Pain management in spinal metastases: the role of percutaneous vertebral augmentation

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Recent technological advances combined with innovative interventional radiology techniques can now offer an alternative less invasive treatment option for many patients with malignant vertebral body infiltration. Percutaneous vertebral augmentation procedures offer less invasive but effective pain relief to many patients with symptomatic spinal metastatic disease. The procedures are image guided and involve the injection of polymethylmethacrylate bone cement into the affected vertebral body. This technique can also be combined with radiofrequency ablation, which may accelerate vertebral stability. In this review, we examine the recent literature surrounding this topic and provide an overview of these emerging techniques.

Key words: kyphoplasty, metastasis, palliative medicine, radiofrequency ablation, spine, vertebroplasty

Introduction

Spinal metastases have a huge impact on the quality of lives of millions of people worldwide. Each year ~5% of cancer patients develop spinal metastases, with the most common primary sites being breast, lung and prostate [1]. Patients with spinal metastases have a median survival of 30 months, and effective palliation of symptoms is the principle clinical objective [2].

The predominant symptom in patients with spinal metastases is pain, which can be of three types: constant localised pain, radicular pain and axial pain. Traditional pain management techniques involve a combination of pharmacology, radiotherapy and surgical procedures. Axial pain is usually related to spinal instability, which can be successfully managed by surgery [3].

Recent technological advances combined with innovative interventional radiology techniques can now offer alternative less invasive treatment options for many patients with malignant vertebral body infiltration. Percutaneous vertebral augmentation procedures such as vertebroplasty, kyphoplasty and skylphoplasty have been in clinical use for a number of years but are currently not used as first-line treatment options in the setting of spinal metastases largely due to a lack of technical expertise in combination with insufficient outcome data from preliminary clinical trials.

The treatment of spinal metastases is extremely challenging due to the frequently observed severe pain and the associated marked debility this patient group experiences. Before the advent of percutaneous vertebral augmentation, multiple techniques were required to achieve a significant improvement in pain relief, which often included extensive surgery. However, oncology patients and oncologists are frequently reluctant to pursue extensive surgery [3]. In comparison, percutaneous vertebral augmentation represents a powerful tool in the management of oncology patients who suffer from painful skeletal metastases due to the minimally invasive nature of the procedure. In this review, we examine the recent literature surrounding this topic and provide an overview of these emerging techniques.

Presentation and current treatment options

The type, location and extent of spinal metastases determine the optimal method of symptomatic management. Although metastases form more frequently in the lumbar spinal region, thoracic metastases are generally more symptomatic due to the smaller calibre of the spinal canal in this region. Approximately 98% of spinal metastases are extradural, of which 80% involve the posterior spinal elements (vertebral body and pedicles) often leading to instability, deformity and pain [4, 5].

There are three main types of pain experienced by these patients as described in the ‘Introduction’ section. An expanding tumour can cause periosteal ‘stretching’ leading to constant localised pain and compression of nerve roots leading to radicular pain. These types of pain are most effectively treated by radiotherapy aiming to reduce the tumour size. Success rates of radiotherapy have been quoted to range from 40% to 70% [3]. Radiotherapy is often the mainstay of treatment in patients who have radiosensitive tumours, who cannot tolerate surgery or who have a poor survival prognosis [3].
However, the onset of pain relief can be delayed for up to 2 weeks following radiotherapy. Furthermore, one in five patients receives no or inadequate alleviation of pain using radiotherapy [3]. Radicular pain can also be effectively treated by nerve root blocks and oral steroids, which decrease perineural vasogenic oedema [6].

Axial pain is frequently associated with pathological vertebral body fracture and spinal instability secondary to destruction of its posterior portion. The options for management in these patients include medical therapy or surgical intervention. Medical management in combination with physiotherapy targets pain control and functional preservation. Analgesia can be achieved with non-steroidal anti-inflammatory drugs and steroids for bony pain, while neuropathic agents such as gabapentin are frequently used for nerve root pain. However, these therapies take time to provide effective pain relief. As the majority of these patients have short life expectancies, the goal is that of rapid symptomatic relief with subsequent improvement in the quality of life. Furthermore, conservative medical therapy may be ineffective or cause inadequate pain relief. However, inadequate pain relief may lead to immobility, which in turn increases the risk of venous thromboembolism, pressure sores, secondary respiratory problems and depression [7].

Traditionally, an alternative to medical therapy for managing axial pain and spinal instability has been open surgical intervention. Surgical spinal procedures are highly invasive in nature and are generally not suitable in this group of patients because of the high surgical risk of complications and the short life expectancy of this patient group. It is in this setting that percutaneous vertebral augmentation techniques offer an attractive alternative with less soft tissue trauma, less blood loss and the use of local anaesthesia, therefore leading to lower morbidity and mortality when compared with open spinal surgery.

**percutaneous vertebral augmentation**

Percutaneous vertebral augmentation procedures were first pioneered by clinicians over 25 years ago but are still not widely used due to lack of awareness and limited availability in mainstream medical care. In 1981, Harrington [8] treated 14 patients with spinal instability secondary to metastases with an open procedure where polymerised cement was used to stabilise the spine; some degree of spinal stabilisation was found in all 14 patients. In 1987, a French radiologist, Deramond, was the first to describe the use of percutaneous acrylic cement injection for the treatment of an aggressive vertebral body haemangioma [9]. Since these first descriptions, there have been many modifications and refinements to such techniques with improved clinical effectiveness [9].

Currently, there are three procedures licensed for clinical use: vertebroplasty, kyphoplasty and skyphoplasty, each of which requires a similar preprocedural workup. A detailed history and clinical examination is a prerequisite and should correlate with imaging findings. Plain radiographs, isotope bone scintigraphy and magnetic resonance imaging are the main radiological techniques used to identify sites of disease that may require treatment.

**vertebroplasty**

Vertebroplasty can be carried out under local anaesthesia combined with sedation in a day-case setting. A recent publication in the British Journal of Anaesthesia reported that infiltration of intraosseous lidocaine combined with continuous intravenous infusion of remifentanil is effective [10]. The procedure is usually carried out in an interventional radiology suite under strict aseptic conditions. As these patients' are often immunocompromised, a prophylactic dose of broad-spectrum antibiotic is recommended; this can be administered intravenously before the procedure or, alternatively, the antibiotic can be impregnated into the bone cement. Vital signs should be monitored throughout.

Vertebroplasty is usually carried out under fluoroscopic guidance using a single-plane fluoroscopy unit with a C-arm or biplane fluoroscopy. This procedure can also be carried out using computed tomography (CT) fluoroscopy; however, most centres reserve this technique for selected difficult cases.

The patient is positioned prone on the fluoroscopy table or the gantry of a CT scanner and initial images are acquired to confirm the targeted level. Local anaesthetic is then infiltrated into the skin, subcutaneous tissues and periosteum. Following this, an 11- or 13-gauge needle is passed along the anaesthetised tract and used to penetrate the cortex of the vertebra using a transpedicular, parapedicular or costopedicular approach (Figure 1). Further images are then acquired to help guide needle placement into the anterior quadrant of the targeted vertebral body, ideally as close to the midline as possible (Figure 2). At this stage, bone biopsies can be taken using a coaxial needle if...
required. Cement is then instilled under close imaging guidance until the anterior two-thirds of the vertebral body is filled and cement is equally distributed on both sides (Figure 3). In larger vertebra such as in the thoracic and lumbar spine, a bipedicular approach may be required to achieve this [11].

Following the procedure, patients require bed rest for 2 h and during this period, their vitals signs and neurology are monitored. Patients are then mobilised, and provided there are no immediate complications, discharge can usually be arranged on the same day. In many centres, a CT scan is carried out before discharge to assess intraosseous cement distribution and to look for signs of cement extravasation into adjacent viscera.

**kyphoplasty**

Kyphoplasty has evolved from vertebroplasty and aims to offer the benefit of analgesia in vertebral fractures in combination with restoration of vertebral body height. The procedure follows the same principles and general exclusion criterion. In kyphoplasty, a general anaesthetic is required. Following insertion of a larger 8-gauge needle into the vertebral body, a balloon-like device is inflated, which restores vertebral body height and creates a cavity into which cement is then injected. The balloon is subsequently removed before cement injection. Polymethylmethacrylate cement is then injected into the cavity in a controlled manner under imaging guidance and allowed to set.

Kyphoplasty has proven beneficial in restoring vertebral body height, and although there is less published data than with vertebroplasty, several recent studies have reported lower rates of cement leakage [12, 13]. A systematic review by Hulme et al. [14] concluded that both procedures provide similar rates of analgesia, and although kyphoplasty is associated with a reduced rate of cement leakage, in many instances, this is not clinically relevant. In addition, kyphoplasty costs 5–10 times more to carry out than vertebroplasty because the equipment is more expensive and because of the requirement for a general anaesthesia [15]. As both procedures have similar rates of pain control, it is therefore difficult to recommend kyphoplasty over vertebroplasty as the procedure of choice even if a significant kyphosis is present.

**skyphoplasty**

Skyphoplasty is the newest edition to the armamentarium of percutaneous vertebral augmentation procedures. This procedure is similar to kyphoplasty, but instead of using an inflatable balloon, a stiff plastic tube is deployed through a cannula and squashed into a ‘popcorn-like’ shape to create the vertebral body cavity. The device is then removed and cement is infiltrated. The skyphoplasty device creates more pressure and in a more predictable direction than kyphoplasty.
and only requires a single insertion site. As it is a fairly new procedure, there is a paucity of published literature comparing it with the other percutaneous vertebral augmentations. One recent study by Foo et al. [11, 16] has shown that skyphoplasty is a safe and effective procedure for relieving pain associated with vertebral compression fractures.

**percutaneous radiofrequency ablation**

In specialist centres, minimally invasive radiofrequency ablation of spinal metastases can be carried out at the same time as percutaneous vertebral augmentation. Following penetration of the vertebral cortex, a partially insulated electrode is passed into the vertebra under CT guidance. This electrode is attached to a radiofrequency generator. When activated, the electrode emits ions, which are converted to heat and cause local cellular damage [17]. This procedure can also be carried out under local anaesthesia and acts synergistically with percutaneous vertebral augmentation to give significant analgesia and increased vertebral stabilisation within 24 h of the procedure. There is also some evidence to show that if radiofrequency ablation is carried out before percutaneous vertebral augmentation, the risk of cement extravasation is reduced [18]. Theories for its mechanism of action include destruction of sensory nerve fibres, reduction of the lesion size and destruction of tumour cells producing nerve-stimulating factors. Results from these procedures combined can give a patient stable and painless vertebra within 24 h of admission with an unstable vertebra [19].

**patient selection**

Percutaneous vertebral augmentation procedures are not only effective for the treatment of spinal metastatic lesions but have also proven of benefit in treating vertebral compression fractures secondary to osteoporosis, benign tumours (haemangioimm, giant cell tumour), other forms of malignant infiltration (myeloma, lymphoma) and trauma [11]. When selecting patients for these procedures, a multidisciplinary approach is essential with input from a radiologist, spinal surgeon and referring clinical specialist. There are a range of different indications and contraindications for these procedures.

Indications for percutaneous vertebral augmentation procedure in patients with spinal metastases are:

- Painful vertebral compression fracture or imminent vertebral compression fracture causing significant disability, such as inability to walk and transfer or perform activities of normal daily living [7].
- Intense intractable pain that is adjacent to the vertebrae that have been diagnosed as fractured or osteolytic by recent imaging [15].

Absolute contraindications are:

- Asymptomatic vertebral compression fracture
- Pain that is responding to medical therapy
- Local or systemic infection
- Uncorrectable coagulopathy
- Allergy to bone cement
- Tumour causing spinal cord compression.

Relative contraindications are: [7, 17, 20]

- Lack of orthopaedic and neurosurgical support.
- Complete or greater than 70% vertebral collapse (as it is difficult to enter the vertebra).
- Patients with five or more metastases. In the past, numerous vertebral body involvement were seen as an absolute contraindication. However, with increasing experience in the procedure, multiple metastases can be treated serially with the most painful metastasis being treated initially followed by treatment of other metastases as required.
- Vertebral fractures with posterior column involvement. Posterior column involvement is technically more challenging and increases the risk of cement extravasation. However, skeletal metastases with posterior column involvement can frequently be treated successfully.
- Nerve root pain and/or radicular pain that is more severe than the axial pain. These patients often need adjunctive treatment with percutaneous vertebral augmentation and nerve root blocks to fully treat the patients' local pain.

**complications**

The overall risk associated with percutaneous vertebral augmentation in the treatment of malignant disease is ≤10% [20, 21]. Minor complications usually relate to local trauma. The most common complication being pain around the injection site, which usually subsides after 48–72 h; this may be combined with bleeding from the puncture site, which is more common if multiple vertebral levels are being targeted or if very vascular lesions are being treated such as metastases from thyroid or renal cell carcinoma. Other complications related to local trauma include rib fractures and fracture of the posterior vertebral elements, which occur in <1% of cases. Other complications include infection and allergic reaction to the cement, which can cause cardiovascular instability [22].

The most feared major complication related to percutaneous vertebral augmentation is cement extravasation with leakage into the epidural space and neural foramina with resultant cord compression and radicular pain. There is also a risk of pulmonary embolism should cement enter the paravertebral venous plexus. Cement extravasation is reported in up to 41% of vertebroplasty procedures but is rarely symptomatic as demonstrated in a study by Gangi et al. [25] who reported on a series of 868 procedures. Cement leakage into the epidural space occurred in just 15 cases, of which 3 became symptomatic but in no case was there spinal cord compression [23–25]. Ensuring good quality imaging and adequate opacification of cement can help avert these rare complications. Overall percutaneous vertebral augmentation procedures are considered safe with a less than 3% incidence of major symptomatic complications [23–25].

**clinical evidence**

To date, there have been numerous published trials on the topic of vertebroplasty for the treatment of tumour-associated spinal fractures. Cumulative analysis of these data demonstrates that
these patients have a significant reduction in pain, with minimal procedure-related morbidity. This reduction in pain has been shown to aid mobility, response to physiotherapy and quality of life [26, 27]. Although there is currently no level 1 evidence for vertebroplasty in the treatment of tumour-associated vertebral fractures, 2009 saw the publication of three randomised controlled trials (RCTs) on the topic of percutaneous vertebral augmentation for the treatment of osteoporosis-associated vertebral fractures. Two of the RCTs showed a trend towards meaningful improvement in pain in the short term when compared with non-surgical management and a placebo-simulated procedure [28, 29]. The third RCT concluded that vertebroplasty was of no benefit in comparison to a simulated procedure in giving short-term pain relief [30]. However, the last two randomised studies involving patients suffering from osteoporotic collapse were heavily criticised for the high crossover rate of patients between the study groups, poor patients selection and control groups. There is currently a need for RCTs to be carried out on the topic of vertebroplasty in the oncological setting.

Emerging evidence has identified that percutaneous vertebral augmentation is an excellent alternative to medical and surgical management in carefully selected patients with vertebral body fractures secondary to skeletal metastases. The ability of this procedure to induce rapid pain relief with minimal interference with adjuvant therapies and minimal comorbidities should make it the first choice of treatment in centres that can offer it.

disclosure
The authors declare no conflict of interest.

references


