Percutaneous cementoplasty for the treatment of extraspinal painful bone lesion, a prospective study

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KEYWORDS
Cementoplasty; Metastases; Myeloma; Pain; Palliative care

Abstract
Purpose: The current gold standard treatment of localized painful bone lesion is radiotherapy but this technique has limitations. Our study aims to demonstrate that cementoplasty is an efficient alternative for these palliative indications when lesions involve extraspinal bones. We prospectively followed 20 patients who received a percutaneous cementoplasty on painful lytic bone lesions between May 2008 and May 2010.
Materials: Seventeen patients also had difficulty walking in relation to the pain experienced. The clinical indication for treatment was severe pain (≥ 4 on the numeric scale) due to bone lesion on CT or MRI. All procedures (except one) were performed under local anesthesia.
Results: Feasibility was 100% without immediate complications. The patients experienced a significant and rapid decrease of their pain (4.1 points, P < 000.1) and this effect was sustained over the long term (7.75 months of follow-up on average). Sixty-four percent of patients treated on the lower limbs and pelvis improved mobility.
Conclusion: In our experience, percutaneous cementoplasty may be a safe and effective palliative treatment for localized painful lytic lesion. Combining CT and fluoroscopic guidance seems to be the safer option because of extravertebral localization. Smart fill of the bone and careful selection of patient determine the effectiveness of the procedure. Diffuse painful lesions and long bone diaphysis should not be good indications.

Bone lesions always raise two fundamental questions for the patient: pain and risk of fracture. When surgery is not possible, the use of cement is a good answer to both problems. Indeed, its stabilization properties were initially used in orthopedic practice while percutaneous intravertebral injection under radiology guidance has been first introduced.

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Figure 1. Patient 5. a, b: lytic lesion of the medial condyle of the femur in the coronal and axial; c: 22-gauge needle for periosteal anesthesia; d: coaxial trocar penetration; e: cement injection and verification of distributed CT and fluoroscopy (not shown); f: condylar lytic zone subjected to compressive stresses filled by cement. The filling of the area allows a consolidation also reducing the risk of fracture; g: pain follow-up shows progressive and lasting disappearance of symptom.
to treat angioma in 1984 [1,2]. Known as vertebroplasty, this technique spread to spine metastasis and osteoporosis fractures indication with many existing series in the literature [3–5]. Much less series concern the cementoplasty on extraspinal lesions. The current gold standard treatment of painful bone metastases is radiotherapy and analgesic indication is an important part in the daily practice in radiation therapy units. Unfortunately, treatment effects appear only 15 days after the start of treatment and leave around 30% of patients incompletely relieved [6]. This paper demonstrates our experience of interventional analgesic treatment of non-vertebral lytic bone lesions by cementoplasty. First outcome was the significant analgesic effect of this technique and second outcome was mobility improving.

Patients and methods

Type of study and population

From May 2008 to May 2010, we prospectively followed 20 patients with lytic hyperalgesic (≥4 on Numeric Scale)
bone lesions treated on a tri-centric technical platform. Exclusion criteria were systemic contraindication. The indication was based on imaging which highlighted one or more extravertebral lytic bone lesions associated or not with extra bone invasion or fracture. Selection of participants was therefore established by a multidisciplinary panel of practitioners on a proper relationship between the pain symptoms and the imaging. Patient characteristics are summarized in Table 1: average age was 67 years old; etiology was metastatic in 13 patients and myeloma in seven patients; average diameter of lesions in the three axes was 29 mm (15–73).

Description of the procedure [7]

All procedures were performed under local anesthesia except one (patient No. 18). They were performed under fluoroscopy (GE Stenoscope C-arm) and CT Scan (Lightspeed8, GE Medical Systems, Milwaukee, WI) at site 1; under CT alone (Brilliance 8; Philips, The Netherlands) at site 2 and under fluoroscopy alone (XperAllura, Philips) at site 3. A long 22-gauge needle was inserted until contact with bone to allow anesthesia on the route and at the peristeum. Then, a 11-gauge trocar vertebroplasty (Osteo-site® Cook 11G) was inserted into the lytic lesion (Fig. 1). Imaging control was realized to verify its correct position. The cement (Osteofirm Cook®) was injected pasty under imaging control. Injection was stopped when the distribution was satisfactory or when a leak was detected.

Data collection

All the data were collected by radiologist by phone or live interview. Hospital Anxiety and Depression scale (HAD) has been collected before carrying out the procedure to analyze the psychological profile of the treated population [8]. During the procedure, the experienced pain and filling of lesion were analyzed. After the procedure, patients were followed clinically at 1 day, 1 week and then monthly (8 months on average). Pain intensity (Numerical Scale, NS) and functional improvement for pelvis or lower limbs lesions responsible for impairment were collected. The scoring was performed using items of the Functional Independence Measure (FIM) score on mobility, toileting and

Figure 2. Charts of average pain felt by the patient after cementoplasty on numerical scale (NS). Histograms of mean reduction in pain after treatment on NS. The nadir of the curve is located at 1 month and the analgesic effect is long lasting. The treatment immediately reduced the pain (4 points on average).

Figure 3. Flow Chart of bone metastasis and normal distribution red marrow in adulthood correlated with the percentage of bone metastases. Haematopoietic marrow lies in the skull, vertebrae, flat bones, the proximal metaphysis of the femur and humerus. Bone metastases preferentially reach skeletal hyper vascularized areas of red marrow.
We also recorded WHO-class painkillers administered and after 3 months, each patient was asked about his satisfaction with the cementoplasty using the score of Patient’s Global Impression of Change (PGIC) on pain [11,12]. No specific radiological monitoring was performed.

**Presentation of results**

Clinical success was defined as improvement of pain score greater or equal to 2 points on NS and as an improvement of greater or equal to 1 point on functional independence measure [11,13]. According international consensus, we
Figure 4. Patient 14. a, b: CT scan MPR coronal and axial view; c, d: cement injection under control CT and fluoroscopy; e: CT scan VR after cementoplasty. The lytic lesion of the distal metaphysis of the fibula leads to a major risk of fracture. The distribution of cement in the lesion that allowed a bone consolidation face to the compressive stresses; f: pain follow-up shows immediate and lasting disappearance of symptom.

distinguish complete response (CR) (pain after procedure = 0) and partial response (PR) (pain reduction of ≥ 2 points) [14]. Cementoplasty was felt to be effective in patients who had a PGIC score less or equal to 3.

Statistical analysis

A survival rate was calculated by Kaplan-Meier method. We used the Wilcoxon Mann-Whitney nonparametric paired method to assess pain improvement. A Spearman correlation test (nonparametric) was conducted between cement volume and tumor size.

Results

The mean survival rate at 12 months was 70% (Table 2). The feasibility was 100% under local or general anesthesia. During the procedure, pain experienced was 4 on average. The mean volume of cement injected was 4.3 ml in average (4—10 ml) and 70% of the lesions were filled to more than
Percutaneous cementoplasty for the treatment of extraspinal painful bone lesion

Figure 5. Patient 15. a, b: CT scan MPR coronal and axial view shows lytic lesion of the proximal femur diaphysis with posterior cortical disruption (arrow); c, d: fine needle enable periosteal anesthesia for intramedullary penetration of the needle for cementoplasty; e: fluoroscopic guidance; f: CT scan MPR coronal view after injection. The cement was distributed only in the upper part of the lesion. This filling is insufficient to expect a consolidation. Significant decrease in background pain despite incomplete filling. The patient is warned of the risk of fracture during the handing over. The treatment did not reduce the pain induced by movement (g).

50% of cement. We had only one leakage of cement and it was along the path of puncture. There were no major complications according consensus classification [15]. We didn’t experienced refracture of cement.

Before treatment, average pain was 6.4. During follow-up, the response was significant in a short time as the average score on NS fell from 6.4 to 2.3 ($P<0.001$) in 24 hours. The analgesic response was 4.1 points on average. The maximum efficiency was obtained at 1 month with a CR in 80% patients and pain less than 2 in other patients. Two patients did not improve and had a PGIC score greater than or equal to 4 (patient 11 and 15). Seventeen patients had difficulty walking. Among them, 11 patients (64%) treated improved significantly their mobility. Reducing pain of one WHO-level was observed in only one patient.

Discussion

Bone pain and metastases discussion is summarized in Figs. 2 and 3. Bone metastases are a public health problem because cancer overall incidence is still increasing (3.2 million/year) and because the skeleton is the third incident site for metastasis after lung and liver [16,17].
Osteolytic lesions predominate (80% due to prostate, breast and lung cancers) and myeloma malignancy is the most frequent cause of lytic bone lesions [18–20]. Bone lesions affect the quality of life of the patient causing intractable pain, nerve compression, pathological fractures and decreased mobility. All these complications are a source of anxiety and depression as a complication of bone metastases in both serious and costly [17]. Bone metastases are preferentially located in areas of red marrow where blood flow is high that is why two thirds of lesions are extraspinal [19,21,22]. Pain is not correlated to the degree of bone injury and the mechanisms are incompletely understood. Some were identified as stress-related periosteal tumor development, microfractures and macro-fractures, cytokines mediating osteoclast, the accompanying nerve damage of the periosteum and surrounding tissues [17,23–25]. However, it explains why bone pain has two components: a painful background and acute peaks during movement. The management of painful bone metastases combines systemic and local therapies. It is justified because quality of life is at least as important as the prognosis for these patients. Bisphosphonates, hormone therapy and chemotherapy have a delayed effect [26]. Only analgesics have an immediate benefit that is why they remain for many patients the ultimate therapeutic option. Nevertheless, if background pain is usually fairly controlled, the pain induced by movement requires higher doses leading to adverse events [27,28].

When a localized painful lesion is identified, surgery is rarely a satisfactory therapeutic option because it is often a too invasive option on a fragile patient. Fractures fixation ordinarily may be accomplished with minimal blood loss or morbidity. In fact, fractures or impending fractures involving the acetabulum necessitate extensive joint reconstruction, with inherent increased potential for morbidity and complications [29]. Radiotherapy is a good solution but it has three limitations. First, it is often unsatisfying because 40% of patients have no response and only 30% have CR according to recent data from the literature [6]. Then, effect is delayed about 15 days because of the mechanism of apoptosis. Finally, because of tissue tolerance, it can be used only once. The vertebroplasty is also a minimal invasive local therapy. It proved its efficacy in benign and malignant pathology by allowing healing and pain control [1,4,5]. The cementoplasty in extraspinal bone tumors is less studied [30,31].

Regarding pain results, one third of patients experienced intense pain (>4) during the procedure which encourages a preference for sedation or general anesthesia if possible. The cementoplasty analgesic effect is major, fast and maintained. Cement necrotizing and embolization properties on afferents responsible for nerve pain are involved in the efficiency mechanism. Moreover it is likely complex involving a mechanical consolidation of the bone reducing periosteum stress [32]. This explains the effectiveness of the technique both on background pain and on kinetic pain. As already shown in the literature we have not found any relationship between tumor volume filling and reduction of pain (< 50% or > 50%, P = 0.802 the first month) [31]. But considering kinetic component, we assume that the quality of the padding is important to maximize analgesic effect by consolidating bearing areas subjected to mechanical stress [33] (Fig. 6). The patient 11 in whom the procedure did not work involved a pelvic pain irradiating to the lower limb. Retrospectively, the pain was probably related to radiation-induced neuropathy showing the importance of pre-procedural patient clinical examination. Clinically bone pain is generally projected next to the anatomical region and typically increased by focal pressure. The series published on extraspinal cementoplasty are few but their results are consistent with our observations showing pain reduction in about 80% cases [27,31–32].

Considering the mobility, one third of lesions affect pelvic bone or lower limb so they cause a rapid reduction in mobility and reduce quality of life. In our series we show an improvement of mobility for two thirds of patients who had a disability before cementoplasty and over 80% of patients are improved on items concerning locomotion. On this point, our results are consistent with observations previously published by Basile et al. and Marcy et al. [31,33].

Regarding complications, they are stratified according Society of International Radiology classification [15]. The risk of bleeding is greater during needle insertion and with hyper vascular metastasis (thyroid, kidney, and melanoma) [34,35]. In these cases, it is recommended to maintain compression for 5 minutes [36]. During injection, it is
Percutaneous cementoplasty for the treatment of extraspinal painful bone lesion

Figure 7. Patient 19. a, b: CT scan MPR coronal and axial view showing lytic lesion with involvement of the acetabulum roof (arrow) and columns (stars); c, d: CT scan placement of the needle for cement injection into the roof of the acetabulum and cement injection control; e: CT scan VR showing a consolidation of the acetabular roof while the filling of the lesion is incomplete. Significant reduction in pain despite the incomplete filling of the lesion (f). We made the choice to consolidate the area subject to higher compressive stresses. The gain on mobility is significant.
difficult to predict cement’s distribution [37]. There is a risk of leakage which can be problematic when intra-articular, in contact with a nerve trunk or on a support zone (Fig. 4). In other cases, it does not need treatment. Notice that contact neuralgia is accessible to infiltration of cortisone. As the rupture of the posterior wall was once a contraindication for vertebroplasty, it is no longer so today with the improvement of the technique. As the same, we believe a thick consistency of the cement and real-time fluoroscopic imaging minimizes the risk of leakage outside close joint line metastases (Fig. 5). In any case if osteolysis adjacent to the joint, injection must be extremely careful to avoid the risk of rapid chondrolysis when intra-articular leakage [38]. Note that the anatomical configuration of extraspinal lesions needs a three-dimensional vision. Thus, we believe that a combination of CT and fluoroscopic guidance makes the procedure safer.

When cancer affects patients, they often acquired bone marrow failure due to disease itself or chemotherapy [39]. In these conditions, it seems legitimate to consider these patients at high risk of infectious complications and to limit this risk by providing a systematic antibiotic prophylaxis (cefazolin [18] as first-line). Moreover some authors advocate the use of antibiotic loaded cement in immuno-suppressed patients [40,41]. High hygiene precautions are also necessary because the injection of cement is related to the establishment of an orthopedic implant with the difference that you can hardly remove it if infected [37,40,42].

The overall rate of infectious complications reported is less than 1%. Biomechanical properties of cement are perfectly adapted to withstand compression fractures that occur in the flat bones and bearing joints such as the vertebrae, the acetabulum, and the femoral condyle (Fig. 1). We treated a lytic lesion of the peroneal malleolus with a satisfactory filling of the tumor (patient 14) and in this case, we can assume that the risk of fracture is reduced by restoring bone strength to face constraints in compression (Fig. 5). However, resistances to twisting stresses are low so it cannot reduce the risk of fracture of lytic diaphyseal lesion (Fig. 6) [43,44]. It seems reasonable to reserve this indication as palliative and inform the patient of the persistence of risk of fracture (Fig. 7). If stabilization is necessary, osteosynthesis should be preferred. Notice that the injection of cement may interfere significantly with surgery which may be necessary thereafter [42,45,46]. Treatment of diaphysis should be only considered for advance palliative cases when surgery is contra indicated.

The clinical impression of change (PGIC) shows that 90% of patients feel positive change after the procedure which corroborates the results for pain. Patient 15 was not completely satisfied because of persistent kinetic pain despite the significant analgesic response on background pain (Fig. 5). As explained, we assume that mobility non-improvement was due to incomplete filling of the lesion that could not provide a good biomechanical stabilization. More than a half of our patients have symptoms of anxiety (60%) or depression (20%) according to HAD score. We imagine it interferes with pain feeling and the effectiveness impression of the procedure even if no significant difference has been showed. The vertebroplasty is not considered a technique of percutaneous tumor ablation in the strict sense. Some authors have studied the heat of the cement during its polymerization to investigate the effect of hypothetic thermal ablation. It is clear that this relative effect is certainly not able to have an oncologic action alone and one should consider cementoplasty for analgesia or stabilizing only [47,48]. Although in our series we did not observe any recurrent disease, some patients have received treatment with radiotherapy and all were treated with chemotherapy. If the therapeutic intent is carcinologic treatment, association with a thermal ablation technique such as cryotherapy or radiofrequency ablation should be considered [43,45,46]. However, for analgesic action, recent studies show no superiority of radiofrequency + cementoplasty versus cementoplasty alone on the treatment of small tumors [23,32]. It seems legitimate to combine thermal ablation technique when tumor involves the surrounding soft tissues. However, cementoplasty appears to be most effective in terms of pain management for weight-bearing bones, probably due to its stabilizing action [40,48,49].

Our study has a recruitment bias related to a majority of women but existing studies have however no sex difference [27,31–33]. The dose reduction of analgesic and WHO-level are not good indicators of the effectiveness excluding five patients with a single lesion. For them, there is no noticeable increase in the WHO-level prescribed painkillers and one resulted in a decrease (patient 13). In fact, cementoplasty allow controlling pain locally identified while other painful lesions may require the taking of analgesics independently of the targeted lesion. Despite the diversity of groups, if we compare the analgesic efficacy in the group with multiple myeloma and solid tumor it does not show significant difference. However, one can assume that there must be differences in the long term given the differences in aggressiveness. Masala et al. report their experience in treating extraspinal injuries myeloma and get similar results in terms of analgesic efficacy [50]. We deliberately restricted the selection of patients with lytic tumors to promote efficiency of the procedure by optimizing the filling of the lesion. Cementoplasty is not a suitable technique to pure osteoblastic lesions because the injection is under heavy pressure that makes difficult to control proper distribution of cement [48,51].

Conclusion

In our experience, the percutaneous cementoplasty is an effective palliative treatment that can be considered at the forefront for pain management of many osteolytic extraspinal bone tumors. It is safe and fast effect. It also allows consolidation of the bone and improved patient mobility. Criteria for successful procedure include proper patient’s selection with precise clinical exam of eligible patients: it is particularly indicated to oligometastatic patient with a well-identified osseous pain. It includes also proper lesion selection because acrylic cement is adapted to flat bones and filling priority areas of constraints helps prevent fractures in compression.

Criteria for safe procedure include careful cement injection when lesion is surrounding bone joint and optimal guidance with combined CT scan and fluoroscopy.
Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


