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REVIEW ARTICLE

High- versus low-viscosity cement vertebroplasty and kyphoplasty for osteoporotic vertebral compression fracture: a meta-analysis

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Abstract

Background To compare high- versus low-viscosity bone cement on the clinical outcomes and complications in patients with Osteoporotic vertebral compression fractures (OVCFs) who underwent percutaneous vertebroplasty (PVP) or percutaneous kyphoplasty (PKP).

Methods PubMed, Embase, and the Cochrane Library were searched for papers published from inception up to February 2021 for potentially eligible studies comparing high- versus low-viscosity cement for PVP/PKP. The outcomes were the leakage rate, visual analog scale (VAS), and Oswestry Disability Index (ODI).

Results Eight studies (558 patients; 279 in each group) were included. The meta-analysis showed that the leakage rate was lower with high-viscosity cement than with low-viscosity cement (OR = 0.23, 95%CI 0.14–0.39, $P < 0.001$; $I^2 = 43.5\%$, $P_{\text{heterogeneity}} = 0.088$); similar results were observed specifically for the disk space, paravertebral space, and peripheral vein, but there were no differences regarding the epidural space and intraspinal space. The VAS was decreased more significantly with high-viscosity cement than with low-viscosity cement (WMD = − 0.21, 95%CI − 0.38, − 0.04, $P = 0.015$; $I^2 = 0.0\%$, $P_{\text{heterogeneity}} = 0.565$). Regarding the ODI, there was no difference between high- and low-viscosity cement (WMD = − 0.88, 95%CI − 3.06, 1.29, $P = 0.426$; $I^2 = 78.3\%$, $P_{\text{heterogeneity}} < 0.001$).

Conclusions There were lower cement leakage rates in PVP/PKP with high-viscosity bone cement than low-viscosity bone cement. The two groups have similar results in ODI, but the VAS scores favor high-viscosity bone cement. Therefore, the administration of high-viscosity bone cement in PVP/ PKP could be a potential option for improving the complications of leakage in OVCFs, while the clinical efficacy of relieving pain is not certain.

Keywords Osteoporotic fractures · Spine · Vertebroplasty · Kyphoplasty · Bone cement · Viscosity

Abbreviations

OVCFs	Osteoporotic vertebral compression fractures
PVP	Percutaneous vertebroplasty
PKF	Percutaneous kyphoplasty
VAS	Visual analog scale
ODI	Oswestry disability index
PKP	Percutaneous kyphoplasty
NOS	Newcastle–Ottawa scale
RCTs	Randomized controlled trials
SD	Standard deviations
ORs	Odds ratios
WMDs	Weighted mean differences
CIs	Confidence intervals

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Introduction

Osteoporosis can lead to osteoporotic vertebral fractures (OVCFs) [1–3]. Because of the aging population, OVCF is one of the major health problems worldwide [1–3]. In the United States, about 700,000 osteoporotic fractures of the thoracic and lumbar spine (most commonly in the thoracolumbar transition zone or midthoracic region) are reported annually [1]. In addition, one in six elderly patients treated in the emergency department for a condition where a lateral chest X-ray is indicated is reported to have an incidental vertebral fracture seen on X-ray [4]. About 20% of the elderly population is > 70 years of

age, and 16% of postmenopausal women will experience OVCFs worldwide [5]. Percutaneous vertebroplasty (PVP) is widely used in patients with OVCFs and accompanying back pain, and percutaneous kyphoplasty (PKP) is a technique based on improved PVP [6, 7]. Bone cement is used in PVP and PKP to treat OVCFs [6, 7].

The use of high-viscosity cement does not completely prevent leakage, and low-viscosity cement is associated with some worries about possible leakage from the vertebra [8]. Previous studies reported that PVP using high-viscosity bone cement in treating OVCFs could significantly reduce the rate of cement leakage and improve operation safety [9–12]. Nevertheless, in terms of clinical efficacy, the advantages of high-viscosity cement are still controversial [8–17]. A 2018 meta-analysis (with the literature search up to 2017) showed that although high- and low-viscosity cement had similar clinical outcomes, high-viscosity cement had a lower risk of leakage in the disk space or vein [18]. Since then, new studies and trials have been performed, and including these new studies in a newly updated meta-analysis could provide additional insights into the use of bone cement. A network meta-analysis also supported the lower risk of leakage for high-viscosity cement in vertebral compression fractures [19].

The authors hypothesized that high-viscosity bone cement is superior to low-viscosity bone cement on the clinical outcome and complications in patients with OVCFs who underwent PVP or PKP. Therefore, this meta-analysis aimed to compare high- vs. low-viscosity bone cement on the clinical outcomes [visual analog scale (VAS) and Oswestry Disability Index (ODI)] and complications in patients with OVCFs who underwent PVP or PKP. The results might help determine the optimal approach for such patients.

Materials and methods

Literature search

The present systematic review and meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [20]. The search strategy and the eligibility criteria were designed according to the PICOS principle [21]. PubMed, Embase, and the Cochrane Library were searched for papers published from inception up to February 2021 for potentially eligible studies using the MeSH terms "Osteoporotic Fractures" and "high viscosity cement" as well as relevant key words, followed by screening based on the eligibility criteria. Two investigators performed the literature search and study selection process independently according to a pre-specified protocol. Discrepancies were solved by discussion.

Eligibility criteria

The eligibility criteria were (1) population: patients with OVCF, (2) exposure: treated with PVP/PKP and high-viscosity bone cement, (3) non-exposed control: treated with PVP/PKP and low-viscosity bone cement, (4) outcomes: leakage rate, VAS, and ODI, and (5) full-text published in English. Case reports, reviews, meta-analyses, letters to the editor, and animal studies were excluded. If more than one paper reported the same study population, only the most recent one matching the eligibility criteria was included (Fig. 1).

Data extraction

The study characteristics (authors and year of publication), patient characteristics (disease, sex, age, and follow-up time), treatment parameters (method of intervention and vertebral body position), and outcomes (leakage rate, ODI, and VAS) were extracted independently by two investigators according to a pre-specified protocol. Discrepancies were solved by discussion until a consensus was reached.

Quality of the evidence

The level of evidence of all included articles was assessed independently by two authors according to the Newcastle–Ottawa scale (NOS) for the cohort studies [22] and the Cochrane RoB 2 tool for the randomized controlled trials (RCTs) [23, 24]. Discrepancies in the assessment were resolved through discussion until a consensus was reached.

Data synthesis

For continuous outcomes, the mean values and standard deviations (SD) were used to compute the odds ratios (ORs) and weighted mean differences (WMDs) and their corresponding 95% confidence intervals (CIs) [24, 25]. The data were analyzed according to the exposure of PVP/PKP with high- versus low-viscosity bone cement.

Statistical analysis

All analyses were performed using STATA SE 14.0 (StataCorp, College Station, Texas, USA). Statistical heterogeneity among the studies was calculated using Cochran's Q-test and the I^2 index. An $I^2 > 50\%$ and Q-test $P < 0.10$ indicated high heterogeneity, and the random-effects model

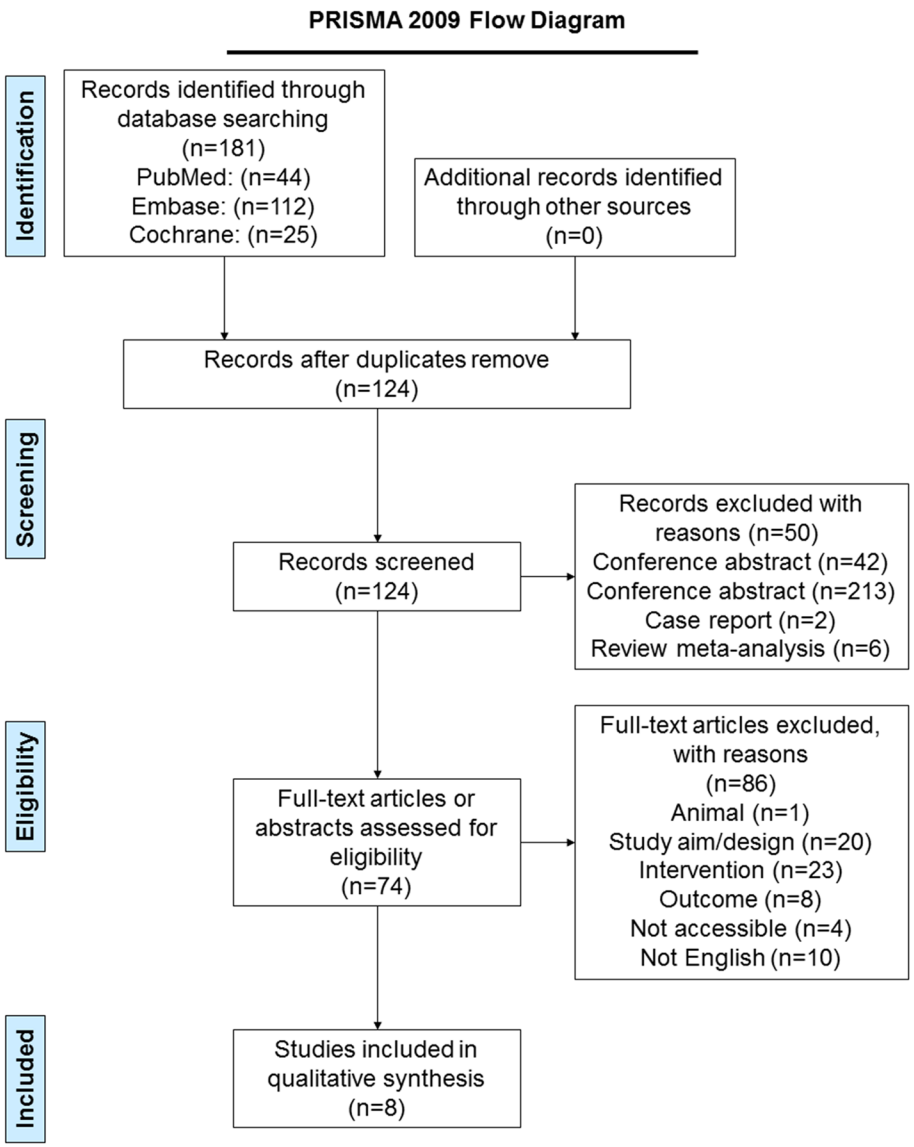

Fig. 1 PRISMA 2009 flow diagram

was used; otherwise, the fixed-effects model was applied. *P*-values < 0.05 were considered statistically different. The potential publication bias was not assessed using funnel plots and Egger's test because the number of studies included in each analysis was < 10, in which case the funnel plots and Egger's test could yield misleading results [24]. Sensitivity analyses were performed by running the meta-analyses and sequentially excluding each study in turn (Table 1).

Results

Study selection

The initial search yielded 181 records. After removing the duplicates, 124 records were screened, and 50 were excluded. Then, 74 full-text articles or abstracts were assessed for eligibility, and 66 were excluded (animal study,

Table 1 Results of VAS and ODI from meta-analysis

Outcome	No. of study	WMD	Lower 95%CI	Upper 95%CI	*P*	I^2 (%)	$P_{heterogeneity}$
VAS	8	−0.208	−0.375	−0.040	0.015	0	0.565
ODI	7	−0.883	−3.057	1.291	0.426	78.3	< 0.001

High-viscosity bone cement versus low-viscosity bone cement

VAS Visual analog scale, *ODI* Oswestry Disability Index, *WMD* weighted mean difference, *CI* confidence interval

$n=1$; study aim/design, $n=20$; intervention, $n=23$; outcome, $n=8$; not accessible, $n=4$; not in English, $n=10$).

Finally, eight papers were included [9–12, 14–16, 26] (Table 2). All studies were from China. There were three RCTs [11, 12, 26] and five cohort studies [9, 10, 14–16]. The studies included 558 patients (279 with high-viscosity cement and 279 with low-viscosity cement. All studies investigated PVP, except one retrospective study in which PVP was performed with high-viscosity cement and PKP was performed with low-viscosity cement [15]. According to the RoB 2 tool, one RCT [11] scored 4 points, and two RCTs [17, 26] scored 5 points (Supplementary Table S1). According to the NOS, one study [15] scored 7 points, and four studies [9, 10, 14, 16] scored 8 points (Supplementary Table S2).

Leakage rate

All eight studies [9–12, 14–16, 26] presented the total leakage rate. The meta-analysis showed that the leakage rate was lower with high-viscosity cement than with low-viscosity cement (OR = 0.23, 95%CI 0.14–0.39, $P<0.001$; $I^2=43.5\%$, $P_{\text{heterogeneity}}=0.088$) (Fig. 2 and Table 3). Specifically, the leakage rate was lower with high-viscosity cement than with low-viscosity cement in the disk space (OR = 0.30, 95%CI 0.17–0.54, $P<0.001$; $I^2=0.0\%$, $P_{\text{heterogeneity}}=0.723$), paravertebral space (OR = 0.40, 95%CI 0.22–0. 73 $P=0.003$; $I^2=0.0\%$, $P_{\text{heterogeneity}}=0.842$), and peripheral vein (OR = 0.28, 95%CI 0.14–0.53, $P<0.001$; $I^2=0.0\%$, $P_{\text{heterogeneity}}=0.972$), while there were no differences regarding the epidural space (OR = 0.25, 95%CI 0.04–1.60, $P=0.143$; $I^2=0.0\%$, $P_{\text{heterogeneity}}=0.749$) and intraspinal space (OR = 0.45, 95%CI 0.14–1.45, $P=0.182$; $I^2=0.0\%$, $P_{\text{heterogeneity}}=0.950$) (Fig. 2 and Table 3).

VAS

All eight studies [9–12, 14–16, 26] presented VAS data. The meta-analysis showed that the VAS was decreased more significantly with high-viscosity cement than with low-viscosity cement (WMD = − 0.21, 95%CI − 0.38, − 0.04, $P=0.015$; $I^2=0.0\%$, $P_{\text{heterogeneity}}=0.565$) (Fig. 3 and Table 3).

ODI

All eight studies [9–12, 14–16, 26] presented ODI data. The meta-analysis showed no difference between high- and low-viscosity cement (WMD = − 0.88, 95%CI − 3.06, 1.29, $P=0.426$; $I^2=78.3\%$, $P_{\text{heterogeneity}}<0.001$) (Fig. 4 and Table 3).

Sensitivity analysis

The sensitivity analyses showed that the meta-analyses for the total leak rate (Fig. S1), VAS (Fig. S2), and ODI (Fig. S3).

Discussion

OVCFs can be treated using PVP or PKP and either low- or high-viscosity cement. Studies suggested different outcomes and safety issues between the two types of cement [8–17]. This meta-analysis aimed to compare high- vs. low-viscosity bone cement on the clinical outcomes and complications in patients with OVCFs who underwent PVP or PKP. The results suggest lower cement leakage rates in PVP/PKP with high-viscosity bone cement than low-viscosity bone cement. PVP/PKP with high- and low-viscosity cement have similar results in ODI, but the VAS scores favor high-viscosity bone cement (Table 2).

In this meta-analysis, a lower risk of cement leakage, in general, was observed with the high-viscosity bone cement compared with the low-viscosity one. This is supported by previous meta-analyses [18, 19]. More specifically, the risk was lower regarding disk space, paravertebral space, and peripheral, while there were no differences regarding the epidural space and intraspinal space. Chen et al. [19] did not analyze the specific leakage in the vertebral compression fractures, while Zhang et al. [18] observed that high-viscosity cement had a lower risk of leakage in the disk space or vein. A retrospective study also showed that high-viscosity cement was less likely to leak in the vein but without difference for disk space, paravertebral area, or intraspinal space [10]. These results of subgroup analysis are not completely consistent with the present analysis. The anatomical characteristics and the filling volume could influence the areas where thinner cement could be more likely to leak, and discrepancies among studies could be due to the techniques used and the exact types and brands of cement being compared.

Bone- and fracture-related parameters, injection methods, and cement properties are the three most important factors influencing the risk of leakage [27]. Indeed, cortical fractures are the most likely to leak [28]. Disk space leakage is mainly due to endplate fracture [29]. Osteoporotic degeneration of the surrounding bone could also influence the leakage rate since Alhashash et al. [13] showed that patients with a *T*-score worse than − 1.8 had a higher risk of leakage if a low-viscosity bone cement were used. Although the methods of PVP and PKP are mature, iatrogenic injury to the endplate or the cortical body can lead to cement leakage [18]. In addition, as for any viscous fluid, the cement will spread along the paths offering the least resistance in the vertebral

Table 2 Literature search and study characteristic

Author, Year	Country	Study design	Disease	No. patients			Age case (years)		Male, *n* (%)		Operation		Vertebrae	Average/whole follow-up time
				Total	HV	LV	HV	LV	HV	LV	HV	LV		
Li, 2020 [14]	China	Retrospective cohort study	OVCF	80	40	40	68.2 ± 6.4	67.4 ± 6.9	11 (27.5%)	13 (32.5%)	PVP	PVP	Thoracic and lumbar T10-L5	12 months
Gao, 2020 [26]	China	RCT	OVCF	70	35	35	68.21 ± 10.87	68.17 ± 10.73	15 (42.86%)	13 (37.14%)	PVP	PVP	Not mentioned	12 months
Tang, 2019 [9]	China	Retrospective cohort study	OVCF	72	38	34	78.50 ± 6.29	78.41 ± 7.77	10 (26.32%)	7 (20.59%)	PVP	PVP	T7-L5	12 months
Zhang, 2017 [10]	China	Retrospective cohort study	OVCF	66	36	30	72.03 ± 7.44	70.43 ± 6.95	24 (66.7%)	20 (66.7%)	PVP	PVP	Thoracolumbar vertebral body T 11-L 2	12 months
Guo, 2017 [11]	China	RCT	OVCF	100	50	50	77.2 ± 8.1	75.4 ± 6.8	25 (50%)	2 8(56%)	PVP	PVP	Not mentioned	HV: 2.5 ± 0.8 years; LV:2.2 ± 1.6 years
Sun, 2016 [15]	China	Retrospective cohort study	OVCF	98	46	52	65.4 ± 2.6	65.2 ± 3.3	12 (26.09%)	14 (26.92%)	PVP	PKP	Not mentioned	HV: 22.7 ± 3.3 months LV: 21.7 ± 2.3 months
Zhang, 2015 [12]	China	RCT	OVCF	32	14	18	75.5 ± 9.3	75.8 ± 9.3	2	3	PVP	PVP	Not mentioned	24.5 months
Zeng, 2015 [16]	China	Retrospective cohort study	Osteoporotic thoracolumbar compression fractures	40	20	20	66.4 ± 9.8	18 (45%)	PVP	PVP	Not mentioned	HV: 2.0 ± 0.6 years; LV: 2.0 ± 0.5 years		

HV high-viscosity bone cement, *LV* low-viscosity bone cement, *OVCF* osteoporotic vertebral compression fracture, *PVP* percutaneous vertebroplasty, *PKP* percutaneous kyphoplasty, *RCT* randomized controlled trial

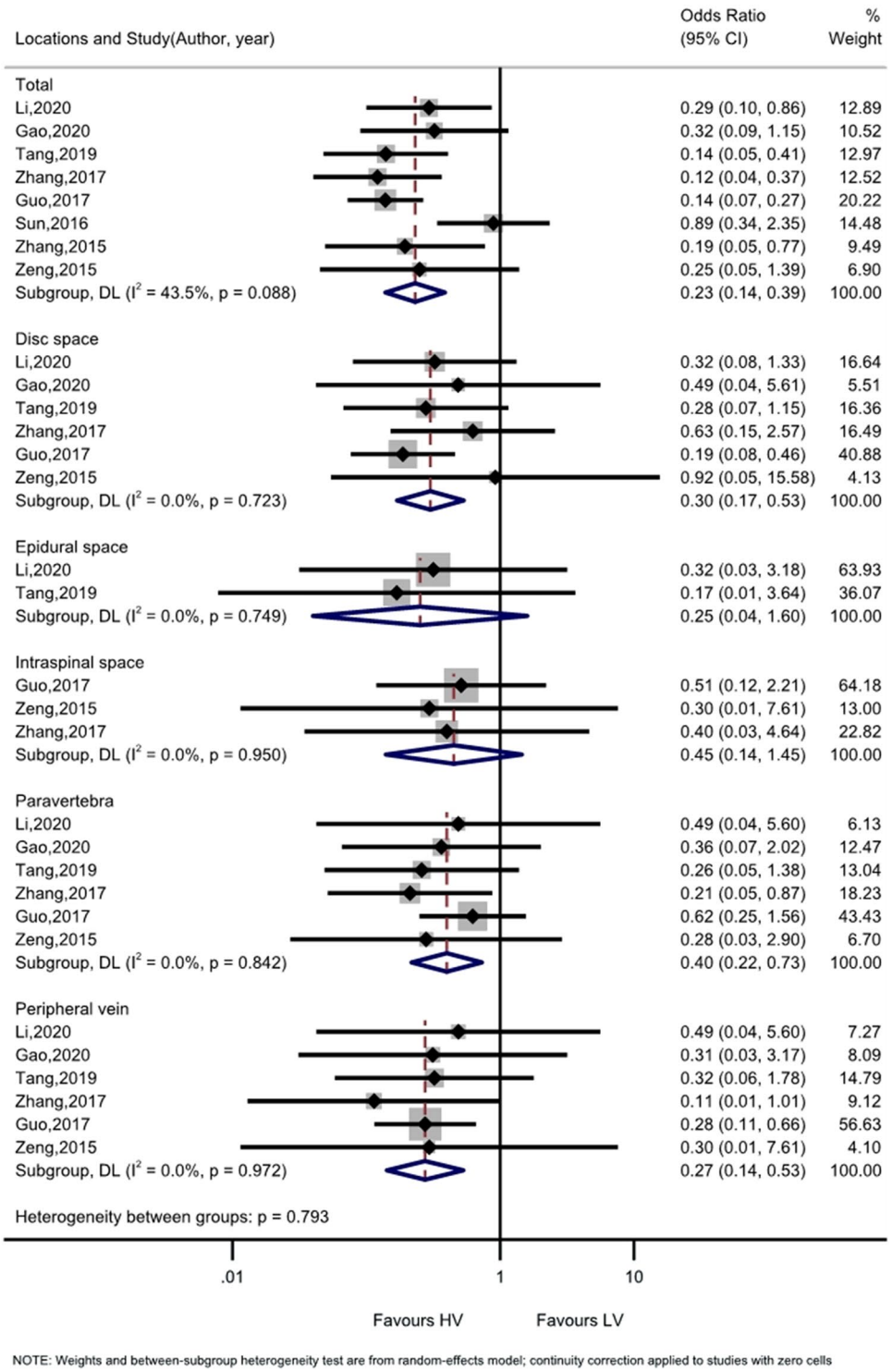

Fig. 2 Forest plot of leakage rate comparing high-viscosity bone cement group with low-viscosity bone cement group

body and fracture [30]. High-viscosity bone cement will spread more uniformly than low-viscosity cement [30, 31], reducing the risk of a leak at one site while the fracture is still not completely filled [18]. Using a gelatin sponge can decrease the risk of vein leakage, but it increases the number of interventions [32].

Regarding the clinical outcomes, the present study showed no difference in the ODI (functional outcome) but a better VAS for pain with the high-viscosity cement. Pain after PVP/PKP can be due to cement leakage, and the present meta-analysis also showed a lower risk of leakage with high-viscosity bone cement. Still, Zhang et al. [18] showed no

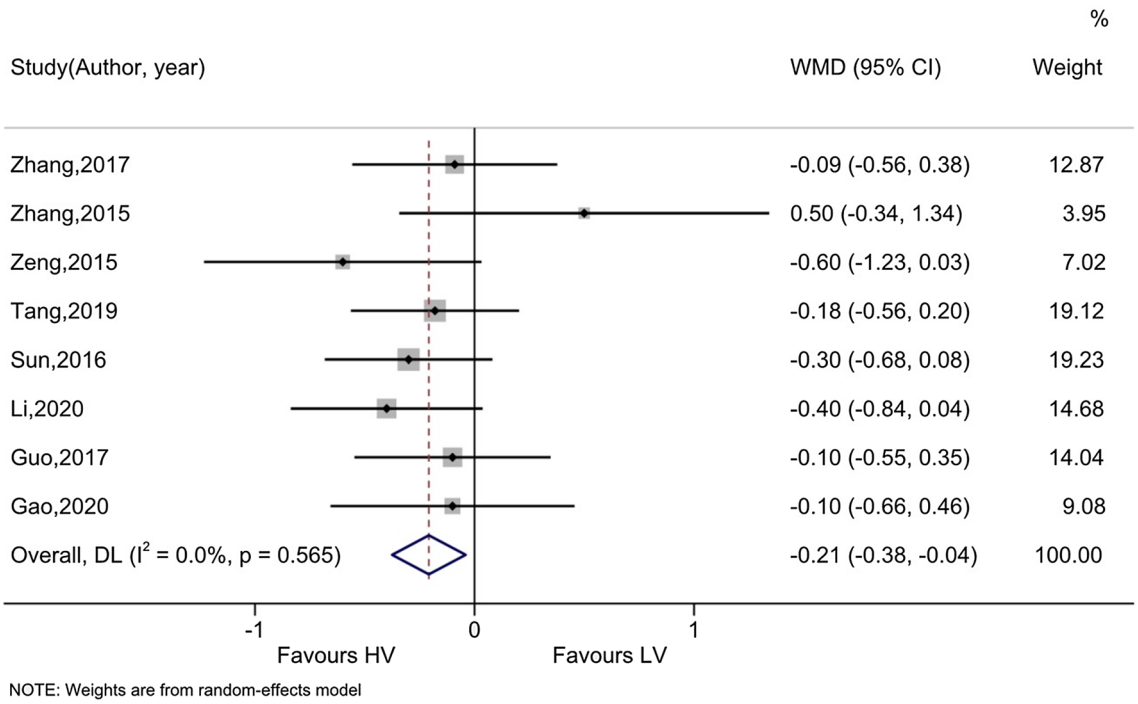

Fig. 3 Forest plot of the visual analog scale (VAS) comparing high-viscosity bone cement group with low-viscosity bone cement group

difference in VAS and ODI between high- or low- viscosity cement. Of course, the studies included in the meta-analyses can influence the results, as well as the evaluation timing of the included studies. Miao et al. [8] also reported no differences in VAS. On the other hand, other studies that did not meet the eligibility criteria of the present meta-analysis nevertheless support a lower VAS with high-viscosity cement [13, 33, 34] and better ODI [13]. Well-designed studies with long-term follow-up are necessary to determine the clinical outcomes between high- and low-viscosity cement in future.

There are three types of osteoporotic compression fractures: wedge, crush (or biconcave), and burst [2]. These fractures have different prognoses [35]. The non-operative management of stable thoracolumbar burst fractures has been advocated for some years [36]. Crush fractures are usually considered complicated, and non-surgical studies often exclude them for the sake of safety and only include, for example, wedge fractures [37]. Furthermore, many studies, such as the ones included in this meta-analysis, do not specify the types of fractures included. Performing a subgroup analysis based on the types of fractures would be of clinical value to determine the efficacy of PVP/PKP in such fractures, but it is impossible for now.

This study has limitations. Most of the included studies were single-center studies, and the bone cement materials they used might be different and have certain

Table 3 Results of the leakage rate from the meta-analysis

Outcome	Subgroup	No. of study	OR	Lower 95%CI	Upper 95%CI	P	I^2 (%)	$P_{heterogeneity}$
Leakage rate	Total	8	0.231	0.139	0.386	< 0.001	43.5	0.088
	Disk space	6	0.301	0.169	0.536	< 0.001	0	0.723
	Epidural space	2	0.252	0.040	1.596	0.143	0	0.749
	Intraspinal space	3	0.450	0.140	1.453	0.182	0	0.950
	Paravertebral	6	0.399	0.218	0.730	0.003	0	0.842
	Peripheral vein	6	0.275	0.142	0.530	< 0.001	0	0.972

High-viscosity bone cement versus low-viscosity bone cement

OR odds ratio, *CI* confidence interval

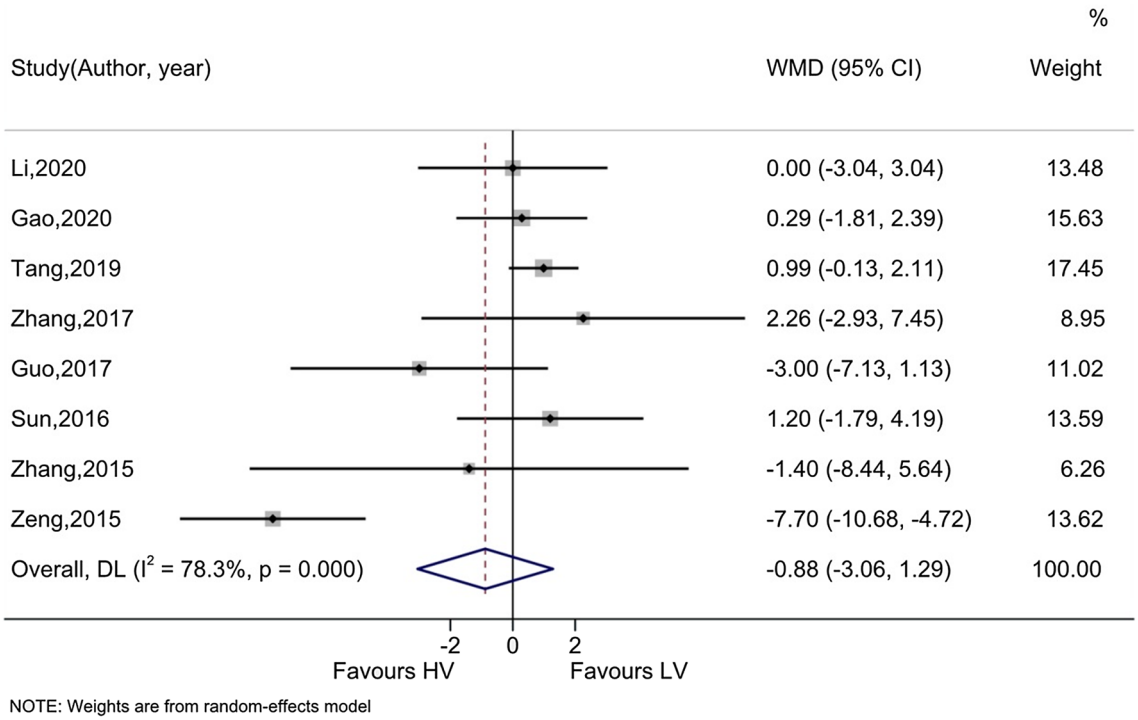

Fig. 4 Forest plot of the Oswestry Disability Index (ODI) comparing high-viscosity bone cement group with low-viscosity bone cement group

heterogeneity. This study direction is relatively new, so the number of reports was small, and there is a lack of high-quality RCT evidence. The included patients have certain heterogeneity, possibly biasing the results. Most studies did not report the exact type of OVCF, preventing a subgroup analysis of cement leakage according to the exact type of fracture. Finally, as for any meta-analysis, the quality of this meta-analysis is limited to the quality of the included studies. Indeed, no cohort study scored higher than 8 points on the NOS, and no RCT scored higher than 5 points on the RoB 2. In addition, one study used high-viscosity cement for PVP and low-viscosity cement for PKP [15], which is bound to bias the results.

In conclusion, compared with low-viscosity bone cement, PVP/PKP using high-viscosity bone cement might improve the VAS with fewer leakage complications. In terms of clinical efficacy, both cement types achieved similar ODI. Future high-quality studies with larger numbers of patients and not limited to single-level OVCFs are encouraged. Long-term follow-up will be necessary to evaluate the safety and efficacy of high-viscosity bone cement.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00586-022-07150-w.

Author contributions QW analyzed and interpreted the patient data regarding osteoporotic vertebral compression fracture. QW performed the statistical analysis, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Data availability The dataset(s) supporting the conclusions of this article is(are) included within the article (and its additional file(s).

Declarations

Conflict of interest The authors declare that they have no competing interests.

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