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High-viscosity versus low-viscosity cement for the treatment of vertebral compression fractures

A meta-analysis of randomized controlled trials

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Abstract

Background: High viscosity cement (HVC) and low viscosity cement (LVC) have been used to treat osteoporotic vertebral compression fractures (OVCFs). Our study was to assess the safety and efficacy of HVC and LVC in treating OVCFs.

Methods: We searched the electronic database for randomized controlled trials of HVC and LVC to treat OVCFs. Random-effects model was performed to pool the outcomes about operation time, visual analogue scale (VAS), bone cement injection volume, oswestry disability index (ODI), bone cement leakage and adjacent vertebral fractures.

Results: Twelve randomized trials were included in the meta-analysis. The 2 groups had similar changes in terms of bone cement injection volume, ODI and adjacent vertebral fractures. The HVC group showed shorter operation time and better VAS score improvement. The bone cement leakage rate of the HVC group was significantly better than LVC group ($P < .00001$). According to the location of bone cement leakage, in the leakages of the veins ($P < .00001$), the intervertebral disc ($P < .00001$), the paravertebral area ($P = .003$) and the intraspinal space ($P = .03$), the HVC group were significantly better than the LVC group.

Conclusions: In terms of bone cement injection volume, ODI and adjacent vertebral fractures, the 2 group are equivalent. HVC had a shorter operation time, lower bone cement leakage rate and better VAS score improvement, compared with LVC.

Abbreviations: CI = confidence intervals, HVC = high-viscosity cement, LVC = low-viscosity cement, MD = mean differences, ODI = oswestry disability index, OVCFs = osteoporotic vertebral compression fractures, PKP = percutaneous kyphoplasty, PVP = percutaneous vertebroplasty, RR = risk ratio, VAS = visual analogue scale, VCF = vertebral compression fracture.

Keywords: cement leakage, high-viscosity cement, meta-analysis, vertebral compression fractures

1. Introduction

Osteoporosis can cause a gradual loss of calcium from bone tissue, resulting in a decrease in bone density and bone strength. In daily work and life, osteoporosis patients are very susceptible to fractures from slight external force, among which the osteoporotic vertebral compression fracture (OVCF) is the most common.[1,2] An OVCF can cause persistent back pain, spinal deformities, spinal cord and nerve damage, and even paralysis, seriously affecting the function of multiple systems.[3–6] Traditional therapies include physical therapy, long-term bed rest, medication and open surgery. Some complications may occur in patients who are bedridden for a long time, such as bedsores, deep vein thrombosis of the lower extremities, pulmonary infections and urinary tract infections.[7] Open surgery is mostly used in patients with symptoms of nerve compression who require the decompression of the spinal canal, and there are complications such as slow postoperative recovery and limited vertebral body movement.[8]

In recent years, with the development of minimally invasive techniques for the spine, more and more scholars have applied percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP) to treating fresh compression fractures of the spine. Compared with open surgery, these 2 minimally invasive surgical methods cause less trauma, effectively strengthen the vertebral body, relieve pain, stabilize the vertebral body, and prevent kyphotic deformities caused by further compression of the vertebral body. In addition, they can enable the patient to get out of bed early and thus avoid related complications caused by long-term bed rest, which can improve the patient's quality of life.[9,10] However, minimally invasive surgery may involve bone cement leakage, the refracture of the responsible vertebral body and adjacent vertebral body, pulmonary embolism, and toxic reactions to bone cement, etc.[11] The most common complication is bone cement leakage, and studies have shown that the incidence of this leakage is 25% to 40%.[12] Bone cement leakage into the intervertebral disc or paravertebral soft tissue generally does not produce clinical symptoms. If it penetrates into the blood

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vessel or spinal canal, it can cause pulmonary embolism and spinal cord compression, and severe cases can cause paralysis and death.[13] Therefore, reducing the leakage of bone cement has become a hot spot for scholars. As the primary parameter of bone cement performance, viscosity is currently considered as the key factor that affects bone cement leakage after surgery.[14] Tang et al[15] retrospectively analyzed the efficacy of high-viscosity cement (HVC) and low-viscosity cement (LVC) to treating OVCF, and they found that HVC can significantly reduce the leakage rate of bone cement and improve the safety of the surgery. A prospective randomized controlled study conducted by Fang et al also showed that HVC had a lower leakage rate of bone cement.[16] However, some scholars believe that bone cement leakage between HVC and LVC are equivalent.[17–19] In addition, the conclusions of researches on the location of bone cement leakage are also different. A prospective study by Guo[20]et al showed that HVC was significantly lower than LVC in terms of the rates of disc leakage and venous leakage, but there was no significant difference between the 2 bone cements in intraspinal and paravertebral leakage. Huang[21] et al found that HVC and LVC displayed significant differences in the rate of venous leakage, but no difference in disc leakage.

To date, several scholars have studied the efficacy, leakage rate and other complications of HVC and LVC, but the number of cases in a single study is small and the strength of the relevant meta-analysis evidence is low. To this end, we conducted a systematic review and meta-analysis to understand the efficacy and safety of HVC and LVC in treating osteoporotic vertebral compression fractures.

2. Materials and methods

2.1. Search strategy

Two independent evaluators conducted a relevant literature retrieval on EMBASE, PubMed, Cochrane Library, Web of Science and China National Knowledge Infrastructure. The following key words were entered for the search: (high-viscosity OR high viscosity) AND (vertebral fracture* OR vertebral compression fracture* OR vertebral compression fracture [VCF*] OR osteoporotic vertebral compression fracture* OR OVCF*). The last search was performed on December 23, 2021, with no language restrictions. Moreover, the reference list of relevant study was also applied to search. Ethics approval is not required as this study is a meta-analysis based on published studies.

2.2. Criteria for selected trials

Studies that met the following criteria were included in the meta-analysis: This study was a randomized controlled trial comparing HVC and LVC; the subjects were diagnosed with a vertebral compression fracture caused by osteoporosis; and the results of the study on the filling and leakage of bone cement and the patient's physical function were reported. The exclusion criteria are as follows: Case reports, reviews, observational studies, basic science experiments; animal or body research; and studies for which data were not available. Repeated published research. Two reviewers independently extracted potentially eligible studies based on the inclusion and exclusion criteria. Differences were resolved through discussion and consultation, and an agreement was reached.

2.3. Data extraction

The 2 evaluators independently extracted the relevant information from each eligible study. Any inconsistencies were resolved by discussion and consultation, and if necessary, the opinion of the third examiner was consulted until all participants reached a consensus. The information included the study design, publication year, study location, intervention details, sample size, VCF level, age, gender distribution, follow-up time, and clinical results. The combined outcome parameters included the surgical parameters (operation time and bone cement injection volume) and clinical indicators including visual analogue scale (VAS), bone cement leakage, adjacent vertebral fractures and oswestry disability index (ODI). The sites of bone cement leakage were classified into the paravertebral regions, intraspinal canal, intervertebral disc space, and peripheral veins. The short-term, mid-term and long-term follow-up times were 1 to 3 months, 6 to 12 months and more than 12 months.

2.4. Quality assessment

Two reviewers independently assessed the risk of bias in the included randomized controlled studies based on the Cochrane review criteria. In addition, the Grades of Recommendation, Assessment, Development and Evaluation approach ranked the strength of evidence for all the merged results. According to the evaluation of the study design, bias risk, consistency, directness and accuracy, the quality of the results was divided into 4 categories: extremely low, low, medium and high.[22]

2.5. Statistical analysis

Continuous outcomes were pooled into mean differences (MD) with 95% confidence intervals (CI). Dichotomous data were expressed as the risk ratio (RR) and 95% CI. The χ^2 ($P < .1$ indicates heterogeneity) and I^2 statistic ($I^2 > 50\%$ indicates high heterogeneity) were used to evaluate the heterogeneity between studies.[23,24]The outcomes were pooled using random effects models. Funnel plots and Egger tests were used to identify the possibility of publication bias. Subgroup analyses were performed based on the locations of cement leakage, the surgical methods and follow-up information. Sensitivity analyses were used to evaluate the source of high heterogeneity. The data analyses were used in Review Manager 5.3. The Egger test was performed using Stata 12.0. P values < .05 were considered statistically significant.

3. Results

3.1. Search results

The 567 relevant studies were preliminarily retrieved from PubMed (n = 53), EMBASE (n = 159), the Cochrane Library (n = 23), Web of Science (n = 115), and China National Knowledge Infrastructure, (n = 217), and 411 remained after repeats were excluded. After a review of the titles and abstracts, the number of articles was reduced to 104. Lastly, through reading the full text, a total of 12 randomized controlled studies[16,17,20,21,25–32] were included in the meta-analysis (Fig. 1). There are 4 articles in English and 8 in Chinese. The characteristics of all the studies are summarized in Table 1.

3.2. Quality assessment

All 12 RCT studies were subject to quality assessment according to the Cochrane review criteria. The risk of bias summary is shown in Figure 2. According to the Grades of Recommendation, Assessment, Development and Evaluation approach, 2 pooled outcomes displayed high quality evidence, 5 showed moderate quality evidence and 2 contained low quality evidence (Table 2).

3.3. Meta-analysis results

3.3.1. Operation time. A total of 7 articles reported the operation time. The operation time of the HVC group was significantly shorter than that of the LVC group (MD: –11.73;

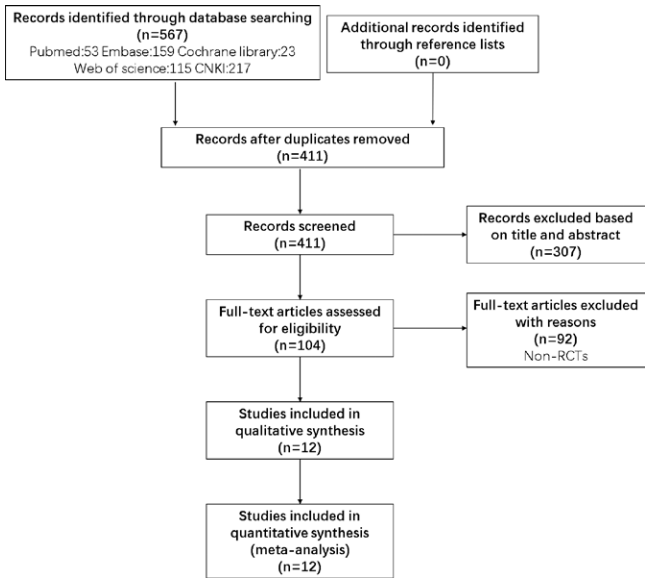

Figure 1. Flow chart of the study selection procedure.

analysis, and the results still showed no significant difference between HVC and LVC (MD: –0.08; 95% CI: –0.18 to 0.02; $P = .10$) with no heterogeneity ($P = .77$, $I^2 = 0\%$) (Fig. 4B).

3.3.3. Bone cement leakage. A total of 12 randomized controlled trials reported bone cement leakage. We performed a subgroup analysis on the amount of bone cement leakage according to the different surgical methods (Fig. 5A). Overall, the bone cement leakage of the HVC group was significantly lower than that of the LVC group (RR: 0.40; 95% CI: 0.29–0.54; $P < .00001$) with high heterogeneity ($P = .0008$, $I^2 = 63\%$). On the subgroup side, for the bone cement leakage, the results revealed a significant difference in the PVP when using HVC versus PVP using LVC (RR: 0.34; 95% CI: 0.28–0.42; [$P < .00001$]) with no heterogeneity ($P = .86$, $I^2 = 0\%$) and PKP using HVC versus PKP using LVC (RR: 0.26; 95% CI: 0.10–0.67; $P = .005$) with no heterogeneity ($P = .69$, $I^2 = 0\%$), while no significant differences were found in the PVP when using HVC versus PKP using LVC (RR: 0.61; 95% CI: 0.26–1.42; $P = .25$) with high heterogeneity ($P = .005$, $I^2 = 77\%$). We removed PVP with HVC versus PKP with LVC for the sensitivity analysis, and the pooled results still showed that the bone cement leakage of the HVC group was significantly lower than that of the LVC group (RR: 0.34; 95% CI: 0.28–0.41; $P < .00001$) with no

Table 1

The characteristics of included studies.

Studies	Country	Surgical methods	Levels of VCF		Sample size (Male/Female)		Mean age (yr)		Follow-up
			HVC	LVC	HVC	LVC	HVC	LVC	
Huang 2014	China	PVP	98	92	30 (6/24)	30 (2/28)	68.1	67.8	2–5 yr
Xu 2014	China	PVP	98	92	30 (6/24)	30 (2/28)	71.3	73.2	2–5 yr
Zhou 2015	China	PVP vs PKP*	56	54	40 (13/27)	40 (10/30)	65.6	66.0	1 yr
Zhang 2015	China	PVP	17	22	14 (2/12)	18 (3/15)	75.5	75.8	1.5–3.5 yr
Li 2016	China	PVP vs PKP*	49	49	49 (19/30)	49 (18/31)	62.1	63.6	3 d
Guo 2017	China	PVP	98	86	50 (25/25)	50 (28/22)	77.2	75.4	HVC:2.5y LVC:2.2y
Yang 2017	China	PVP	45	45	45 (28/17)	45 (26/19)	54.4	56.3	NA
Liu 2018	China	PVP HVC vs.LVC	64	68	47 (6/41)	46(5/41)	64.27	65.33	1 yr
		PKP HVC vs.LVC	66	67	44 (4/40)	46(6/40)	64.55	63.99	
Wang 2019	China	PKP	42	48	42 (14/28)	48 (15/33)	65.34	66.42	3 mon
Fang 2019	China	PVP	100	100	100 (40/60)	100 (42/58)	70.23	71.14	1 yr
Alhashash 2019	Germany	PVP	37	36	30 (12/18)	30 (13/17)	68.63	71.53	2 yr
Lv 2020	China	PVP vs.PKP*	33	33	33 (15/18)	33 (13/20)	73.06	73.39	1 yr

PKP = percutaneous kyphoplasty, PVP = percutaneous vertebroplasty.

HVC = high-viscosity cement, LVC = low-viscosity cement, VCF = vertebral compressive fracture, NA = not available, d = days, m = months, y = years.

*PVP using HVC versus PKP using LVC.

95% CI: –13.10– –10.36; $P < .00001$) with low heterogeneity ($P = .08$, $I^2 = 46\%$) (Fig. 3).

3.3.2. Bone cement injection. A total of 8 randomized controlled trials reported the bone cement injection volumes. We performed a subgroup analysis on the bone cement injection quantity according to different surgical methods (Fig. 4A). In general, there was no significant difference between HVC and LVC in the amount of bone cement injection (MD: –0.49; 95% CI: –1.03 to 0.04; $P = .07$) with high heterogeneity ($P < .00001$, $I^2 = 98\%$). In terms of subgroups, for the injected cement volume, the results revealed no significant difference with PVP when using HVC versus PVP using LVC (MD: –0.11; 95% CI: –0.23 to 0.01; $P = .08$) with no heterogeneity ($P = .72$, $I^2 = 0\%$) and PKP using HVC versus PKP using LVC (MD: –0.03; 95% CI: –0.21 to 0.15; $P = .75$) with no heterogeneity ($P = .41$, $I^2 = 0\%$). A significant difference was found for PVP when using HVC versus PKP using LVC (MD: –1.44; 95% CI: –2.46 to 0.43; $P = .005$) with high heterogeneity ($P < .00001$, $I^2 = 98\%$) We removed PVP with HVC versus PKP with LVC for the sensitivity heterogeneity ($P = .93$, $I^2 = 0\%$) (Fig. 5B).

In addition, we performed a subgroup analysis of bone cement leakage according to its location (Fig. 6). The pooled results for the leakages of the veins (RR: 0.24; 95% CI:0.17–0.34; $P < .00001$), the intervertebral disc (RR: 0.36; 95% CI: 0.25–0.54; $P < .00001$), the paravertebral area (RR: 0.53; 95% CI: 0.35–0.81; $P = .003$) and the intraspinal space (RR: 0.40; 95% CI: 0.18–0.90; $P = .03$) in the HVC group were significantly reduced compared with those in the LVC group with no heterogeneity.

3.3.4. VAS, ODI and adjacent vertebral fracture. We extracted data on the VAS and ODI from the included randomized controlled trials, and we performed a subgroup analysis based on the length of the follow-up time. On the whole, for the VAS, the HVC group was significantly lower than the LVC group (MD: –0.11; 95% CI: –0.19 to 0.04; $P = .003$) with low heterogeneity ($P = .006$, $I^2 = 45\%$). In terms of subgroups, the results revealed no significant differences at the preoperative time (MD: –0.06; 95% CI: –0.21 to –0.09; $P = .45$)

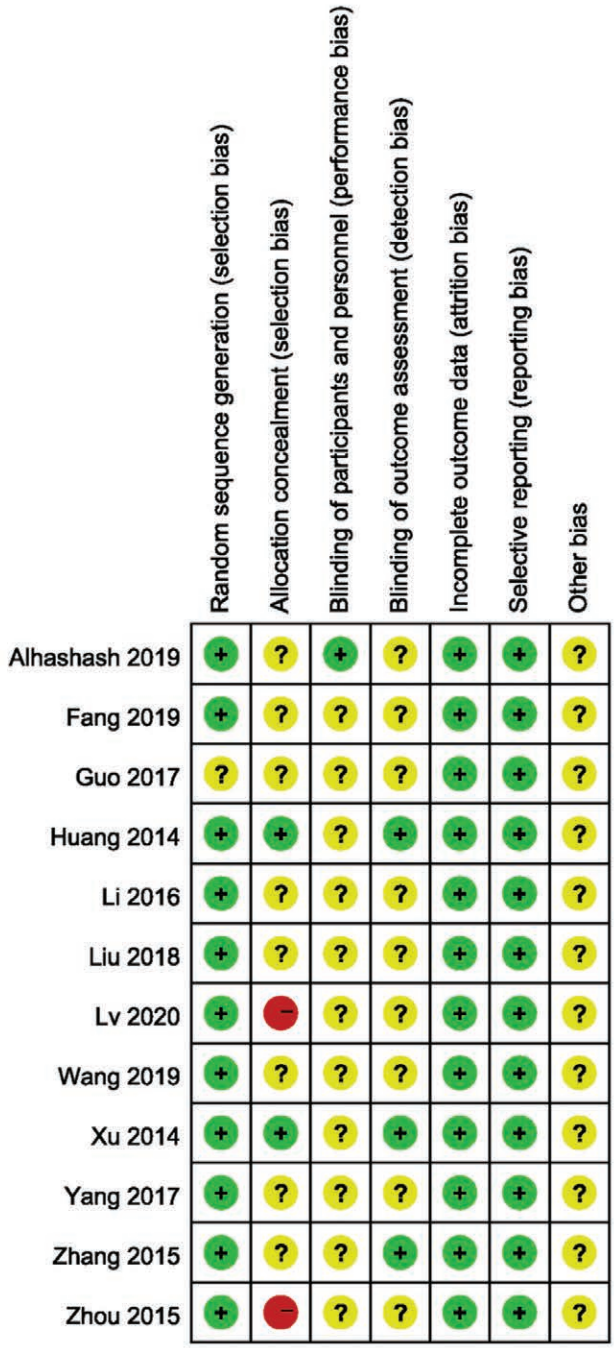

Figure 2. Risk of bias summary of RCTs.

with no heterogeneity ($P = .54$, $I^2 = 0\%$) within 7 days post-operation (MD: –0.04; 95% CI: –0.12 to 0.04; $P = .36$) with no heterogeneity ($P = .62$, $I^2 = 0\%$), midterm follow-up (MD: –0.04; 95% CI: –0.13 to 0.04; $P = .30$) with no heterogeneity ($P = .38$, $I^2 = 0\%$) and long-term follow-up (MD: –0.29; 95% CI: –0.73 to 0.15; $P = .20$) with high heterogeneity ($P = .07$, $I^2 = 62\%$), and a significant difference was present at the short term follow-up (MD: –0.27; 95% CI: –0.47 to –0.06; $P = .01$) with high heterogeneity ($P = .002$, $I^2 = 74\%$) (Fig. 7).

For the ODI, on the whole, the pooled results revealed no significant differences between the HVC group and the LVC group (MD: 0.50; 95% CI: –0.01 to 1.02; $P = .06$) with low heterogeneity ($P = .17$, $I^2 = 22\%$). In terms of subgroups, the results revealed no significant differences at the preoperative time (MD: 0.07; 95% CI: –1.71 to 1.84; $P = .94$) with low heterogeneity ($P = .12$, $I^2 = 39\%$) within 7 days post-operation (MD: –0.01; 95% CI: –1.04 to 1.01; $P = .98$) with no heterogeneity ($P = .40$, $I^2 = 0\%$), midterm follow-up (MD: 0.24; 95% CI: –0.78 to 1.26; $P = .64$) with no heterogeneity ($P = .19$, $I^2 = 37\%$) and long-term follow-up (MD: 1.06; 95% CI: –0.94 to 3.06; $P = .30$) with low heterogeneity ($P = .14$, $I^2 = 48\%$), and a significant difference was found at the short term follow-up (MD: 0.88; 95% CI: 0.08–1.67; $P = .03$) with no heterogeneity ($P = .68$, $I^2 = 0\%$) (Fig. 8).

A total of 5 articles have reported on adjacent vertebral fractures. No significant difference was found between the HVC group and the LVC group (RR: 1.32; 95% CI: 0.60–2.90; $P = .50$) with low heterogeneity ($P = .35$, $I^2 = 10\%$) (Fig. 9).

3.3.5. Publication bias. The funnel plots for bone cement leakage (Fig. 10A), VAS (Fig. 10B) and ODI (Fig. 10C) showed no obvious publication bias, and the Egger test results on bone cement leakage ($t = 0.43$, $P = .678$), VAS ($t = –0.38$, $P = .709$) and ODI ($t = –0.56$, $P = .578$) also showed no obvious evidence of publication bias.

4. Discussion

In recent years, PVP and PKP have become important minimally invasive surgical techniques for treating osteoporotic vertebral compression fractures. However, care must be taken when performing this operation, because there is a risk of bone cement leakage. Bone cement leakage is closely related to the quality of the vertebrae, fracture-related factors, bone cement factors, and bone cement injection methods. Short-term activity does not affect the established vertebral fracture morphology at the moment of the fracture, and the operational steps and bone cement injection pattern have been streamlined, therefore, improving the properties of the bone cement to reduce the leakage rate has become the focus of research. Fluidity and viscosity are important properties of bone cement. The diffusion velocity and filling degree of bone cement are directly affected by its viscosity. One study[33] found that the viscosity of bone cement was an independent risk factor for bone cement leakage. Compared with LVC, HVC has the characteristics of a short mixing liquid period, high instantaneous viscosity, long injection time, low polymerization temperature, and dispersion of bone cement, etc.[34] Since the advent of HVC, many researchers have evaluated its safety and effectiveness; however, its effect on the efficacy and leakage rate of vertebral compression fractures remains controversial.[17–19,35,36]

At present, 1 meta-analysis has compared the efficacy of HVC and LVC in treating vertebral compression fractures.[37] The meta-analysis concluded that HVC and LVC both had the same satisfactory effect. In addition, in terms of bone cement leakage, the incidence of leakage was higher with HVC was lower than with LVC, especially in the peripheral vein and intervertebral disc space, but there was no significant difference in the paravertebral and intraspinal areas. However, this meta-analysis only included 2 randomized controlled trials and 5 cohort studies, and the methodological quality of one randomized controlled trial was very low, so the research results had some limitations.

Our meta-analysis results showed that the operation time of the HVC group was significantly shorter than that of the LVC group, but the amount of bone cement injection between the 2 groups were equivalent. The subgroup analysis showed that there was a significant difference in the amount of bone cement injection in this subgroup of PVP versus PKP, and there was no difference in the other 2 groups. Due to high heterogeneity, after this subgroup was eliminated, the results still indicated that there was no difference in the bone cement injection volume between the 2 HVC and LVC groups. This finding is consistent with the study by Zhang et al.[37] In our analysis, the amount of injected

Table 2

Summary of strength of evidence with regard to the outcomes.

Outcomes	Studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Operation time	7	Serious †	No	No	No	Moderate
Injected cement volume	8	Serious †	Serious ‡	No	No	Low
Cement leakage	12	Serious †	Serious ‡	No	No	Low
VAS scores	9	Serious †	No	No	No	Moderate
ODI	8	Serious †	No	No	No	Moderate
Cobb angle	3	No	No	No	Serious ⊹	Moderate
Adjacent vertebral fracture	5	No	No	No	Serious ⊹	Moderate
Injected cement volume *	6	No	No	No	No	High
Cement leakage *	9	No	No	No	No	High

VAS = Visual analog scale, ODI = Oswestry Disability Index.

* Injected cement volume after the sensitivity analysis.

† Serious risk of selection bias.

‡ Significant heterogeneity existed across the trials.

⊹ Wide confidence intervals are around the estimate of the effect or total population size is less than 400.

* Cement leakage after the sensitivity analysis.

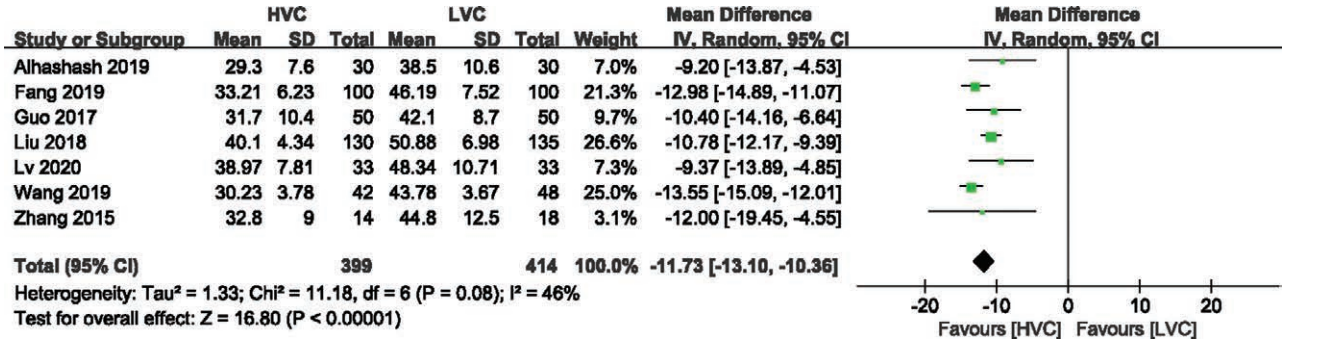

Figure 3. Meta-analyses of operation time between high-viscosity cement (HVC) and low-viscosity cement (LVC). HVC = High-viscosity cement, LVC = Low-viscosity cement.

bone cement was not directly related to its viscosity, but to the operation method. Some scholars have shown that the amount of bone cement injection in the PKP group is significantly greater than that in the PVP group. They believe the reason is that the balloon is inserted into the vertebra before the injection of bone cement during the PKP operation, creating a low-pressure injection environment compared with the high-pressure environment in the PVP, and PKP may be injected with more sufficient bone cement.[38] Therefore, because of the different surgical methods, the PVP versus PKP subgroup has high heterogeneity, and the amount of bone cement in the injection is significantly different. In addition, because the HVC does not have a liquid phase during the mixing process, it can instantly reach high viscosity, which makes the injectable period long, which is convenient for operations and shortens the injection and hardening time, so the operation time for a single vertebral body is significantly reduced.

In terms of bone cement leakage, our meta-analysis results suggest that the HVC group leakage was significantly lower than that of the LVC group, which is consistent with Rapan et al[39] and Lador et al[40] because the high viscosity of bone cement has strong resistance to pressure and resistance to distortion, and a better intraoperative enhancement effect, and its match accurately addresses the bone cement injection system to achieve good control. The subgroup analysis showed that there was no difference in bone cement leakage in the PVP versus PKP subgroup, and the other 2 groups showed significant differences. Due to high heterogeneity, after this subgroup was excluded, the results still indicated that the bone cement leakage for HVC was significantly lower than that of the LVC group. We believe that bone cement leakage is not only related to bone cement viscosity, but also to surgical methods. Due to the balloon technique used in PKP surgery, a low-pressure injection environment is created in the vertebral body, thereby reducing the leakage of low-viscosity bone cement, which may cause no significant difference in bone cement leakage in the PVP versus PKP subgroup. Hu et al[38] also showed that the leakage rate for bone cement in the PKP group was lower than that in the PVP group. In this paper, a subgroup analysis on different positions of bone cement leakage was performed. The results showed that in the paravertebral region, intraspinal space, intervertebral disc space, and peripheral vein region, the bone cement leakage in the HVC group was significantly lower than that in the LVC group. Habib et al[41] used an in vitro bone cement leakage model to compare high-viscosity bone cement with low-viscosity bone cement, and they found that high-viscosity bone cement was superior to low-viscosity bone cement in terms of reducing leakage and the uniformity of distribution. Baroud et al[42] reported a correlation between bone cement viscosity and the leakage rate of bone cement from vertebral veins. The results of a randomized controlled study by Fang et al[16] showed that the rate of bone cement leakage in the spinal canal, intraspinal space and intervertebral disc space of the HVC group was significantly lower than that of the LVC group. The results of this meta-analysis are consistent with these findings. The high-viscosity bone cement has the characteristics of instantaneous high viscosity, low polymerization temperature and a long injection time. The surgeon can apply pressure under X-ray fluoroscopy through a special transmission device to control the injection amount and the flow of bone cement more accurately in the injured vertebra, and it is advantageous for the surgeon to inject bone cement into the injured vertebrae more accurately during the operation, and when the bone cement is close to the paravertebral area, intraspinal space and vertebral venous plexus, the cement can be stopped in time. Jung et al[43] used low-viscosity bone cement PVP to treat 20 cases of osteoporotic vertebral compression fractures. The most common type of postoperative bone cement leakage was intervertebral disc leakage (with

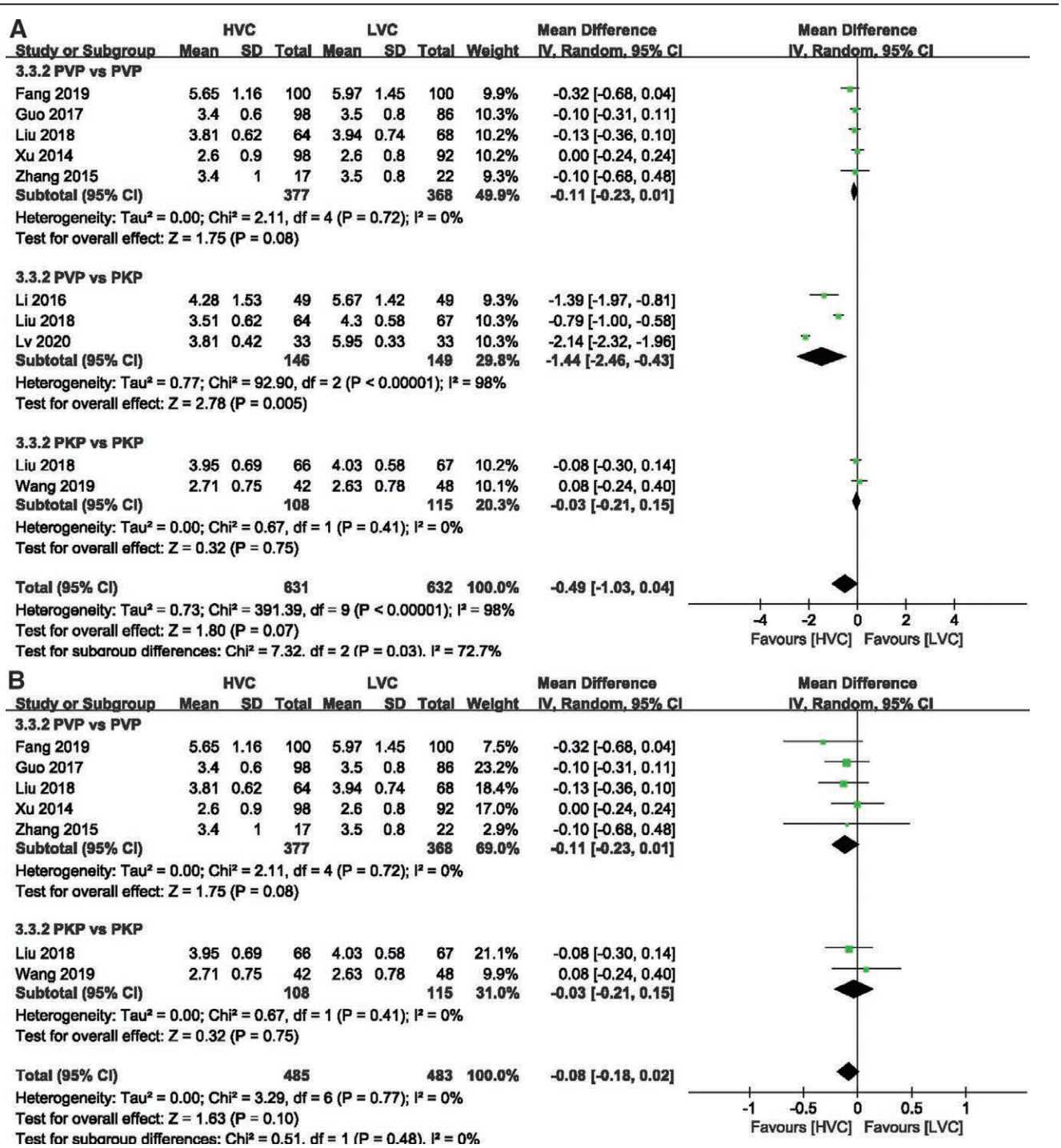

Figure 4. (A) Subgroup analysis of injected cement volume based on different surgical methods. (B) Sensitivity analysis of injected cement volume based on different surgical methods.

leakage rates as high as 65.0%). Loeffel et al[44] concluded that fractures are likely to cause the endplate of cartilage to break due to basic diseases such as osteoporosis, and it is more likely that the puncture needle penetrates the cartilage plate during the operation, at which time the bone cement will enter the intervertebral disc along the fracture. The author believes that the dispersion difference caused by the difference in bone cement viscosity is an important factor that affects the bone cement leakage of the intervertebral disc, the bone cement has higher viscosity and lower fluidity, and it is cloud-like during its injection flow instead of having a finger flow, which makes the dispersion of high-viscosity bone cement in the injured vertebrae more uniform, simultaneously increasing the flow resistance in the injured vertebra. Therefore, the flow force of bone cement along the retrograde bone trabecula and the damaged upper and lower cartilage endplate is also lower than that of the low-viscosity bone cement, and the possibility of breaking through the upper and lower endplates is reduced.

We define 1 to 3 months as a short-term follow-up, 4 to 12 months as a mid-term follow-up, and more than 12 months as a long-term follow-up. A total of 9 randomized controlled trials reported data on VAS. The meta-analysis results showed that the VAS score of the HVC group was lower than that of the LVC group, indicating that the clinical effect of HVC was better

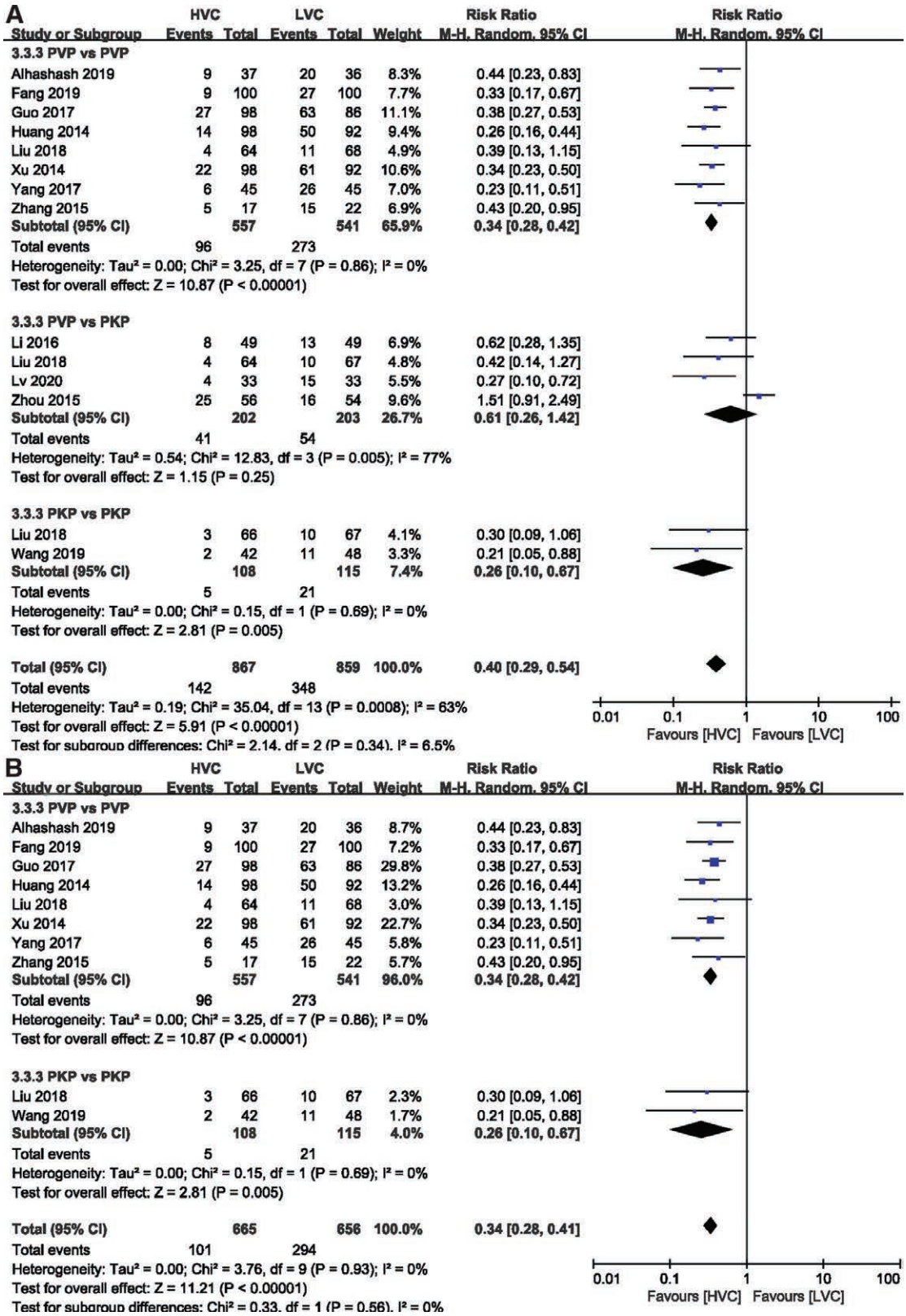

Figure 5. (A) Subgroup analysis of cement leakage based on different surgical methods. (B) Sensitivity analysis of cement leakage based on different surgical methods.

than that of LVC. A further analysis of the subgroup showed that there were no significant differences between the 2 groups before surgery, mid-term and long-term follow-up, and in the short-term follow-up alone, the VAS score of the HVC group was less than that of the LVC, but this subgroup was highly heterogeneous. If a sensitivity analysis of the subgroup was excluded, no significant difference could be found between the 2 groups. The study by Guo et al[20] also showed that 3 months after surgery, the VAS score of the HVC group was significantly lower than that of the LVC group. Additionally, more studies

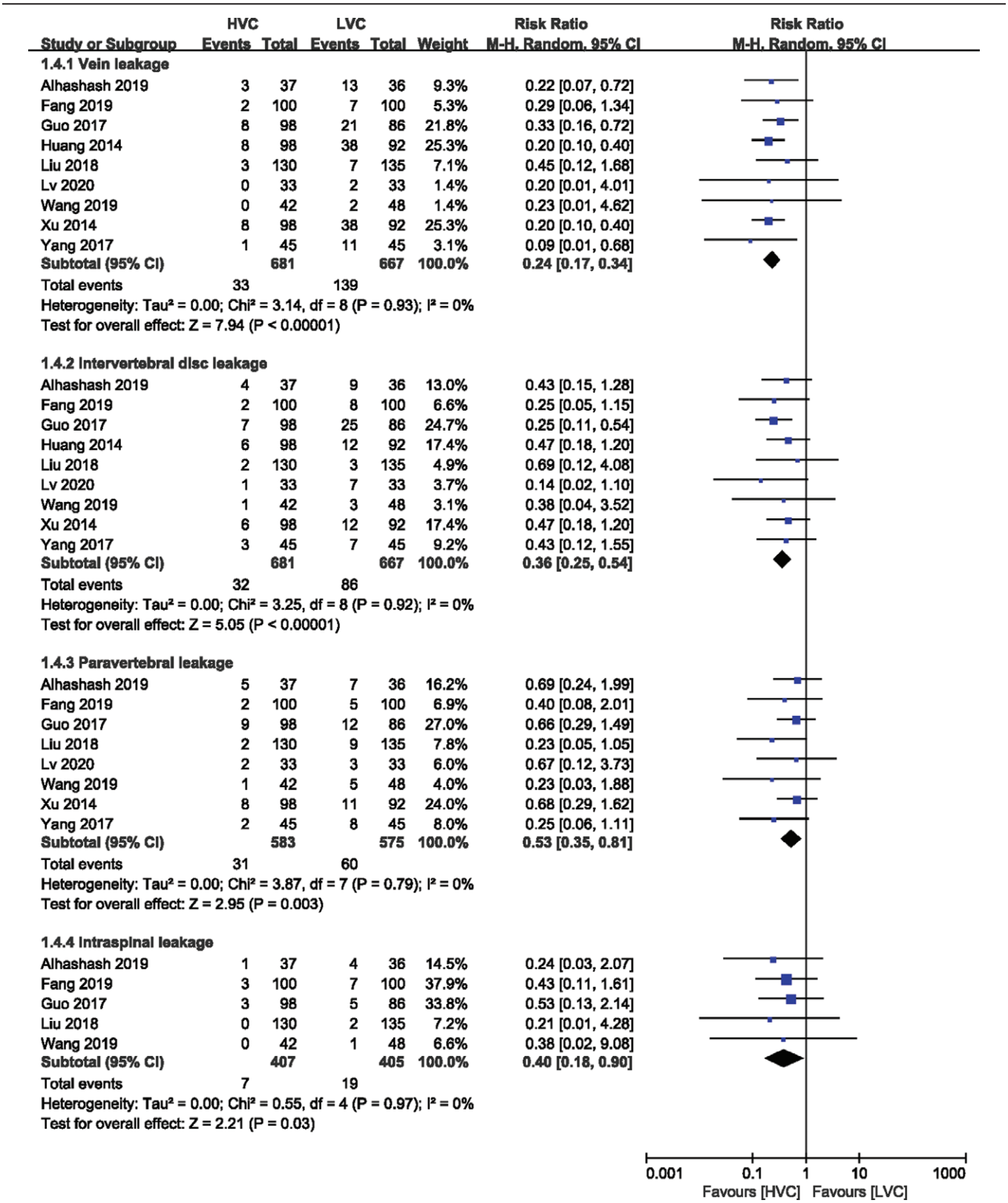

Figure 6. Subgroup analysis of cement leakage based on different locations of cement leakage.

suggest that there is no significant difference in the VAS between HVC and LVC.[25,27,32] At present, the clinical effect of HVC is at least equivalent to that of LVC. In the future, more large-sample multi-center prospective randomized controlled studies are needed to determine whether HVC is superior to LVC in terms of VAS. In addition, for ODI, there is no significant difference between HVC and LVC.

The pooled results showed no statistically significant difference between HVC and LVC in the incidence of postoperative adjacent vertebral fractures. This finding is consistent with the results of Alhasash et al[25] and Zhang et al.[31] According to reports, the probability of recurrence for new fractures in patients with osteoporotic vertebral fractures after minimally invasive surgery is 5.5% to 52%.[45] Alhasash et al believed that

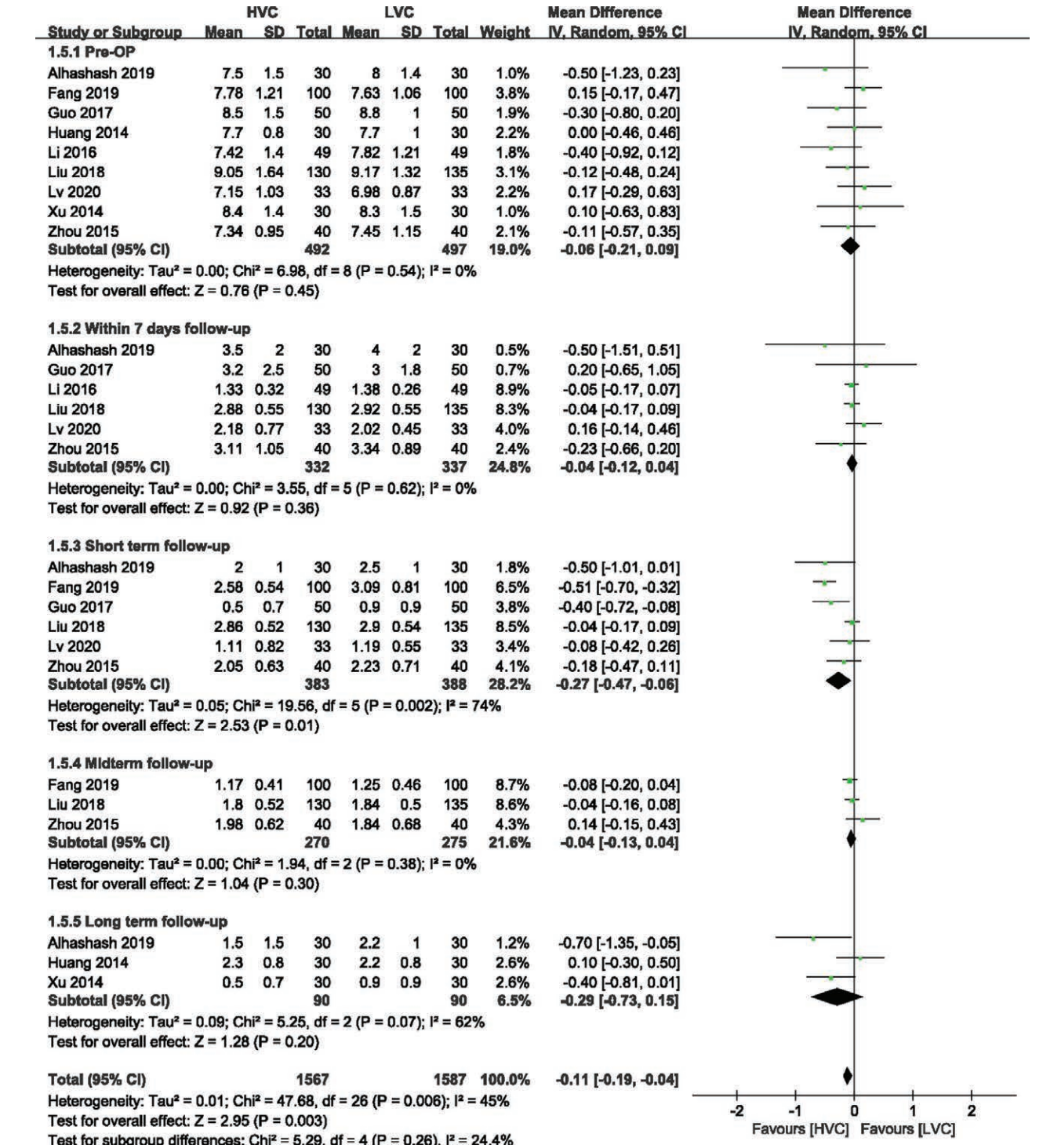

Figure 7. Subgroup analysis of visual analog scale based on the length of follow-up time before and after surgery.

the bone cement viscosity was not an important risk factor for new vertebral fractures after surgery. Rho YJ[46] thinks that the leakage of intervertebral disc bone cement can increase the risk of fracture, specifically postoperative adjacent vertebral fractures, perhaps after the injection of vertebral body bone cement, although its strength is comparable to that of normal vertebral bodies. However, compared with the osteoporotic vertebral body in the adjacent segment, its strength is clearly too high and its elastic modulus increases. After bone cement penetrates the intervertebral disc space, it will cause a change in the stress distribution in the intervertebral disc and reduce the buffer effect of the intervertebral disc. After the patient resumed weight-bearing activities, the adjacent vertebral body was subjected to greater stress, resulting in fracture. However, Ren et al[45] and Alhasash et al believed that the postoperative occurrence of new vertebral fractures was unrelated to disc leakage. At present, many scholars recognize that a risk factor for new postoperative fractures is the discovery of multiple initial fractures before surgery.[45,47–49]

Our research has some advantages. First, this is the latest and most comprehensive meta-analysis to evaluate the effectiveness and safety of HVC and LVC in the treatment of VCF. Second, we used the Cochrane bias risk and classification

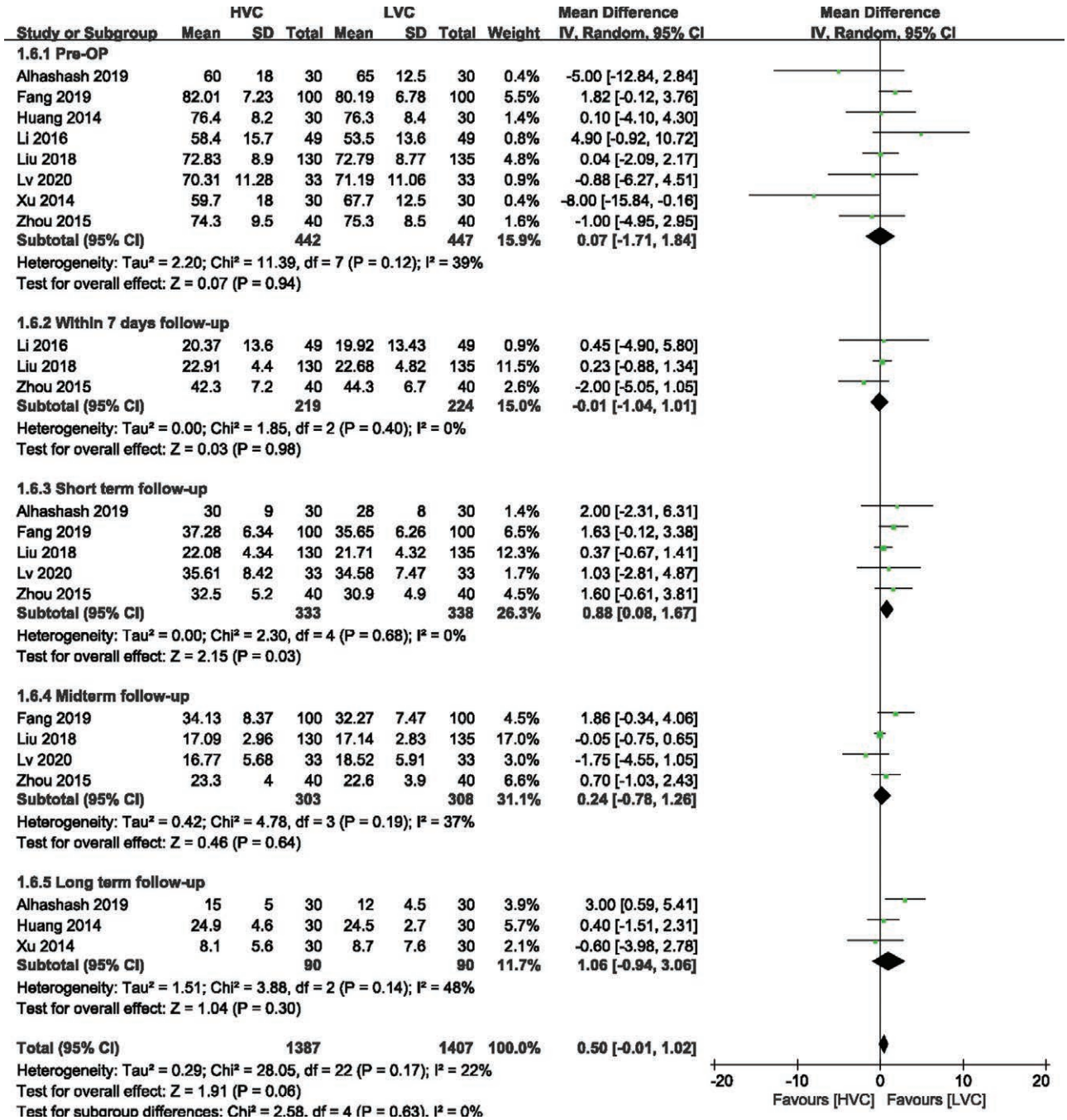

Figure 8. Subgroup analysis of oswestry disability index based on the length of follow-up time before and after surgery.

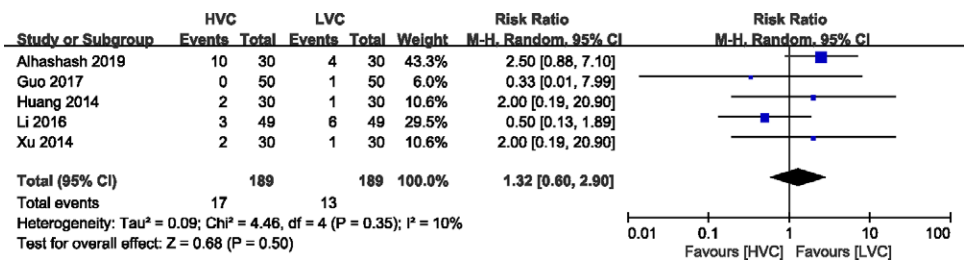

Figure 9. Meta-analyses of adjacent vertebral fractures between high-viscosity cement (HVC) and low-viscosity cement (LVC). HVC = High-viscosity cement, LVC = Low-viscosity cement.

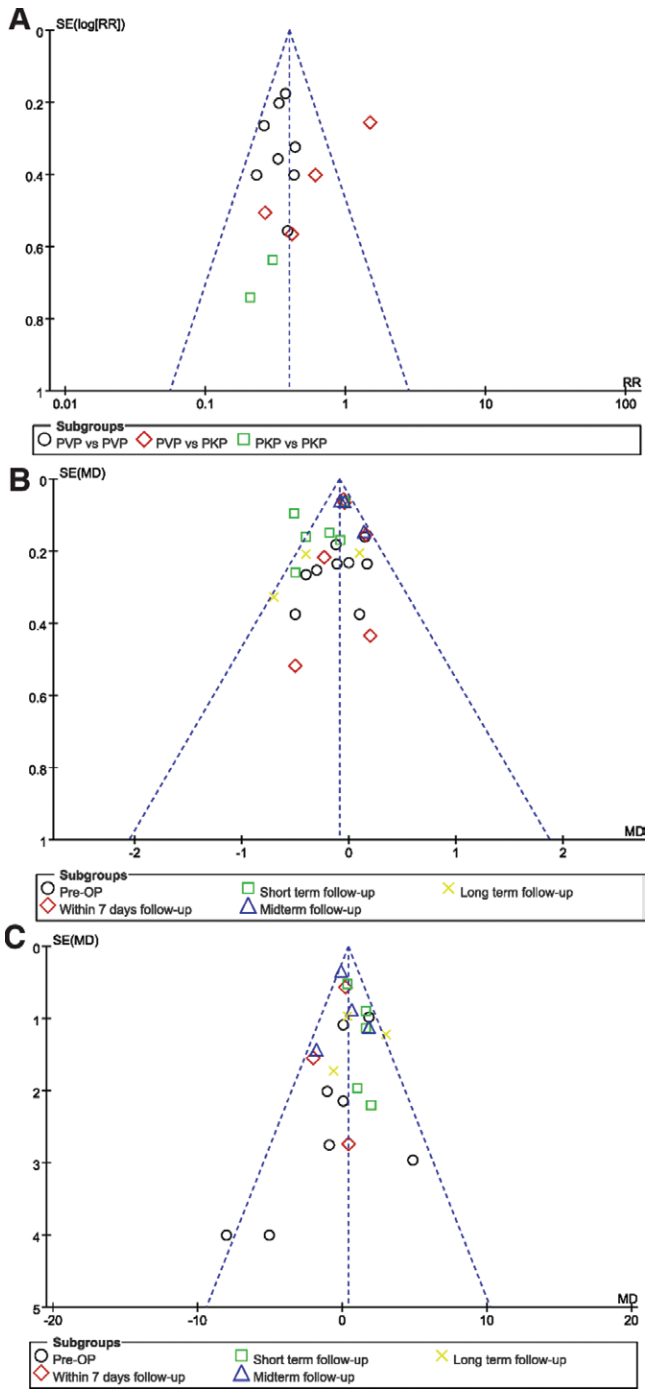

Figure 10. (A) The funnel plot for the cement leakage. (B) The funnel plot for the visual analog scale.(C) The funnel plot for the oswestry disability index.

method to assess the quality of the evidence. Other advantages include rigorous search strategies, including only randomized controlled trials, no language restrictions, publication bias tests, subgroup analyses and sensitivity analyses to ensure the consistency and accuracy of the results. However, our research also has some limitations. First, due to inadequate blindness, significant heterogeneity or imprecision, several of the pooled results consisted of low-quality evidence. Second, 11 of the 12 included studies were conducted in China, which could limit the application of the results to other populations.

5. Conclusions

Compared with LVC, HVC had a shorter operation time, lower bone cement leakage rate and better VAS score improvement, but in terms of bone cement injection volume, ODI and adjacent vertebral body fractures, the 2 are equivalent. More large-sample, multi-center, high-quality studies and longer-term follow-ups are needed to evaluate the effectiveness and safety between the 2 bone cements.

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