Systematic Review and Meta-Analysis

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Efficacy of percutaneous vertebroplasty treatment of spinal tumors

A meta-analysis

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Abstract

Objective: To evaluate the function of percutaneous vertebroplasty (PVP) treatment to pain relief and life quality for patients with spinal tumors.

Methods: Articles about the researches on the treatment of spinal tumors by PVP in PubMed, Embase, and the Chinese Biomedical Literature database from January 1, 2015 to December 31, 2013. The keywords "spinal tumors," "efficacy," and "vertebroplasty" were firstly scanned to exclude all irrelevant articles. Then, the final inclusion of studies was determined by reading the full text of the remaining articles. The citation lists of all retrieved articles were scanned to identify other potentially relevant reports. RevMan5.2 was used to analyze pain intensity visual analog scale (VAS) and Karnofsky performance scores (KPS) within each research. Combined HRs (hazard ratio) were calculated using fixed- or random- effects models according to the heterogeneity.

Results: Twenty-six studies involving 1351 patients met our selection criteria. Meta-analysis results among 10 case-control studies showed that the combined HR was −2.83 [95% confidence interval (CI) −2.92, −2.73; $P < .0001$], indicating a 2.83-fold decrease of pain in PVP group. For 12 single-arm studies, a significantly decrease of pain after PVP treatment (HR = −4.79, 95% CI −5.00, −4.57, $P < .0001$) was also found in PVP group. In addition, for KPS analysis, the combined HR was 16.31 (95% CI 14.31, 18.31; $P < .0001$), which indicated that PVP treatment was associated with a 16.31-fold increase of KPS. The combined HR was 0.58 (95% CI 0.35, 0.96; $P = .04$) for complication analysis.

Conclusions: PVP treatment of spinal tumor is significantly associated with better pain relief and life quality, which could improve the outcome in metastatic spinal tumor patients.

Abbreviations: ACP = American College of Radiology, ASNR = American Society of Neuroradiology, ASSR = American Society of Spine Radiology, CI = confidence interval, HRs = hazard ratio, KPS = Karnofsky performance scores, PVP = percutaneous vertebroplasty, SIR = Society of Interventional Radiology, SNIS = Society of Neurointerventional Surgery, VAS = visual analog scale.

Keywords: efficacy, meta-analysis, spinal tumors, vertebroplasty

1. Introduction

Bone disease contributes substantially to morbidity and mortality in patients with cancer. Based on the statistics from the American Cancer Society, there will be 2970 new cases and 1490 deaths of cancer of the bones and joints in 2015.[1] Thus, bone tumors are posing a potential threat to public health and seeking for an efficient strategy is of great significance.

Percutaneous vertebroplasty (PVP), initially described in patients with symptomatic vertebral hemangioma, has been established as a safe and effective treatment for osteoporotic vertebral fractures and vertebral metastatic lesions.[2] Compared with radiotherapy alone, this procedure provides immediate structural support, and stabilizes and reinforces the remaining bone structure.[3] The conflicting conclusions might result from the rarity of bone tumor cases. When the sample size was not enough, the statistical power to gain the underlying answer would be low and the probability to make mistakes would be considerable.

To provide a theoretical basis for the prevention of bone tumor, a meta-analysis was performed to pool all relevant published data to investigate the efficacy of PVP for the treatment of spinal tumors.

2. Methods

2.1. Search strategy

We searched the electronic databases PubMed, Embase, and the Chinese Biomedical literature database from January 1, 2009 to December 31, 2015. The keywords "spinal tumors," "efficacy,"

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The authors declare conflict of interests.

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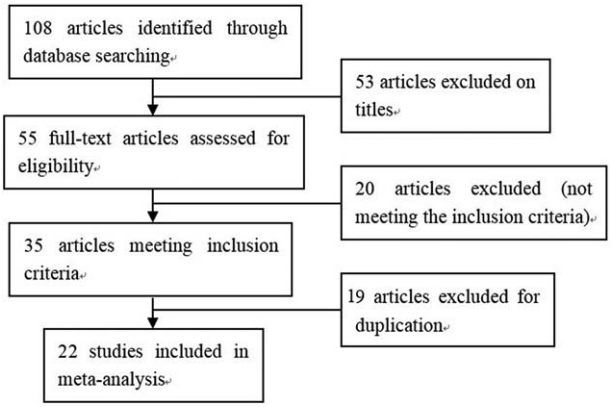

Figure 1. Flow chart of the literature search strategy to identify cohort studies on breast cancer risk and physical activity.

and "vertebroplasty" were firstly scanned to exclude all irrelevant papers. Then, the final inclusion of studies was determined by reading the full text of the remaining articles. The citation lists of all retrieved articles were scanned to identify other potentially relevant reports.

2.2. Selection criteria

The search results were screened according to specific inclusion and exclusion criteria as follows. Inclusion criteria: research limited to human bone tumor; the study was published in English or Chinese; evaluation of pain relief; peer-reviewed and published original articles; and letters reporting original research work. Exclusion criteria: key information was incomplete to provide the required data; nonoriginal researches, letters referring comments or opinions to articles, reviews, and articles published in a book. If patients were enrolled from the same institutions during the same period, the most recently published data were included in the study.

2.3. Data extraction

Titles and abstracts were screened for eligibility. Two reviewers performed the search and assessed the studies independently, and the inclusion of a study was decided by consensus. The following items were recorded from each study: the first author's name, year of publication, language, cohort size, diagnosis, and follow-up time.

2.4. Statistical analysis

After collecting and classifying the information, the data were analyzed utilizing SPSS version 13.0.

Data combining was performed using RevMan version 5.2 (free software downloaded from http://www.cochrane.org). Heterogeneity across studies was evaluated by the I^2 statistic, which represents the percentage of total variation across studies that is attributable to heterogeneity rather than to chance.

3. Results

3.1. Description of studies

As shown in Figure 1, 108 articles were identified, of which 82 articles were excluded after screening titles or abstracts because they were irrelevant to this study or unsuitable for the inclusive criteria. Finally, 22 studies were included into this study with 10 studies of case-control study, 12 studies of single-arm studies for visual analog scale (VAS) studies and 4 studies for Karnofsky performance scores (KPS) analysis.

3.2. Meta-analysis of pain relief after PVP treatment among case-control studies

Pain relief, assessed by VAS score, was analyzed in 10 case-control studies and in a total of 690 cases (Table 1).[4–13] The results showed significant between-study heterogeneity ($P < .0001$, $I^2 = 98\%$), and a random-effects model was used. The combined HR (hazard ratio) was −2.83 [95% confidence interval (CI) −2.92, −2.73; $P < .0001$] (Fig. 2A), which indicated that PVP treatment was associated with a 2.83-fold decreased risk of pain, in comparison with control studies. Patients exhibited excellent improvement of pain during the follow-up.

3.3. Pain relief before and after treatment by PVP among single-arms studies

As shown in Table 2,[14–25] there are 12 single-arm studies with 534 cases included, evaluating the efficacy of PVP to pain scales in tumor patients. The VAS score was evaluated respectively, before and after treatment of PVP. A random-effects model was used to combine HRs because of the heterogeneity among the studies ($P < .0001$; $I^2 = 89\%$). Identically, the results of the meta-analysis showed a significantly decrease of pain after PVP treatment (HR = −4.79, 95% CI −5.00, −4.57, $P < .0001$) (Fig. 2B).

Table 1

Characteristics of the case-control studies evaluating VAS scores[4–13].

Author	Year	Language	Cohort size		Diagnosis	Follow-up
			Case	Control		
Ke et al[4]	2015	English	6	3	Metastatic Tumors	7 days
Yang et al[5]	2009	English	40	40	Metastatic spinal tumors	6 months
Yang et al[6]	2013	English	50	50	Spinal Osteoblastic Metastasis	1 year
Yang et al[7]	2012	English	38	38	MM-associated spinal fracture	5 years
Xie et al[8]	2009	Chinese	45	45	Metastatic spinal tumors	1 year
Chen et al[9]	2014	Chinese	83	54	Metastatic spinal tumors	1 day
Wang et al[10]	2012	Chinese	46	20	Spinal tumors	3 months
Gao et al[11]	2015	Chinese	27	21	Spinal tumors	3 months
Pan[12]	2014	Chinese	27	27	Spinal tumors and metastatic spinal tumors	1 day
Zhang M[13]	2015	Chinese	16	14	Spinal tumors and metastatic spinal tumors	1 day

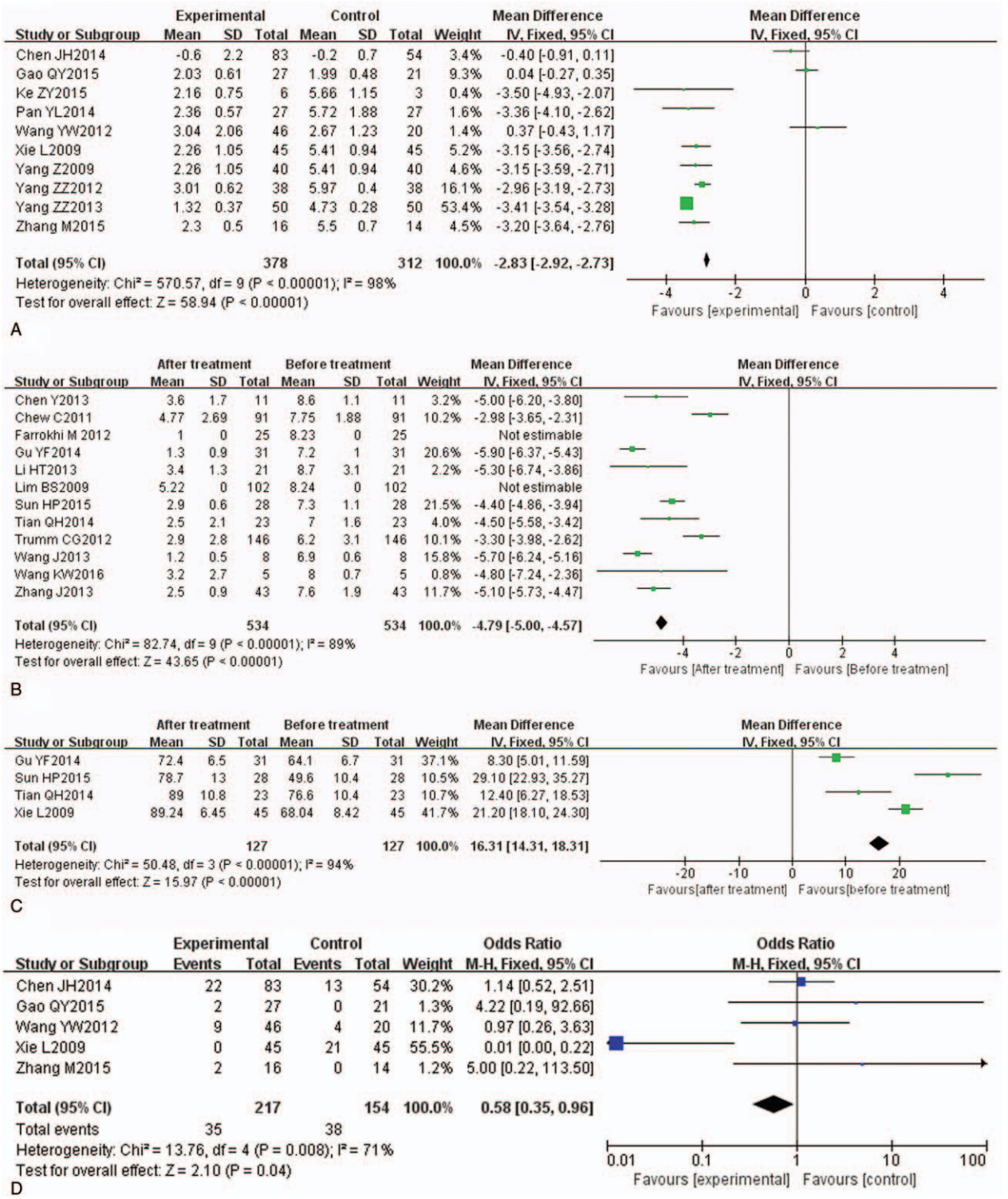

Figure 2. Results of meta-analysis. A, Forest plot of the hazard ratio (HR) for VAS among case-control studies (B) Forest plot of the hazard ratio (HR) for VAS among single-arms studies (C) Forest plot of the hazard ratio (HR) for KPS among studies (D) Forest plot of the hazard ratio (HR) for compliance.

3.4. Meta-analysis results of KPS

Four studies including 127 cases evaluated the impact of PVP on the KPS of patients (Table 3).[8,14,15,25] The results showed significant between-study heterogeneity ($P < .0001$, $I^2 = 94\%$), and a random-effects model was used. The combined HR was 16.31 (95% CI 14.31, 18.31; $P < .0001$) (Fig. 2C), which indicated that PVP treatment was associated with a 16.31-fold increase of KPS (Fig. 3).

3.5. Complications

Five studies including 217 cases evaluated the impact of PVP on the complications of patients. The results showed significant

Table 2

Characteristics of the single-arms studies according to VAS relief[14–25].

Author	Year	Language	Cohort size	Diagnosis
Sun et al[14]	2015	English	28	Metastatic spinal tumors
Gu et al[15]	2014	English	31	Metastatic spinal tumors
Chen et al[16]	2013	English	11	Metastatic spinal tumors
Farrokhi et al[5,17]	2012	English	25	Metastatic spinal tumors
Zhang et al[18]	2013	English	43	Osteolytic spinal metastases
Wang et al[19]	2016	English	5	Thoracic and lumbar spine tumor
Trumm et al[20]	2012	English	146	Spinal malignancy
Chew et al[21]	2011	English	91	Myeloma and spinal metastases
Wang et al[22]	2013	English	8	Vertebral hemangioma
Lim et al[23]	2009	English	102	Osteolytic metastatic spinal disease
Li et al[24]	2013	Chinese	21	Metastatic spinal disease
Tian et al[25]	2014	Chinese	23	Metastatic spinal disease

between-study heterogeneity ($P=.008$, $I^2=71\%$), and a random-effects model was used. The combined HR was 0.58 (95% CI 0.35, 0.96; $P=.04$) (Fig. 2D).

3.6. Publication bias

Twelve studies evaluating VAS/KPS were examined by Begg test. Visual inspection of the funnel plot showed asymmetry suggesting publication bias. Sensitivity analysis was performed using the trim and fill method, which conservatively imputes hypothetical negative unpublished studies or omits certain studies to mirror the positive studies that cause funnel plot asymmetry.

4. Discussion

Bone is the third most common site for metastatic disease (after lung and liver).[26] As reported, spinal metastatic disease occurs in up to one-third of all cancer patients, like breast, prostate, lung, kidney, or thyroid cancers. Notorious for causing severe pain, bone metastases are also the major reasons for pathologic fracture, life-threatening hypercalcemia, spinal cord compression, immobility, and ultimate mortality in patients affiliated with advanced cancers.[27]A lot of progress has been made in the medical management of bone metastases including surgery approaches and radiation therapy, and targeted medical therapy. However, these strategies are at best only palliative and do not improve overall patient survival.[28] Metastatic disease of the spine can manifest in many ways. Pain is present in virtually all cases and can be severe enough that basic activities such as walking become nearly impossible. The challenges to identify more effective and specific molecularly targeted therapy to prevent and cure bone metastases and enhance the quality of life in these patients remain daunting. In this study, the included participants were overall metastatic spinal tumor.

Table 3

Characteristics of studies included in the meta-analysis according to KPS scales[8,14,15,25].

Author	Year	Language	Cohort size	Dignosis
Sun et al[14]	2015	English	28	Metastatic spinal tumors
Gu et al[15]	2013	English	31	Metastatic Spinal Tumors
Xie et al[8]	2009	Chinese	45	Metastatic Spinal Tumors
Tian et al[25]	2014	Chinese	23	Metastatic Spinal Tumors

PVP is a well-known percutaneous procedure effective in relieving pain, in comparison with open surgery. According to the guidelines published by the Society of Interventional Radiology (SIR) in 2003, the common indications for PV include osteoporotic vertebral compression fracture older than 2 weeks and refractory by medical therapy, painful vertebra with extensive osteolysis or invasion secondary to benign or malignant tumor, and painful vertebral fractures associated with osteonecrosis.[29] In 2009, the American College of Radiology (ACR), the American Society of Neuroradiology (ASNR), the Society of Neurointerventional Surgery (SNIS), the American Society of Spine Radiology (ASSR), and the SIR collaboratively prepared the official practice guidelines for vertebroplasty.[30] Presently, a meta-analysis was proceeded to evaluate the efficacy of PVP to pain relief. Pain assessment according to VAS was performed for all 22 included studies. Sensitivity analyses were performed to ensure that the results were reliable and valid. Finally, results indicated a significant decrease of pain scales after PVP treatment, implying the efficacy of PVP in pain relief of metastatic spinal tumor patients. In addition, life quality assessment according to KPS was performed for 4 studies and the KPS score was improved outstandingly after PVP treatment. In contrast, the complication rate was increased in PVP group. But the result may be inaccurate, because PVP group was mostly regarded as control other than experimental group in the study, in comparison with PKP (percutaneous kyphoplasty). Recently, several studies have proved the better safety of PKP than PVP. However, PKP has a longer operation time and higher material cost than PVP.[31] To confirm this evaluation, a large multi-center randomized controlled trial (RCT) should be conducted.

We acknowledge certain limitations of our study. First is the lack of a control group undergoing conservative treatment or PVP, especially with respect to the incidence of cement leakage. Second, the participants were relatively small. Third, the general status, previous treatment, life expectancy, and tumor type of the cancer patient may all influence the treatment outcome. With much more studies being published, the influence factors of PVP treatment efficacy should be explored in the near future. Because of limited evidence regarding the therapeutic aspects of these tumors, no definite protocol can be formulated for their treatment and the best mode of therapy should be individualized for each case. Additional high-quality data are necessary to draw more reliable conclusions.

In conclusion, our comprehensive meta-analysis of all published studies showed that PVP is significantly associated

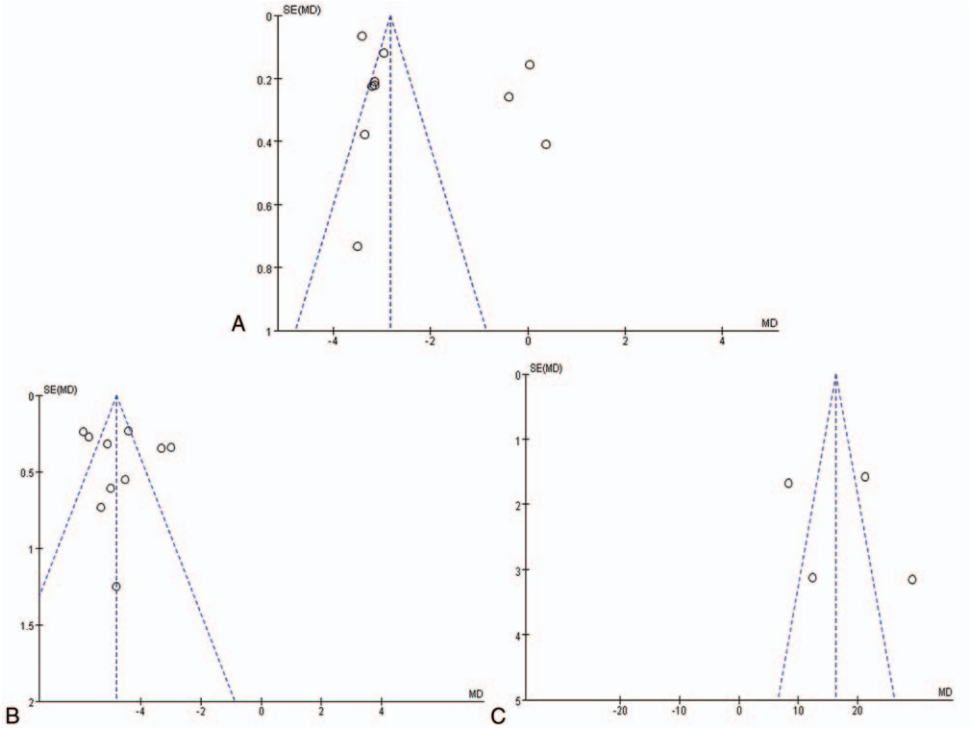

Figure 3. Funnel plot for VAS in case-control studies (A), single-arm studies (B), and KPS (C).

with pain relief and life quality in metastatic spinal tumor patients. It seems that PVP can improve the outcome in these patients.

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