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**Author:** Muijs, Sander Paul Jan  
**Title:** Percutaneous vertebroplasty for painful long-standing osteoporotic vertebral compression fractures: indication, clinical outcome, cement Leakage & classification  
**Date:** 2012-09-20
S.P.J. Muijs

1Department of Orthopaedic Surgery, Leiden University Medical Center, Leiden, The Netherlands.
General Discussion
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The (R)evolution of Percutaneous VertebroPlasty
Since 1984, in which Deramond performed the first PVP, vertebroplasty gained enormous popularity due to the encouraging outcomes of numerous follow-up studies. Sometimes, vertebroplasty was considered, a “magic intervention” by patients (and some doctors too), that could cure all types of chronic back pain.

Due to two widely discussed papers in the New England Journal of Medicine, this highly positive perspective made a 180 degree turn and promptly PVP was believed to be a worthless procedure by many healthcare providers.

As a result, today PVP for OVCFs is no longer part of the standard insured medical costs in the Netherlands. Although questions concerning the effectiveness of PVP in specific patient groups and the precise working mechanism of the procedure remain, the current research presented in this thesis (which was initiated before other “critics” appeared), does however not support this acute discarding of the PVP procedure, which is based on rather awkward methodology of that research.

Patient Selection and Indications
Not unlike other medical interventions, the outcome of PVP is highly dependent on selecting the correct indications for a specific medical problem. As such, in general, patient selection is the keystone of a successful treatment outcome.

In acute OVCFs, patients should be confined to a period of at least 6-8 weeks of conservative treatment (in which up to 85% of the OVCFs will spontaneously heal), whilst strict inclusion criteria for PVP should be met - including a thorough physical examination, plain radiography and MR Imaging - before PVP should be considered (see also, Chapter 7, this thesis).

The triad of indication criteria for painful long-standing OVCFs includes: I) incapacitating pain at the fractured level, with focal point tenderness, which increases if pressure is applied to the spinous process of the fractured vertebra, II) unresponsiveness to at least 6-8 weeks of conservative treatment and III) intravertebral BME on MR Imaging.
The research presented in the current thesis, showed no correlation between the volume of intravertebral BME and the outcome of PVP for long-standing OVCFs (see also, Chapter 2, this thesis). Other authors showed, that when treating patients without any signs of intravertebral BME, the outcome is significantly worse.15, 16 Thus, these studies suggest that the mere presence of and not the volume of intravertebral BME should be used as part of the indication criteria strategy. Pathophysiologically this might be explained by the fact that the presence of intravertebral BME shows that part of the fractured vertebral body still is in the early phase of the fracture healing cascade, with subsequent micro-movement in the unconsolidated vertebral body.17

Next to VCFs due to osteoporosis (aetiology of the majority VCFs), painful (pending) compression fractures due to aggressive haemangioma, multiple myeloma or bone metastasis and trauma are included in the indication spectrum for PVP.18–20 These patients with disseminated or primary vertebral malignant disease have generally a poor general health condition (i.e. co-morbidity, chemotherapy), which makes them non-eligible for extensive spinal (resection) surgery. But, since PVP is performed under local anaesthesia and is performed in day-care, PVP provides a treatment modality with an acceptable cost effectiveness for the patient and an immediate improvement of Quality of Life, mainly due to pain relief.21, 22 The PVP procedure in metastatic bone destruction may be performed in combination with radio frequency ablation using CT-fluoroscopy guidance.23–26

The value of routine bone biopsy during every PVP for any presumed osteoporotic VCF, shows an unsuspected malignancy rate of 3.8% in our population, with no signs of malignancy at MR Imaging. Thus we advocate a vertebral body bone biopsy during every PVP procedure, in order to early diagnose an unexpected malignancy, which can be treated, like multiple myeloma (see also, Chapter 3 of this thesis).
Clinical Outcome in Long-Standing OVCFs

In literature, the clinical outcome of a PVP is usually presented in pain rating scales i.e. the visual analogue scale (VAS). Next to pain, other possible improvements in daily functioning can be as important as a decrease in pain, for example increased mobility despite presence of (less) pain, which will improve the overall Quality of Life.

In order to make the PVP procedure more easily comparable to other (surgical) interventions and to potentially calculate effect sizes, Chapter 4 of this thesis, evaluates the short-form 36 (SF 36) Quality of Life questionnaire in a prospective three year follow-up study on patients treated for long-standing OVCFs. This study showed a durable and significant improvement in both the domains of physical function, bodily pain and the physical component score and in both summary SF 36 scores, thus indicating a significant and durable overall increase in the Quality of Life after a PVP.

Registration and Complications

During the last decade, registration of medical implants in order to facilitate monitoring of implant survival and (long-term) complications, has become more important despite its presence for hip prostheses since 1979. Registration of implants is a powerful tool to evaluate both the quality of an implant and the possible (long-term) complications. An important advantage, if such registration relates practice descriptive statistics and performance to the overall national level (i.e. “mirror information), is that quality at local levels will be improved.

In essence, the injection of non-absorbable bone cement into a vertebral body, which will stay in-situ for life, can also be seen as an implant. Therefore at least the type and volume of the injected cement and the vertebral levels should be registered.

Although cement leakage as a complication is present in up to 88%, severe complications are rare. The latter underscores the importance of a registry, which enables to identify rare complications earlier. Severe complications occur mainly in cases of high-volume cement leakage. Leakage of cement into the neural foramen or spinal canal can cause neurological injury. Next to a massive leakage, leakage into the intervertebral disc, may alter biomechanical stresses around adjacent vertebral bodies and may even pose an increased risk for new fractures. Due to the fact that new OVCFs tend to form adjacent to an old fracture (even in patients who are not previously treated with PVP), large series (i.e. registries) are needed to proof if PVP is a potential threat to adjacent vertebrae.
In our institution, a post-procedural CT-scan is part of the standard treatment protocol. On the necessity of the standard post-procedural CT-scan some debate exists in literature. Some authors feel that there is no need for a standard postoperative CT-scan due to the fact that the (acute) complication rate in PVP is low.\textsuperscript{33} The radiation dose of a CT-scan of the spine is also a point of concern, since the patient is exposed to more than 5 times the effective radiation dose compared to an AP and lateral plain radiograph of the spine.\textsuperscript{34,35} If the worldwide registration of cement leakages is found to be important, a post-operative CT-scan will be mandatory.

Leakages are best detected using post-procedural CT-scan.\textsuperscript{32} The use of CT-scan versus a plain X-ray results in an increased detection rate of more than 50\% of cement leakages.\textsuperscript{29} The exact anatomical position, the volume of the leakage as well as leakages in the basivertebral venous system can be more easily assessed with CT.\textsuperscript{29} In this thesis, the development of a new CT-based leakage classification system was described (see also, Chapter 6, \textit{this thesis}). So far, no anatomical based classification system for cement leakage had been published, making it impossible to conduct uniform registration of the most common complication of PVP.

The use of a low-viscosity PMMA-cement showed to triple the risk of cement leakage when compared to a medium viscosity PMMA cement (see also, Chapter 5, \textit{this thesis}). Still new types of PVP cement with different viscosities and an unknown outcome in terms of cement leakage and possible complications are being introduced to the market and used in the clinical setting without any phased introduction to the market with good clinical control to prevent (long-term) complications.\textsuperscript{28,36} The latter underscores the need for a cement leakage classification system with good validity in order to offer the best patient care possible: primum non nocere.
References


DISCUSSION & SUMMARY


Editorial - Further Opinion

Alistair Ross¹

¹Associate Editor, The Journal of Bone and Joint Surgery.

The battle over the treatment of patients with a painful osteoporotic vertebral fracture is hotting up nicely. On one side, the protagonists of vertebroplasty are carrying out a considerable number of these procedures and claiming significant, prolonged pain relief for their patients; on the other, the evidence-based medicine brigade can find no evidence that the procedure has anything other than a placebo effect. In their instructional review, Muijs, van Erkel and Dijkstra consider the place of percutaneous vertebroplasty in the 15% of patients who fail to respond to 12 weeks of conservative treatment. In its favour, they cite Eck et al who, in 2008, reported a meta-analysis of the literature to date and found a mean, statistically significant, improvement of 5.68 (SD+/−1.24) in post-operative VAS level. More recently, however, two randomised controlled studies were published in the New England Journal of Medicine (the Australian and INVEST studies) which cast doubt on its efficacy.

In the midst of this debate, the potential for causing harm should not be overlooked. Eck et al reported a 17.9% risk of new fracture, usually at an adjacent level, after vertebroplasty and a 19.7% risk of cement leak. Complications may be catastrophic and are usually related to leakage of large volumes of cement.

The indications for the procedure, whether effective or not, are now fairly clear. Patients with an osteoporotic fracture with more than 15% loss of anterior vertebral height, severe pain which is unresponsive to all reasonable modalities of conservative treatment, tenderness over spinous process of the fractured vertebra and bone marrow oedema on MRI imaging with fat suppression may be considered for treatment. It is the timing of this treatment that raises a number of issues. In the literature to date patients have been treated as early as one week after their fracture and as late as 12 months. Of the major randomised studies, the Vertos II study only included patients with back pain for six weeks or less, the Australian and INVEST studies included patients with back pain for up to a year. The Vertos II study showed that vertebroplasty gave greater pain relief than conservative treatment and concluded that the pain relief is immediate, sustained for at least a year, and is significantly greater than that achieved with conservative treatment. The Australian and INVEST studies concluded that vertebroplasty conferred no additional benefit over placebo or sham treatment.
These studies are not really comparable as they clearly study different populations. Given that the pain of an osteoporotic vertebral fracture will probably settle within 12 weeks in 85% of patients, it seems paradoxical to study a group in which the pain has been present for less than six weeks. Similarly, is it reasonable to study groups of patients who have been in pain for anything between a few weeks and a year?

One further piece of evidence should be considered. Since the article by Muijs et al was accepted for publication, the authors of the Australian and INVEST studies have combined their findings in a meta-analysis to try to identify any subgroups which would benefit from vertebroplasty. They have concentrated on patients with fractures of recent onset (<6 weeks) and patients in severe pain and have still failed to show any benefit from vertebroplasty over placebo.

Muijs et al are certainly correct in concluding that indisputable evidence in favour or against the effectiveness of percutaneous vertebroplasty is still lacking and that further studies are needed. When these are planned, not only should the inclusion and exclusion criteria be crystal clear but the investigators should undoubtedly narrow down the population studied by duration of symptoms: perhaps 3 to 6 months would be sensible in the first instance. Otherwise, how are we to know if we should advise vertebroplasty, and if so, who to treat and when?
References


