

Unilateral versus bilateral percutaneous vertebroplasty for osteoporotic vertebral compression fractures in elderly patients

A meta-analysis

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Abstract

Objective: To contrast the effects and complications in unilateral and bilateral percutaneous vertebroplasty (PVP) for osteoporotic vertebral compression fractures in elderly patients.

Methods: Multiple databases were adopted to search relevant studies, and the articles eventually satisfied the criteria were included. All the meta-analyses were conducted with the Review Manager 5.2. To estimate the quality of each article, risk of bias table was performed.

Results: Finally, 627 patients were enrolled in 9 studies and ultimately met the eligibility criteria. The unilateral and bilateral surgical samples were 314 and 313, respectively. The meta-analysis showed no significant difference in Visual Analog Scale/Score (VAS) (MD = -0.05, 95% confidence interval [CI] [-0.24, 0.13], $P = .57$), Oswestry Disability Index (ODI) score (MD = 0.03, 95% CI [-0.57, 0.62], $P = .93$) and cement leakage (OR = 1.00, 95% CI [0.67, 1.50], $P = 1.00$) between unilateral group and bilateral group. The surgery time of unilateral PVP is much less than that of bilateral PVP (MD = -8.42, 95% CI [-13.17, -3.66], $P = .0005$). Patients with bilateral PVP surgery have been injected more cement than patients with a unilateral surgery (MD = -2.56, 95% CI [-2.79, -2.33], $P < .00001$).

Conclusion This study demonstrated unipedicular approach is the preferred surgical technique for treatment of osteoporotic vertebral fracture (OVF) compared with bilateral PVP since unipedicular approach injects less cement and cost less surgery time.

Abbreviations: CIs = confidence intervals, ODI = Oswestry Disability Index, OVF = osteoporotic vertebral fracture, VAS = Visual Analog Scale/Score.

Keywords: elderly, osteoporotic vertebral compression fractures, percutaneous vertebroplasty

1. Introduction

Osteoporosis is a skeletal system disease resulting in increased bone brittleness and easy to be fractured. Fractures usually occur in the chest and lumbar segments of the hip and spine.^[1-3] Osteoporotic vertebral fracture (OVF) is a common fracture in the elderly. OVF suffers from severe back pain, pulmonary dysfunction, spinal deformity, abdominal limitation, impaired mobility, chest contents, and clinical depression, which have an impact on the quality

of life of patients.^[4,5] Several studies suggested that population distribution of OVF patients is 8% in women and 27% in men.

The pain caused by osteoporotic vertebral compression fractures in the elderly significantly reduced the quality of life in old patients. OVF has traditionally been treated with enough rest, physical therapy and antiresorptive medications.^[6,7] Patients are often with multiple system complications, and conservative treatment requires stay in bed for a long time. It might further aggravate osteoporosis, and induce complications such as respiratory and urinary infection. Since Galibert reported percutaneous vertebroplasty (PVP) for the treatment of vertebral hemangiomas in 1987, PVP has been widely used in the clinical treatment of osteoporotic vertebral compression fractures.^[8,9] The procedure involves inserting a needle into a fractured vertebra and injecting polymethylmethacrylate (PMMA) or other bone cement into the fractured vertebra under radiation control. After injection of cement, the pain pathway in the surrounding tissues seems to be altered by various stimuli.

In the past decades, PVP is a safe and effective treatment. Both unilateral and bipedal operations had satisfactory results, consistent with those before surgery. However, studies have shown that compared with bilateral PVP, unilateral PVP surgery has a better therapeutic effect.^[10]

The aim of this meta-analysis is to contrast the safety and effectiveness of unilateral and bilateral PVP for treatment in osteoporotic vertebral compression fractures. Because of the

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inconsistent results of the 2 treatments, a meta-analysis is necessary to verify the differences in the efficacy and complication rates of unilateral and bilateral PVP surgery.

2. Materials and methods

Ethical approval was not necessary because this is a meta-analysis. All data were available on the internet.

2.1. Search strategy

To search out all of the relevant published citations, multiple electronic databases including Pubmed, Springer, EMBASE, EMBASE, OVID, and China Journal Full-text Database were applied, without language restrictions. To maximize the search accuracy, the following MeSH terms were assembled with the Boolean operator “AND”:

- (1) osteoporotic vertebral compression fractures or OVF;
- (2) percutaneous vertebroplasty or vertebroplasty or PVP or VP;
- (3) unilateral or bilateral or unipedicular or bipedicular related articles with all publication statuses (published, unpublished, in press, and in progress) published from January 2000 to January 2018 were systematically searched and reviewed.

Two authors in our team searched the literature independently and examined the reference lists to obtain the additional relevant studies that not identified.

2.2. Citation selection

The other 2 authors independently and carefully chose the citations in the process. They sifted through the titles and abstracts of the articles identified by the proposed electronic search criteria, and then obtained the full text of the studies that might meet the criteria and reviewed them to see if the studies might be relevant.

The relevant research in this study must meet the following criteria:

- (1) A randomized control trial or controlled clinical trial study;
- (2) Sample size more than 10;
- (3) Adult patients with OVFs;
- (4) Comparison between unilateral and bilateral PVP;
- (5) Available Exclusion Criteria

Exclusion criteria:

- (1) Non-randomized studies;
- (2) Studies lacking outcome measures or comparable results;
- (3) Studies on other diseases other than OVF.

After reading the full text of the articles, the characteristics from each study using a standard data extraction were extracted: the first author's name, year of publication, nation, age range of patients, sex distribution (male/female), sample size (asthmatics/cough), follow-up period, and other parameters.

2.3. Data extraction

The 2 reviewers read the full text independently and extracted features from each study using the Excel 2010 standard data extraction table. Data extracted from these studies included the first author's name, year of publication, year of onset, average age of patients, sample size (unilateral/bilateral), gender distribution (male/female), outcome measurements, and follow-up time. Results Measurements, including Visual Analog Scale/Score

(VAS), Oswestry Disability Index (ODI), operative time, cement injection volume, and cement leakage results, were collected to estimate differences between unilateral and bilateral PVP.

2.4. Statistical analysis

The meta-analyses were conducted with the software Review Manager 5.2 (The Cochrane Collaboration, 2011) to compare the clinical effects between unilateral and bilateral PVP in elderly patients among selected articles. As continuous outcomes, standard mean difference (SMD) with 95% confidence intervals (CIs) was performed. In discontinuous outcomes, odds ratio (OR) with 95% CIs were conducted. A *P* value < .05 was considered to be statistically significant. The heterogeneities in this study were assessed using the I^2 index. We chose the random-effect model when the heterogeneity I^2 statistic > 50%, otherwise the fixed-effect model was applied.

In addition, the quality of the studies was assessed with sensitivity analysis and bias analysis. Risk of bias table of the included studies was independently assessed according to the Cochrane Handbook for Systematic Reviews of Interventions by 2 members of our team. Also if any occurrence of poor agreement and no consensus could be achieved, a third investigator was the adjudicator.

3. Results

3.1. Search results

After preliminary screening, a total of 1030 titles and abstracts were preliminarily reviewed in these electronic databases, 9 of which eventually met the eligibility criteria. Other 1021 articles excluded duplicate, unrelated studies, inappropriate data, inappropriate comparisons, reviews, no controls, other diseases, other operations or incomplete articles. The flow chart reflecting the search process can be seen in Figure 1, including the reasons for exclusion.

3.2. Characteristics of included studies

Table 1 provides detailed characteristics of the study. The table lists the name of the first author, the year of publication, the year of onset, the average age of the patient, sample size (unilateral/bilateral), gender distribution (male/female), outcome measurements, and follow-up time. All these articles were published from 2000 to 2018. A total of 627 patients were included in 9 studies, of which 314 were unilateral surgical specimens and 313 were bilateral surgical samples. The sample size is between 30 and 130. All patients were elderly patients.

3.3. Quality assessment

The bias table in the Review Manager 5.2 Tutorial was used to evaluate the risk of each study by applying the criteria of evaluating design-related bias. The quality of included studies was evaluated by the risk of bias table, and the evaluation in this study was shown in Figure 2. In the 9 articles, 1 trial showed problem in patient selection and 1 showed problem in allocation bias. Overall, all the trials were out of risk.

3.4. Meta-analysis about operating time

Nine included studies involve in operating time for unilateral and bilateral PVP. The forest plot for the operating time in unilateral and bilateral PVP groups was shown in Figure 3. The

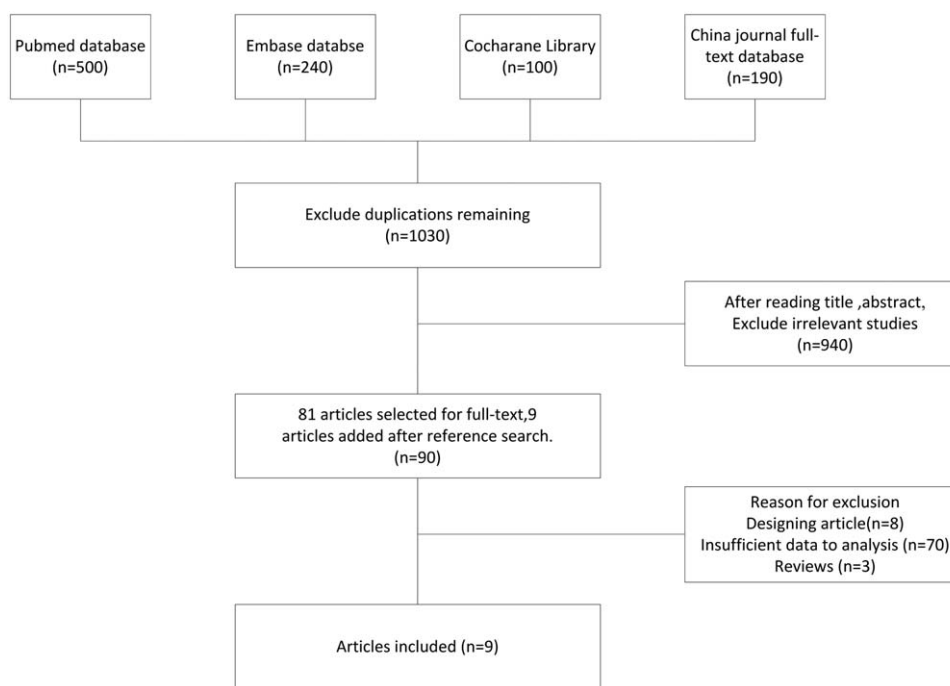


Figure 1. Flow diagram of the study selection.

meta-analysis suggested that there was significant difference of the operating time in unilateral group and bilateral group (MD = -8.42, 95% CI [-13.17, -3.66], $P = .0005$; P for heterogeneity < .00001, $I^2 = 98\%$). The operating time in bilateral group was more than that in unilateral group.

3.5. Meta-analysis about VAS score

All studies involved in the VAS score between unilateral and bilateral PVP groups. As shown in the forest plot (Fig. 4). The result of meta-analysis showed that the difference of VAS

score between unilateral and bilateral PVP was not significant (MD = -0.05, 95% CI [-0.24, 0.13], $P = .57$; P for heterogeneity = .007, $I^2 = 44\%$).

3.6. Meta-analysis about the ODI score

There are 9 studies about the comparison of ODI score. The forest plot for the ODI score was shown in Figure 5. All these 9 studies showed no significant differences of ODI score between unilateral and bilateral PVP (MD = 0.03, 95% CI [-0.57, 0.62], $P = .93$; P for heterogeneity = .73, $I^2 = 0\%$).

Table 1

Characteristics of studies included in the meta-analysis.

Study	Year	Language	Country	No. of patients, female/male	Age range, mean	Groups	n	Years of onset
Xu ^[11]	2018	English	China	51/25	74.5 ± 10.7	unilateral bilateral	30 46	January 2013 to January 2016
Amoretti ^[12]	2018	English	France	29/15	72.4 ± 8.5	unilateral bilateral	24 20	December 2010 to November 2013
Senturk ^[13]	2018	English	Turkey	40/29	71.5 ± 8.8	unilateral bilateral	33 36	January 2011 to May 2015
Zidan ^[14]	2018	English	Egypt	40/37	69.4 ± 7.9	unilateral bilateral	39 38	June 2010 to May 2015
Ozsoy ^[15]	2018	English	Turkey	12/12	70.3 ± 8.2	unilateral bilateral	10 14	May 2012 to March 2015
Sun ^[16]	2018	English	Korea	60/70	71.3 ± 8.1	unilateral bilateral	70 60	January 2014 to January 2017
Shao ^[17]	2018	Chinese	China	18/12	73.2 ± 2.6	unilateral bilateral	17 13	January 2015 to September 2016
Feng ^[18]	2014	Chinese	China	80/37	72.5 ± 3.3	unilateral bilateral	61 56	February 2010 to February 2012
Yin ^[19]	2009	Chinese	China	38/22	75.4 ± 2.4	unilateral bilateral	30 30	May 2007 to March 2009

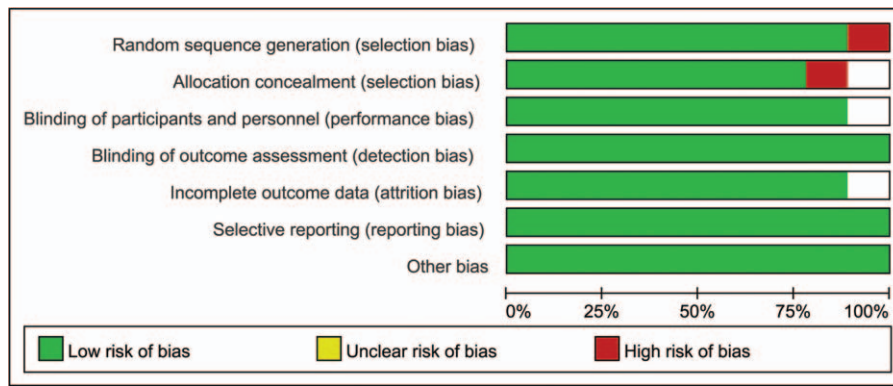


Figure 2. Assessment of the quality of the included studies: low risk of bias (green hexagons), unclear risk of bias (blank hexagons), and high risk of bias (red hexagons).

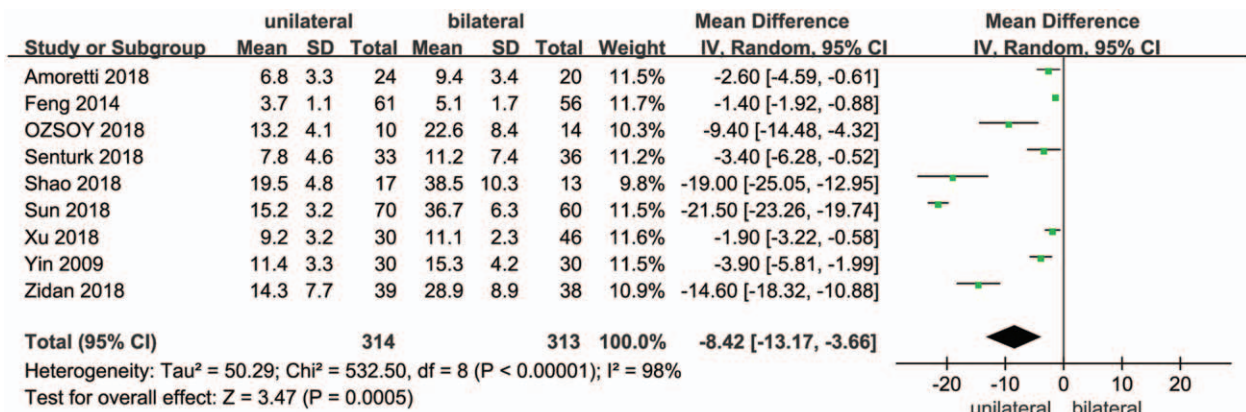


Figure 3. A forest plot for the operating time in unilateral and bilateral PVP groups. PVP=percutaneous vertebroplasty.

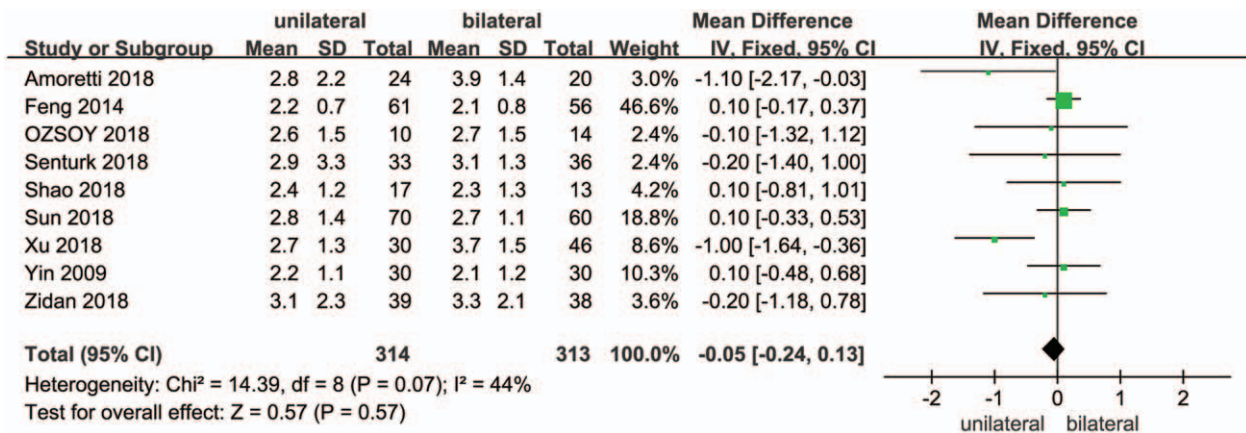


Figure 4. A forest plot for the VAS score in unilateral and bilateral PVP groups. PVP=percutaneous vertebroplasty, VAS=Visual Analog Scale/Score.

3.7. Meta-analysis about the injected cement volume

All the 9 studies on the cement volume injected in PVP have shown the statistically significant difference between unilateral and bilateral PVP. The result of meta-analysis indicated that in

bilateral PVP surgery, patients with OVF have been injected more cement than patients in a unilateral surgery (MD = -2.56, 95% CI [-2.79, -2.33], P < .00001; P for heterogeneity = 0.65, I² = 0%). The forest plot for the injected cement volume was shown in Figure 6.

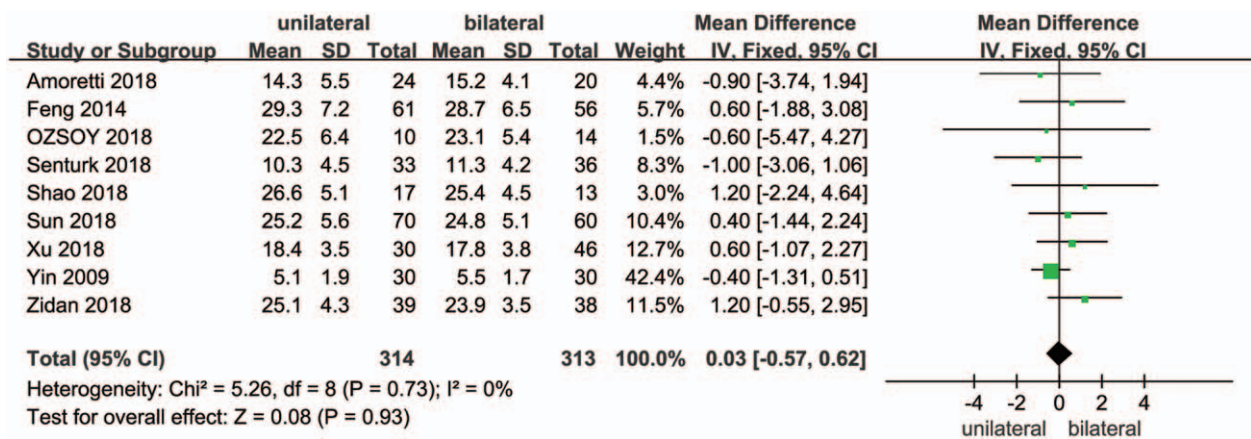


Figure 5. A forest plot for the ODI score in unilateral and bilateral PVP groups. ODI=Oswestry Disability Index, PVP=percutaneous vertebroplasty.

3.8. Meta-analysis about the cement leakage

There are 9 studies are about the cement leakage in unilateral and bilateral PVP groups. The result of meta-analysis showed that no difference of cement leakage between unilateral and bilateral PVP was not significant (OR=1.00, 95% CI [0.67, 1.50], $P=1.00$; P for heterogeneity = .98, $I^2=0\%$) (Fig. 7).

3.9. Sensitivity analysis

According to the results of meta-analyses, the heterogeneities of operating time was very high ($I^2 > = 95\%$). As shown in Figure 8, the high heterogeneity of operating time was probably attributed to the different results in each study. When the article of Sun in 2018 was excluded, I^2 changed from 98% to 92%.

3.10. Bias analysis

A funnel plot for the studies about operating time in unilateral and bilateral PVP groups was performed (Fig. 9). All the studies were included in the plot. The result showed that there existed some publication bias since the symmetrical characteristic of the funnel plot was not good.

4. Discussion

Osteoporosis is a progressive and metabolic bone disease. The main manifestations are the increase of bone brittleness, the decrease of bone mass and the decrease of bone strength.^[20-22] It is one of the important factors that affect the quality of life in the elderly, and the most common complication is the osteoporotic compression fracture of the thoracolumbar spine.

PVP is one of the mainstream treatments for OVF, which can rapidly relieve pain and stability of vertebral fractures. However, the choice of surgical approach remains controversial.^[23,24] Some researchers believe that bilateral PVP is more effective in relieving pain, which is related to the distribution of bone cement in the vertebral body. In recent years, unilateral PVP has been increasingly used in surgery, reduced exposure time to radiation, reduced risk of cement leakage, and complications. Bilateral PVP showed increased operation time and injected cement volume, while unilateral PVP reduced operation time, surgery-related complications and radiation exposure.

VAS is a psychometric response scale used in questionnaires, which is to measure the subjective characteristics or attitudes that cannot be directly measured. Studies adopt VAS to estimate pain relief after PVP surgery. In this research, VAS score between

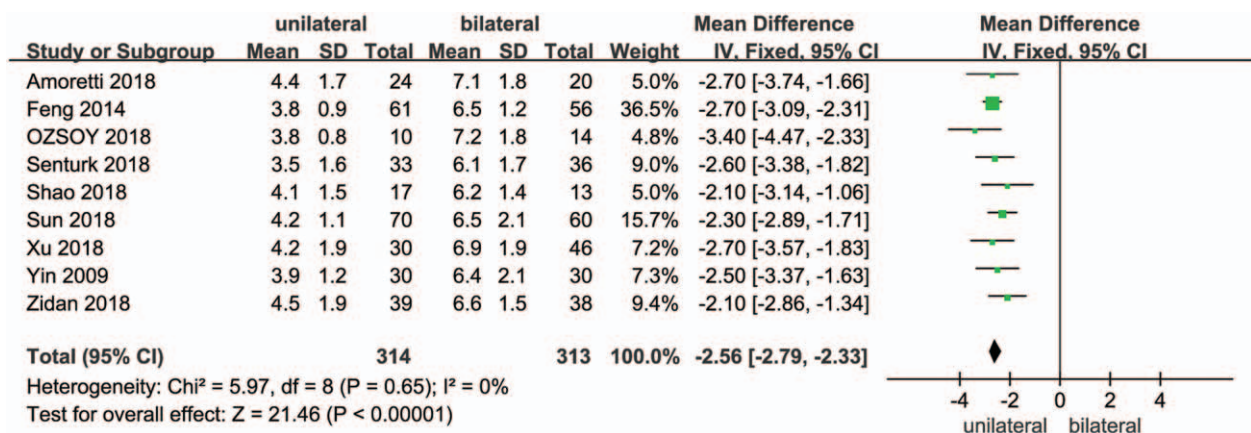


Figure 6. A forest plot for the injected cement volume in unilateral and bilateral PVP groups. PVP=percutaneous vertebroplasty.

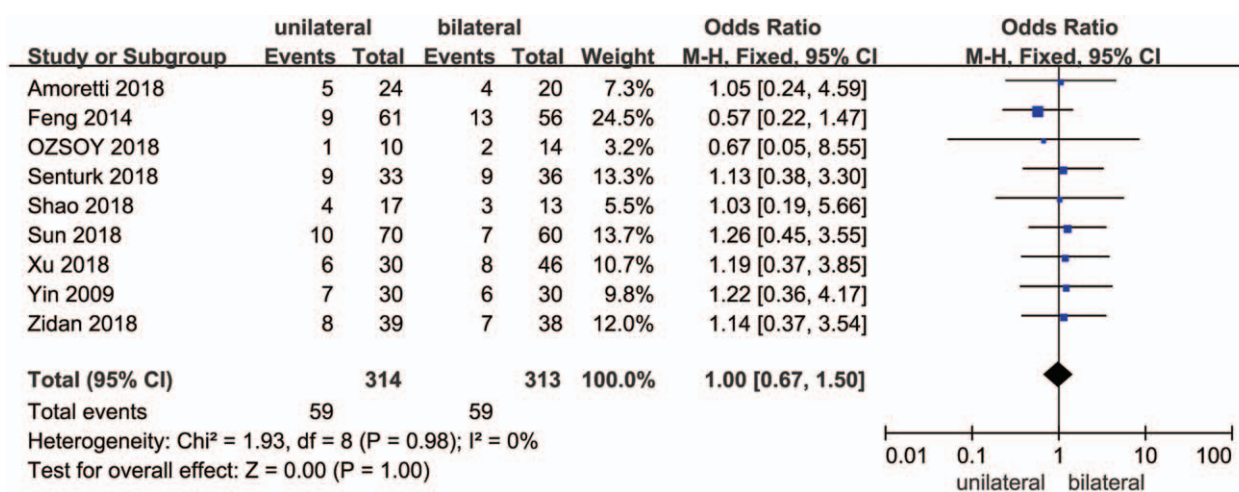


Figure 7. A forest plot for the cement leakage in unilateral and bilateral PVP groups. PVP=percutaneous vertebroplasty.

unilateral and bilateral PVP was not significant (MD = -0.05, 95% CI [-0.24, 0.13], P = .57; P for heterogeneity = .007, I² = 44%). This indicated that the pain relief of unilateral group was as much as that of bilateral group. ODI is an index that used by clinicians and researchers to quantify disability for low back pain. The results showed that the ODI score of unilateral PVP was similar to that of bilateral PVP (MD = 0.03, 95% CI [-0.57, 0.62], P = .93; P for heterogeneity = .73, I² = 0%). Cement leakage is a common complication of vertebroplasty. Symptoms of nerve irritation with compression of nerve roots may be caused by the leakage. Difference of cement leakage between unilateral and bilateral PVP was not significant (OR = 1.00, 95% CI [0.67, 1.50], P = 1.00; P for heterogeneity = .98, I² = 0%). Yu reported that the effects of unilateral and bilateral PVP had no difference.^[25] Patients with severe vertebral deformation were recommended to adopt bilateral PVP while unilateral PVP was preferred when degree of vertebral compression is not large.

There is significant difference of the operating time in unilateral group and bilateral group (MD = -8.42, 95% CI [-13.17, -3.66], P = .0005; P for heterogeneity < .00001, I² = 98%). The operating time in unilateral group was less than bilateral group. The patients in bilateral group have been injected more cement than patients in a unilateral surgery (MD = -2.56, 95% CI

[-2.79, -2.33], P < .00001; P for heterogeneity = .65, I² = 0%). Qi suggested that unilateral PVP as the advantages of low incidence of cement injection, short exposure time and short operative time.^[26]

In the comparison between PVP and conservative therapy, PVP had a better clinical effect. Mattie and Rachele reported that the effect of PVP exceeded the effect of conservative therapy with respect to pain relief in patients with osteoporotic compression fractures.^[27,28]

The results in this study supported that the unipedicular PVP is a faster treatment for comparable spinal deformity contrasted with the bipedicular approach. It also improves the cost-effectiveness of the procedure for injecting less cement and reduces the operation time, thereby reducing the risk of disease. However, there exists controversy about the effect of PVP that the clinical effect of PVP and placebo have no difference.^[29] Some surgeons believe that PVP better effect in the relieving acute pain than conservative treatment, but in the long-term efficacy the difference between PVP and placebo had no significance.^[30] The clinical efficacy of PVP needs to be further researched

However, some limitations still existed in this research. First, the more indicators in both unilateral and bilateral groups could be analyzed, and it could be evaluated in the future. Second, more

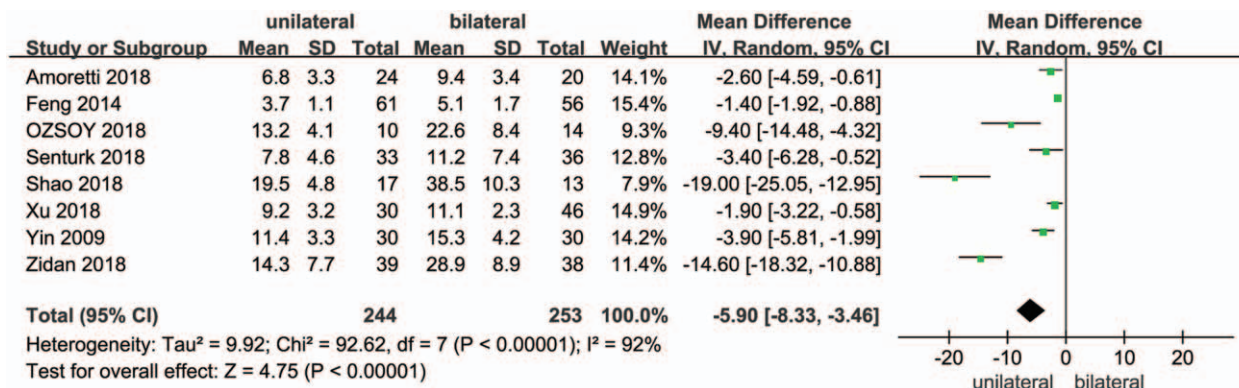


Figure 8. A forest plot for the sensitivity analysis in operating time.

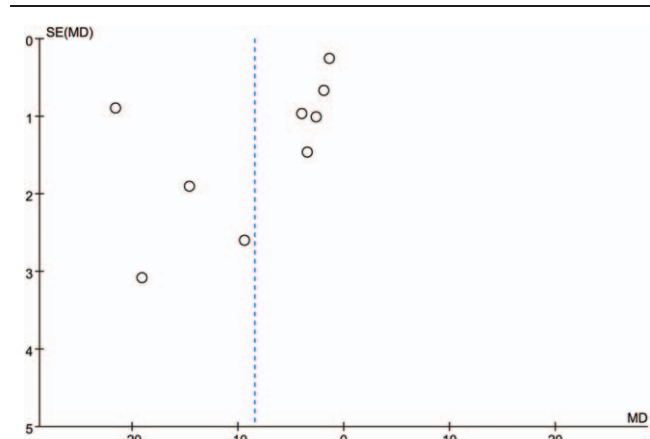


Figure 9. A funnel plot for the studies about operating time in unilateral and bilateral PVP groups. PVP=percutaneous vertebroplasty.

articles could be involved, which could be conducted in the further research. Third, the comparison among unipedicular approach, bilateral PVP and conservative therapy could be conducted in the future.

Author contributions

Conceptualization: Yingchun Chen.

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Project administration: Lin Zhang.

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Supervision: Yingchun Chen.

Validation: Er-nan Li, Li-xiang Ding.

Writing – review & editing: Yingchun Chen.

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