Vertebroplasty: An alternative therapy for painful osteoporotic vertebral fractures which do not respond to conservative treatment? Review and update

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Summary
Purpose: To review and update the available literature of vertebroplasty: a procedure for treating painful compression fractures of the thoracic and lumbar spine that don’t have responded to a conservative treatment.

Material and methods: A review of the literature was performed about the procedure, indications, complications and results based on PubMed and academic Google using the following keywords: vertebroplasty, compression vertebral fractures, polimetilmetacrilato, PMMA and osteoporosis.

Results: Description of the procedure, indications and complications. Several studies with few number of patients have indicated a high rate of successes an a low rate of complications. Recently, two double blind, randomized clinical trials have been published, comparing vertebroplasty with a simulation of it. The results of these studies don’t support the realization of vertebroplasty for the treatment of pain in osteoporotic compression fractures.

Conclusions: The clinical results of vertebroplasty were promising. Recently, the publication of two randomized clinical trials with greater evidence than previous ones, contradicts it. Several questions without answer arise: Can this procedure be effective in a subgroup of patients? Could be effective in medium-long term? Are there other options to treat patients that don’t respond to conventional treatment?

Key words: Vertebroplasty, Vertebral compression fractures, Polimetilmetacrilato, PMMA and Osteoporosis.
Introduction

Osteoporosis has been called the silent epidemic of the 21st century. Fractures represent its most frequent complication. They can happen in any part of the body. Those of greater importance due to their consequences, costs and degree of incapacity are the vertebral, proximal femoral and distal radial. All add to the index of morbimortality, always produce a degree of incapacity and, in some case, increase mortality.

The prevalence of this disease means that approximately 40% of white women over 50 years of age and 13% of men, will suffer some osteoporotic fractures during their lives.

The vertebrae are the most common location. Thus, the EVOS study (European Vertebral Osteoporosis Study, a multi-centred European study), stated that in the European population over 50 years of age, one in five women and one in eight men had a vertebral fracture. Similar results have been obtained in various epidemiological studies in different areas of Spain.

Around 60% of vertebral fractures (VF) are asymptomatic, for which reason the epidemiology is not known precisely. However, the EVOS study revealed that the incidence of VF is four times greater than fracture of the hip. It is estimated that in the year 2000 9 million osteoporotic fractures occurred in the world, of which 1.4 million were clinical VF. 34.8% of total fractures occurred in Europe, where the prevalence of VF is 12% at 60 years, and 25% in women and 17% in men at 75 years.

The prevalence of morphometric VF in the Spanish population over 50 varies between 15% and 27% in women. One in four patients with VF will suffer a second VF during the following two years and 26% will suffer a non-vertebral fracture in the following year.

Various studies have shown that osteoporotic vertebral compression fractures represent an important cause of morbidity in patients affected by osteoporosis. It is estimated that in the United States some 70,000 patients a year suffer from it, and it is expected that this incidence will increase in parallel with the increasing age of the population. It represents a significant economic cost of nearly 700 million dollars a year.

Even though, as has already been said, around 60% of vertebral fractures can be asymptomatic, it is also certain that one of the fundamental consequences of these fractures is pain, which can be intense, with disabling functional incapacity, which can be controlled with difficulty through non-invasive treatments (conventional analgesics, rest, physiotherapy…).

Since 1987, vertebroplasty (VP) has been developed as a reliable and minimally invasive alternative therapy.

Vertebroplasty is a minimally invasive technique which consists of an injection of a material (polymethylmethacrylate, calcium triphosphate, or other) into the body of a vertebra, with the aim of reducing the pain and augmenting its mechanical resistance.

The mechanism of its analgesic action is not clear. There are various hypotheses, notable among which is that the restoration of the mechanical integrity of the vertebra could mean a reduction in “micromovements” across the treated section, or that it is the result of local heat, chemical or vascular effects of the cement on the free nerve endings.

The substance most commonly used is polymethylmethacrylate (PMMA), a synthetic polymer used for the cementation of bone prostheses.

Procedure and technique

The procedure is carried out by puncturing the affected vertebral body, controlled fluoroscopically or by means of CAT (Computerised Axial Tomography), or both at the same time. There are four access routes to the vertebral bodies: anterolateral (for the cervical vertebrae), parapedicular, lateral (for the lumbar vertebrae only) and transpedicular. The last route is that most used.

The procedure is generally carried out with local anaesthetic and sedation, but epidural anaesthesia, rachianaesthesia or (very occasionally) general anaesthesia can be used. In VP the vertebral body is punctured using needles, through one of the aforementioned access routes, guided by means of digital fluoroscopy or CAT. Sometimes one can take advantage of the technique to carry out a biopsy if the aetiology of the vertebral fracture is not clear. When the needle reaches the third vertebral anterior, the cement mixture is injected under fluoroscopic control strictly to the posterior extension of the cement with the help of a mechanical injector (Figure 1). There are various injecting devices on the market which, usually, mix the cement internally and connect direct to the needle (Figure 2).

The technique usually takes half an hour for each vertebra; it is not recommended that more than three vertebrae are consolidated in a single session. The indications and contraindications of this technique are listed in Tables 1 and 2.

Results

There are various studies with a limited number of patients which, in general, demonstrate a high rate of success and a low rate of complications.

However, a systemic review published in 2006 to assess the efficacy and safety of the technique in osteoporotic vertebral fractures which included 1136 interventions in 793 patients, concluded that an evaluation of the efficacy of percutaneous vertebroplasty, would require clinical trials with long-term follow up. The level of pain measured using the VAS (Visual Analogue Scale) with a score of 0 to 10 improved significantly, from 7.8 to 3.1 (60.3%) immediately after the vertebroplasty. The short-term complications varied between 0.4% and 75.6%. The most frequent was the leak of cement out of the vertebral body (from 3.3% to 75.6%). Even though the majority were asymptomatic, in 2.4% they were devastating.
After the systematic review, the authors concluded that there was insufficient data to ensure efficacy. The procedure has a low rate of complications but those can be very severe. Of the 15 studies reviewed, 11 were prospective, 3 retrospective and only one a clinical trial.

Another recently published study compares the effects of optimum conventional treatment for pain against vertebroplasty in patients with vertebral compression fractures. It consists of a prospective study, randomised, which evaluated the patients on day one and two weeks after, using the quality of life scale (QUALEFFO) and incapacity questionnaire (Roland-Morris Disability (RMD)). The study included 18 patients treated with vertebroplasty and 16 patients treated conventionally. Those patients in whom vertebroplasty had been carried out had an improvement in pain, mobility and functionality significantly better than those receiving conservative treatment.

Now in progress is the clinical trial VERTOS II, which intends to estimate the cost-effectiveness of vertebroplasty compared to conservative therapy in terms of the reduction in pain, quality of life, complications, secondary fractures and mortality. It consists of a multi-centric study, which intends to recruit 100 patients in each group, following up for 12 months. It is hoped that this study will greatly clarify current questions with respect to vertebroplasty.

The departments of radiology of the Mayo Clinic College of Medicine and the Baylo University Medical Center carried out a retrospective review of the first 1000 patients on whom they have carried out percutaneous vertebroplasty (independently of the underlying cause for which it was indicated), with the objective of putting together a prospective database.

Different variables were collected, including studies of images and of clinical visits, and they carried out telephone interviews with each patient. The study evaluated pain, on a subjective and visual scale, changes in mobility, the use of analgesic medication, and used incapacity questionnaires (Roland Morris Questionnaire). They found a dramatic improvement in all the parameters evaluated after vertebroplasty. The improvement in pain, mobility, use of analgesics and Roland-Morris score were evident immediately after vertebroplasty and remained for two years after follow up. There was a low level of complications after the procedure. The most frequent was rib fracture. In accord with these results, they conclude that professionals, in recommending this treatment for pain due to compression fracture, can inform patients that it is a technique with a high rate of success and a low rate of complications.

In spite of these studies suggesting a positive effect of treatment with vertebroplasty, compared with other conservative treatments, there are no randomised double blind clinical trials published.

Very recently the first two randomised double blind clinical trials have been published comparing vertebroplasty carried out with the injection of polymethylmethacrylate, with control patients on whom the procedure was carried out, but without the injection of this material.

The INVEST study of Kallmes et al., included 131 patients (vertebroplasty in 68 and simulation of vertebroplasty in 63). The results regarding pain and functional capacity after one month were similar in the treated and control groups, with a tendency towards an improvement in pain in the vertebroplasty group, although not significant. In both groups improvement was observed 3 days after the procedure, but were similar at 3 months. The authors concluded that the improvement in the pain and functional capacity associated with osteoporotic compression fractures in patients treated with vertebroplasty were similar to that in the control group. Another trial, Buchbinder et al., included 71 patients (carrying out vertebroplasty in 35 and a simulation in 36). The results with regard to pain, quality of life and functional capacity after a week, and at 1, 3 and 6 months, are similar in both groups. As before, the pain improved in both groups of patients.

These two trials had some limitations, fundamentally that they did not take into account other medical treatments which were taken and which could have affected the results.
These findings question the indication of vertebroplasty for the treatment of patients with recent osteoporotic vertebral fractures.

**Complications**

The rate of complications described in the literature in the case of vertebroplasty in osteoporotic fractures, is low, between 1 and 3%. The most frequent is the leak of cement from the vertebra, the majority of times without clinical repercussions. On occasions severe complications have been described, such as infection, neurological failure after the leak of cement into the medullar canal, pulmonary embolism and pneumothorax, all with a very low frequency.

Occasionally hypertension and arrhythmia have been described, ascribed to the polymerisation of polymethylmethacrylate, for which reason cardiovascular monitoring is necessary continually during the procedure.

In the recently published clinical trials the rate of complications does not differ from those described previously.

**Conclusions**

Different series of published studies endorsed this technique as efficacious and safe, with a level of scientific evidence grade III.

Despite the fact that the clinical results of vertebroplasty were promising, the recent publication of two randomised clinical trials, with a higher grade of evidence than those published earlier, contradicts them.

The huge incidence of osteoporotic vertebral fractures which cause pain and significant incapacity in patients is an evident fact in numerous studies. The management of pain is a problem in daily clinical practice. We had confidence in the effectiveness and the very low rate of complications in this technique. After the publication of these clinical trials, questions are emerging which need to be answered: could the placebo effect of the simulated vertebroplasty through puncture and/or the effect of local anaesthetic be responsible for the similar results in both groups? And what of the superiority of the intervention, be it with cementation or simulated, over the conservative treatment? Could this technique be effective in a sub-group of patients as Kallmes et al. suggest? If this were the case, in which sub-group of patients? We have evidence of its lack of effectiveness in the short-to-medium-term, but in the long-term? In the face of the morbidity and incapacity which frequently produces secondary pain in these fractures, what other therapeutic alternatives do we have left for patients who don’t respond to conventional treatment?

It is now even more important, if possible, to continue and/or carry out clinical trials which bring us answers to these questions.

And in the meantime? It becomes even more important to create a specialised and multidisciplinary approach around the management of pain. Likewise, adequate information and communication between the doctor and patient to evaluate the therapeutic options available, the current state of knowledge around this invasive technique and the possible risks and benefits, will permit the individualisation of the indication to the various alternative therapies.

**Bibliography**


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**Table 1. Indications for vertebroplasty**

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<th>Indications</th>
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<tr>
<td>- Osteoporotic vertebral fractures with moderate</td>
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<td>to severe pain which does not respond to a normal</td>
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<td>analgesic treatment</td>
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<td>- Painful vertebral metastasis</td>
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<td>- Multiple myeloma with fractures in the vertebral body</td>
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<td>- Painful haemangiomas of the vertebral body</td>
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<td>- Painful osteonecrosis in the vertebral body</td>
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<td>- Reinforcement of pathological vertebral body</td>
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<td>before stabilising surgery</td>
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**Table 2. Contraindications**

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<tr>
<td>- Absolute:</td>
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<tr>
<td>a. Asymptomatic vertebral fractures</td>
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<tr>
<td>b. Improvement with conservative therapy</td>
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<tr>
<td>c. Local or systemic infection</td>
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<tr>
<td>d. Non-correctable coagulopathy</td>
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<tr>
<td>e. Myelopathy by intracranial bone fragment which comprises medulla</td>
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<tr>
<td>f. Allergy to the cement or to the contrast contained in the cement</td>
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<tr>
<td>- Relative:</td>
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<tr>
<td>a. Fracture of the posterior wall of the vertebral body</td>
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<tr>
<td>b. Tumour which invades the epidural space without causing neurological symptoms</td>
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<tr>
<td>c. Compression fracture with diminution of vertebral height 0 or of &gt; 75-80%</td>
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<tr>
<td>d. Fractures older than one year</td>
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