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The efficacy of percutaneous vertebroplasty for vertebral metastases associated with solid malignancies

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ABSTRACT

Background: Percutaneous vertebroplasty appears beneficial for patients with acute compression fractures of multiple aetiologies including myeloma, osteoporosis and trauma. There are few reports on its use in the setting of metastatic solid malignancy.
Methods: We identified all individuals who had undergone percutaneous vertebroplasty at our institution since 2004 and focused on those with metastatic solid malignancies. Their clinical characteristics and outcomes were investigated.
Results: From 136 cases that underwent percutaneous vertebroplasties, 19 were performed mainly in breast, prostate, lung and renal cancers. Of these 19 cases, 10 patients (53%) were treated for solitary lesions, 3 (16%) were injected at two levels and the remaining 6 cases (31%) underwent cement injection at three levels. The majority of individuals (84%) reported short- and long-term symptomatic improvements. At a median follow-up of one year, six patients have died.
Conclusions: Percutaneous vertebroplasty appears as an effective palliative procedure in patients with compression fractures secondary to metastatic solid malignancy. Its use can be successfully combined with other treatment modalities (radiotherapy and chemotherapy).

1. Introduction

Painful vertebral metastases are a debilitating and common complication of a number of solid malignancies most frequently occurring in prostate, breast and lung cancers. The incidence of vertebral metastases has been reported to range from 30% to 70% depending on the primary tumour. Approximately, 10% of cancer patients will present with symptoms related to vertebral metastases and of these, 40–70% will have involvement at multiple levels.[1] The increasing frequency of vertebral metastases is a reflection of the prevalence of these primary cancers, increasing survival times and the predilection of these types of malignancies to metastasis to the bones.

Vertebral metastases are traditionally managed through a combination of surgery, radiation and medical therapy. Surgical intervention is usually palliative, focusing on pain control, maintaining neurological function and spinal stabilisation as its aims. Radiotherapy is useful in alleviating vertebral pain in around 70% of the cases, but delayed benefits of 2–6 weeks are

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common.[2] Its use is further limited by a maximum-tolerated dose to the spinal cord and does not provide stabilisation. The medical therapeutic options include analgesics, bisphosphonates, corticosteroids and in certain cases chemotherapy. Classically, percutaneous vertebroplasty using polymethylmethacrylate (PMMA) cement is undertaken in cases with refractory painful metastases in whom conservative therapy, defined as traditional escalation of analgesia and bed rest, has failed. Based on this study and our observations of the morbidity associated with severe back pain,[3] long-term bed rest and the side-effects associated with the high doses of traditional analgesics, we propose that it should be considered as the first line adjunct treatment option for pain control in these cases.

Percutaneous vertebroplasty is an invasive procedure that is performed under radiological guidance, and has been successfully applied in the pain management of vertebral haemangiomas,[4] compression fractures secondary to osteoporosis[5] or myeloma.[6,7] It has been shown to be a safe and efficacious 'day case' procedure that can rapidly improve pain, as well as strengthen the underlying bone involved.[8] To date, a number of case series have been published on the use of percutaneous vertebroplasty in osteoporotic fractures,[9–11] but there are few data specifically reviewing its use in spinal metastases, the majority of these are case reports.[12–14]

To investigate this further, we reviewed 136 patients who underwent percutaneous vertebroplasty of 1–3 vertebrae over a 4-year period at Imperial Healthcare NHS Trust, London, specifically focusing for this study on identifying features in those with solid malignant disease who benefited most from this intervention.

2. Patients and methods

All percutaneous vertebroplasties performed between the years 2004 and 2008 by the Imperial Healthcare NHS Trust Department of Interventional Radiology were retrospectively reviewed. These cases were identified on the departmental register, which recorded every percutaneous vertebroplasty case that was undertaken in an electronic prospective manner.

Each case was reviewed by a consultant radiologist on the radiology imaging picture archiving and communication system (PACS) along with the formal vertebroplasty report. Data were abstracted from the electronic medical records and the following information was collated: age, gender, diagnosis, date of vertebroplasty, position of lesion, performance status, other treatments including surgery, radiotherapy, chemotherapy and pain team involvement, and benefit from treatment. Patients were individually contacted through telephone to assess their benefit from the intervention. They were specifically asked if they felt that the vertebroplasty had alleviated their level of pain and then score their pain categorically as mild, moderate or severe, to describe their mobility and analgesic requirements post-procedure and assessed for performance status based on the European Cooperative Oncology Group (ECOG) performance status scale. This was compared to the documented pain score, analgesic requirements, mobility and performance status before they had been referred for vertebroplasty at the pre-procedure clinic.

Prior to the procedure, all patients reported the presence of severe back pain centred around or immediately adjacent to the diseased vertebral body. In some cases, there was an associated band-like sensation of constriction. Based on the medical records prior to the procedure, patients reported that the pain was poorly controlled by oral analgesics, was impeding mobility and their daily activities. Each case had a histologically confirmed diagnosis of cancer, and a nuclear medicine bone scan reporting the presence of vertebral metastasis, a computer tomography (CT) scan consistent with malignant vertebral disease, plain films and/or a magnetic resonance imaging (MRI) of the spine. Each patient was reviewed by the neurosurgical multidisciplinary team who were meeting to discuss surgical options including fixation, debulking or vertebroplasty. Percutaneous vertebroplasty was considered in the cases that were not amenable to surgical fixation and debulking based on the performance status of the patient or disease status of the cancer. It was undertaken as a palliative procedure and exclusion criteria included acute spinal cord compression that requires immediate surgery (even in these cases, vertebroplasty combined with surgery is a feasible option). Many cases have more than three vertebrae involved, but only three vertebrae are injected at one sitting to reduce the possibility of fat embolisation.

Percutaneous vertebroplasty can be performed under local anaesthesia but general anaesthesia is often preferable for both the patient and the operator. It is performed under fluoroscopy or CT guidance with the patient under sedation lying in either the prone or the lateral decubitus position. For the treatment of a cervical lesion, CT guidance is preferable as this provides better visualisation of the carotid vessels. The vertebroplasty needle is fluoroscopically guided into the diseased bone, and PMMA cement is injected into the malignant bone cavity. Access may be transpedicular or paravertebral depending on the level of the vertebrae under treatment. The PMMA cement is made up from 9.0 g of Kyphx HV-R fluid, which has a high viscosity, radio-opaque bone cement (99.1% methylmethacrylate, 0.9% N,N-dimethyl-p-tolvidine, 75 ppm hydroquinine) mixed with 20.0 g of Kyphx cement powder (68% methyl methacrylate–styrene copolymer, 30% barium sulphate and 2% benzoyl peroxide), and injected via a 7 guage, 160 mm long Gishen bone biopsy needle (rocket trephine needle) using both 1 ml and 2.5 ml luer locks. The cement is allowed to thicken to the consistency of toothpaste prior to injection to reduce the risk of extravasation. Following completion of the procedure, patients are monitored for up to four hours post-operatively. They should remain recumbent during this period to prevent weight bearing whilst the PMMA cement hardens.

In the future, it is possible that vertebroplasty maybe considered as the first line treatment option for pain control in vertebral metastases, and surgery may be considered as the second line of treatment if vertebroplasty has failed to relieve the symptoms.

3. Results

A total of 136 cases were identified and of these cases, 19 (14%) were undertaken on patients with solid tumours includ-

Table 1 – Characteristics of patients who underwent vertebroplasties for pain control in metastatic bone disease secondary to solid malignancies.

Age/sex	Primary cancer	Vertebral level injected	No. of sites	Immediate benefit	Analgesic reduction	Benefit at follow-up	Follow-up (months)
60 (F)	Breast	T12	1	Yes	Yes	Yes	10
86 (F)	Breast	L1	1	Yes	Yes	Yes	6
73 (F)	Breast	T12, L1, L3	3	Yes	Yes	Yes	19
64 (F)	Breast	T12	1	Yes	Yes	Yes	19
44 (F)	Breast	T7	1	Yes	Yes	Yes	8
84 (F)	Breast	T10, T12, L1	3	Yes	Yes	Yes	4
69 (F)	Breast	T7, T9, L3	3	Yes	Yes	Yes	7
72 (F)	Breast	L4	1	Yes	Yes	Yes	3
89 (M)	Prostate	L3, L4, L5	3	No	No	Yes	9
75 (M)	Prostate	T6,T7	2	Yes	Yes	Yes	14
79 (M)	Prostate	L2	1	Yes	Yes	Yes	19
71 (M)	Prostate	T12, L1, L2	3	No	No	No	3
82 (M)	Lung	Sacrum	1	Yes	No	No	4
48 (M)	Lung	T7, T8	2	Yes	Yes	Yes	12
49 (F)	Renal	L4, T10, T12	3	Yes	Yes	Yes	5
73 (M)	Renal	T6	1	No	No	No	38
75 (M)	Oesophageal	L2	1	Yes	Yes	Yes	6
79 (F)	Adenoid cystic	L1	1	Yes	Yes	Yes	16
57 (F)	Cervix	L2, L4	2	Yes	Yes	Yes	17

ing breast, prostate, lung, renal cell and oesophageal cancers. Those individuals with multiple myeloma were excluded in this report. The most common tumour category was breast cancer, followed by prostate cancer (Table 1). The mean age was 70 years (range 44–89 years).

Following the percutaneous vertebroplasty procedure, the post-procedure reports documented that 16 patients (84%) described an immediate benefit within the first 24–48 h, of which four patients reported alleviation of pain on waking from the procedural anaesthetic. There was one reported complication of pain at the site due to a small amount of PMMA cement leakage around the site used directly in the vertebroplasty procedure. This patient received simple analgesia after the procedure and the pain resolved within 24 h; The patient subsequently had a good result from the vertebroplasty with good long-term pain control. At follow-up, these 16 individuals continued to derive benefit from the vertebroplasty with a marked reduction in their analgesic requirement and improved mobility. Of the remaining three patients, one reported that there was no change in his symptoms, one reported some improvement but required a repeat of the procedure at one of the three levels injected and the other described increasing pain at follow-up (Table 2).

Percutaneous vertebroplasty was carried out predominantly in the thoracic and lumbar regions to treat pain and stabilise compression fractures related to metastatic bone involvement (Figs. 1 and 2). In one case, cement was injected into the sacrum, which specifically resulted in only partial pain relief. Ten cases (53%) were treated for solitary lesions, three (16%) were injected at two levels and the remaining six cases (31%) underwent PMMA cement injection at three levels.

Table 2 – Summary of Results (immediate benefit was assessed in hospital and long-term benefit at 3 months).

Immediate benefit (Pain and mobility)	84.2% (16/19)
Long-term benefit (Pain and mobility)	84.2% (16/19)
Step down in analgesic requirement	78.9% (15/19)
Worsening pain	5.3% (1/19)
Complication rate	5.3% (1/13)

All cases included in this report had metastatic disease, and percutaneous vertebroplasty was undertaken with palliative intent. The mean follow-up period measured 12 months (range of follow-up 3–38 months); since the time of the procedure, six patients have died.

4. Discussion

Percutaneous vertebroplasty is a minimally invasive treatment option which can help to alleviate pain associated with vertebral metastases without epidural compression. In September 2003, the National Institute for Clinical Excellence (NICE) in the United Kingdom (UK), approved the use of percutaneous vertebroplasty in patients with painful spinal metastases refractory to conservative measures. Percutaneous vertebroplasty is performed under fluoroscopy or CT with the patient under sedation lying in either the prone or the lateral decubitus position. The vertebroplasty needle is fluoroscopically guided into the diseased bone, and PMMA cement is injected into the malignant bone cavity. The injection of the acrylic bone cement leads to strengthening of the vertebra, thereby preventing further compression of the affected vertebral body, and thus stabilisation against vertebral collapse due to tumour necrosis.[8]

Patients with evidence of acute cord compression or disruption of the posterior border of the affected vertebra should be managed with either emergency surgical decompression or radiotherapy although we consider cement into the verte-

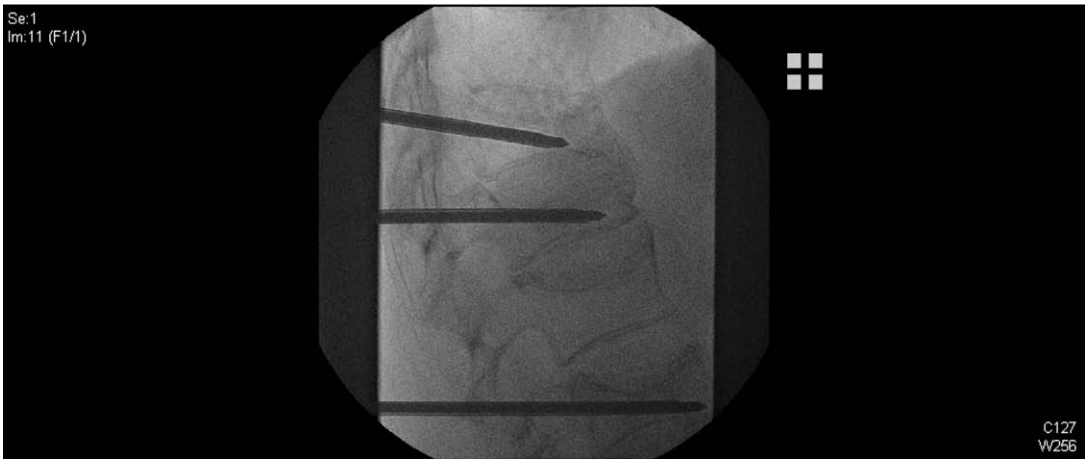

Fig. 1 – Insertion of needles.

bral body followed by laminectomy to potentially decrease the extent of surgery, as therapeutically possible. The inability to lie prone for the procedure is overcome by doing the procedure with the patient in the lateral position. Neither age nor performance status is a contra-indication to percutaneous vertebroplasty that can be carried out under moderate sedation and local anaesthesia. Only three vertebrae are injected at any one sitting, so if more vertebrae are involved and painful, these can be dealt with on a separate occasion.

The main complication associated with percutaneous vertebroplasty is leakage of cement posteriorly into the spinal canal. Extravasation of contrast into the canal may cause nerve root irritation or cord compression, but occurs in less than 0.5% of the cases. Leakage around the site of injection superiorly, inferiorly or laterally is invariably irrelevant. Filling of small veins whilst the cement is liquid can occur and may lead to a fat embolus due to embolisation of fat triggered by cement leaking into the small veins. Theoretically, there is a risk of infection, but from our experience to date none of our patients have reported any complications from infection. Based on the other studies, the overall risk of infection from vertebroplasty in all types of patients including those with osteoporotic fractures is less than 0.5%, and the risk of further fractures in the adjacent vertebrae following vertebroplasty is around 1%. From our series and other published reports, percutaneous vertebroplasty appears safe with a low rate of complications between 5% and 10% in metastatic disease.[6,15] More than 80% of patients will experience significant pain relief, leading to an improvement in their mobility.[6,15]

As mentioned, this procedure has been successfully applied in the pain management of haemangiomas,[4] osteoporosis[5] and myeloma.[6,7] Its present use in the UK for metastatic lesions from solid tumour remains relatively infrequent possibly due to the limited published data in spinal metastases and a lack of access to this procedure, which is only carried out by specialist radiologists with experience in this procedure. At the time of the NICE overview in 2003 on percutaneous vertebroplasty, only six centres in the UK were performing the procedure. In the United States of America (USA), vertebroplasty is widely utilised in the setting of osteoporotic crush fractures. An analysis carried out by Gray et al. of vertebroplasties performed in the USA from 2001 to 2005 based on fee-for-service data from medicare claims enrolees showed that the rates of primary vertebroplasty almost doubled from 14,142 cases in 2001 to 29,090 cases in 2005.[16] This increase was believed to reflect changes in clini-

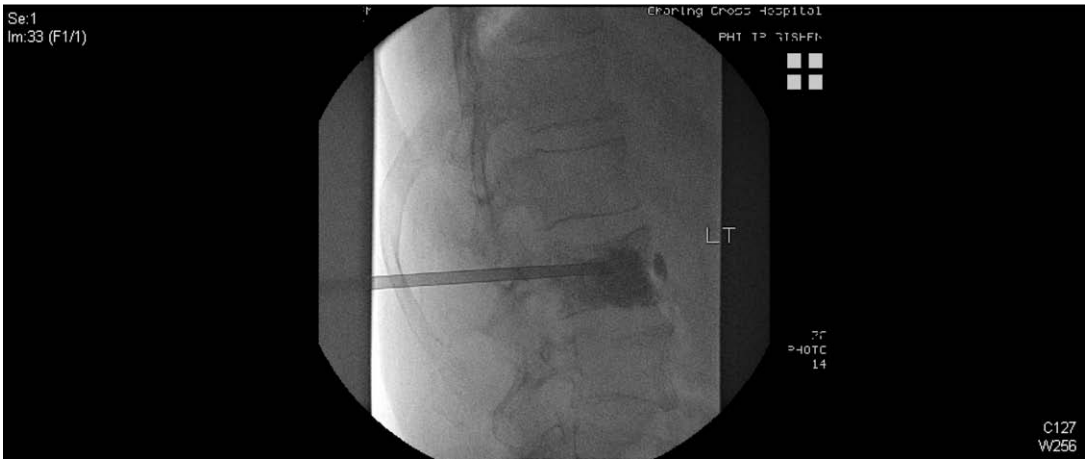

Fig. 2 – Placement of PMMA cement into a thoracic vertebral lesion.

cal opinion, patient demand, medical insurance coverage policies and the availability of vertebroplasty relative to other treatment approaches. However, the use of percutaneous vertebroplasty in metastatic solid malignancy whilst probably higher in the USA than in the UK still appears to be relatively limited. The largest series reported specifically in percutaneous vertebroplasty other than this report is by Weill et al., who reported on 18 cases in spinal metastases.[15]

Patients with vertebral metastatic disease often suffer from persistent debilitating pain. Percutaneous vertebroplasty should be considered as a major and useful treatment option to alleviate pain. Although it does not improve the survival outcome, palliation is a reasonable goal when life expectancy is short and can reduce complications associated with long-term bed rest, which maybe particularly relevant for 'older' patients. The estimated cost of a percutaneous vertebroplasty is 300 sterling pounds, which includes the material cost of the vertebroplasty kit-PMMA cement, Khypx mixer, Rocket trephine needle, luer locks, syringes and a day procedure bed for up to four hours. In the long run, cost benefits from this procedure will derive from reduced analgesic requirements and avoidance of complications of long-term bed rest and impaired mobility. This will ultimately result in significant potential savings from reduced in-patient admissions for pain control, home care costs, community nursing, out-of ours access to primary care and clinical services.

The results of this study are comparable to the findings from other groups such as Gangi et al., who demonstrated favourable outcomes in 83% of patients with malignant lesions.[17] The success of vertebroplasty in the metastatic setting has been best demonstrated in the thoracic and lumbar regions, but its use in the cervical region has also been reported.[18] As well as stabilisation, local tumouricidal effects around the cement area have been noted in a postmortem study of six individuals.[19] Percutaneous vertebroplasty can be used to complement radiotherapy with a rapid reduction in pain management from 1 to 3 d while maintaining structural support within the affected vertebra(e).[20] Murray et al. demonstrated *in vitro* that cement is not affected by radiotherapy nor is potential radiation therapy affected by the injection of cement into the vertebral column.[21] If vertebroplasty is to be undertaken in conjunction with radiotherapy, it has been recommended that vertebroplasty is performed prior to radiotherapy for optimal results.[15]

Limitations of this study include a small number of patients and the absence of a prospectively completed questionnaire. Further work can aim to randomise patients to intervention with this procedure versus other approaches including symptomatic care alone.

5. Conclusion

This study illustrates that percutaneous vertebroplasty can be beneficial within 48 h in 84% of patients with acute, centrally localised back pain related to metastatic vertebral disease. Up to three vertebral levels maybe injected at one sitting with good results. Its use has been shown to offer significant pain relief, leading to better mobility and symptom control particularly in the palliative setting. In the future, it is possible that vertebroplasty maybe considered as the first line treatment option for pain control in vertebral metastases, before consideration of more invasive surgery. Vertebroplasty may be undertaken prior to or during radiotherapy and chemotherapy. For optimal results its use before radiotherapy has been recommended. Its value as a complementary therapy to radiation, chemotherapy and surgical intervention is currently under utilised in the UK, and it should be considered as an additional treatment modality for patients with severe pain in metastatic vertebral disease.

Conflict of interest statement

None declared.

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