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Percutaneous vertebroplasty: Multi-centric results from EVEREST experience in large cohort of patients

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ABSTRACT

Purpose: The purpose of this study was to prospectively evaluate results and complications of percutaneous vertebroplasty (PV) performed in 6 different Italian Centres belonging to the European VERtebroplasty REsearch Team (E.VE.RES.T) in a large series of patients.

Materials and methods: Follow-up was obtained in 4547 patients (3211 females and 1336 males; mean age 70.2 years) that underwent PV for a total of 13,437 treated vertebrae. Procedures were performed by using fluoroscopic guidance or combined CT-fluoroscopic guidance. All patients underwent PV in local anaesthesia except for second cervical vertebrae treated with a trans-oral approach that required general anaesthesia.

Results: 4004 out of 4547 (88.0%) patients reported significant pain relief (difference $> \text{or} = 2$ point in pain evaluated with an 11-point visual analogue scale; $p < 0.0001$) within 48 h: an average of 7.7 ± 0.4 dropped to 1.8 ± 0.6 in the osteoporotic patients; 8.3 ± 0.4 to 2.4 ± 0.4 in metastases; 8.3 ± 0.4 to 1.7 ± 1.0 in myeloma; 6.2 ± 3.5 to 0.3 ± 0.2 in angioma and 7.4 ± 0.4 to 1.4 ± 0.9 in trauma. 430 osteoporotic patients (13%) were retreated for a subsequent fracture; in 302/430 patients (70.2%), the new fracture occurred in the contiguous vertebra. No major neurologic complications were reported and the most frequent minor complication was venous leakage (20.5%).

Conclusions: This large series of patients confirms that percutaneous vertebroplasty is an effective and safe procedure in the treatment of vertebral fractures. Best results are obtained in the treatment of myeloma and trauma.

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1. Introduction

Vertebral fractures are a common cause of pain and disability and are associated with increased mortality; interventions that effectively manage pain and shorten recovery time would be of great benefit [1,2].

Percutaneous vertebroplasty (PV) is a minimally invasive procedure in which bone cement polymethylmethacrylate (PMMA) is injected, using a needle positioned under CT or fluoroscopic guidance, into a vertebral body to treat pain associated with a vertebral compression fracture. The cement functions as an internal cast in the vertebra to provide pain relief and structural stabilization [3,4].

Some observational studies suggested that there is pain reduction after this procedure is performed [5–7] but the efficacy of PV is still debated [8–10]; in fact not only is the short-term efficacy of

Table 1
Patient's population.

Centre	Male	Female	Osteoporosis	Metastasis	Myeloma	Angioma	Trauma	Others
Torino	480	1469	1289	344	81	29	120	86
Bergamo	117	262	333	12	11	8	13	2
Pisa	159	403	439	53	41	12	17	0
Cagliari	108	305	303	19	2	7	81	1
Roma	202	422	483	96	23	3	4	15
Napoli	270	350	473	120	10	15	0	2
Total	1336	3211	3320	644	168	74	235	106

vertebroplasty unproven, but some authors hypothesized that after PV an increased risk of subsequent vertebral fractures may occur [8].

The purpose of our study was to prospectively evaluate the effectiveness of PV performed in 6 different Italian centres belonging to the European VERtebroplasty REsearch Team (E.VE.RES.T) in a large series of patients.

2. Methods and materials

Follow-up was collected in 4547 consecutive patients (3211 females and 1336 males; mean age 70.2 years, age range 20–101 years) suffering from back-pain due to vertebral compressive fractures (VCFs) and was referred to the Interventional Radiology Unit of the six EVEREST centres. Patients underwent treatments from January 2002 to January 2008. Treated VCF were caused by osteoporosis, malignancy (metastasis or myeloma), trauma and symptomatic aggressive angioma.

PV was performed in case of painful VCFs that failed to respond to conventional medical therapy, such as minimal or no pain relief with medication or narcotic doses that are intolerable.

According to the different aetiology, diagnosis of painful VCF was also assessed by rheumatologists, oncologists, orthopaedics and neurosurgeons.

Inclusion criteria were: VCF detected by plain X-ray or computed tomography (CT), with bone marrow oedema on magnetic resonance (MR) (hyper-intensity in correspondence of the painful vertebral body due to bone marrow oedema at Short-Tau Inversion Recovery (STIR) sequences), local back pain with single-point pressure on examination, and poor or no response to medical therapy. Exclusion criteria were asymptomatic stable fracture, clinically effective medical therapy, osteomyelitis of target vertebra, non-correctable coagulation disorders, local or systemic infections. Moreover, patients with back pain due to other spinal sources (i.e.: facet joint syndrome and discogenic pain) were excluded.

All the procedures were performed in day-surgery under fluoroscopic or combined (computed tomography and fluoroscopic) guidance by expert interventional radiologists. Combined approach with CT and fluoroscopy was performed in 4.5% of the patients, whereas in the 95.5% the only fluoroscopy was used. PV was carried out as previously described by others authors [11,12].

All procedures were performed in local anaesthesia except for the trans-oral approach on the second cervical vertebra that required general anaesthesia; 3–4 ml of lidocaine 2% was administered percutaneously and 3–4 ml of ropivacaine 7.5% close to the periosteum. Patient pressure, heart rate and oxygen saturation were monitored during the entire procedure. Antibiotic therapy was also administered (2 g Cefamizid).

Bevel-edge 10–15 Gauge needles were used in order to have greater directionality. The needles had been positioned using antero-posterior and latero-lateral view under fluoroscopic guide. The radiopaque bone cement (PMMA) was injected under continuous fluoroscopic monitoring in order to check the spreading of the PMMA and to minimize the risks of symptomatic leakages.

After the procedure the patients were kept 2 h in hospital for clinical monitoring and then discharged; general anaesthesia during trans-oral approach required an overnight hospitalization.

Prophylactic vertebroplasty was performed in patients with a higher risk of a new fracture (long-term corticosteroid therapy osteoporosis) within a normal vertebra between two collapsed bodies in the thoraco-lumbar junction as reported by some authors [13].

Patients were evaluated at baseline and through a one-year follow-up (maximum follow-up: 12 months) for pain relief using an 11-point visual analogue scale (VAS) with zero considered as no pain and 10 as the most severe pain. Evaluation at each follow-up point included pain response using VAS, physical examination and X-ray at 48 h and one month, and physical examination at three months and one year. A reduction of a minimum 2 points in VAS score was considered as a positive result [14].

Patients were fully informed of potential treatment-related side complications and provided signed informed consent before each procedure in accordance with the Declaration of Helsinki. PV has been offered as a standard treatment for painful vertebral collapses at EVEREST Centres since 2002. Outcomes data were collected in a prospectively maintained database and this analysis was approved by the Internal Review Board.

For each patient location and type of pathology was evaluated. The percentage of refractures (follow-up: 12 months) and new treatments was also calculated. Moreover, the analysis of complications was performed.

T student analysis was performed to compare the different groups. *P* values less than .05 were considered to indicate a statistically significant difference.

3. Results

Patient's population is summarized in Table 1; the most significant percentage (>99%) of treated levels was thoracic and lumbar (Table 2). The average number of VCFs treated with vertebroplasty in the same patient was three, for a total of 13,437 fractures. Main pathology was osteoporosis (73%), followed by metastases (14%), trauma (5%), myeloma (4%), symptomatic angioma (2%) and others (Kummell's disease, lymphoma) (2%). Diseases prevalence rate in the analyzed population is given in Table 3.

In the analysis of pain relief after the PV we observed that 4004 out of 4547 (88.0%) patients had significant pain relief ($p < 0.0001$)

Table 2
Treated vertebrae.

Centre	Cervical	Thoracic	Lumbar	Sacral
Torino	35	3730	4275	24
Bergamo	0	336	451	1
Pisa	3	534	568	5
Cagliari	0	555	633	4
Roma	0	504	737	12
Napoli	0	294	730	6
Total	38	5953	7394	52

Table 3
 Disease prevalence rate.

Centre	Osteoporosis (%)	Metastasis (%)	Myeloma (%)	Angioma (%)	Trauma (%)	Others (%)
Torino	66.1	17.6	4.2	1.5	6.2	4.4
Bergamo	87.9	3.2	2.9	2.1	3.4	0.5
Pisa	78.1	9.4	7.3	2.1	3.1	0
Cagliari	72.6	4.6	0.5	1.7	19.6	0.2
Roma	77.4	15.4	3.7	0.5	0.6	2.4
Napoli	76.3	19.3	1.6	2.4	0	0.4
Total	73	14	4	2	5	2

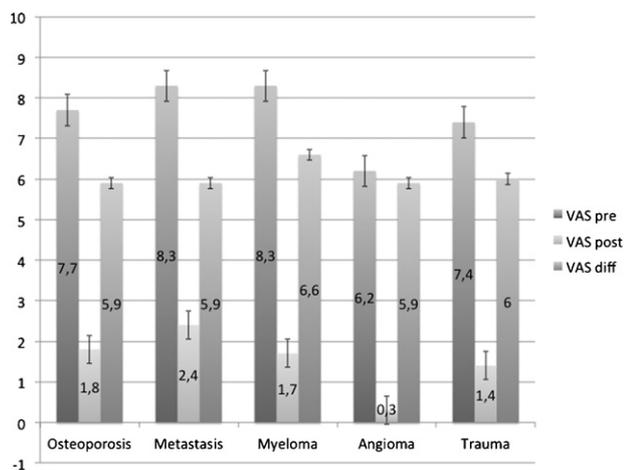


Fig. 1. Pain evaluation: VAS score.

within 48 h: average VAS of 7.7 ± 0.4 significantly dropped to 1.8 ± 0.6 ($p < 0.001$) in the osteoporotic patients; 8.3 ± 0.4 to 2.4 ± 0.4 ($p < 0.001$) in metastases; 8.3 ± 0.4 to 1.7 ± 1.0 ($p < 0.001$) in myeloma; 6.2 ± 3.5 to 0.3 ± 0.2 ($p < 0.001$) in symptomatic angioma and 7.4 ± 0.4 to 1.4 ± 0.9 in trauma ($p < 0.001$). According to the different types of pathology, the pain relief showed a statistically significant reduction for each category. In the 12 months follow-up (Fig. 1) we did not find statistically significant differences in the pain relief compared to the 48 h results. In particular, in the osteoporotic patients the VAS was 2.1 ± 0.8 versus 1.8 ± 0.6 ($p > 0.05$), in the metastatic patients was 2.9 ± 0.5 versus 2.4 ± 0.4 ($p > 0.05$), in the patients with myeloma it was 1.9 ± 0.7 versus 1.7 ± 1.0 ($p > 0.05$), in the patients with symptomatic angioma it was 0.4 ± 0.3 versus 0.3 ± 0.2 ($p > 0.05$), in the patients with trauma it was 1.5 ± 1.1 versus 1.4 ± 0.9 ($p > 0.05$). Of the 4547 patients treated, only 10.5% were re-treated for a subsequent fracture, above all for osteoporosis (13%) followed by myeloma (7.7%) (Fig. 2). In 302 out of 430 osteoporotic retreated patients (70.2%), the new fracture occurred in the contiguous vertebra. We performed <3 levels in 8% ($n = 274$)

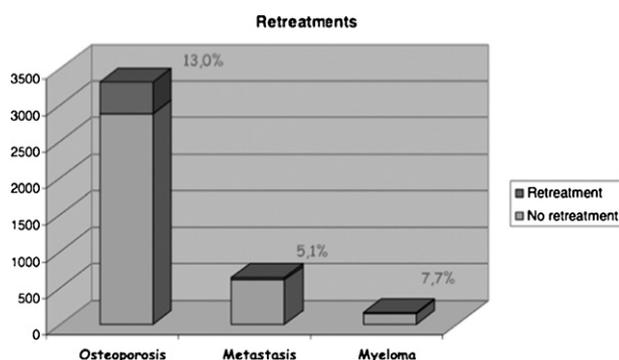


Fig. 2. Percentage of retreatments of new fractures.

of retreated osteoporotic patients, and >3 in 5% ($n = 156$). In 5% ($n = 153$) of cases the new fracture occurred above the treated vertebra, in 4% ($n = 149$) of cases below. Prophylactic vertebroplasty was performed in 74 patients. By comparing the combined guidance (CT-fluoroscopy) and fluoroscopy we did not find any statistically significant difference in the VAS reduction according to the different pathology ($p > 0.05$).

No major neurological complications were reported and we observed minor complications in 32.9% of cases. The most frequent minor complication was the venous leakage (20.5% of the cases). The complications are summarized in Table 4.

4. Discussion

To evaluate the effectiveness of PV in a large population may be important because of the non-concordant data published in the last years about the efficacy of PV in the painful VCF treatment [2,9,10]. In particular, in 2009 Kallmes et al. [9] published in the New England Journal of Medicine a randomized trial based paper where they stated that “improvements in pain and pain-related disability associated with osteoporotic compression fractures in patients treated with vertebroplasty were similar to the improvements in a control group”. These results were further confirmed by Buchbinder et al. [2]. However, in a recently published paper by Klazen et al. [10], it was demonstrated that in a subgroup of patients with acute osteoporotic vertebral compression fractures and persistent pain, PV is effective and that immediate pain relief is maintained for at least one year.

By analysing the composition of our population, from the 6 EVEREST centres, we observed that it was mainly composed of patients with osteoporosis (73%). The composition of the different types of pathologies was similar in all 6 centres.

Our results indicate a significant pain relief after PV within 48 h. In particular we observed that among the different types of pathologies the best results were obtained by the osteoporosis, trauma and myeloma. Our results are concordant with previous publications [15,16]; in fact Anselmetti et al. [16] by analyzing a population of 106 patients affected by myeloma and treated with PV, observed a statistically significant decrease in the VAS score ($p = 0.001$). Klazen et al. [10] analyzed 202 patients with acute osteoporotic vertebral fracture (101 with PV and 101 with conservative treatment) and demonstrated that PV gave better results compared to the

Table 4
 Complications.

Centre	Venous leak	Discal leak	Canal leak	Pulm. embolism	Haematoma	Infection
Torino	452	200	0	22	1	2
Bergamo	142	53	0	3	1	0
Pisa	79	65	3	6	0	0
Cagliari	105	60	0	11	0	0
Roma	72	63	0	2	0	0
Napoli	80	49	2	1	0	0
Total	930	490	5	45	2	2

conservative treatment at 1 month, 2 month and 1 year follow-up ($p=0.0001$). Knavel et al. [17] shown that vertebroplasty can be successfully and safely used in patients with traumatic non-osteoporotic compression fractures in a retrospective analysis of 15 patients.

In 10.5% of the cases it was necessary to re-treat the patients for the occurrence of a new fracture. These new fractures occurred at the same rate as they would in patients who did not have vertebroplasty [18]. In particular we observed that the higher incidence was present in osteoporotic patients (13%). Our incidence of re-fracture is markedly lower compared to Li et al. [19]. This difference can be due to some factors: first of all Li et al. suggested brace protection for at least 3 months after PVP. Moreover they administered in all patients calcium supplementation and calcitonin nasal spray oral bisphosphonate.

In the 430 osteoporotic patients we performed <3 levels in 8% of retreated osteoporotic patients, and >3 in 5%. In 5% of cases the new fracture occurred above the treated vertebra, in 4% of cases below. These results are concordant with the study results of Trout et al. [20] that demonstrate an association between vertebroplasty and new vertebral fractures; in particular they demonstrated that after PV, patients are at increased risk of new-onset adjacent-level fractures and, when these fractures occur, they occur sooner than nonadjacent level fractures. Serious complications from vertebroplasty are rare, involving less than five percent of cases. As with other procedures, however, complications can occur. Some of the most common complications of vertebroplasty include problems with anaesthesia, thrombophlebitis, infection and cement leakage. In our analysis no major neurological complications were reported and we observed minor complications in 32.9% of cases. The most frequent minor complication was the venous leakage (20.5% of the cases) followed by disc leakage. In 45 cases we observed pulmonary embolism and in 4 cases the rupture of the needle occurred. The procedural and peri-procedural complications of PV are well described in the literature and the incidence we observed is within the expected range. In 2 cases we observed infection. Infection following spine procedures is rare but can be a very serious complication. Some infections may show up early, within the first few days after the procedure. Deeper infections that spread into the bones and soft tissues of the spine are harder to treat.

This study has some limitations: firstly, this is not a randomized study and no control group is present; secondly, this is a multi-centric analysis and clinical outcome can vary depending upon several different physicians evaluations; thirdly, analgesic medical therapy, oncological treatments and therapy for osteoporosis were not considered in the analysis and these therapies can significantly affect the clinical outcome if pain relief is the main parameter. However, the present study represents one of the largest series of patients that underwent percutaneous vertebroplasty and can add other evidence to the effectiveness and safety of vertebral augmentation.

This study results indicate that PV is an effective and safe procedure in the treatment of vertebral fractures. The best results are obtained in the treatment of myeloma and trauma.

Conflict of interest

All Authors declare to have no conflicts of interest.

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