Percutaneous osteoplasty for extraspinal metastases

Qinghua Tian, Yongde Cheng, Chungen Wu *

ABSTRACT

As an extension of percutaneous vertebroplasty (PVP), percutaneous osteoplasty (POP) refers broadly to percutaneous bone cement injected into various parts of the body and narrowly to cement injected into extraspinal bone lesions. POP mainly includes such surgeries as percutaneous sacroplasty, percutaneous acetabuloplasty, percutaneous femoral osteoplasty, and percutaneous iliac osteoplasty (Figure 1). Currently, POP is a positive and an effective treatment for extraspinal bone lesions in that it can rapidly relieve pain, effectively prevent pathological fractures, and partially inactivate tumors, with few complications. The aim of this review is to detail the POP techniques and report their safety and efficacy in the treatment of extraspinal metastases.

Keywords: percutaneous osteoplasty; percutaneous vertebroplasty; extraspinal metastases.

Department of Radiology, the Affiliated Sixth People's Hospital, Shanghai Jiaotong University, Shanghai 200233, China.

* **Correspondence:** Chungen Wu, Email: 18930177559@163.com

CLINICAL-APPLICATION BACKGROUND

Bone is one of the most frequently involved sites for many common cancers such as breast, prostate,
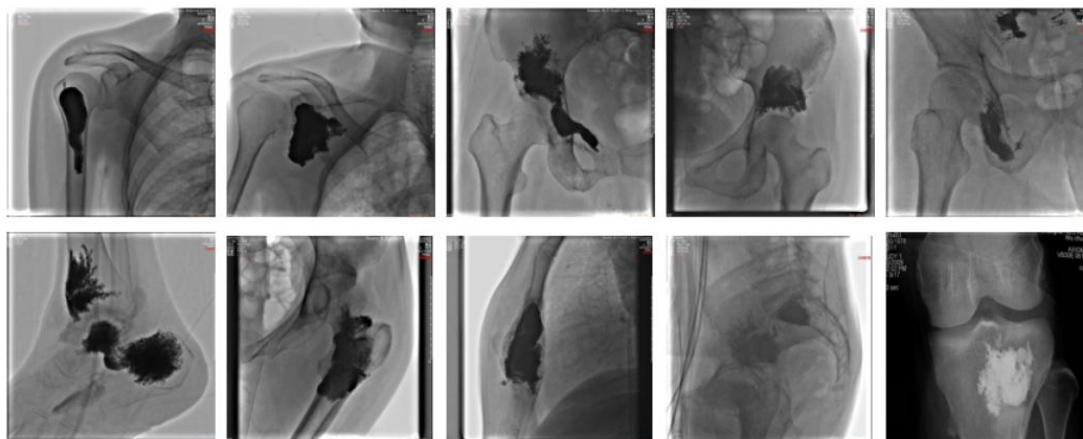

Figure 1. Percutaneous osteoplasty.

lung and kidney cancers and multiple myeloma. Bone metastases are preferentially located in areas of red marrow where blood flow is higher, which accounts for two-thirds of the lesions to be extraspinal (1,2). Current methods for treatment of painful extraspinal metastases combine systemic and local therapies, including surgery, radiotherapy, chemotherapy, and narcotic sedatives. When a localized painful lesion is identified, surgery is rarely a satisfactory therapeutic option because it is often too invasive for a fragile patient. Radiotherapy is a good solution but has some limitations, such as delayed effect and tissue tolerance (3). Bisphosphonates, hormone therapy, and chemotherapy (especially phosphonic acid) are effective in breast cancer, multiple myeloma, and metastatic carcinoma, but their clinical efficiency is not particularly obvious because of the delayed effect and short survival time (4). It is estimated that at least 45% of patients with bone metastases suffer from intractable pain due to not receiving adequate treatment (5). This has prompted the search for new therapies to relieve pain, such as radiofrequency ablation (RFA), cryoablation, microwave ablation (MWA), POP, and magnetic resonance–guided ultrasound (6-8). RFA treatment can significantly reduce the use of opioids, and an ongoing preliminary study shows that MWA is also very promising (7). However, early research suggests that ablation has obviously delayed effects and cannot strengthen bones; therefore, it is not the best choice for preventing impending pathological fracture lesions.

As an extension of PVP, POP was first put forth by Zhou et al. (9) and has proven highly effective in relieving pain from extraspinal metastases, alone or in combination with other techniques. It can reduce the risk of a pathological fracture, achieve pain regression and improve mobility (8,10).

MECHANISM

The principle of pain relief in POP is based on the consolidation of the weakened and pathological cancerous bone and on the combined chemical and thermal cytotoxic effect produced during cement polymerization. Due to strong stress resistance and high hardness, the injection of bone cement into the lesion site can increase bone strength and prevent microfractures. Therefore, POP is more suitable for treatment of weight-bearing bone damage and most impending pathological fractures. Meanwhile,

polymerization of bone cement can necrotize peripheral nerve endings and tumor cells, thus alleviating pain. The toxicity of the bone cement monomer may also play a role in POP's anti-tumor effect and shrinking of tumor volume (11-13).

INDICATIONS

Inclusion criteria are normally as follows: patients with intense and focal pain associated with evidence from plain X-ray films and computed tomography (CT) or magnetic resonance imaging (MRI) of osteolytic bone lesion with or without impending bone fractures; unsatisfactory response to conventional pain therapy; life expectancy of > 3 months; age > 18 years and sound mental condition; and provision of informed consent.

Exclusion criteria are as follows: non-correctable coagulation disorders (platelets 90,000, international normalized ratio 1.50); systemic or local infection; and distance between the lesion and vessels or vital organ < 10 mm. Lost integrity of the cortical bone is not an exclusion parameter.

OSTEOPLASTY TECHNIQUES

The Biochemical index and coagulation function should be detected before POP. The surgery must be carried out under strict aseptic conditions and under local anesthesia, and vital signs should be monitored during the operation. Broad-spectrum antibiotics can be used for patients with insufficient immune function. POP can be divided into 2 equally important components: needle placement and cement injection. Well-chosen imaging guidance is of utmost importance for precise lesion targeting, uncomplicated needle placement, accurate visualization of cement distribution, and early detection of leaks. Biplane fluoroscopy or dual guidance with a mobile C-arm placed in front of the computed-tomography (CT) gantry is suggested, with the latter being required in cases of difficult-to-access extraspinal lesions.

Extraspinal-osteoplasty patients may be positioned prone, supine or lateral decubitus, depending on the exact anatomic location of the lesion. The adequate access point, puncture angle and distance from skin to lesion can be determined beforehand via CT and/or magnetic resonance imaging (MRI). In order to avoid critical nerves and blood vessels, the shortest puncture distance is recommended. In cases of

acetabuloplasty, the anterior lateral approach can avoid injury to the femoral nerve, while the posterior approach can avoid injury to the sciatic nerve. A small incision is made at the puncture site after anesthesia using 2% lidocaine. A dedicated beveled vertebroplasty needle, 18−10 gauges in diameter, is advanced into the bone lesion. A bevel tip is preferable, as this feature allows easy repositioning and precise steering of the needle. In most cases, the simple pressure of the operator's hands on the needle is sufficient to correctly place it into the lesion; it can be assisted by surgical hammer when a hard bone is encountered.

Polymethyl methacrylate (PMMA) can be successfully used for bone metastases, whereas a biological osteoconductive calcium phosphate bone cement is preferable for benign lesions. A sterile 2, 5 or 10 mL Luer Lock polypropylene syringe, or a dedicated pressure injector, can be used to inject the cement into the bone lesion. The cement can be slowly injected under real-time surveillance; the injection must be stopped immediately if any leakage occurs. Post-operative CT scan is performed to observe the distribution of bone cement and leakage. More than 1 lesion can be treated in the same session, depending on the doctor's experience and the patient's physical condition. For hypervascular bone metastases, it is recommended that bony angiography be used to predict the flow and distribution of bone cement and help prevent the occurrence of leakage.

There have been some recent improvements in bone cement injection techniques. Kawai describes POP using a cement-filled catheter for a pathological fracture of the humerus, after which the patient experienced immediate pain relief and improved limb mobility (14). Sun reported that for patients with multiple osteolytic metastases in the same humerus, the POP technique of a cement-filled catheter with multiple side holes is feasible and may be advantageous over regular POP (10,15).

As for metastases located in the long bones, it has been argued that POP alone should be contraindicated because osteoplasty alone provides inadequate consolidation during weight bearing (16,17). To improve mechanical consolidation of osteoplasty, several authors have proposed combining osteoplasty with the insertion of different types of devices in the femur, such as pins, nails, or cannulated screws (18-25). Tian et al. reported that a modified trocar needle was implanted into the proximal femur through a bone puncture needle sheath parallel to the vertical and horizontal axis of the femoral neck and the vertical axis of the thighbone respectively before PMMA injection (18). In 2012, Deschamps et al. reported 100% technical success for osteoplasty combined with the insertion of 3 cannulated screws along the inferior cortical femoral neck and against the upper cortical femoral neck. PMMA was then injected around the screws (25).

CLINICAL OUTCOMES

POP has proven to be highly effective for relieving pain in case of extraspinal metastases, alone or in combination with other techniques such as ablation (8,26-33).

Iannessi et al. demonstrated that 17 patients with painful extraspinal bone lesions who were treated with POP experienced a significant, rapid, and long-lasting decrease in their pain (4.1 points; $P < 0.1$; 7.75 months of follow-up on average) (29). Sun et al. performed POP for 51 consecutive patients with painful bone metastases outside the spine; all patients experienced a satisfying resolution of painful symptoms at 3 months follow-up (27). In Masala et al.'s study, 39 patients with painful extraspinal bone lesions from multiple myeloma underwent POP, which provided long-lasting pain relief with frequent tumor control and a significant reduction in the use of analgesic drugs (30). Anselmetti et al. reported that POP with PMMA achieved significant pain relief in 50 patients with painful extravertebral lytic bone metastases that were nonresponsive to conventional therapy (8). Cazzato et al. systematically reviewed the current evidence for POP of long bones and reported that it is safe, offering good pain relief and recovery of impaired limb function (31). Tian et al. combined POP with RFA for painful extraspinal bone metastases in 38 patients and achieved immediate pain relief and function improvement (32). Pusceddu et al. applied MWA and osteoplasty in patients with painful bone metastases of the femur and acetabulum and achieved promising results, which suggests that the combination is safe and effective in treating painful bone metastases which are at a high risk of fracture (33).

COMPLICATIONS

Cement leakage, pathological fracture, infection, allergy, and bleeding are the common events with POP (16,34). There are more likely to be complications when there is cortical destruction, soft-tissue invasion or hypervascular bone metastasis.

Bone cement leakage is the most common complication of POP, including leakage into blood vessels, joints, and soft tissues. The risk of leakage can be problematic when intra-articular, in contact with a nerve trunk or on a support zone. In any case of osteolysis adjacent to the joint, injection must be administered with extreme care to avoid the risk of rapid chondrolysis in the event of intra-articular leakage (35). In Weill et al.'s study, the incidence of leakage into the surrounding soft tissue was 28% and that into the hip joint was 11%, but only 1 case showed symptoms (26). Kelekis et al. observed that the incidence of leakage into the hip joint was 28% and reported that a leakage in the obturator foramen resulted in continued pain, which was treated by RFA of the pudendal nerve (28). Intraosseous venography before injection of bone cement has been advocated as a way to identify sites of potential venous leakage during the procedure. Note that the anatomical configuration of extraspinal lesions needs a 3-dimensional imaging. Therefore, we believe that a combination of CT and fluoroscopic guidance makes the procedure safer.

The risk of bleeding is greater during needle insertion and in hypervascular metastases (thyroid, kidney and melanoma) (34). In these cases, it is recommended that the surgeon maintain compression for 5 minutes or implement trans-catheter arterial embolization (TAE) to effectively reduce bleeding (36,37). The overall rate of infectious complications reported is < 1%. Fat embolism is also a matter of concern. Bone cement injection can cause bone marrow fat to be squeezed into the blood, leading to fatal pulmonary embolism. Bone cement injection can cause bone marrow fat to be squeezed into the blood, leading to fatal pulmonary embolism or to hypotension and arrhythmias. The entry of bone cement into the circulatory system may also result from secondary fat embolism after bone marrow replacement (11). Patients may have transient fever and local pain after POP, and the degree of pain is positively correlated with the amount of bone cement injected. However, total pain relief occurs after 24 hours. Few patients are allergic to bone cement, and fatal allergies are extremely rare.

The biomechanical properties of cement are perfectly adapted to withstand compression fractures that occur in the flat bones and weight-bearing joints such as the acetabulum or the femoral condyle. POP alone cannot provide adequate consolidation during weight bearing for metastases that are located in the long bones and that often cause pathological fractures. Therefore, the rate of fractures despite osteoplasty is very high in the literature. In a retrospective analysis of 21 consecutive patients, fractures occurred in one-third of patients and were significantly more frequent if associated with a > 30 mm cortical rupture (8,16,38).

OUTLOOK

At present, there are 2 main research hotspots in POP: the development of new bone cement and the combination therapy mode with POP.

PMMA is the most widely used cement, with several decades of application in orthopedic surgery. Older-generation PMMA cements had to be mixed with barium sulfate, tungsten, or tantalum powder because of their inherently low radiopacity (39). The high temperature during PMMA polymerization results in thermocoagulation of tumor cells locally, but may also damage healthy adjacent tissues, such as neural roots and the spinal cord itself, in cases of severe leakage. Moreover, PMMA is nonreactive to new bone formation. Newer filler materials for POP are composite cements and calcium phosphate cements (CPCs) (40-42). CPCs are the most expensive bone cements on the market but have the best compatibility and osteogenic induction (43). Some experts add a variety of osteogenesis-inducing growth factors and antitumor drugs into the cement, making it a carrier of antitumor treatment (44-46). However, these studies remain in the experimental stage, a long distance from clinical application. Future development will focus on improving the cure rate with good bone conduction, bone inducement and tumor filling materials; and restoring the anatomical structure and physiological characteristics of bone to a greater extent.

The combination of POP and multiple other methods in the treatment of benign and malignant extraspinal tumors is another hotspot in the current research; it has had a better clinical effect, with a pain relief rate of 95–100% (5). Tian et al. evaluated a combination of RFA and POP in 38 patients with 54 painful extraspinal bone metastases and achieved inspiring results (32). RFA before cement injection

has the advantage of decreasing tumor cell spread, either mechanically through the formation of an ablation shell barrier or via embolization of necrotic tumor cells. In addition, RFA may result in thrombosis of the venous plexus, which should decrease the risk of cement extravasation. Pusceddu et al. demonstrated the effectiveness of CT-guided percutaneous MWA and POP in patients with painful bone metastases at high risk of fracture. In their study, mean reduction of VAS score and improvement in surviving patients' walking ability were 90% and 100%, respectively (33). Masala et al. (47). reported mean VAS score reductions of 79%, 6 months post-treatment in patients treated with radiofrequency and osteoplasty and 71% in those treated with cryoablation and POP.

Various factors should be considered in the management of extraspinal metastases: tumor histological characteristics, the patient's physical condition, disease progress, the degree of bone destruction, and the purpose of treatment (radical or palliative). For metastases resistant to conventional therapy (radiation, chemotherapy or a combination), POP provides a new and promising method that can effectively relieve pain, strengthen bones, and inactivate some tumors so as to improve the patients' quality of life.

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