

Review Article

# Vertebroplasty or kyphoplasty as palliative treatment for cancer-related vertebral compression fractures: a systematic review

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## Abstract

**BACKGROUND CONTEXT:** Percutaneous vertebroplasty (PVP) and kyphoplasty (KP) are minimally invasive treatment options for vertebral compression fractures (VCFs) due to malignancy.

**PURPOSE:** To perform a systematic review evaluating the effectiveness and safety of vertebral augmentation for malignant VCFs.

**STUDY DESIGN:** Systematic review.

**STUDY SAMPLE:** Studies on PVP or KP for VCFs in patients with malignant spinal lesions.

**OUTCOME MEASURES:** Visual Analog Scale (VAS) for pain, Oswestry Disability Index (ODI), Karnofsky Performance Score (KPS), and complications were extracted from eligible studies.

**METHODS:** Using Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, studies published between January 1, 2000 and January 3, 2018 were identified by combining the results of a report by Health Quality Ontario with an updated literature search.

**RESULTS:** The review identified two randomized controlled trials, 16 prospective studies, 44 retrospective studies, and 25 case series for a patient sample size of 3,426. At the earliest follow-up, pain improved from 7.48 to 3.00 with PVP, and from 7.05 to 2.96 with KP. ODI improved from 74.68 to 17.73 with PVP, and from 66.02 to 34.73 with KP. KPS improved from 66.99 to 80.28. Cement leakage was seen in 37.9% and 13.6% of patients treated with PVP and KP, respectively. Symptomatic complications (N = 43) were rare.

**CONCLUSIONS:** This review showed clinically relevant improvements in pain, ODI, and KPS in patients with VCFs due to malignancy treated with either PVP or KP. Cement leakage is common, but rarely symptomatic. Percutaneous vertebroplasty and KP are safe and effective palliative procedures for painful VCFs in patients with malignant spinal lesions. © 2019 Elsevier Inc. All rights reserved.

**Keywords:** Cancer; Kyphoplasty; Malignant spinal lesions; Palliative treatment; Vertebroplasty; Vertebral compression fractures

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## Introduction

In 2012 there were 14.1 million new cancer cases worldwide [1]. The frequency of metastasis to the spine depends on the primary cancer, with the majority being breast, lung, and prostate [2]. Between 5% and 10% of all cancer patients develop spinal metastases during the course of their disease, presenting as debilitating back pain in the thoracic or lumbar area [3]. Treatment options for patients with spinal metastasis are usually palliative, focusing on improving

the quality of remaining life of patients and their families by reducing or completely eliminating pain.

Vertebral augmentation, including percutaneous vertebroplasty (PVP) and kyphoplasty (KP), has been used as a minimally invasive treatment option for vertebral compression fractures (VCFs). The procedure is considered to be well suited for treatment of patients with malignant spine disease because it can be done under local anesthesia and provides rapid pain relief [4].

Percutaneous vertebroplasty and KP provide stability within the fractured vertebral body by preventing microscopic movement and macroscopic collapse. It has also been suggested that polymethylmethacrylate (PMMA) bone cement induces exothermic reactions that are toxic to nerve endings [5].

Vertebral augmentation was developed in the late 80s for the treatment of vertebral hemangiomas and osteolytic vertebral tumors [6]. It has since gained popularity for treatment of osteoporotic fractures. Under fluoroscopy, the needle is inserted through the pedicles [7]. Polymethylmethacrylate is injected into the vertebral body, still under imaging guidance, to minimize extravasation into the spinal canal. The surgeon may elect to obtain a biopsy prior to cement injection. Studies have shown underlying malignancy in around 5% of all patients [8,9] in whom the VCFs were initially thought to be due to osteoporosis. In contrast to PVP, during KP a small balloon is inserted and inflated inside the vertebral body to restore height prior to cement injection [7].

Percutaneous vertebroplasty and KP can be performed under local anesthesia, which prevents prolonged immobilization [10]. This is of particularly great importance when considering comorbidities and the degree of debility of this study population. Use of local anesthesia also provides the possibility of performing PVP and KP on an outpatient basis, allowing these patients to spend more time with their family.

The aim of this study was to perform a systematic review, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, to evaluate the effectiveness and safety of vertebral augmentation for cancer-related VCFs.

## Materials and methods

The pool of articles in this review consists of articles identified from the Health Technology Assessment performed by Health Quality Ontario (HQO) fulfilling the eligibility criteria, combined with articles identified from an updated literature search by the authors (Fig. 1). The HQO search included results from January 1, 2000 to October 2014. Additional articles published from October 2014 to January 2018 were identified by the authors by using Ovid MEDLINE, Ovid EMBASE, and Cochrane Library. The search strategy was nearly identical to the HQO search strategy, with a single optimization. Details on the search

strategy can be found in the Appendix. All articles identified by HQO and during the new search were evaluated. Abstracts were reviewed by two authors independently. In the case of discrepancy, the articles were discussed and consensus on eligibility was established. Finally, the reference lists of the included studies were screened for potentially relevant studies not included in the original search.

Inclusion criteria were:

- English publications available in full text.
- Published between January 1, 2000, and January 3, 2018.
- Reports involving vertebral augmentation techniques for cancer-related VCFs.

Exclusion criteria were:

- Experimental or animal studies involving evaluations of technology performance.
- Clinical reports not involving technical or clinical outcomes.
- Studies involving vertebral augmentation techniques not performed percutaneously under imaging guidance.
- Clinical studies mainly involving patients with osteoporotic or traumatic VCFs.
- Studies involving vertebral augmentation techniques performed simultaneously with spinal surgical interventions (including radio frequency ablation).
- Narrative reviews and opinions or commentaries.

Information on study design, patient characteristics, performed procedure, outcomes at all follow-ups, and complications were extracted from the HQO review and the additional articles. Follow-ups were categorized using six intervals for data presentation purposes (Table 2). The primary efficacy outcome was level of pain measured by the Visual Analog Scale (VAS) [11]. Secondary outcomes included the Oswestry Disability Index (ODI) [12], Karnofsky Performance Score (KPS) [13], complications, and rate of cement leakage.

The articles were evaluated as a whole and divided into two groups, reporting results on vertebroplasty and KP, separately. Two articles [14,15] presented data on both procedures but did not differentiate when reporting outcomes. These were allocated according to the most frequently performed procedure. Weighted averages on the patient demographics (Table 1) as well as VAS and ODI scores at each follow-up for articles in the two groups were calculated (Table 2). Weighted averages for KPS are presented without differentiating between treatment with PVP and KP since only a few studies reported this outcome (Table 2). All data expressed as means were weighted according to sample size.

## Results

Two hundred forty-three articles were identified during the new search in addition to the 150 articles from HQO. Seventy-three records were excluded based on review of the abstract and 85 articles from HQO did not fulfill the eligibility criteria. Thirty-six full-text records were excluded

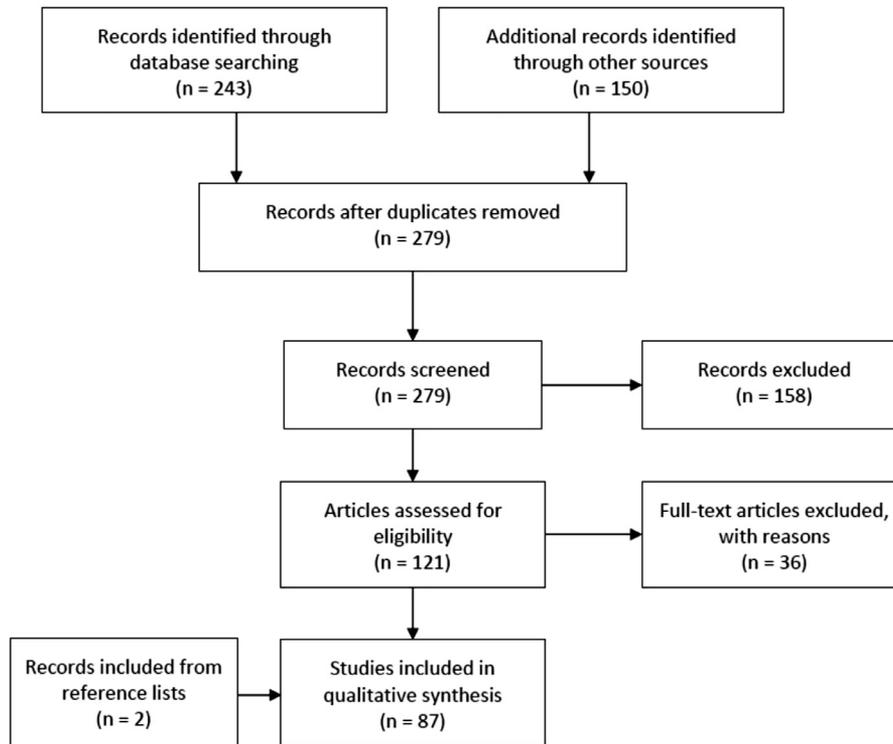


Fig. 1. Flow chart depicting study selection.

according to the exclusion criteria. Two additional studies were identified from reference lists of included articles. In total, 87 articles [4,5,14–98] were included in qualitative synthesis. The spreadsheet containing all extracted information is accessible (see Table, Supplemental Digital Content).

The results were comprised of two randomized controlled trials, 16 prospective studies, 44 retrospective studies, and 25 case series or reports.

We identified a total number of 3,426 patients. Among these 2,091 patients were treated with PVP and 1,335 with KP. Patient demographics regarding age, gender, and mean number of treated levels are summarized in Table 2. The most frequent primary malignancies were multiple myeloma (35.5%), lung (18.7%), and breast (18.6%). Cement leakage occurred in 37.9% of PVPs and in 13.6% of KPs. Symptomatic complications related to the operative procedure were reported in 43 cases. These included radiating pain, transient chest pain, radiculopathy without palsy, hemothorax, hematoma, radicular neuritis, asymptomatic and symptomatic pulmonary embolisms, bilateral leg motor deficits, cauda equina, and complete paraplegia.

We identified 56 studies reporting VAS for pain. Thirty-five of these were PVP studies and 21 were KP studies. Eighteen studies used ODI score as an outcome, comprised of five PVP studies and 13 KP studies. Eight studies reported KPS, including both PVP and KP studies.

Patients treated with PVP experienced pain relief after surgery with improvements in VAS from 7.48 preoperatively to 3.00 postoperatively. Patients treated with KP also

experienced pain relief with improvements in VAS from 7.05 preoperatively to 2.96 postoperatively. These improvements persisted during the subsequent follow-ups (Table 2, Fig. 2). Oswestry Disability Index scores in the PVP group improved from 74.68 at baseline to 17.74 at the earliest follow-up (<4 weeks postoperatively). Oswestry Disability Index scores in the KP group improved from 66.02 at baseline to 34.73 at the earliest follow-up. These initial improvements both plateaued to 30 at the remaining follow-up periods (Table 2, Fig. 2). Karnofsky Performance Score measured with no regard to surgical procedure improved from 66.99 preoperatively to 80.28 postoperatively. This improvement persisted during the subsequent follow-ups (Table 2, Fig. 2).

## Discussion

To our knowledge, this is the first systematic review with meta-analysis evaluating treatment efficacy and safety of cancer-related VCFs using PVP or KP. This systematic review involving 3,426 patients demonstrates clinically relevant improvements in VAS, ODI, and KPS [99–101]. Especially encouraging is the improvements in ODI which are greater than the threshold for substantial clinical difference [100] and can be interpreted as change from crippling back pain to moderate disability [12]. Although cement leakage was common, symptomatic complications were only seen in around 1% of cases. The data indicate a substantially lower cement leakage rate when performing KP compared to PVP. This difference might be partially due to

Table 1  
Patient demographics

	PVP	KP	Total
Total no. of patients, N (%)	2091 (61.0)	1335 (39.0)	3426 (100.0)
Weighted mean age, y (N)	62.56 (2,009)	63.16 (1,272)	62.79 (3,281)
Gender, N (%)			
Female	1101 (52.7)	652 (48.8)	1753 (51.1)
Male	972 (46.5)	665 (49.8)	1637 (47.8)
Unknown	18 (0.9)	18 (1.3)	36 (1.1)
Primary malignancy			
Adenocarcinoma of unknown primary site	1	2	3
Bladder	11	6	17
Breast	466	171	637
Cervix	0	14	14
Colorectal	32	37	69
Esophagus	1	4	5
Gall bladder	1	5	6
Gastrointestinal	10	9	19
Germ cell cancer	0	3	3
Glioblastoma	1	0	1
Head and neck cancer	9	5	14
Histiocytosis	1	0	1
Kidney	46	21	67
Leukemia	0	3	3
Liver	23	29	52
Lung	357	282	639
Lymphoma	15	18	33
Mastocytosis	0	2	2
Melanoma	0	4	4
Mesothelioma	0	1	1
Multiple myeloma	694	522	1216
Neuroendocrine	10	0	10
Ovary	7	4	11
Pancreas	10	4	14
Prostate	65	50	115
Sarcoma	15	7	22
Stomach	33	33	66
Thymus	3	0	3
Thyroid	15	3	18
Unknown/other	228	106	334
Urinary tract	8	0	8
Uterus	10	0	10
Vagina	0	1	1
Vulva	0	1	1
Mean number of treated levels per patient (N)	2.26 (2,005)	1.95 (859)	2.17 (2,864)
Cement leakage, N (%)	1157 (37.9)	206 (13.6)	1419 (31.1)
Symptomatic complications (N)	35 (2,024)	8 (909)	43 (2,933)

N, number of patients.

a difference in tumor configuration and vertebral body destruction rather than the technique alone. However, this finding may not be clinically important, considering the low incidence of symptomatic complications. Studies including osteoporotic fractures found similar leakage rates and the same disparity between vertebroplasty and KP [102]. The leakage rate for PVP in studies published prior to October 2014 was substantially different from more recent studies (41.7% and 27.4%, respectively), indicating a refinement of the procedure. This difference was not seen when performing KP. In order to reduce the risk of confounding, studies involving other vertebral augmentation

methods, or supplementary tumor-controlling strategies such as radiation were excluded.

The major limitations of this study are the heterogeneity of reported outcomes, primary malignancies, and design of the included studies. The number and location of the treated levels and the volume of cement injected were not consistently reported across the studies. Approximately a third of the papers did not contain any outcome measure used for the pooled analysis of efficacy, but exclusively contributed to the collective evaluation of safety. Datasets reporting Short Form 36, Roland Morris Disability Questionnaire, and Eastern Cooperative Oncology Group were

Table 2  
Outcome measures

	Preoperative	<4 wk	≤6 wk	<6 mo	<1 y	≥1 y
VAS (N)						
PVP	7.48 (1,445)	3.00 (1,147)	2.90 (606)	2.50 (370)	2.85 (784)	2.98 (260)
KP	7.05 (1103)	2.96 (814)	2.99 (222)	3.12 (318)	3.55 (204)	3.09 (375)
ODI (N)						
PVP	74.68 (226)	17.73 (190)	32.25 (67)	31.68 (67)	29.88 (81)	28.93 (103)
KP	66.02 (592)	34.73 (275)	38.54 (156)	37.35 (381)	30.16 (162)	32.45 (301)
KPS (N)						
PVP and KP	66.99 (611)	80.28 (609)	83.11 (263)	83.92 (263)	82.02 (265)	79.08 (110)

N, number of patients.

not included because of a small sample size of these studies. In addition, articles presenting qualitative descriptions or unvalidated scales for pain, mobility, and quality of life were only included in evaluation of safety. The analysis of efficacy does not take the primary malignancy into account. Therefore, if a certain type of primary cancer acts as a prognostic predictor, our data analysis does not allow the identifying of this. This field of research is obviously limited by the sparse amount of randomized controlled trials. Only one included study, the Cancer Patient Fracture Evaluation study, compared vertebral augmentation to nonsurgical management using a randomized design [21]. This study reports rapid pain relief and improvement of quality of life.

The construction of pooled follow-ups for VAS, ODI, and KPS were necessary to allow a transparent presentation of the results. This presents challenges when interpreting the results, since data in the same follow-up category could be collected at different times. KPS was only reported in eight studies and were evaluated with no respect to surgical procedure to present a meaningful number of patients.

As can be expected in studies of patients with terminal disease, the sample size throughout the follow-up period diminishes. This may lead to an overestimation of the efficacy, since only the patients with the best general condition and the largest effect of the treatment are participating in the follow-ups. However, the available data shows that the largest improvement is seen soon after the PVP or KP, and the improvement is maintained throughout the follow-up period. The majority of randomized controlled trials on vertebral augmentation are solely including patients with osteoporotic VCFs [103]. Spontaneous healing of osteoporotic VCFs is reported to occur within 3 months [104], but the natural course of malignant lesions is an area of speculation. This difference in study population makes it difficult to compare our results with previously published studies evaluating the effectiveness of vertebral augmentation.

Vertebral augmentation with either PVP or KP is a minimally invasive and safe procedure for painful VCFs in patients with malignant spinal lesions, which make the procedures ideal for palliative treatment. This review showed clinically relevant improvements in VAS for pain, ODI,

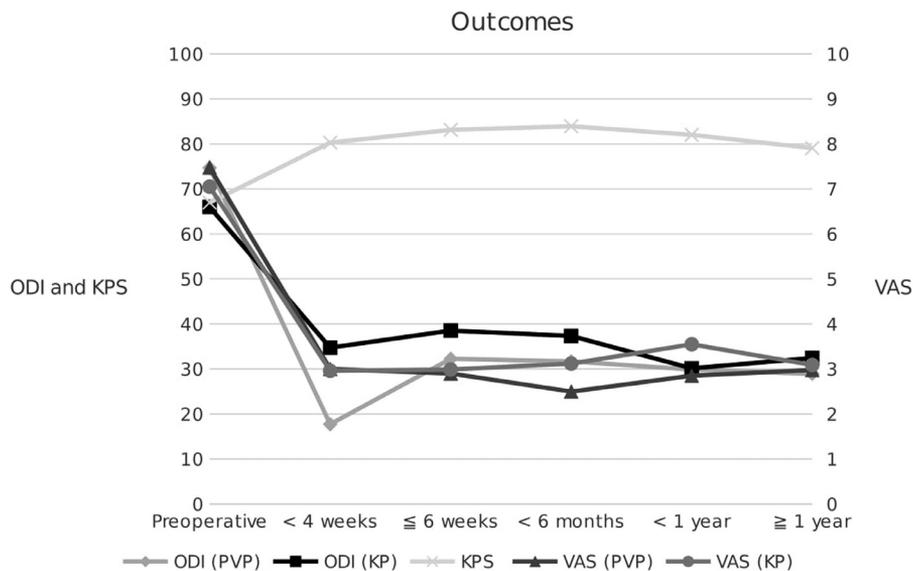


Fig. 2. Graph illustrating VAS, ODI, and KPS at follow-ups. VAS, Visual Analog Scale; ODI, Oswestry Disability Index; KPS, Karnofsky Performance Score.

and KPS. Cement leakage is common, but rarely symptomatic. Our results do not indicate any difference between PVP and KP in improving VAS for pain, ODI, and KPS. Treatment outcomes with PVP and KP appear to be similar. The choice of procedure should remain a matter of surgical preference, institutional tradition, and the possible need for vertebral height restoration. To control for confounders and the risks of bias, blinded randomized controlled trials should be performed.

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## Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.spinee.2019.02.012>.

## Appendix. Literature Search Strategy

#	Search	Results
1	Spinal Fractures/ use mesz,coch or spine fracture/ use emez	31.439
2	Fractures, Compression/ use mesz,coch or compression fracture/ use emez	6.966
3	((spinal or spine or vertebr* or compression) adj2 fracture*) or VCF).ti,ab.	38.863
4	or/1-3	55.590
5	exp Multiple Myeloma/	108.245
6	Spinal Neoplasms/ use mesz, coch or exp spine tumor/ use emez	18.100
7	(myeloma* adj (plasma-cell* or multiple*) or myelomas#s or ((spinal or spine*) adj (neoplasm* or tumor* or cancer* or metastas#s))).ti,ab.	12.068
8	or/5-7	132.682
9	and/4,8	2.476
10	Kyphoplasty/	3.488
11	Vertebroplasty/ use mesz,coch or percutaneous vertebroplasty/ use emez	6.719
12	(kyphoplast* or vertebroplast* or (vertebr* or cement spinal) adj augment*) or percutaneous osteoplast* or (balloon adj2 (spine or spinal or vertebr*))).ti,ab.	9.408
13	or/10-12	11.054
14	9 and 13	806
15	limit 14 to (english language and yr="2014 -Current")	243

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