Percutaneous Vertebroplasty Combined with Zoledronic Acid for the Treatment of Painful Osteolytic Spinal Metastases in Patients with Breast Cancer

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ABSTRACT

Purpose: To assess retrospectively the efficacy and safety of percutaneous vertebroplasty (PVP) combined with zoledronic acid (ZA) for the treatment of painful osteolytic spinal metastases from breast cancer.

Materials and Methods: PVP was performed in 43 patients with breast cancer and painful osteolytic spinal metastases; 126 vertebrae were treated. The patients subsequently received 4 mg ZA via a 15-minute intravenous infusion every 4 weeks for 12 months. Pain and quality of life (QoL) were assessed using a visual analog scale (VAS) and Karnofsky performance scale (KPS), respectively, 24 hours before PVP and 24 hours, 1 month, 3 months, 6 months, and 12 months after PVP. Skeletal-related events (SREs) were assessed for 12 months following the intervention.

Results: The mean VAS scores decreased significantly from 7.6 ± 1.9 at 24 hours before PVP to 3.6 ± 1.4 at 24 hours, 2.0 ± 1.5 at 1 month, 2.8 ± 1.6 at 3 months, 3.1 ± 0.8 at 6 months, and 2.5 ± 0.9 at 12 months after the intervention ($P < .05$). KPS scores increased significantly after the combination treatment ($P < .05$). Compared with previous studies without PVP or ZA treatment, this patient group had a lower incidence of SREs. No major complications were observed.

Conclusions: PVP combined with ZA was shown to be a highly effective and safe combination therapy to relieve pain and improve QoL in patients with osteolytic spinal metastases from breast cancer. The combination therapy also prevented the occurrence of SREs.

ABBREVIATIONS

KPS = Karnofsky performance scale, PVP = percutaneous vertebroplasty, QoL = quality of life, SMR = skeletal morbidity rate, SREs = skeletal-related events, VAS = visual analog scale, ZA = zoledronic acid

Approximately 70% of patients with advanced breast cancer develop bone metastases, most commonly affecting the spine (1). Vertebral pain is usually the first and dominant clinical symptom in patients with spinal metastases. Along with pain, other consequences of spinal metastases include pathologic fracture, spinal cord compression, radiation or surgery to bone, and hypercalcemia of malignancy. The aforementioned consequences are usually defined as skeletal-related events (SREs). Progressive pain and SREs result in reduced quality of life (QoL) and functional independence (2). Patient survival may also be significantly reduced following the occurrence of SREs (3). The treatment of patients with spinal metastases from breast cancer is aimed at relieving pain, improving QoL, preventing the occurrence of SREs, and prolonging survival.

Conservative treatment of painful spinal metastases includes analgesia, chemotherapy, hormonal therapy, and radiation therapy. However, these modalities usually cannot prevent the progression of spinal deformity resulting

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from pathologic fractures or provide immediate stabilization to an unstable vertebral segment (4,5). Surgical options such as open reduction and internal fixation are theoretically possible but are rarely performed because of poor bone stock and multiple underlying comorbidities (6). Percutaneous vertebroplasty (PVP) is a minimally invasive, radiologically guided procedure. PVP offers a less invasive therapeutic option to provide pain relief and biomechanical stability in patients with metastases to the spine.

In recent years, many studies have evaluated the effects of PVP on pain relief and QoL improvement in patients with spinal metastases (7–9). Because bisphosphonates have been part of the standard treatment of bone metastases for approximately 10 years (10,11), bisphosphonates should have been administered concomitantly in those studies. However, no studies concerning PVP have taken the effects of bisphosphonates into account. The purpose of this retrospective study was to evaluate the efficacy and safety of PVP combined with zoledronic acid (ZA) for the treatment of painful osteolytic spinal metastases from breast cancer, with an assessment of pain relief and QoL improvement and the prevention of SREs.

MATERIALS AND METHODS

Patient Selection

This study was approved by the local ethics committee, and informed written consent was obtained from all patients before treatment. Between July 2007 and December 2011, 48 consecutive female patients with breast cancer and painful osteolytic spinal metastases received the treatment of PVP combined with ZA. Five patients were excluded because of treatment with bisphosphonates before PVP. The remaining 43 patients had a mean age of 57.3 years ± 8.1 (range, 32–74 y). Of patients, 40 (93.0%) completed the ZA treatment for 12 months, 2 discontinued the treatment after 8 months for financial reasons because ZA was not covered by the national medical insurance at that time, and 1 patient completed the treatment protocol for 6 months but died of liver metastasis from breast cancer 7 months after PVP. Follow-up for 12 months was completed for 42 patients.

All patients had histologically diagnosed breast cancer and clinical and imaging evidence of osteolytic spinal metastases. A biopsy of the spine confirming metastatic bone disease from breast cancer was performed in 38 patients. Imaging studies included spine magnetic resonance imaging, computed tomography (CT), and bone scans or positron emission tomography. Each patient underwent a CT scan (Sensation 4 or 16; Siemens, Forchheim, Germany) of the involved vertebrae before and after PVP. CT findings obtained before PVP enabled radiation oncologists to classify spinal metastases as osteolytic, osteoblastic, or mixed lesions. The distribution of bone cement in the vertebrae and cement leakage were analyzed on CT scans performed after PVP.

The clinical indications for PVP were in accordance with the Society of Interventional Radiology (SIR) quality improvement guidelines (12) and confirmed by an interdisciplinary team of medical oncologists, radiation oncologists, surgeons, and interventional radiologists before intervention. The indications included (*i*) excruciating pain with adverse effects (eg, constipation, urinary retention, confusion) to opioid treatment or development of opioid tolerance in patients with formerly controlled pain; (*ii*) intractable pain refractory to chemotherapy and radiation therapy; and (*iii*) extensive osteolysis secondary to malignant infiltration with or without fracture of the affected vertebral body. All treated patients met at least one of these criteria. Asymptomatic displacement of a fracture fragment producing spinal canal narrowing, radiculopathy, extension of the tumor into the spinal canal with or without cord compression, and collapse of the posterior vertebral body wall were regarded as relative contraindications to PVP. Absolute contraindications included improvement of pain with analgesic therapy, asymptomatic vertebral fracture with low risk for biomechanical instability and collapse, active local or systemic infections, uncorrectable coagulopathy, and allergy to bone cement or opacification agents.

PVP Procedure and ZA Treatment

The same interventional radiologist performed all procedures. PVP was performed under sterile conditions with local anesthesia. Antibiotics were not administered before the procedure. Most procedures were performed with the patient in a prone position. A unilateral transpedicular approach was used most often reserving a bipedicular approach for cases in which the unilateral approach resulted in unsatisfactory filling. For cervical vertebral bodies, anterolateral access was performed with the patient lying in a supine position. The affected vertebrae were localized fluoroscopically with a biplanar C-arm. Small skin incisions were made, and 11-gauge or 13-gauge hollow needles (Murphy M2; Cook, Inc, Bloomington, Indiana) were inserted and driven with gentle hammer blows under fluoroscopic guidance. The goal was to place the needle tip in the anterior one third of the vertebral body or at the center of the osteolysis. Finally, polymethyl methacrylate bone cement (SpinePlex; Stryker, Kalamazoo, Michigan) was injected through the hollow needles into the vertebral body under continuous observation by biplanar fluoroscopy. If any cement leakage was detected, the injection was stopped at once. A CT scan of the treated bone level was immediately performed for documentation of the cement distribution.

After the procedure, patients were admitted to the hospital for 2–3 days for observation. Generally 2 days