# Vertebroplasty or kyphoplasty as palliative treatment for cancer-related vertebral compression fractures

## a systematic review

Sørensen, Simon Thorbjørn; Kirkegaard, Andreas Ole; Carreon, Leah; Rousing, Rikke; Andersen, Mikkel Østerheden

*Published in:*
The Spine Journal

*DOI:*
10.1016/j.spinee.2019.02.012

*Publication date:*
2019

*Document version:*
Accepted manuscript

*Document license:*
CC BY-NC-ND

*Citation for pulished version (APA):*
Sørensen, S. T., Kirkegaard, A. O., Carreon, L., Rousing, R., & Andersen, M. Ø. (2019). Vertebroplasty or kyphoplasty as palliative treatment for cancer-related vertebral compression fractures: a systematic review. *The Spine Journal*, *19*(6), 1067-1075. https://doi.org/10.1016/j.spinee.2019.02.012


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

Simon Thorbjørn Sørensen MS-VI ,
Andreas Ole Kirkegaard MS-VI , Leah Carreon MD, prof. ,
Rikke Rousing MD, PhD , Mikkel Østerheden Andersen MD

PII: S1529-9430(19)30073-7
DOI: https://doi.org/10.1016/j.spinee.2019.02.012
Reference: SPINEE 57876

To appear in: *The Spine Journal*

Received date: 13 October 2018
Revised date: 19 February 2019
Accepted date: 20 February 2019

Please cite this article as: Simon Thorbjørn Sørensen MS-VI , Andreas Ole Kirkegaard MS-VI , Leah Carreon MD, prof. , Rikke Rousing MD, PhD , Mikkel Østerheden Andersen MD , Vertebroplasty or kyphoplasty as palliative treatment for cancer-related vertebral compression fractures: a systematic review, *The Spine Journal* (2019), doi: https://doi.org/10.1016/j.spinee.2019.02.012

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

Authors:

- Simon Thorbjørn Sørensen, MS-VI – Center for Spine Surgery & Research, Middelfart Hospital
- Andreas Ole Kirkegaard, MS-VI - Center for Spine Surgery & Research, Middelfart Hospital
- Leah Carreon, MD, prof. - Center for Spine Surgery & Research, Middelfart Hospital
- Rikke Rousing, MD, PhD - Center for Spine Surgery & Research, Middelfart Hospital
- Mikkel Østerheden Andersen, MD - Center for Spine Surgery & Research, Middelfart Hospital

Corresponding author:

Simon Thorbjørn Sørensen, Østre Hougvej 55, 5500 Middelfart, Denmark
Phone: +4530238440
E-mail: sisoe13@student.sdu.dk
Fax number: +4563484281

Funding: None

Drug Statement: The Manuscript does not contain information about medical device(s)/drug(s).

**Abstract**

Background Context: Percutaneous vertebroplasty (PVP) and kyphoplasty (KP) are minimally invasive treatment options for VCFs due to malignancy.

Purpose: To perform a systematic review evaluating the effectiveness and safety of vertebral augmentation for malignant vertebral compression fractures (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 PRISMA 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 2 RCTs, 16 prospective studies, 44 retrospective studies, and 25 case series for a patient sample size of 3426. 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. PVP and KP are safe and effective palliative procedures for painful VCFs in patients with malignant spinal lesions.

**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).
PVP and KP provides 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). PMMA 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).

PVP 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 (PRISMA) guidelines, to evaluate the effectiveness and safety of vertebral augmentation for cancer-related vertebral compression fractures.

**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 (Figure 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 vertebral compression fractures

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 vertebral compression fractures
- 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 kyphoplasty 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 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 2 randomized controlled trials, 16 prospective studies, 44 retrospective studies, and 25 case series or reports.

We identified a total number of 3426 patients. Among these 2091 patients were treated with PVP and 1335 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. 18 studies used ODI score as an outcome, comprised of 5 PVP studies and 13 KP studies. 8 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, Figure 2). ODI scores in the PVP group improved from 74.68 at baseline to 17.74 at the earliest follow-up (<4 weeks postoperatively). ODI 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, Figure 2). KPS 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, Figure 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 3426 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 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 kyphoplasty (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 was 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 (SF-36), Roland Morris Disability Questionnaire (RMDQ), and Eastern Cooperative Oncology Group (ECOG) were 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 (CAFE) study, compared vertebral augmentation to non-surgical 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 8 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 vertebral compression fractures 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, 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.

**References**


1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86.
2. Patel LR, Camacho DF, Shiozawa Y, Pienta KJ, Taichman RS. Mechanisms of cancer cell metastasis to the bone: a multistep process. Future Oncol. 2011;7(11):1285-97.
3. Bilsky MH, Lis E, Raizer J, Lee H, Boland P. The diagnosis and treatment of metastatic spinal tumor. Oncologist. 1999;4(6):459-69.
4. Alvarez L, Perez-Higueras A, Quinones D, Calvo E, Rossi RE. Vertebroplasty in the treatment of vertebral tumors: postprocedural outcome and quality of life. Eur Spine J. 2003;12(4):356-60.
5. Trumm CG, Jakobs TF, Zech CJ, Helmberger TK, Reiser MF, Hoffmann RT. CT fluoroscopy-guided percutaneous vertebroplasty for the treatment of osteolytic breast cancer metastases: results in 62 sessions with 86 vertebrae treated. J Vasc Interv Radiol. 2008;19(11):1596-606.
6. Galibert P, Deramond H, Rosat P, Le Gars D. [Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty]. Neurochirurgie. 1987;33(2):166-8.
7. Zoarski GH, Stallmeyer MJ, Obuchowski A. Percutaneous vertebroplasty: A to Z. Tech Vasc Interv Radiol. 2002;5(4):223-38.
8. Mukherjee S, Thakur B, Bhagawati D, Akmal S, Arzoglou V, Yeh J, et al. Utility of routine biopsy at vertebroplasty in the management of vertebral compression fractures: A tertiary center experience. Journal of Neurosurgery: Spine. 2014;21(5):687-97.
9. Hansen EJ, Simony A, Carreon L, Andersen MO. Rate of unsuspected malignancy in patients with vertebral compression fracture undergoing percutaneous vertebroplasty. Spine. 2016;41(6):549-52.
10. Chen KY, Ma HI, Chiang YH. Percutaneous transpedicular vertebroplasty with polymethyl methacrylate for pathological fracture of the spine. J Clin Neurosci. 2009;16(10):1300-4.
11. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. Psychol Med. 1988;18(4):1007-19.
12. Fairbank JC, Pynsent PB. The Oswestry Disability Index. Spine (Phila Pa 1976). 2000;25(22):2940-52; discussion 52.
13. Mor V, Laliberte L, Morris JN, Wiemann M. The Karnofsky Performance Status Scale. An examination of its reliability and validity in a research setting. Cancer. 1984;53(9):2002-7.
14. Audat ZA, Hajyousef MH, Fawareh MD, Alawneh KM, Odat MA, Barbarawi MM, et al. Comparison if the addition of multilevel vertebral augmentation to conventional therapy will improve the outcome of patients with multiple myeloma. Scoliosis and Spinal Disorders. 2016;11(1):47.
15. Majeed H, Bommireddy R, Klezl Z. Cement augmentation for vertebral fractures in patients with multiple myeloma. Acta orthopaedica Belgica. 2014;80(4):551-7.

16. Anselmetti GC, Manca A, Montemurro F, Hirsch J, Chiara G, Grignani G, et al. Percutaneous vertebroplasty in multiple myeloma: prospective long-term follow-up in 106 consecutive patients. Cardiovasc Intervent Radiol. 2012;35(1):139-45.
17. Anselmetti GC, Manca A, Montemurro F, Tutton S, Chiara G, Battistella M, et al. Vertebroplasty using transoral approach in painful malignant involvement of the second cervical vertebra (C2): a single-institution series of 25 patients. Pain Physician. 2012;15(1):35-42.
18. Barragan-Campos HM, Vallee JN, Lo D, Cormier E, Jean B, Rose M, et al. Percutaneous vertebroplasty for spinal metastases: complications. Radiology. 2006;238(1):354-62.
19. Basile A, Cavalli M, Fiumara P, Di Raimondo F, Mundo E, Caltabiano G, et al. Vertebroplasty in multiple myeloma with osteolysis or fracture of the posterior vertebral wall. Usefulness of a delayed cement injection. Skeletal Radiol. 2011;40(7):913-9.
20. Basile A, Tsetis D, Cavalli M, Fiumara P, Di Raimondo F, Coppolino F, et al. Sacroplasty for local or massive localization of multiple myeloma. Cardiovasc Intervent Radiol. 2010;33(6):1270-7.
21. Berenson J, Pflugmacher R, Jarzem P, Zonder J, Schechtman K, Tillman JB, et al. Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial. Lancet Oncol. 2011;12(3):225-35.
22. Bosnjakovic P, Ristic S, Mrvic M, Miljkovic AE, Vukicevic T, Marjanovic G, et al. Management of painful spinal lesions caused by multiple myeloma using percutaneous acrylic cement injection. Acta Chir Iugosl. 2009;56(4):153-8.
23. Botton E, Edeline J, Rolland Y, Vauleon E, Le Roux C, Mesbah H, et al. Cementoplasty for painful bone metastases: a series of 42 cases. Med Oncol. 2012;29(2):1378-83.
24. Burton AW, Reddy SK, Shah HN, Tremont-Lukats I, Mendel E. Percutaneous vertebroplasty--a technique to treat refractory spinal pain in the setting of advanced metastatic cancer: a case series. J Pain Symptom Manage. 2005;30(1):87-95.
25. Calmels V, Vallee JN, Rose M, Chiras J. Osteoblastic and mixed spinal metastases: evaluation of the analgesic efficacy of percutaneous vertebroplasty. AJNR Am J Neuroradiol. 2007;28(3):570-4.
26. Chen G, Luo ZP, Zhang H, Nalajala B, Yang H. Percutaneous kyphoplasty in the treatment of painful osteoblastic metastatic spinal lesions. J Clin Neurosci. 2013;20(7):948-50.
27. Chen L, Ni RF, Liu SY, Liu YZ, Jin YH, Zhu XL, et al. Percutaneous vertebroplasty as a treatment for painful osteoblastic metastatic spinal lesions. J Vasc Interv Radiol. 2011;22(4):525-8.
28. Chen L, Su IC, Ni CF, Wang ZT. Percutaneous vertebroplasty performed with an 18-gauge needle for treatment of metastatic severe compression fracture of the cervical vertebral body. J Vasc Interv Radiol. 2014;25(9):1413-7.
29. Chen LH, Hsieh MK, Niu CC, Fu TS, Lai PL, Chen WJ. Percutaneous vertebroplasty for pathological vertebral compression fractures secondary to multiple myeloma. Arch Orthop Trauma Surg. 2012;132(6):759-64.
30. Chew C, Ritchie M, O'Dwyer PJ, Edwards R. A prospective study of percutaneous vertebroplasty in patients with myeloma and spinal metastases. Clin Radiol. 2011;66(12):1193-6.
31. Corcos G, Dbjay J, Mastier C, Leon S, Auperin A, De Baere T, et al. Cement leakage in percutaneous vertebroplasty for spinal metastases: a retrospective evaluation of incidence and risk factors. Spine (Phila Pa 1976). 2014;39(5):E332-8.

32. Dalbayrak S, Onen MR, Yilmaz M, Naderi S. Clinical and radiographic results of balloon kyphoplasty for treatment of vertebral body metastases and multiple myelomas. J Clin Neurosci. 2010;17(2):219-24.
33. Diamond TH, Hartwell T, Clarke W, Manoharan A. Percutaneous vertebroplasty for acute vertebral body fracture and deformity in multiple myeloma: a short report. Br J Haematol. 2004;124(4):485-7.
34. Dudeney S, Lieberman IH, Reinhardt MK, Hussein M. Kyphoplasty in the treatment of osteolytic vertebral compression fractures as a result of multiple myeloma. J Clin Oncol. 2002;20(9):2382-7.
35. Eleraky M, Papanastassiou I, Setzer M, Baaj AA, Tran ND, Vrionis FD. Balloon kyphoplasty in the treatment of metastatic tumors of the upper thoracic spine. J Neurosurg Spine. 2011;14(3):372-6.
36. Farrokhi M, Nouraei H, Kiani A. The Efficacy of Percutaneous Vertebroplasty in Pain Relief in Patients with Pathological Vertebral Fractures due to Metastatic Spinal Tumors. Iran Red Crescent Med J. 2012;14(9):523-30.
37. Garland P, Gishen P, Rahemtulla A. Percutaneous vertebroplasty to treat painful myelomatous vertebral deposits-long-term efficacy outcomes. Ann Hematol. 2011;90(1):95-100.
38. Hentschel SJ, Rhines LD, Shah HN, Burton AW, Mendel E. Percutaneous vertebroplasty in vertebra plana secondary to metastasis. J Spinal Disord Tech. 2004;17(6):554-7.
39. Huber FX, McArthur N, Tanner M, Gritzbach B, Schoierer O, Rothfischer W, et al. Kyphoplasty for patients with multiple myeloma is a safe surgical procedure: results from a large patient cohort. Clin Lymphoma Myeloma. 2009;9(5):375-80.
40. Huegli RW, Schaeren S, Jacob AL, Martin JB, Wetzel SG. Percutaneous cervical vertebroplasty in a multifunctional image-guided therapy suite: hybrid lateral approach to C1 and C4 under CT and fluoroscopic guidance. Cardiovasc Intervent Radiol. 2005;28(5):649-52.
41. Julka A, Tolhurst SR, Srinivasan RC, Graziano GP. Functional outcomes and height restoration for patients with multiple myeloma-related osteolytic vertebral compression fractures treated with kyphoplasty. J Spinal Disord Tech. 2014;27(6):342-6.
42. Knight JR, Heran M, Munk PL, Raabe R, Liu DM. C-arm cone-beam CT: applications for spinal cement augmentation demonstrated by three cases. J Vasc Interv Radiol. 2008;19(7):1118-22.
43. Kobayashi T, Arai Y, Takeuchi Y, Nakajima Y, Shioyama Y, Sone M, et al. Phase I/II clinical study of percutaneous vertebroplasty (PVP) as palliation for painful malignant vertebral compression fractures (PMVCF): JIVROSG-0202. Ann Oncol. 2009;20(12):1943-7.
44. Konig MA, Jehan S, Balamurali G, Bierschneider M, Grillhosl A, Boszczyk BM. Kyphoplasty for lytic tumour lesions of the spine: prospective follow-up of 11 cases from procedure to death. Eur Spine J. 2012;21(9):1873-9.
45. Korovessis P, Vardakastanis K, Vitsas V, Syrimpeis V. Is Kiva implant advantageous to balloon kyphoplasty in treating osteolytic metastasis to the spine? Comparison of 2 percutaneous minimal invasive spine techniques: a prospective randomized controlled short-term study. Spine (Phila Pa 1976). 2014;39(4):E231-9.
46. Kushchayev S, Kushchayeva Y, Theodore N, Preul MC, Clark OH. Percutaneous vertebroplasty for thyroid cancer metastases to the spine. Thyroid. 2010;20(5):555-60.
47. Lane JM, Hong R, Koob J, Kiechle T, Niesvizky R, Pearse R, et al. Kyphoplasty enhances function and structural alignment in multiple myeloma. Clin Orthop Relat Res. 2004(426):49-53.

48. Lee B, Franklin I, Lewis JS, Coombes RC, Leonard R, Gishen P, et al. The efficacy of percutaneous vertebroplasty for vertebral metastases associated with solid malignancies. Eur J Cancer. 2009;45(9):1597-602.
49. Li Y, Gu YF, Sun ZK, Wu CG, Li YD, Wang W, et al. Comparison of percutaneous vertebroplasty with and without interventional tumour removal for malignant vertebral compression fractures with symptoms of neurological compression. Eur Radiol. 2013;23(10):2754-63.
50. Lim BG, Lee JY, Lee MK, Lee DK, Kim JS, Choi SS. Kyphoplasty for the treatment of vertebral compression fractures in a cancer patient with neurological deficits and anterior vertebral wall destruction. Pain Physician. 2011;14(6):539-44.
51. Lykomitros V, Anagnostidis KS, Alzeer Z, Kapetanos GA. Percutaneous anterolateral balloon kyphoplasty for metastatic lytic lesions of the cervical spine. Eur Spine J. 2010;19(11):1948-52.
52. Masala S, Anselmetti GC, Marcia S, Massari F, Manca A, Simonetti G. Percutaneous vertebroplasty in multiple myeloma vertebral involvement. J Spinal Disord Tech. 2008;21(5):344-8.
53. Masala S, Anselmetti GC, Muto M, Mammucari M, Volpi T, Simonetti G. Percutaneous vertebroplasty relieves pain in metastatic cervical fractures. Clin Orthop Relat Res. 2011;469(3):715-22.
54. Mazumdar A, Gilula LA. Relief of radicular pain in metastatic disease by vertebroplasty. Acta Radiol. 2010;51(2):179-82.
55. McDonald RJ, Trout AT, Gray LA, Dispenzieri A, Thielen KR, Kallmes DF. Vertebroplasty in multiple myeloma: outcomes in a large patient series. AJNR Am J Neuroradiol. 2008;29(4):642-8.
56. Mikami Y, Numaguchi Y, Kobayashi N, Fuwa S, Hoshikawa Y, Saida Y. Therapeutic effects of percutaneous vertebroplasty for vertebral metastases. Jpn J Radiol. 2011;29(3):202-6.
57. Mont'Alverne F, Vallee JN, Guillevin R, Cormier E, Jean B, Rose M, et al. Percutaneous vertebroplasty for multiple myeloma of the cervical spine. Neuroradiology. 2009;51(4):237-42.
58. Murphy KJ, Nwankwo IJ, Gailloud P. Percutaneous vertebroplasty in the treatment of blastic vertebral column metastasis from breast cancer. J Vasc Interv Radiol. 2007;18(2):321-3.
59. Pflugmacher R, Kandziora F, Schroeder RJ, Melcher I, Haas NP, Klostermann CK. Percutaneous balloon kyphoplasty in the treatment of pathological vertebral body fracture and deformity in multiple myeloma: a one-year follow-up. Acta Radiol. 2006;47(4):369-76.
60. Pflugmacher R, Taylor R, Agarwal A, Melcher I, Disch A, Haas NP, et al. Balloon kyphoplasty in the treatment of metastatic disease of the spine: a 2-year prospective evaluation. Eur Spine J. 2008;17(8):1042-8.
61. Ramos L, de Las Heras JA, Sanchez S, Gonzalez-Porras JR, Gonzalez R, Mateos MV, et al. Medium-term results of percutaneous vertebroplasty in multiple myeloma. Eur J Haematol. 2006;77(1):7-13.
62. Rodriguez-Catarino M, Blimark C, Willen J, Mellqvist UH, Rodjer S. Percutaneous vertebroplasty at C2: case report of a patient with multiple myeloma and a literature review. Eur Spine J. 2007;16 Suppl 3:242-9.
63. Saliou G, Kocheida el M, Lehmann P, Depriester C, Paradot G, Le Gars D, et al. Percutaneous vertebroplasty for pain management in malignant fractures of the spine with epidural involvement. Radiology. 2010;254(3):882-90.

64. Seo SS, Lee DH, Kim HJ, Yoon JW, Kwon OS, Kim KH. Percutaneous vertebroplasty at C7 for the treatment of painful metastases -A case report. Korean J Anesthesiol. 2013;64(3):276-9.
65. Shimony JS, Gilula LA, Zeller AJ, Brown DB. Percutaneous vertebroplasty for malignant compression fractures with epidural involvement. Radiology. 2004;232(3):846-53.
66. Simony A, Hansen EJ, Gaurilcikas M, Abildgaard N, Andersen MO. Pain reduction after percutaneous vertebroplasty for myeloma-associated vertebral fractures. Dan Med J. 2014;61(12):A4945.
67. Sun G, Jin P, Li M, Lui X, Li F, Xie Z, et al. Three-dimensional C-arm computed tomography combined with fluoroscopic guided pediculoplasty for treatment of vertebral body metastasis with lytic pedicle. Technol Cancer Res Treat. 2012;11(2):169-74.
68. Sun G, Li L, Jin P, Liu XW, Li M. Percutaneous vertebroplasty for painful spinal metastasis with epidural encroachment. J Surg Oncol. 2014;110(2):123-8.
69. Sun G, Wang LJ, Jin P, Liu XW, Li M. Vertebroplasty for treatment of osteolytic metastases at C2 using an anterolateral approach. Pain Physician. 2013;16(4):E427-34.
70. Tancioni F, Lorenzetti M, Navarria P, Nozza A, Castagna L, Gaetani P, et al. Vertebroplasty for pain relief and spinal stabilization in multiple myeloma. Neurol Sci. 2010;31(2):151-7.
71. Tran Thang NN, Abdo G, Martin JB, Seium-Neberay Y, Yilmaz H, Verbist MC, et al. Percutaneous cementoplasty in multiple myeloma: a valuable adjunct for pain control and ambulation maintenance. Support Care Cancer. 2008;16(8):891-6.
72. Trumm C, Jakobs T, Pahl A, Stahl R, Helmberger T, Paprottka P, et al. CT fluoroscopy-guided percutaneous vertebroplasty in patients with multiple myeloma: analysis of technical results from 44 sessions with 67 vertebrae treated. Diagn Interv Radiol. 2012;18(1):111-20.
73. Trumm CG, Pahl A, Helmberger TK, Jakobs TF, Zech CJ, Stahl R, et al. CT fluoroscopy-guided percutaneous vertebroplasty in spinal malignancy: technical results, PMMA leakages, and complications in 202 patients. Skeletal Radiol. 2012;41(11):1391-400.
74. Tseng YY, Lo YL, Chen LH, Lai PL, Yang ST. Percutaneous polymethylmethacrylate vertebroplasty in the treatment of pain induced by metastatic spine tumor. Surg Neurol. 2008;70 Suppl 1:S1:78-83; discussion S1:-4.
75. Vrionis F, Hamm A, Stanton N, Sullivan M, Obadia M, Miguel RV. Kyphoplasty for tumor-associated spinal fractures. Tech Reg Anesth Pain Manag. 2005;9(1):35-9.
76. Woo JH, Park HS, Han JI, Kim DY. Vertebroplasty for the compression of the dorsal root ganglion due to spinal metastasis. Pain Physician. 2013;16(4):E405-10.
77. Yoon JY, Kim TK, Kim KH. Anterolateral percutaneous vertebroplasty at C2 for lung cancer metastasis and upper cervical facet joint block. Clin J Pain. 2008;24(7):641-6.
78. Zou J, Mei X, Gan M, Yang H. Kyphoplasty for spinal fractures from multiple myeloma. J Surg Oncol. 2010;102(1):43-7.
79. Bae JW, Gwak H-S, Kim S, Joo J, Shin SH, Yoo H, et al. Percutaneous vertebroplasty for patients with metastatic compression fractures of the thoracolumbar spine: clinical and radiological factors affecting functional outcomes. The spine journal : official journal of the North American Spine Society. 2016;16(3):355-64.
80. Chih YP, Wu WT, Lin CL, Jou HJ, Huang YH, Chen LC, et al. Vertebral Compression Fracture Related to Pancreatic Cancer With Osteoblastic Metastasis: A Case Report and Literature Review. Medicine (Baltimore). 2016;95(5):e2670.

81. Gorospe L, Blanchard-Rodriguez MJ, Chinea-Rodriguez A. Cement pulmonary embolism after percutaneous vertebroplasty in multiple myeloma. Asian cardiovascular & thoracic annals. 2016;24(4):400-1.
82. Jurczyszyn A, Czepko R, Banach M, Godlewski B, Czepko RA, Maslowski P, et al. Percutaneous Vertebroplasty for Pathological Vertebral Compression Fractures Secondary to Multiple Myeloma--Medium-Term and Long-Term Assessment of Pain Relief and Quality of Life. Advances in clinical and experimental medicine : official organ Wroclaw Medical University. 2015;24(4):651-6.
83. Kosse A, Nakhla JP, Yassari R, Abramowicz AE, Brook A. Retained needle after cement injection during vertebral augmentation and its management strategy. BMJ Case Reports. 2016;2016:012180.
84. Li Z, Ni C, Chen L, Sun Z, Yang C, Zhao X, et al. Kyphoplasty versus vertebroplasty for the treatment of malignant vertebral compression fractures caused by metastases: a retrospective study. Chinese medical journal. 2014;127(8):1493-6.
85. Malhotra K, Butler JS, Yu HM, Selvadurai S, D'Sa S, Rabin N, et al. Spinal disease in myeloma: cohort analysis at a specialist spinal surgery centre indicates benefit of early surgical augmentation or bracing. BMC cancer. 2016;16:444.
86. Markmiller M. Percutaneous balloon kyphoplasty of malignant lesions of the spine: a prospective consecutive study in 115 patients. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2015;24(10):2165-72.
87. Milojkovic N, Homsi S. Polymethylmethacrylate pulmonary embolism as a complication of percutaneous vertebroplasty in cancer patients. The Journal of the Arkansas Medical Society. 2014;111(7):140-2.
88. Molloy S, Sewell MD, Platinum J, Patel A, Selvadurai S, Hargunani R, et al. Is balloon kyphoplasty safe and effective for cancer-related vertebral compression fractures with posterior vertebral body wall defects? Journal of surgical oncology. 2016;113(7):835-42.
89. Noriega DC, Kruger A, Ramajo RH, Ardura F, Munoz M, Sahin S. Long-Term Benefits of Percutaneous Anatomical Restoration of Vertebral Compression Fractures Linked to Malignancy. Turkish neurosurgery. 2016;26(4):608-14.
90. Rajah G, Altshuler D, Sadiq O, Nyame VK, Eltahawy H, Szerlip N. Predictors of delayed failure of structural kyphoplasty for pathological compression fractures in cancer patients. Journal of neurosurgery Spine. 2015;23(2):228-32.
91. Sun H, Yang Z, Xu Y, Liu X, Zhang Y, Chen Y, et al. Safety of percutaneous vertebroplasty for the treatment of metastatic spinal tumors in patients with posterior wall defects. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2015;24(8):1768-77.
92. Tian Q-H, Sun X-Q, Lu Y-Y, Wang T, Wu C-G, Li M-H, et al. Percutaneous Vertebroplasty for Palliative Treatment of Painful Osteoblastic Spinal Metastases: A Single-Center Experience. Journal of vascular and interventional radiology : JVIR. 2016;27(9):1420-4.
93. Tome-Bermejo F, Pinera AR, Duran-Alvarez C, Roman BLS, Mahillo I, Alvarez L, et al. Identification of risk factors for the occurrence of cement leakage during percutaneous vertebroplasty for painful osteoporotic or malignant vertebral fracture. Spine. 2014;39(11):E693-E700.

94. Wang K-W, Wang H-K, Lu K, Liang C-L, Chen Y-W, Liliang P-C. Fluoroscopically Guided C2 Percutaneous Vertebroplasty: A Surgical Technique Note on an Anterior Ascending Approach. Pain physician. 2016;19(4):E625-9.
95. Wang Y, Liu H, Pi B, Yang H, Qian Z, Zhu X. Clinical evaluation of percutaneous kyphoplasty in the treatment of osteolytic and osteoblastic metastatic vertebral lesions. International journal of surgery (London, England). 2016;30:161-5.
96. Xie P, Zhao Y, Li G. Efficacy of percutaneous vertebroplasty in patients with painful vertebral metastases: A retrospective study in 47 cases. Clinical neurology and neurosurgery. 2015;138:157-61.
97. Zhang HT, Chen GD, Yang HL, Luo ZP. Percutaneous Kyphoplasty in the Treatment of Osteoblastic-related Spinal Metastases. Clin Spine Surg. 2017;30(2):80-4.
98. Zhang JJ, Zhou Y, Hu HY, Sun YJ, Wang YG, Gu YF, et al. Safety and efficacy of multilevel vertebroplasty for painful osteolytic spinal metastases: a single-centre experience. European Radiology. 2017;27(8):3436-42.
99. Lee JS, Hobden E, Stiell IG, Wells GA. Clinically important change in the visual analog scale after adequate pain control. Acad Emerg Med. 2003;10(10):1128-30.
100. Glassman SD, Copay AG, Berven SH, Polly DW, Subach BR, Carreon LY. Defining substantial clinical benefit following lumbar spine arthrodesis. J Bone Joint Surg Am. 2008;90(9):1839-47.
101. Ringash J, O'Sullivan B, Bezjak A, Redelmeier DA. Interpreting clinically significant changes in patient-reported outcomes. Cancer. 2007;110(1):196-202.
102. Gu CN, Brinjikji W, Evans AJ, Murad MH, Kallmes DF. Outcomes of vertebroplasty compared with kyphoplasty: a systematic review and meta-analysis. J Neurointerv Surg. 2016;8(6):636-42.
103. Buchbinder R, Johnston RV, Rischin KJ, Homik J, Jones CA, Golmohammadi K, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev. 2018;4:CD006349.
104. Rousing R, Hansen KL, Andersen MO, Jespersen SM, Thomsen K, Lauritsen JM. Twelve-months follow-up in forty-nine patients with acute/semiacute osteoporotic vertebral fractures treated conservatively or with percutaneous vertebroplasty: a clinical randomized study. Spine (Phila Pa 1976). 2010;35(5):478-82.

**Figure legends:**

Figure 1: Flow chart depicting study selection.

Table 1: Patient demographics. N = Number of patients.

Table 2: Outcome measures. N = Number of patients.

Figure 2: Graph illustrating VAS, ODI, and KPS at follow-ups.

**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 myelomatos#s or ((spinal or spine*) adj (neoplasm* or tumo?r* 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 |

Figure 1

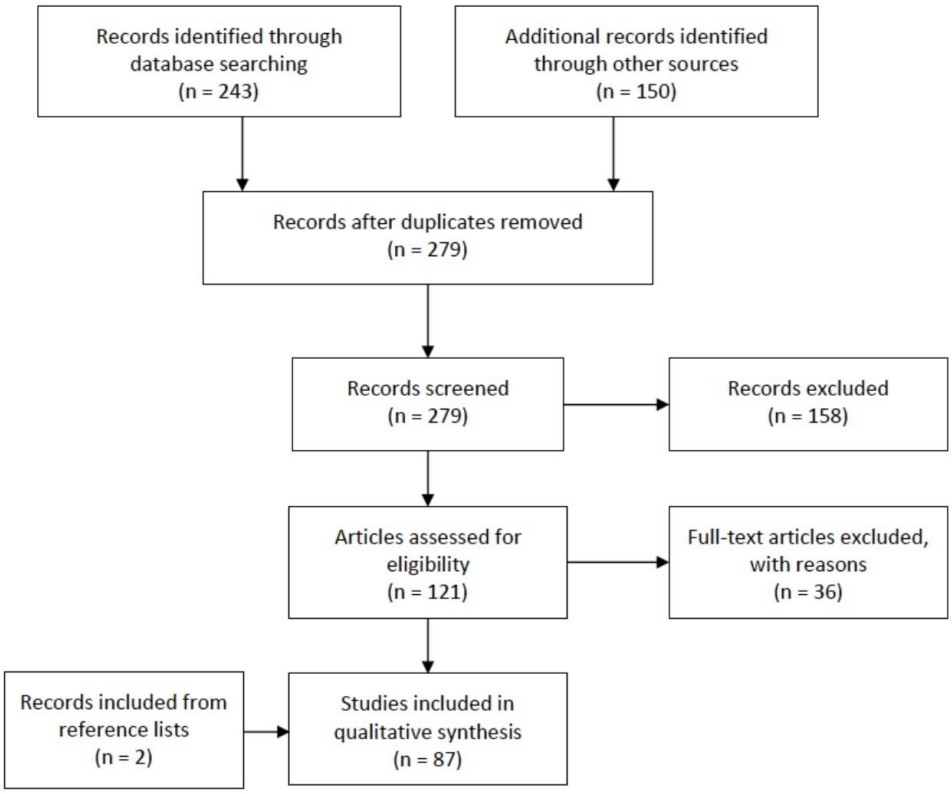
Records identified through database searching (n = 243)
Additional records identified through other sources (n = 150)
Records after duplicates removed (n = 279)
Records screened (n = 279)
Records excluded (n = 158)
Articles assessed for eligibility (n = 121)
Full-text articles excluded, with reasons (n = 36)
Records included from reference lists (n = 2)
Studies included in qualitative synthesis (n = 87)

Figure 2

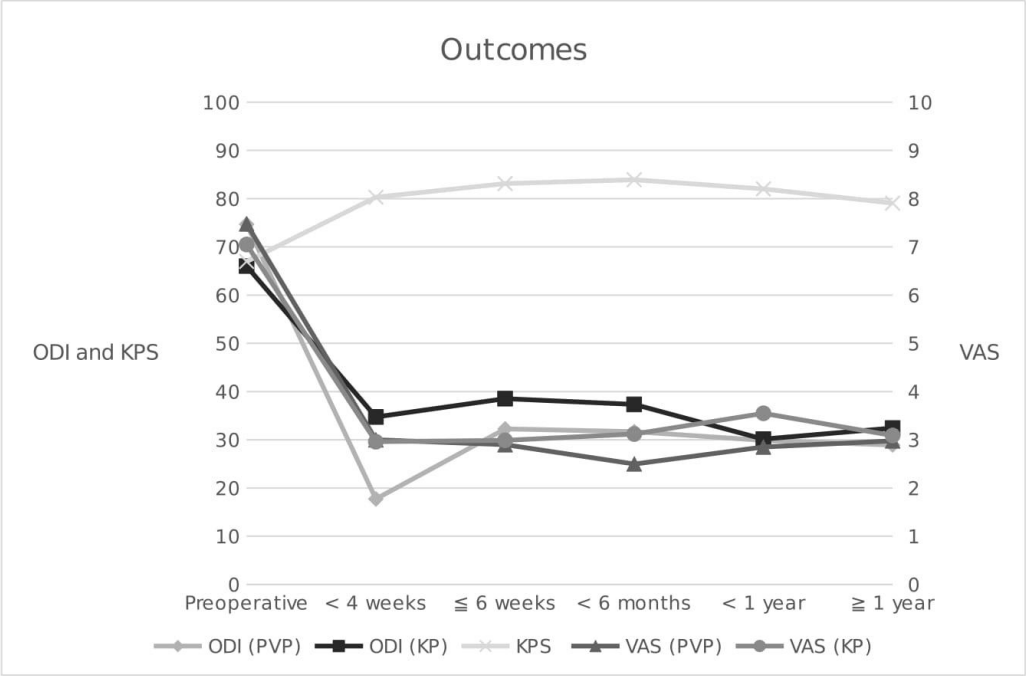
Outcomes
ODI and KPS
VAS
100
90
80
70
60
50
40
30
20
10
0
10
9
8
7
6
5
4
3
2
1
0
Preoperative
< 4 weeks
≦ 6 weeks
< 6 months
< 1 year
≧ 1 year
ODI (PVP)
ODI (KP)
KPS
VAS (PVP)
VAS (KP)

Table 1:

| | PVP | KP | Total |
|---|---|---|---|
| Total no. of patients, N (%) | 2091 (61.0) | 1335 (39.0) | 3426 (100.0) |
| Weighted mean age, Years (N) | 62.56 (2009) | 63.16 (1272) | 62.79 (3281) |
| 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 (2005) | 1.95 (859) | 2.17 (2864) |
| Cement leakage, N (%) | 1157 (37.9) | 206 (13.6) | 1419 (31.1) |
| Symptomatic complications (N) | 35 (2024) | 8 (909) | 43 (2933) |

Table 2:

| | Preoperative | < 4 weeks | ≤ 6 weeks | < 6 months | < 1 year | ≥ 1 year |
|---|---|---|---|---|---|---|
| VAS (N) | | | | | | |
| PVP | 7.48 (1445) | 3.00 (1147) | 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) |