Percutaneous Vertebroplasty for Tumoral Fractures. 15 years Experience of a Multidisciplinary Support and Review of the Literature

Vertebroplastia percutânea para fraturas tumorais. 15 anos de experiência de uma estrutura multidisciplinar e revisão da literatura

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ABSTRACT

The pain management in oncologic patients requires a multidisciplinary approach. Considering bone metastases, multiple myeloma and lymphoma, percutaneous procedures like vertebroplasty can provide rapid pain relief. However, percutaneous vertebroplasty must be placed in order to not delay systemic therapy or other modalities of treatment. In this article, we described our 15 years' experience in collaborating with a multidisciplinary team, reviewing literature and special issues percutaneous vertebroplasty for spinal tumoral fractures.

Key words: Percutaneous vertebroplasty; Tumoral fractures; Bone metastases; Multiple myeloma

INTRODUCTION

Pain is a common symptom in oncologic patients and the pain relief is an important chapter. Medication with important side effects and aggressive surgery might not be adapted to all patients, and even not efficient16.

Statistically, bone metastases are the first pain agent in cancer patients²⁶. Considering that 5% to 10% of all cancer patients develop spinal metastasis and might suffer from a severe back pain, adjuvant therapies like radiotherapy and percutaneous vertebroplasty (VT) take important place as part of the oncologic treatment¹³,³¹.

Since Galibert et al. described for the first time the technique of percutaneous VT in 1987¹¹, more than two thousand publications have appeared to discuss indications, complications and results in the different pathologies. Furthermore the polemics about real efficacy in the osteoporotic group confronted the public with some questions about patient selection and indications, and originated a storm (and brain storm also) in the medical and industry communities.

Considering VT for tumoral fractures, and metastatic, multiple myeloma (MM) and lymphoma are included, the different authors converge to a common opinion about the benefits
of VT to pain relief. The indication and the best moment to perform the VT is an issue because these patients present a complex medical management, so decisions must be taken in a multidisciplinary environment31.

In this article, more than to give numbers of our experience performing VT for spinal metastases, MM or lymphoma, the objective will be to share the experience of 15 years collaborating in an interdisciplinary team in charge of secondary malignant bone diseases, discuss the better time to perform the VT, expose specific issues and present a recent review of the literature.

Clinical Pathway: from the diagnosis of the tumoral spinal lesion up to the indication of VT

At our institution the majority of patients with bone secondary malignant diseases are presented in a weekly colloquy composed by specialists since 1997: oncologists, hematologists, radiotherapists, diagnostic radiologists specialized in bone diseases, neurosurgeons, orthopedists and interventional neuroradiologists. Despite relief of the pain, these cases are announced to the weekly colloquy because not only the symptomatic metastases warrant a treatment, but also instable lesions that can quickly progress and become symptomatic.

The clinical pathway is summarized on the organization chart (Fig. 1).

The diagnosis is generally given by standard radiography, CT (PET or not) and/or MRI and the patient will be evaluated by the physician responsible for the oncologic treatment. This group is constituted by different specialists (e.g. hematologists, pneumonologists, gynecologists, urologists; not only oncologists) and has the responsibility to coordinate all attitudes concerning the patient, evaluating life expectancy and giving priority to one therapy or permitting their association. For example chemotherapy is not compatible with invasive procedures if hematological problems and severe immunosuppression are present. The oncologic treatment follows a complex therapeutic strategy and the concerned specialists must respect it.

The physician responsible for the oncologic treatment who wants to present a case of bone metastases or MM sends an e-mail to the oncologist responsible for the colloquy, with the name of the patient, birthday date and the main subject to be discussed. Oncologists from private clinics can also join the discussion and in this case it is clear that they must carry radiologic records. This oncologist will prepare a list will all patients and will send to the participants by e-mail up to 2 hours before the starting time. The diagnostic radiologist will prepare in advance the radiologic files for the discussion in order to be able to answer the questions that sometimes extend to other organs affected by the cancer.

After complete exposition of the clinical situation, the concerned specialists give their opinion. If more than one specialist is concerned, the coordination between them is established at this time, avoiding many phone calls and shortening the waiting time for the patient.

The coordination is provided by the oncologist responsible for the colloquy. This person centralizes all requests, organizes hospitalizations, sends letters to the corresponding physicians and looks after the presence of the different specialists.

Concerning specifically the spinal metastases, MM or lymphoma, the decision to perform a VT or not comes from the interventional neuroradiologists.

The main indications of VT are painful vertebral fractures caused by metastatic disease or multiple myeloma29. Osteolytic fractures with 50-60% involvement of vertebral body, even if not painful, can also benefit from prophylactic VT to prevent collapse and secondary neurologic compressive symptoms33. Hypercalcemia secondary to severe lytic process can also
improve after VT.

How far should the conservative treatment be maintained before indicating VT? Muscle deconditioning, fast bone loss, deep venous thrombosis, depression and pulmonary diseases can be present as side effects of bed rest and narcotic analgesia, and VT can be performed in a preventive way. In this respect, multidisciplinary discussions changed traditional concepts and the physician responsible for the oncologic treatment acknowledged VT as a reliable technique with acceptable risks and complications.

Contra-indications to VT respect general conditions of all invasive procedures, like local or general infection or non-correctable coagulation disorders and allergy to any element used for VT (cement, needle). Even technically difficult, VT for vertebra plana (loss of more then 70% of height) is not an absolute contra-indication, considering that patient relief is possible and the complications are not frequent.

The colloquy is also the opportunity to ask for complementary exams. If possible patients will be submitted to a CT scan to evaluate the lesions (lytic or blastic) and MRI for the epidural and soft tissues extensions. Concerning osteoblastic metastases, bone hardness can prevent the vertebral approach and cement injection and radiotherapy is preferable to VT.

Another relative contra-indication to VT is the presence of important compression by epidural tumoral extension. In this situation combined therapy with VT to stabilize the vertebra and posterior surgical decompression followed by radiotherapy is more adapted.

In a retrospective data collection from 2005 to 2011, we performed 426 VT, and 255 VT (59.8%) in a context of metastases, multiple myeloma or lymphoma. As frequently showed in the literature, prostatic, breast and pulmonary metastases were the most common lesions found in our cases. Only 6.6% were not presented at the colloquy. The reasons were the intensity of pain, important spine instability or adaptation to the timing of the treatment that could not wait for the interdisciplinary discussion.

Specific technical issues concerning patients with tumoral fractures

All invasive procedures in oncologic patients are exposed to higher risk of complications and VT is not an exception. Weight loss, immunosuppression and debilitiated state may strongly interfere with the immediate follow up period. Patients can be considered more sensitive to developing infection, despite infection in this situation not being described as frequently as thought in the literature. Prophylactic antibiotics are routinely administered in most centers and seem to be enough to avoid infectious complications. The use of antibiotic powder mixed with the cement is not currently used, but recommended by some authors.

Another inconvenient is the patient position on the table. The ventral decubitus can be uncomfortable for the very painful patients. The anesthesia team disposes of different types of narcosis and analgesics with short-life considered quite adapted to this situation, and the intervention can be performed under local anesthesia plus sedation or general anesthesia without hurting the patient. One special situation is lung cancer, the primary tumor in 14% of patients treated by VT and the pulmonary metastases of others tumors. Patients can present severe dyspnea, oxygen dependence and impossibility to lie flat on the back. Moreover, sedation in ventral decubitus is contra-indicated as the risk of apnea during the intervention exists and the general anesthesia is not well accepted either, considering the difficulty to extubate the patient with bad pulmonary function and the short life expectation. For these particular cases the lateral decubitus is helpful despite the difficulty to install the patient and the non-ergonomic position for the operator. The anesthesiologist keeps visual contact with the patient and the doses of narcotics and analgesics will be better monitored. The lateral decubitus is preferable to sitting position where the visibility is compromised by the difficult to have a frontal view, quite important to pedicle approach.

The anatomical landmarks like pedicles, anterior and posterior wall are not easily seen in osteolytic fractures. The transpedicular technique provides a safe approach to the thoracic and lumbar vertebra, avoiding additional bleeding in the paravertebral muscles and soft tissues (sometimes present in the posterolateral approach) and is preferential for percutaneous VT. But it can be technically difficult if the pedicles are not visualized; the adjacent pedicles from superior and inferior levels might be useful as reference if the patient does not have severe spine deformity. Additionally, high thoracic levels have small pedicles and the risk of complication is more important than in lumbar levels. Even if not frequent, one major complication of needle malposition is the epidural hematoma caused by medial pedicle wall breach that can
happen with a bad visualization of pedicles. For difficult cases we performed transpedicular approach by XperCT guidance system when the general anesthesia was permitted with safe needle implantation in a short time intervention.

The cervical region is more affected by tumoral than osteoporotic fractures. Our experience with cervical VT is limited to 24 cases (9.4% of cases), with only 2 cases by transoral approach and all cases were tumoral. The approach is anterolateral for C3 to C7-D1 levels passing between the carotid artery laterally and esophagus medially. C1 and C2 can be acceded by transoral approach.

The treatment of several vertebral levels in one session is another quite particular situation that concerns tumoral fractures, especially MM. Patients with MM might present diffuse spinal fractures that limit mobilization and need high doses of analgesics. Multilevel VT was considered not safe by some authors if performed in more than three levels per session, but it can be performed in several fractured vertebrae and the limit will be determined by the capacity to tolerate table positioning and general anesthesia. From 255 VT for secondary tumoral bone disease, we found 58 cases of multilevels VT (22.7% of VT) in this retrospective data review (2 or 3 levels VT in 42 patients), even under local anesthesia. Painful patients or patients with 4 or more affected levels (16 VT) were treated under general anesthesia. 7 levels were treated in a context of MM (Table 1). We could account 362 levels treated by VT, with a mean of 1.42% levels per VT.

### Table 1

<table>
<thead>
<tr>
<th>Number of levels treated per session</th>
<th>VT for metastases or MM</th>
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<tbody>
<tr>
<td>1</td>
<td>197 (77.2%)</td>
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<tr>
<td>2</td>
<td>27 (10.5%)</td>
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<tr>
<td>3</td>
<td>15 (5.8%)</td>
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<tr>
<td>4</td>
<td>12 (4.7%)</td>
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<tr>
<td>5</td>
<td>1 (0.4%)</td>
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<tr>
<td>6</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>7</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>255</strong></td>
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Pain Relief: VT X Radiotherapy and review of the literature

The evaluation of pain treatment is variable in the literature but the common element is the utilization of analgesic medications. The pain control is defined by completely stopping analgesic drugs or enough pain relief that allows reduction of 50%.

The pain relief is found in 50-97% of patients submitted to VT for metastases and nearly 90% for multiple myeloma. Some reviews demonstrated that 70-90% of patients had improved function secondary to pain control by VT. The immediate amelioration is present in 90% of patients and stays under control for prolonged time in 67% of them. The pain recurrence is strongly associated to new lesions and oncologic evaluation, and re-fracture of treated vertebra is unusual.

Kyphoplasty (KP) is also considered as efficient as VT for tumoral fractures with less risks of leakage. KT provides height restoration and better vertebral filling, but there is no evidence that these two elements are concerned in the mechanisms of pain relief.

VT and radiotherapy are complementary adjuvant therapies for spinal metastases and MM, with slight differences in timing action and effectiveness. VT provides immediate stabilization and rapid pain relief contrasting to radiotherapy that will take weeks to produce the same effect. Radiotherapy achieves pain control in 55 to 83% of patients at 1 month. However radiotherapy carries clear growth control that is not proved with cement injection; the presence of epidural metastases is a typical indication of radiotherapy to avoid future compressive symptoms. The cement does not interfere with the beneficial radiation effects leading to a conclusion that the association of both VT followed by radiotherapy constitute a desirable therapeutic association.

Cement Kynetics: local effects, leakage and complications

The most common cement utilized is basically composed of polymethylmethacrylate (PMMA), easy to prepare, with rare systemic reactions and not costly. PMMA will strengthen the vertebra, avoiding new fracture, bonding and stopping intra-fracture movements that normally would set off the pain. Additionally PMMA becomes solid by a polymerization reaction that generates heat and consequently thermal effects...
on the tumor (necrosis), destruction of nerve endings on periosteal and paravertebral tissues, but there is no correlation between cement volume and pain relief. The necrosis of the tumor by the thermic reaction could be considered as an indirect agent for the oncological treatment but no clear benefit was demonstrated with systematic images (CT or MRI) before and after vertebroplasty\textsuperscript{17,29}.

One important point about this cement is its capacity to resist to compression forces, the main mechanism responsible for vertebral and hip (acetabulum) fractures. Long diaphyses bones are more subject to torsion forces and the strengthening provided by PMMA seems not to be adapted\textsuperscript{12}.

Considering vertebroplasty in a tumoral context, Hulme et al. found cement leakage in 41\% of treated vertebrae after systematic review of 69 studies\textsuperscript{15}, including intradiscal or not. Other authors reported leaks in 72.5\% of cement injections\textsuperscript{10}, constituting the most frequent adverse effect, mainly in tumoral context with cortical infraction and hypervasculization\textsuperscript{3,23}.

Cement leakages can be classified in vascular (venous and arterial) and nonvascular (discal, puncture trajectory, paravertebral). Vascular leaks are often venous and concern the epidural plexus, foraminal plexus and less frequently the vena cava. Despite being quite impressive in the control by CT scan, the clinical manifestation related to cement leaks is rare. Radicular pain after leakage into the foraminal plexus was described in few patients and successfully treated with nonsteroidal anti-inflammatory drugs or corticosteroids. Significant neural compression (epidural leak) and symptomatic pulmonary embolism (vena cava leak) are rare. Barragan-Campos et al. showed that the vascular leakage is more frequent (78.5\%) than the nonvascular (21.5\%), and all patients with nonvascular leaks were asymptomatic. Radicular pain occurred in 3.4\% of patients and treated only with medicaments. In this article 1 patient developed symptomatic pulmonary embolism (117 patients treated) and the patient died 8 days after procedure even receiving oral anticoagulation\textsuperscript{3}. Based on 255 VT performed from 2005 to 2011, we have no severe complication. 1 case of small migration of cement in the vena cava remained asymptomatic. No intra-canal cement leakage or important intra-foraminal with decompression by surgery was necessary in our retrospective data review.

Chew et al. made a review of the literature and showed that serious complications, including pulmonary embolism, deep vein thrombosis, haemotherax and neuropathy requiring decompression surgery, were found in 0 to 11.5\% of patients, and mortality in 0 to 7\%\textsuperscript{7}.

Cement leakage into the disk was often condemned in the osteoporosis and vertebroplasty articles. Actually, as in our own experience and literature, there is no direct association between postprocedural pain, subsequent fracture rate and intradiscal leakage\textsuperscript{18,19}. In this situation, the most common strategy is to wait some seconds or minutes to inject the cement, changing the orientation of the needle in order to achieve adequate cement filling. If there is no more time to do it or the cement continues to fill the disk space, a second needle should be placed. Despite no important relationship between cement leakage into the disk space and bad patient outcome, the injection of cement should be stopped temporarily as well.

**CONCLUSION**

Vertebral metastases and multiple myeloma are common cause of pain in oncologic patients and their relief is part of a complex therapeutic chart that requires a multidisciplinary management. The weekly colloquy at our institution exists since 1997 and provides an optimal organization for the pain management of these patients.

VT for tumoral fractures provides rapid relief of pain and immediate stabilization when compared to radiotherapy with low complication rates. The conservative treatment with bed rest, analgesics and corticosteroids is considered first option for stable fractures without compressive symptoms, but the decision to perform VT should be taken as soon as possible to avoid side-effects of analgesics drugs and the general immobility\textsuperscript{20}.

**REFERENCES**


Narata et al. present in this article their experience on treating metastatic vertebral tumors, with focus on pathological fractures. They describe the routine at the institution and the decision making support for the use of percutaneous vertebroplasty as a part of the multidisciplinary treatment of such patients.

Despite the advances in oncological treatment and increasing long term survival of patients, quality of life and pain control remains a challenge for those who treat these patients. Regarding this, the authors show how they deal with this complex cases and describe their large series. It is know that the complications of vertebroplasty are more common when treating tumoral fractures in comparison with osteoporotic/compression vertebral fractures; although kyphoplasty may not be more efficient concerning pain control, the risks of leakage can be reduced with this procedure (Eck et al.) - what maybe can justify the expensiveness of the procedure. Nevertheless, the authors refere no cases of leakage through the spinal canal with need of decompression - a complication well describe in the literature (Lee et al.). Moreover, although clinical results regarding pain control are possibly the same, as the authors said, from the evidence based point of view the results of khiphoplasty are more consistent (Berenson et al.); well controlled studies comparing these two methods are necessary for a more consistent conclusion about the superiority of one of the methods.

Since treating patients with systemic disease, often requires more than one modality of treatment, the model of a multidisciplinary approach described by the authors is to be copied by those how deal with these complexes cases.