

# The surgical management and treatment of metastatic lesions in the proximal femur

## A mini review

Helin Feng, MD<sup>a</sup>, Jin Wang, MD<sup>a</sup>, Jianfa Xu, MD<sup>a</sup>, Wei Chen, MD<sup>b</sup>, Yingze Zhang, MD<sup>b,\*</sup>

### Abstract

Review current treatments of metastatic lesions in the proximal femur.

We reviewed published literature related to diagnosis and surgical treatments and summarized current treatment options.

Surgical management mainly consist of internal fixation, hip replacement, and percutaneous femoroplasty (PFP) which has been newly applied in clinical practice.

An appropriate series of treatments is necessary for patients to avoid the occurrence of paraplegia and prolong survival time.

**Abbreviations:** CT = computed tomography, ECT = emission computed tomography, MRI = magnetic resonance imaging, PET = positron emission tomography, PFN = proximal femoral nail, PFP = percutaneous femoroplasty, PMMA = polymethylmethacrylate, PVP = percutaneous vertebroplasty, SPECT = single-photon emission tomography.

**Keywords:** metastases, percutaneous femoroplasty, proximal femur, surgery

## 1. Introduction

Metastasis accounts for 90% death of cancer patients. In theory, cancer cells can metastasize anywhere in the body but they usually predominate at one site more often than others. Besides lung and liver, bone is the most common site invaded by cancers and actually nearly all types of cancer can metastasize to the bones, particular for breast cancer, prostate cancer, and multiple myeloma.<sup>[1]</sup> Many factors caused by cancer cells or arisen by the bone marrow microenvironment in response to cancer cells are keys to activation of osteoclastic bone resorption and regulation of osteoblastic activity in bone metastasis.<sup>[2–4]</sup> Bone metastasize presents a strong correlation with tumor growth in bone which has been referred to the “vicious cycle”, in which tumor cells promote bone metastasize by osteoclasts, and osteoclastic bone destruction causes the activation of growth factors in the microenvironment that further promote tumor progression.<sup>[5]</sup> In addition to portending a dismal prognosis, bone metastases cause significant morbidity including bone pain, fractures, hypercalcemia, spinal cord compression, and other nerve compression syndromes.<sup>[6]</sup> The spine, proximal femur, and

pelvis are the most common sites of bone metastases.<sup>[7,8]</sup> Among femur metastatic tumors, 50% of the lesions occur in the femoral neck, 30% occur in the subtrochanteric site, and 20% occur in the intertrochanteric site. These lesions lead to severe bone pain and a high incidence of pathological fractures.<sup>[9]</sup> The goal of proximal femoral metastasis treatment is to relieve pain, restore weight-bearing abilities, and improve the quality of the patient’s remaining life. The treatment of proximal femoral metastases includes nonsurgical and surgical approaches. The nonsurgical approaches include radiation therapy and pharmacologic treatment such as bisphosphonate while the surgical approaches include internal fixation, hip prostheses replacement, and percutaneous femoroplasty (PFP).<sup>[10]</sup> Because the femur is a major weight-bearing bone with minimal space for surgical errors, the operative procedure must be carefully planned and meticulously executed, with the aim of achieving durable reconstruction. Therefore, all pertinent information must be carefully considered before surgical treatment, such as the location of the metastasis, the extent of bone involvement and the number of metastatic lesions, the perceived effects on other therapies, the type of primary cancer, and the expected life span. PFP represents a promising treatment option for alleviating the pain and weakness associated with metastatic lesions of the femur. PFP resulted in significant pain relief in the affected limbs and significantly improved quality of life. In this review, we have summarized the advances in diagnosis and treatment options for proximal femur metastases.

## 2. Diagnosis

Proximal femoral metastases can cause severe pain and even pathological fractures, which can negatively affect a patient’s quality of life. The evaluation of patients with proximal femoral metastases should be performed according to a systematic method.<sup>[11]</sup> One should never assume that proximal femoral metastasis need to be treated in a specific manner without a definite diagnosis, particularly when determining whether the patient has multiple metastases or multiple myeloma. x-Ray is the

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<sup>a</sup> Department of Orthopedics, The Fourth Hospital of Hebei Medical University,

<sup>b</sup> Department of Orthopedics, The Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, China.

\* Correspondence: Yingze Zhang, The Third Hospital of Hebei Medical University, Shijiazhuang, China (e-mail: yzling\_liu0311@126.com).

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most commonly used method for the diagnosis of bone disease. However, computed tomography (CT) is more advantageous in diagnosis of osteoclastic, osteoblastic, and mixed images of metastases,<sup>[12–14]</sup> which is frequently used to assess proximal femur stability. Apart from this, CT plays vital roles in operative planning and postoperative assessment, allowing for *accurate* measurement of the femoral cortices.<sup>[15]</sup> However, when there is a demand for a precise image of soft tissues and bone structures, magnetic resonance imaging (MRI) is preferred.<sup>[16]</sup> Besides accurately detecting bone metastases, MRI offers sensitive and specific detection of early proximal femoral metastases and is able to reveal early pathological changes in the marrow.<sup>[17]</sup> Other examinations such as emission computed tomography (ECT), single-photon emission tomography (SPECT), and positron emission tomography (PET) have their respective advantages. ECT can detect regions of remodeling that are relevant to bone metastases, infection and bone fractures. SPECT<sup>[18,19]</sup> provides better sensitivity and specificity for cancer and metastasis diagnoses. PET is also applied to the staging of systemic diseases in tumor patients.<sup>[20–22]</sup> Additionally, if multiple myeloma is suspected, serum immune electrophoresis and bone marrow aspiration should be performed to obtain a definite diagnosis.

Rougraff et al<sup>[23]</sup> recommended that the standard diagnostic strategy for patients without a definite primary site should include an x-ray of the affected limb, a whole-body bone scan, laboratory studies, and CTs of the chest, abdomen, and pelvis. These procedures identified the primary lesion in 85% of patients. If the patient has no history of tumors or a definite diagnosis is needed, a needle biopsy is a better choice for the diagnosis of bone metastasis.

### 3. Surgical management

The proximal femur is the most common site of mechanical failure in metastatic patients due to its load-bearing function and continuous axial and torsional stresses. Approximately, 10% of patients with metastatic disease will sustain a pathologic fracture, and 65% of all fractures that occur in the femur require surgery.<sup>[24]</sup> Although the majority of tumor patients with skeletal metastases are in the advanced stages of cancer, invasive surgical treatment is usually performed in patients with proximal femur metastases. The relevant stereoscopic surgical treatments fall into two general categories: internal fixation and endoprosthetic replacement.<sup>[25–27]</sup> Percutaneous vertebroplasty, which is associated with mild trauma and good analgesic effects, is an effective and widely accepted operational option for patients with vertebral tumors through clinical practice.<sup>[28–32]</sup> However, the development and evolution of the use of bone cement outside of the spine<sup>[8,31]</sup> has rendered the injection of bone cement a potential treatment option for proximal femur metastases. The

concept of percutaneous vertebroplasty has been developed to PFP after being applied to the treatment of femoral metastases. PFP provides a less invasive therapeutic option that offers pain relief and biomechanical stability to patients with proximal femoral metastases. All patients benefited from the new technique as previous studies shown.<sup>[10,33]</sup>

#### 3.1. Evaluations prior to surgical treatments

In addition to considering the patient's general systematic conditions, Mirel scoring system, which is the most widely used tool for describing the risk of pathologic fracture, should always be taken into account.<sup>[34]</sup> These criteria include the location of the lesion, the extent of the lesion, the pain that occurs with walking, and the lytic or blastic nature of the lesion. If the patient has a score >9, the risk of pathologic fracture is >33%, and the patient requires prophylactic surgery, such as internal fixation or prosthetic replacement. Mirel criteria reveal the risk of pathologic fracture and can facilitate initial decisions regarding surgical planning (Table 1). Van der Linden et al<sup>[35]</sup> argued that axial cortical involvement >30 mm is associated with a higher risk of fracture in cases of proximal femoral metastasis. For these impending fractures, the most appropriate strategies are surgical interventions which can provide mechanical stability before a fracture occurs.

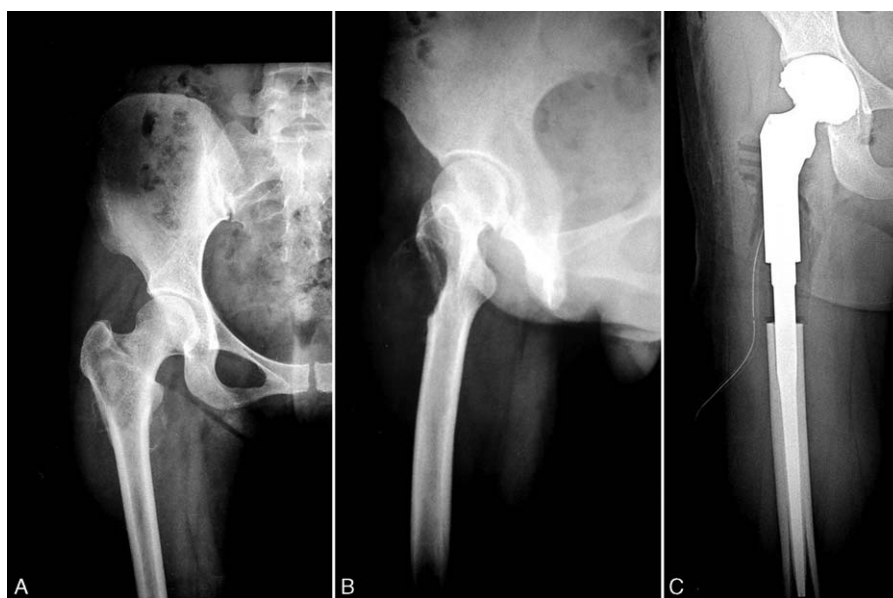
#### 3.2. Treatment with prosthetic replacements

Once a fracture occurs in cases of metastatic lesions, nonsurgical treatments always have inevitable limitations; for example, catagmatic bone cannot be sufficiently immobilized, which prevents recovery and results in sustained pain.<sup>[36,37]</sup> Because pathologic fractures often exhibit delayed union or even non-union, prosthetic replacements are recommended for patients who have suffered such fractures. Prosthetic replacements not only reconstruct the destroyed lesion but are also used to salvage failed internal fixations or nonsurgical treatments. Standard prostheses are widely used for lesions located in the femoral head and neck. However, if a standard prosthesis is inadequate, particularly when there is substantial bone loss in the peritrochanteric region, tumor prosthesis can be applied. Additionally, if the integrity of the acetabulum is sufficient, bipolar hemiarthroplasty is a better option for patients because the complication rate of this procedure is lower than that of a total hip replacement (4% vs. 22.2%).<sup>[38,39]</sup> Paul suggested that impending femoral neck lesions should be treated with arthroplasty.<sup>[34]</sup> In brief, prostheses are an excellent choice for the treatment of proximal femoral metastases in patients with good general fitness and life expectancy. Although the risks of dislocation and infection are high, this method ensures major

**Table 1**  
Mirel's scoring system for the risk of pathologic fracture.

Variable	Score		
	1	2	3
Site	Upper limb	Lower limb	Peritrochanter
Pain	Mild	Moderate	Activity-related
Lesion type	Blastic	Mixed	Lytic
Size	Less than one-third of the cortical diameter	One- to two-thirds of the cortical diameter	More than two-thirds of the cortical diameter

NOTE: A score of 7 or lower indicates that the patient should be treated with radiation only, and a score of 8 or higher indicates that the patient should undergo prophylactic surgical fixation. Adapted with permission from Mirels H. Metastatic disease in long bones. A proposed scoring system for diagnosing impending pathological fractures. *Clinton Orthop Relat Res* 1989; (249):256-64.



**Figure 1.** Surgical treatment of a proximal femoral metastatic tumor (prosthetic replacement). (a and b) The preoperative hip x-ray shows the metastatic lesions in the right proximal femur; (c) the postoperative hip x-ray shows prosthetic replacements.

local tumor control, and the complication and failure rates are not significantly higher than those of osteosynthesis, especially when the latter procedure is associated with curettage and the use of adjuvant cement (Fig. 1).

### 3.3. Treatment with internal nail fixation

Pathologic intertrochanteric or subtrochanteric fractures may be treated with a cephalomedullary nail or with a prosthetic replacement.<sup>[25–27,34,40]</sup> The indications for choosing a prosthetic replacement or a cephalomedullary nail are still not clear. Piatek et al<sup>[41]</sup> argued that treatment with a gamma nail or a proximal femoral nail may be appropriate for subtrochanteric metastases with a distance to trochanter >20 mm. In general, if the bone in the femoral neck and head is adequate to support the implant, nailing is preferred.<sup>[34]</sup> Several studies have demonstrated that patients can achieve satisfactory pain relief and marked clinical improvement with improved weight-bearing ability following internal nail fixation operations.<sup>[24,42,43]</sup> When the surgery is performed, proximal reaming should also be performed as carefully and gently as possible to avoid lateral cortical fracture and embolization. Adequate bone available proximally for fixation is necessary, and distal interlocking is mandatory.<sup>[34]</sup>

For patients with impending intertrochanteric or subtrochanteric fractures, the bone can be stabilized with cephalomedullary nailing because head and neck fixation can be adequate.<sup>[24,34,40,43]</sup> The use of intramedullary devices is a traditional treatment method for long bone metastases, particularly those in the proximal femur. These devices have relatively low rates of mechanical failure (2–22%) and incidence of death from cardiopulmonary complications ranges (1–10%).<sup>[38,44–46]</sup> Considering the abovementioned factors, the treatment method of nailing may be well suited for patients with good proximal bone stock.

### 3.4. Treatment with PFP

The first application of polymethylmethacrylate (PMMA) bone cement was conducted by Deramond et al.<sup>[47]</sup> They injected

PMMA into C2 vertebra affected by vertebral hemangiomas and observed remarkable chronic pain relief.<sup>[48]</sup> Gradually, the use of PMMA following an analogous percutaneous and minimally invasive manipulation method with the assistance of radiology guidance has been found to be favorable for vertebral fractures associated with osteoporosis and painful vertebra with broad osteolysis or invasion secondary to a tumor.<sup>[49]</sup> An effective and minimally invasive surgical technique is desired for the management of many advanced cancers in patients with severe bone pain who cannot tolerate a major surgery and in patients for whom radiotherapy has already been ineffective and therefore only desire pain relief, minimal trauma, and reduced costs. PMMA may possess many advantages for achieving these goals, including bio-inertness, ease of management, relatively high biomechanical strength, and extended sustainability. The injection of bone cement can strengthen the transmission of bone-to-implant and implant-to-bone forces.<sup>[50]</sup> Previous studies have demonstrated the efficiency of bone cement injection in proximal femoral metastases.<sup>[10,33,51]</sup> PFP is a minimally invasive therapy that can provide a facile but effective reinforcement of the proximal femur and reduce the risk of fracture<sup>[52,53]</sup> (Fig. 2).

Main indications for the PFP treatment of proximal femoral metastases include the following: patients present with steady vital signs, without severe heart or lung disease, or topical inflammation and ulceration; the lesion site should involve primarily osteolytic damage, and the cortex around lesion should be complete, particularly within the calcar femorale; pathological fractures must not be present. And these components are recommended for: PFP is not recommended for osteoblastic metastases. Given the large volume of bone cement injected in a topical position, the injection should be performed before the bone cement becomes solidification. During the operation, pulse oximetry should be monitored closely to avoid pulmonary embolism. Bone cement leakage represents a common complication of PFP. In the event of leakage, the needle should be repositioned by fluoroscopy to prevent further leakage. In addition, compression of the osteoclasia or soft tissue lump can



**Figure 2.** Surgical treatment of a proximal PFP. (a) The preoperative hip x-ray shows the metastatic lesions in the left proximal femur; (b) the postoperative hip x-ray shows bone cement injection in proximal femoral metastases. PFP (femoral metastatic tumor). PEP = percutaneous femoroplasty.

cause cancerous cells to transfer into blood, which could accelerate the process of metastasis.

Regarding weight-bearing capacity and biomechanical stabilization after PFP, the injection of bone cement can sufficiently strengthen and reinforce the destroyed bone. Several studies have shown that cement injections performed in different ways can result in different outcomes. Hayashi et al<sup>[54]</sup> claimed that filling the femoral neck with bone cement could improve the mechanical stability of the hip (when loads are applied to the greater trochanter) and protect against fractures of the proximal femur. Palumbo et al<sup>[55]</sup> reported that bicortical cement columns spanning from the superior to inferior femoral neck cortices play important roles in restoring the integrity of the femoral neck and improving the load-bearing capacity of the proximal femur. Beckmann et al<sup>[56]</sup> showed that single central and centrodorsal bone cement filling patterns significantly improve the mechanical stability of the hip, but double craniocaudal augmentation degenerates the skeleton and results in markedly reduced peak loads and decreased energies to the point of failure. Sutter et al<sup>[53]</sup> reported that 15 mL of cement is inadequate to reinforce the proximal femur and there is little biomechanical advantage to placing the cement in the proximal femur when compared with placing it in the trochanter.

Why is PFP so effective? The chemotoxicity and thermal necrosis during exothermic polymerization might account for the possible mechanisms of PMMA in pain relief.<sup>[57,58]</sup> PFP may alleviate pain via the damage of the sensitive nerve endings in periosteum.<sup>[59]</sup> The role of methylmethacrylate (MMA), a component of PMMA, in cell toxicity, neurotoxicity, and chemotoxicity remains unclear and opposite opinions have arisen in previous studies.<sup>[49,60]</sup> After ruling out the “chemical effect” and “thermal effect” as probable causes of pain relief, “mechanical stabilization” can be regarded as the second most likely reason for pain relief. In a previous study, PMMA was found to restore the mechanical stability of the bone by stabilizing the micro-motions of micro-trabecular fractures, which are the most frequently observed histologic change in patients. At

present, the most likely mechanism of pain relief is the mechanical stabilization.<sup>[10,61]</sup> Our previously PFP procedures performed and observed an encouraging curative effect, however, the proposed indications should be strictly followed, as shown Table 2.<sup>[10]</sup>

#### 4. Overview and conclusion

By the time metastatic tumors are diagnosed, patients have advanced disease; thus, even with the recent advances in the treatment of primary cancers, the survival of patients with bone metastases remains poor.<sup>[62,63]</sup> The goals of treatments of proximal femoral metastatic tumors (particularly surgical treatments) are to maximize pain relief, prevent pathologic fractures, provide mechanical stabilization, and enable weight-bearing. For patients with pathologic fractures and ossified metastatic tumors in the proximal section of the femur, prosthetic replacement

**Table 2**

#### Main indications and recommendations for the PFP treatment of proximal femoral metastases.

##### Indications

1. Patients present with steady vital signs, without severe heart or lung disease, or topical inflammation and ulceration
2. The lesion site should involve primarily osteolytic damage, and the cortex around lesion should be complete, particularly within the calcar femorale
3. Pathological fractures must not be present

##### Recommendations

1. PFP is not recommended for osteoblastic metastases
2. Given the large volume of bone cement injected in a topical position, the injection should be performed before the bone cement becomes solidification
3. During the operation, pulse oximetry should be monitored closely to avoid pulmonary embolism
4. Bone cement leakage represents a common complication of PFP. In the event of leakage, the needle should be repositioned by fluoroscopy to prevent further leakage

PEP = percutaneous femoroplasty.

following proximal femoral resection is an appropriate operative choice. Internal nail fixation may be suitable for patients with good proximal bone stock. For patients without fractures and with continuous cortical bone metastatic tumors, PFP may be an attractive option when the goal is to simply relieve pain. The importance of careful and appropriate preoperative assessment before the execution of any therapeutic procedure should be emphasized. A carefully considered multidisciplinary approach will provide patients the best opportunity for an improved quality of life and maximal satisfaction. The patient provided written informed consent for the publication of these pictures and the study was approved by the Human Ethics and Research Ethics committees of the Fourth Hospital of Hebei Medical University.

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