



EFFECTIVENESS OF CEMENTOPLASTY FOR VERTEBRAL AUGMENTATION IN MULTIPLE MYELOMA: A CASE SERIES

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Abstract – Objective: Multiple myeloma (MM) is a neoplasm characterized by the proliferation of somatically mutated plasma cells that tend to expand within the bone marrow and affect multiple locations throughout the bone marrow. When it is located in vertebral areas it causes bone lesions with pain, kyphosis, walking impairments, and disability. Different types of treatments are available. The goal of this study is to report our experience regarding the treatment of vertebral fractures from multiple myeloma using cementoplasty.

Patients and Methods: From January 2012 to December 2015, 38 patients with multiple myeloma and multilevel vertebral fractures were treated. Seventeen patients underwent conservative treatment (group 1), and 21 patients underwent vertebral augmentation with percutaneous cementoplasty (group 2). Both groups were clinically evaluated at 1, 6 and 12 months using a visual analogic scale (VAS) for pain, SF-36 and ODI Score Questionnaires. Radiographic evaluation was performed to verify the quality of cementoplasty and complications.

Results: Mean follow-up was 23.7 months. Mean VAS score in group 1 decreased from 7.1 pre-operatively to 3.9 at final follow-up ($p<0.05$). In group 2, this score decreased from 7.3 pre-operatively to 2.3 at final follow-up ($p<0.05$). Mean SF-36 values in group 1 increased from 34.1 pre-operatively to 58.6 at final follow-up ($p<0.05$), while in group 2 increased from 31.5 pre-operatively to 76.9 at final follow-up ($p<0.05$). Mean ODI score in group 1 decreased from 73.3 pre-operatively to 44.9 at final follow-up ($p<0.05$), while in group 2 decreased from 77.5 pre-operatively to 23.1 at final follow-up ($p<0.05$). Complications were seen in one (4.8%) case of cement leakage.

Conclusions: Our study shows that cementoplasty is a safe and effective option to treat vertebral lesions in patients with multiple myeloma.

KEYWORDS: Multiple myeloma, Vertebral lesion, Vertebral augmentation, Cementoplasty.

INTRODUCTION

Multiple myeloma (MM) is a neoplasm characterized by proliferation of B-lymphocytes and plasma cells in the bone marrow and determines bone fragility¹. The annual incidence is 6 in 100,000 in Western countries². The vertebrae are the most frequent localization of bony lesions with a rate

of 50 to 80%^{3,4} due to the increased survival in patients with this disorder and consequently increased morbidity. The bone anomaly results in vertebral compression fractures, osteolysis, and osteoporosis^{5,6}. The most common symptoms are pain, kyphosis, walking impairments, and disability, which can limit common daily activities⁷. Conservative treatment including bisphosphona-



tes, immunomodulatory agents, proteasome inhibitors, immunotherapeutic drugs and radiotherapy cannot always solve this clinical problem⁸⁻¹⁰. Surgical management with decompressive laminectomy is indicated for unstable fractures or in presence of bone fragments protruding from a fracture¹¹; however, this treatment can produce severe complications including destabilization of the spine, pain, and neurological alterations¹². Vertebral augmentation techniques such as cementoplasty have been shown to reduce pain and the use of analgesic drugs, improving functional disability with a low rate of complications¹³⁻¹⁶. The treatment consists of percutaneous injection of a balloon filled with polymethylmetacrylate (PMMA) at level of the fractured vertebrae¹⁷. The aim of this study is to report our experience regarding the treatment of vertebral fracture linked to multiple myeloma using cementoplasty technique.

PATIENTS AND METHODS

Patients

From January 2012 to December 2015, 38 patients affected by multiple myeloma with multilevel vertebral fractures and back pain, were treated in our Institute. The procedures followed were in accordance with the Ethical Standards of the Responsible Committee on Human Experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. The diagnosis of multiple myeloma was obtained with clinical evaluation and imaging studies including X-ray in standard projections, computed tomography (CT), and magnetic resonance imaging (MRI), and confirmed by histological findings after bone marrow aspiration and biopsy. All patients received chemotherapy and radiotherapy, according to standard protocols in the same center. Zoledronic acid therapy was applied to treat bone lesions. The cohort was 26 (68.4%) men and 12 (31.6%) women. The average age was 57 ± 7.1 years (range 43 to 71). Seventeen patients with an average age of 56.2 ± 6.5 years (range 45 to 70) with a single vertebral lesion (9 thoracic and 8 lumbar) underwent conservative treatment with anti-inflammatory medication, orthopedic brace, and protected weight bearing with crutches (Group 1); 21 patients with an average age of 57.7 ± 7.7 years (range 43 to 71) underwent multilevel vertebral augmentation with percutaneous vertebral cementoplasty in addition to medical therapy (Group 2). There were 39 surgically augmented vertebrae: 14 thoracic and 25 lumbar vertebrae (Table 1). Cementoplasty procedures were performed under

TABLE 1. Study groups.

	Group 1	Group 2	Total
Patients	17	21	38
Male	10	16	26
Female	7	5	12
Average age (years)	56.2 ± 6.5 (45-70)	57.7 ± 7.7 (47-71)	57 ± 7.1 (43-71)
Thoracic vertebrae	9	14	23
Lumbar vertebrae	8	25	33

local anesthesia and neuroleptic analgesia. With patients in the prone position, an average of 2.7 cc (range 2-3.4) of PMMA was injected according to the size of the vertebra. Less volume was needed for the thoracic spine and more volume was needed for the lumbar spine¹⁸. The most common technique was the unilateral pedicular approach, that reached the anterior third of the vertebra close to the midline in the A-P radiographic view (Figure 1). We performed vertebral augmentation of the three vertebral bodies in the same surgical intervention. Weight bearing occurred on the same day as the surgery. Both groups were clinically evaluated at 1, 6 and 12 months using the Visual Analogic Scale¹⁹ (VAS) for pain, SF-36²⁰ and ODI Score Questionnaires²¹. Radiographic evaluation was performed in operated group to verify the quality of cementoplasty and to individuate complications.

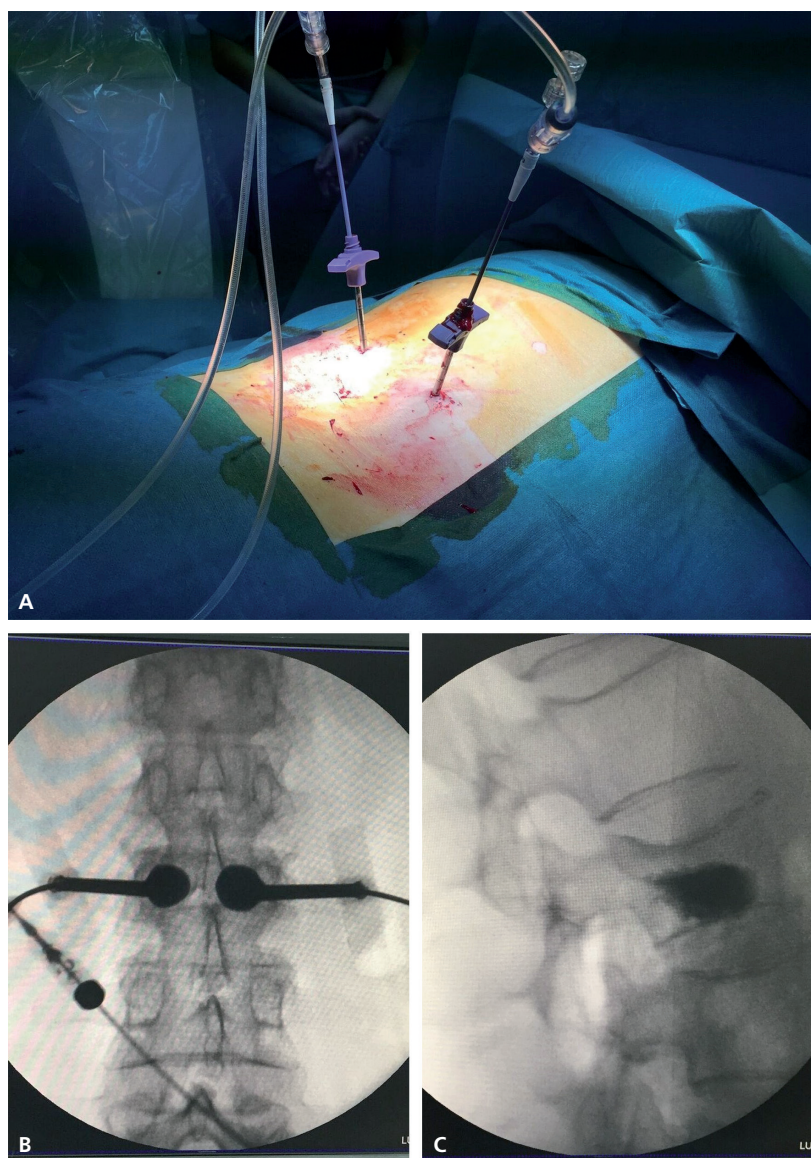
Statistical Analysis

Qualitative data were expressed as absolute frequencies and relative percentages, while quantitative data were expressed as mean, standard deviation (SD) and range. The normality of VAS, SF-36 and ODI were tested with the Kolmogorov-Smirnov test. Then, a Friedman's test was used to compare VAS and MRC scores between the different follow-up times. A Wilcoxon signed-rank test was used for post hoc analyses.

RESULTS

The mean follow-up was 23.7 ± 5.7 months (range 14 to 36). The mean VAS score in group 1 decreased from 7.1 ± 1.2 (range 5 to 9) pre-operatively to 3.9 ± 1.0 (range 1 to 5) at final follow-up ($p < 0.05$). The mean intermediate values were 4.1 ± 1.0 at 1 month and 3.6 ± 1.3 at 6 months after the beginning of treatment. Group 2 decreased from 7.3 ± 0.7 (range 6 to 8) pre-operatively to 2.3 ± 0.8 (range 1 to 4) at final follow-up ($p < 0.05$) with mean intermediate values of 2.6 ± 1.0 at 1 month and 2.4 ± 0.9

Fig. 1. *A*, Percutaneous injection of balloons; *B*, Balloons filled with polymethylmethacrylate (PMMA); *C*, Augmented vertebra.



at 6 months after surgery (Figure 2). The mean SF-36 values in group 1 increased from 34.1 ± 3.8 (range 28 to 41) pre-operatively to 58.6 ± 7.1 (range 39 to 69) at the final follow-up ($p < 0.05$) with mean intermediate values of 53.0 ± 9.6 at 1 month and 57.5 ± 8.4 at 6 months after the beginning of treatment. Group 2 increased from 31.5 ± 5.3 (range 24 to 41) pre-operatively to 76.9 ± 5.8 (range 68 to 86) at the final follow-up ($p < 0.05$) with mean intermediate values of 67.4 ± 6.0 at 1 month and 76.3 ± 4.6 at 6 months after surgery (Figure 3). The mean ODI score in group 1 decreased from 73.3 ± 8.0 (range 55 to 83) pre-operatively to 44.9 ± 7.2 (range 33 to 59) at the final follow-up ($p < 0.05$) with mean intermediate values of 57.5 ± 7.3 at 1 month and 44.5 ± 6.7 at 6 months after the start of treatment. Group 2 decreased from 77.5 ± 3.5 (range 68 to 85) pre-operatively to 23.1 ± 4.9 (range 18 to 35) at the

final follow-up ($p < 0.05$) with mean intermediate values of 31.8 ± 4.8 at 1 month and 24.2 ± 5.6 at 6 months after surgery (Figure 4). In group 2, the radiographic evaluation showed that kyphosis did not get worse due to the mechanical stabilization of the treated vertebrae. The only reported complication was in one case (4.8%) of cement leakage.

DISCUSSION

Vertebral lesions are frequently observed in patients with MM (Figure 5). Often, they are the first sign of disorder. The estimated frequency is over 60% of bone lesions occurring in MM^{3,4}. This high value is comparable to that of metastasis affecting breast, prostate and lung cancer²².

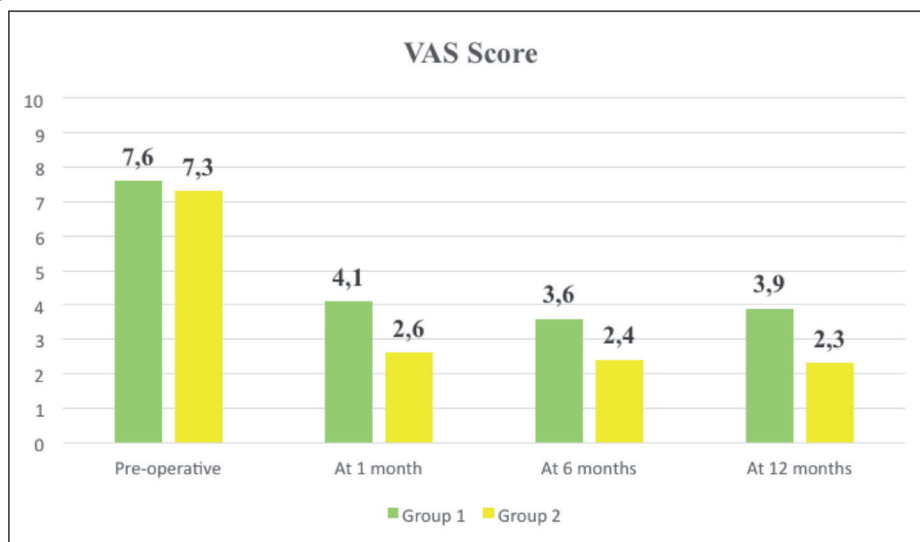
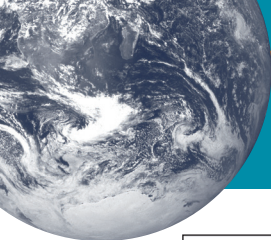


Fig. 2. VAS score variation: conservative treatment (group 1) vs. cementoplasty (group 2).

Fig. 3. SF-36 values variation: conservative treatment vs. cementoplasty.

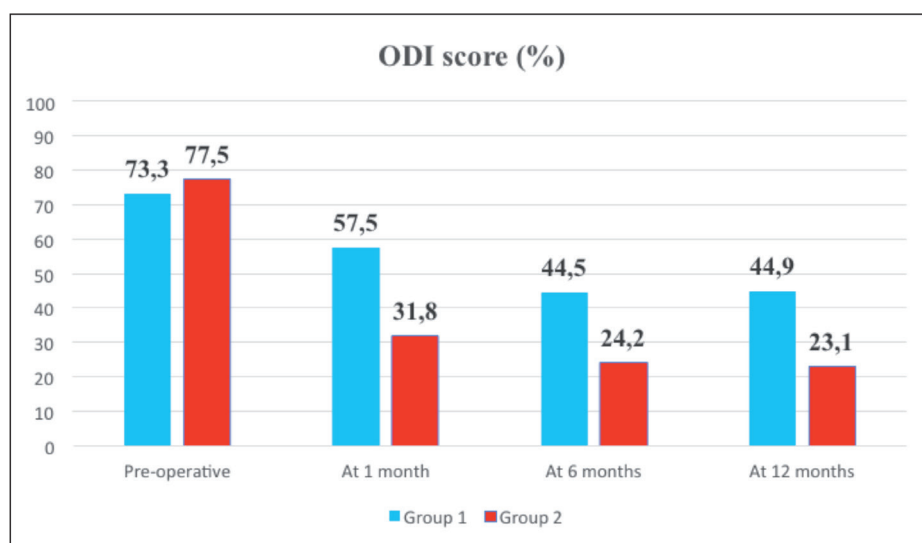
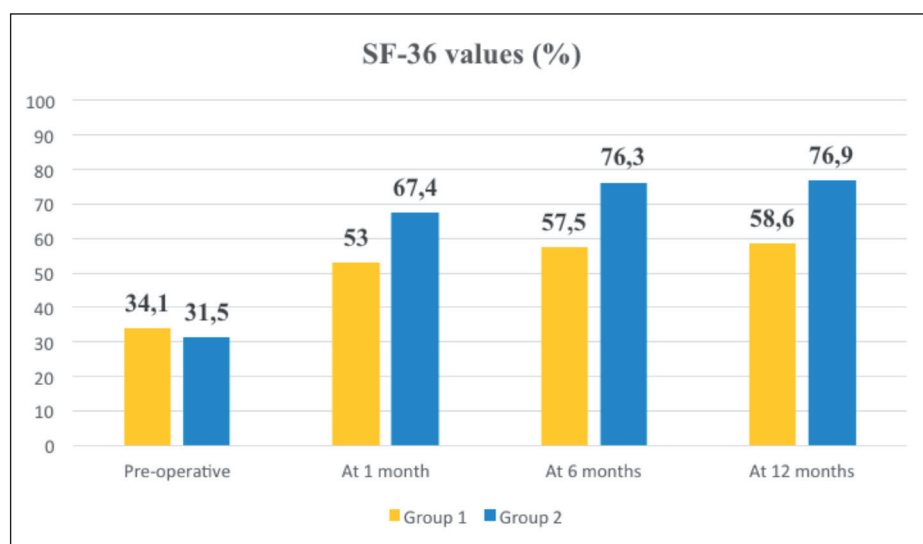


Fig. 4. ODI score variation: conservative treatment vs. cementoplasty.



Fig. 5. 55 years old male patient with multiple vertebral lesions MM-related.

Vertebral involvement may be explained by the pathogenesis of bone-related MM-vertebral bodies contain a high amount of hematopoietic bone marrow, and this marrow plays a key role in osteoblastogenesis²³. In particular, reciprocal stimulation between neoplastic cells and osteoclasts cause generalized osteoporosis and osteolysis – these are mainly located in vertebral bodies²⁴. The D6-L4 vertebrae are the most commonly involved regions of the spine⁵ as reported in this series. The diagnosis is possible due to instrumental evaluation in patients with back pain and worsening kyphosis. Whole body skeletal X-ray is the first exam for diagnosis, but it can often underestimate initial lesions^{25,26}. CT offers higher sensitivity in detecting spinal lesion, evaluating alterations in bone mineralization²⁵ and defining the correct level where the biopsy must be performed²⁷. MRI is sensitive and specific at detecting both vertebral compression fractures and spatial evaluation of neural damage²⁸. Recent studies²⁹ have reported fluorodeoxyglucose (FDG)-positron emitting tomography (PET) as diagnostic instrument in MM, but the value of this exam is limited by low proliferative activity of neoplastic plasma cells. Treatment of MM-related vertebral lesions is based on association of medical, surgical, and minimally invasive techniques⁸⁻¹⁶. In general, medical treatment consists of anti-myeloma drugs to reduce bone loss. Whilst patients treated with a high dose of dexamethasone could have a higher bone loss and need to be counteracted with bisphosphonates, drug combinations, targeting both myeloma cells and

bone marrow microenvironment (thalidomide and lenalidomide), could be potentially useful in inducing disease response and halting bone resorption³⁰. Denosumab is widely described in the literature as novel drug acting specifically on bone disease. It is a fully human monoclonal antibody that targets RANK-L and inhibits osteoclastogenesis³¹. Radiotherapy is a good treatment option due to optimal and long-lasting local control for bone lesion in MM. A dosage of 30 Gy in 10 fractions is useful in the early phases of this disorder⁹. Physiotherapy may be useful in patients with vertebral lesions. A review by Gan et al³² showed the benefits of exercise therapy in patients with MM with improvements in quality of life and physiological aspects. In our study, 17 patients had only one level of vertebral lesions or were incompatible with surgical treatment. These subjects were prescribed a specific training program to avoid the negative impact of medical treatment. Our statistical analysis showed a satisfactory reduction of pain with moderate improvement in quality of life as indicated from the SF-36 and ODI Questionnaire. Decompressive laminectomy was frequently performed in the past, but caused residual instability of the vertebral column, possible delay at the beginning of antimyeloma therapy after surgery, and a reduction in the sensitivity of neoplastic cells to treatment with steroids and radiotherapy¹¹. Vertebral augmentation techniques (cementoplasty) are distinguished from vertebroplasty and kyphoplasty and have been used for 30 years to treat osteoporotic vertebral fractures. These techniques offer good results in reducing pain and have been extended to treat metastatic vertebral fractures³³⁻³⁵. Excellent outcomes in treating vertebral MM lesions were reported in different studies with over 80% improvement in rest or activity pain^{13-16,33-35}. In our series, the 21 patients in group 2 were treated with cementoplasty and had excellent outcomes. These represented a statistically significant decrease in VAS value and ODI Score and a significant increase in SF-36 score compared to the conservative treatment group. Vertebral augmentation had a low incidence of complication-mainly from cement leakage from damaged vertebrae. This rare event may lead to serious complications such as non-responsive vertebral pain and pulmonary embolism^{36,37}. In our series, only one patient had a cement leakage at the D10 level, but with no relevant consequence. The main disadvantages of cementoplasty are its higher costs and complexity. It should be performed as early as possible to improve the vertebral strength and avoid the progression of alteration in the spine mechanics³⁸.



CONCLUSIONS

Our study showed that cementoplasty is a minimally invasive and effective option for the surgical treatment of vertebral lesions in patients with multiple myeloma. The procedure is relatively safe due to a low rate of complications. Compared to conservative treatment, cementoplasty resulted in a major decrease in pain and an improvement in quality of life.

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CONFLICT OF INTERESTS:

The authors declare that there is no conflict of interests regarding the publication of this paper.

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