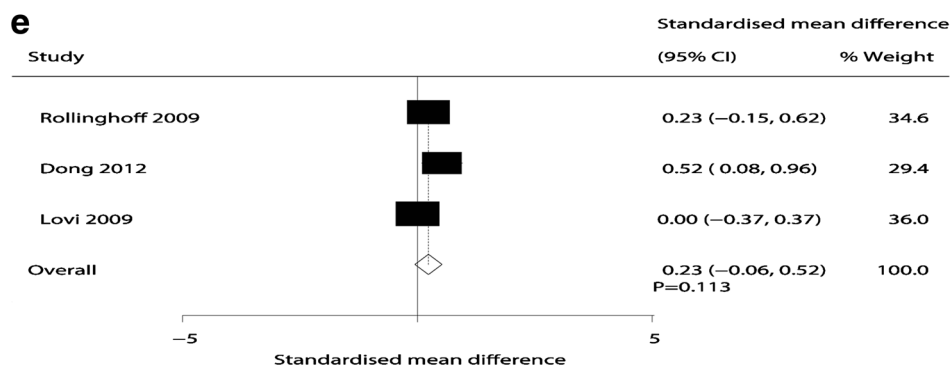
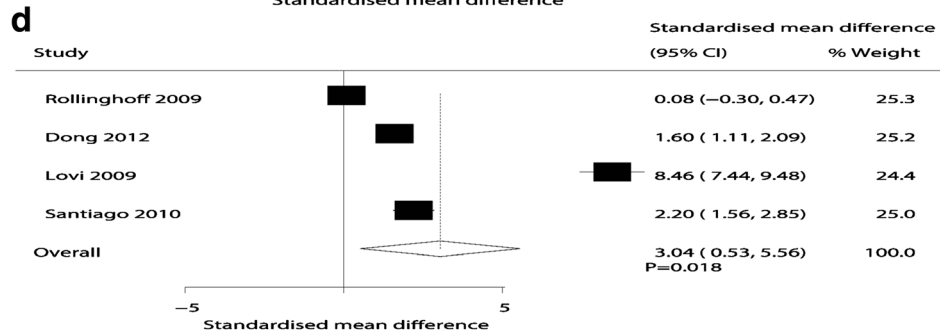
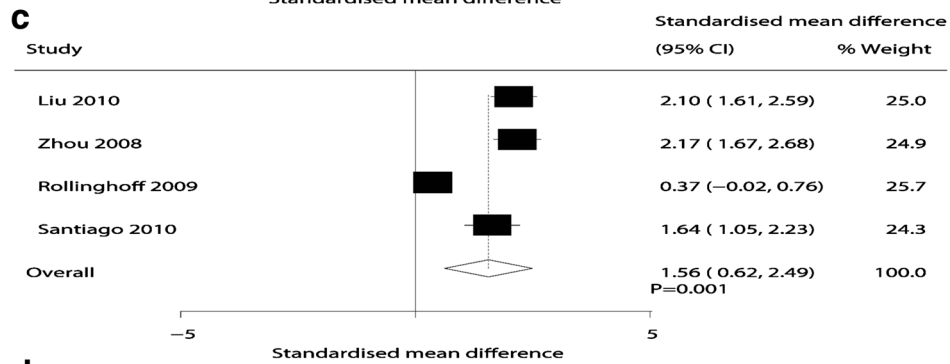
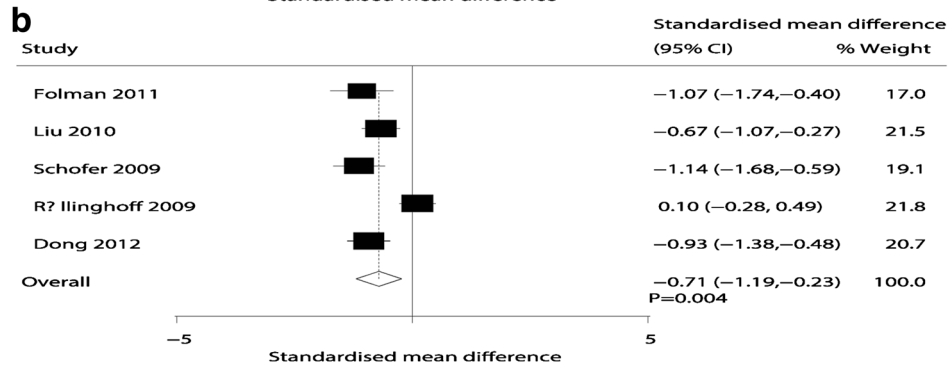
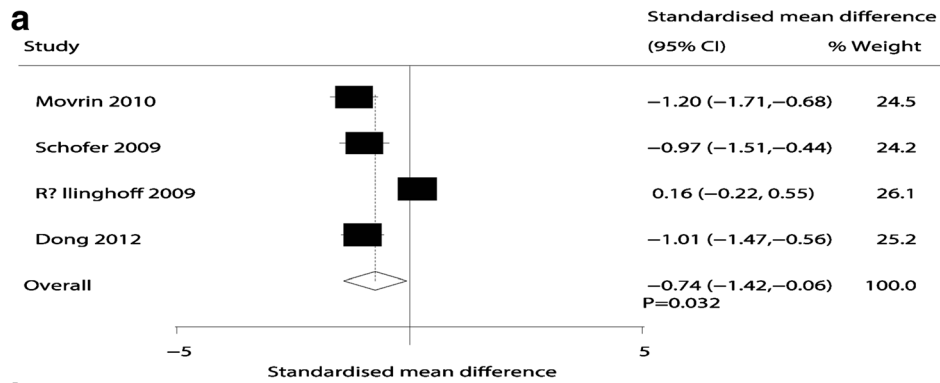
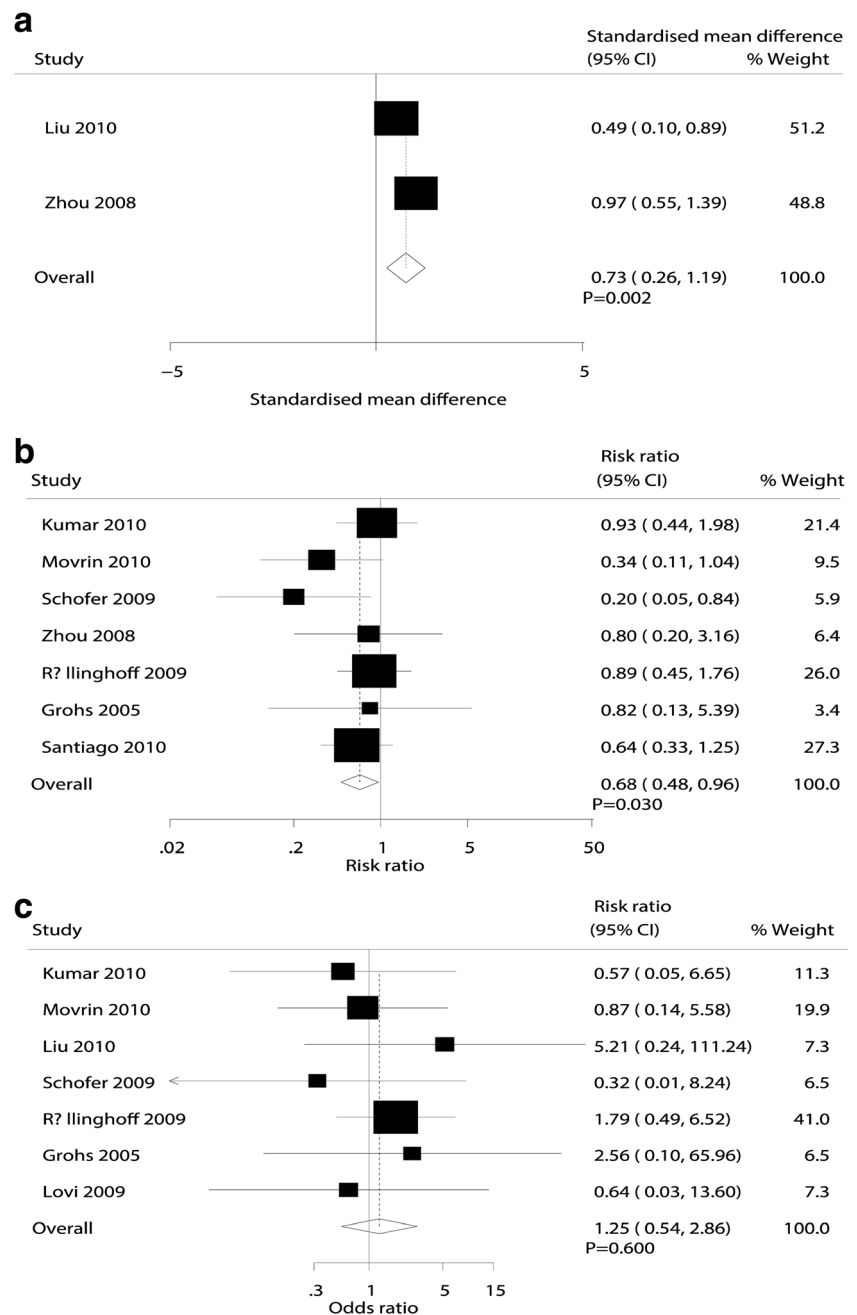


Fig. 6 Forest plot and pooled data of operation time, incidence of cement leakage, and adjacent-level fractures in KP and VP (**a** operation time, **b** cement leakage, **c** adjacent-level fractures)



outcomes varied among studies. Further, individual variation also increased the difficulty of accurate measurement of pain, including characteristics such as pain threshold, level of activity, and analgesia [56], all of which increased the risk of heterogeneity. Third, the population involved in this meta-analysis included patients with OVCFs, regardless of the primary cause of fractures (tumor or trauma, for example) due to the absence of studies investigating the OVCFs population. Fourth, the results of the meta-analysis suggest no significant differences between pain relief attributed to KP and VP. Measuring pain via VAS scores was not clearly associated with the anatomical site

of the painful fracture and failed to really evaluate the effect of intervention. As a result, evaluating the efficacy of interventions was of no benefit. Fifth, no available studies tried to correct for the presence of degenerative changes at the spine, which may affect the outcome of any osteoplastic intervention at the spine. Finally, as KP and VP showed a similar effect in improving the quality of life, it was suggested that KP was preferable to VP for treating OVCFs without considering the economic burden. However, other studies reported that KP was more cost-effective than VP or nonsurgical management in treating patients with vertebral body fractures.

Conclusions

The current study provides useful recommendations by showing that both VP and KP had a similar effect on short-term pain relief, posterior vertebral body weight, and adjacent-level fractures. Compared with VP, KP was more effective for long-term VAS, short- and long-term ODIs, and functional improvements in kyphosis angle, anterior vertebral body height, and mean vertebral body height with a significantly reduced risk of incidence of cement leakage. Due to some risk of selection bias in this study, further large-scale RCTs are needed to verify the treatment outcomes.

Compliance with ethical standards

Conflicts of interest None.

Sources of financial support None.

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