

Surgical Treatment of Metastatic Femoral Fractures: Achieving an Improved Quality of Life for Cancer Patients

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Abstract. *Background: The femur is the most common long bone affected by metastatic carcinoma. We report our experience regarding treatment of metastatic femoral fracture using femoral head prosthesis (FHP) or intramedullary nailing (IM nail) with augmentation by polymethylmethacrylate (PMMA). Patients and Methods: Thirty-five complete fractures in 33 patients were treated surgically. Metastatic lesions were present in the femoral head to neck region (n=9), trochanteric to shaft region (n=23) and supracondylar region (n=3). Results: Eight out of 9 patients with proximal femoral metastasis reconstructed by FHP were later able to walk outdoors. For the 11 patients with trochanteric metastasis, the short type of gamma nail was used for bony fixation. In two patients the inserted IM nails were broken. All other cases showed excellent clinical outcomes. For the 12 patients with femoral shaft metastasis, the long type of gamma nail was inserted. Nine cases showed excellent clinical outcomes without any serious complications. Conclusion: FHP is indicated for metastases in the femoral head to neck region. IM nailing is best indicated when the lesion is located in the proximal to mid shaft and the patient's life expectancy is <6 month.*

Improvements in the treatment of primary cancers have led to increased survival times but also to an increased number of patients with skeletal-related metastatic events. Pathological fractures caused by metastatic tumors usually occur in the late disease stage and are accompanied by severe pain, instability and acute loss of function (1). The femur is the most common long bone affected by metastatic carcinoma and this directly influences daily living activities and the quality of life of cancer patients (2).

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Adequate treatment of femoral metastasis provides immediate pain reduction, stability, increased mobility and local tumor control, thus easing the need for nursing care. Bisphosphonate treatment or radiotherapy for sensitive cancers helps to decrease skeletal complications (3) (Table I) but are not indicated for complete fractures. Because of poor results with conservative treatment, operative stabilization is now the recommended therapy for pathological femur fracture. However, the surgical indications and appropriate procedures for metastatic femur fracture are still controversial (1). Patients with a short life expectancy and inoperable condition are not suitable candidates for surgery. However, advances in adjuvant treatment and the increased survival of patients with metastatic bone disease have motivated surgeons to practice more aggressive treatments (4). This has led to the application of invasive surgical techniques, such as those already used for the treatment of primary sarcoma of bone, including curative resection and megaprosthesis (5-7).

Several factors must be considered in the treatment of femoral metastasis, including the location, estimated prognosis, nature of the fracture (complete or impending) (8) and general patient condition and wishes. Consequently, the treatment should be tailored to suit each individual case. We report here our experience treatment of metastatic femoral fracture using femoral head prosthesis (FHP) or intramedullary nailing (IM nail) with augmentation by polymethylmethacrylate (PMMA). We discuss the selection of different modalities and surgical procedures that may be appropriate for each cancer patient.

Patients and Methods

Patients. Since 2006 in the outpatient clinic of our institute, we experienced 62 consecutive cases with metastatic lesion of the femur, including lymphoma. The diagnoses were made using clinical history, radiographs, bone scintigrams, positron emission tomography and other imaging modalities. Amongst these cases, 35 complete fractures in 33 patients were treated surgically. The mean age of patients was 65.3 years (range, 32 to 81) and there were 19 men and 14 women. Metastatic lesions were present in the femoral

Table 1. Treatment options for metastatic femoral fracture.

Treatment	Metastatic lesion	Estimated prognosis	Katagiri score (9)	Tumor resection	Goal of ADL	Weight bearing
Conservative Casting with Bisphosphonate or Anti-RANKL antibody Radiotherapy	Any	<3 months	0-2	None	Changing position on the bed Wheel chair	None
Megaprosthesis	Femoral neck to intertrochanteric	>1 year	>6	Wide	Full activity Outdoor walk	Full
Femoral head prosthesis	Femoral head to neck	>3 months	3-5	Intra-lesional	Full activity Outdoor walk	Full
Intramedullary nailing with locking screw	Subtrochanteric, femoral shaft to supracondylar	3-6 months	3-5	None	Wheel chair	None
		>6 months	>6	Intra-lesional Cryosurgery Adriamycin cement augmentation	Partial limitation Indoor walk	Partial to full

RANKL, Receptor activator of nuclear factor kappa-B ligand; ADL, activity of daily living;

head to neck region (n=9), trochanteric to shaft region (n=23) and supracondylar to condylar region (n=3). The primary tumors were kidney (n=10), lung (n=7), thyroid (n=4), lymphoma or myeloma (n=4), prostate (n=3), liver (n=2), breast (n=2), esophagus (n=2) and bladder (n=1). All patients were followed-up for at least one year or until death.

Operative indications . The operative indications used in this study for femur metastasis were: (i) pain relief that could not be controlled even with opioid drugs; (ii) tumor progression that was rapid and tumor size that had become uncontrollable; (iii) instability of the fracture site that could not be controlled by cast or splint.

If at least one of these conditions was met, the doctor in charge was consulted regarding: (i) whether the survival prognosis was estimated to be more than 3 months and (ii) whether the general patient condition allowed surgical intervention.

If both these conditions were met, surgical treatment was recommended to the patient. The estimated prognosis was obtained by the Katagiri score (9) and from the opinion of the doctor in charge.

Surgical procedure. Preoperative local imaging studies included plain radiographs, computed tomography and magnetic resonance imaging. Careful attention was paid to the extent of tumor involvement, cortical breakthrough and soft tissue extension. In 26 patients, selective arterial embolization of the metastatic lesion was performed the day before surgery in order to decrease intraoperative blood loss.

Different operative procedures were used depending on the site of the metastatic lesion. For proximal metastasis that extended into the femoral head and across the neck, the tumor was exposed through a posterior approach in the lateral position and removed by intra-articular resection. After careful curettage of residual tumor, a FHP was inserted into the intramedullary cavity and fixed with

PMMA containing gentamicin and adriamycin. None of the patients in this study were reconstructed by megaprosthesis. For trochanteric, subtrochanteric, femoral shaft and supracondylar metastasis, the proximal part of the metastatic lesion was reamed and the tumor carefully curated. Cryosurgery was performed as an adjuvant resection and involved freezing the tumor cavity by direct pouring of liquid nitrogen followed by thawing with warm saline. This was repeated three times. An antegrade IM nail with locking screw was used for reconstruction. For proximal metastases a short nail type was applied, while for femoral shaft metastases a long nail type was used. After stabilization of the femoral fracture, PMMA was applied to fill the bone cavity defect (Figure 1).

Evaluation. The following items were evaluated retrospectively: bony union at final follow-up, local recurrence, performance status both pre- and postoperative, local and systemic complications, activity of daily living and survival time after surgery. The performance status (PS) scoring system followed that of the Eastern Cooperative Oncology Group (10).

Results

FHP reconstruction. For the 9 patients with proximal femoral metastasis reconstructed by FHP, 8 were later able to walk outdoors with or without a T cane and maintained this ability until the final stages of life. The mean PS improved from a preoperative score of 2.6 to a postoperative score of 1.7. Eight patients survived longer than their estimated prognosis. One case with metastasis from renal cell cancer died 2 months after surgery without improvement in their PS, while another case suffered massive bleeding due to lack of embolization before operation.



Figure 1. A 63-year-old male with renal cancer metastasis (left). After careful curettage of tumor, cryosurgery was performed as an adjuvant resection. An antegrade long IM nail with locking screw was used for reconstruction. After stabilization of the femoral fracture, PMMA was applied to fill the bone cavity defect (right).



Figure 2. A 66-year-old male with renal cancer metastasis (left). The tumor resection and PMMA augmentation was not performed because the prognosis was estimated to be poor. This patient walked with full weight bearing against our recommendation and the stem was broken three weeks after surgery (right).

Intramedullary nail with locking screw reconstruction. For the 11 patients with trochanteric to subtrochanteric metastasis, the short type of gamma nail was used for bony fixation. In two patients the inserted IM nails were broken at the fracture site. In a case with kidney cancer metastasis, the tumor resection and PMMA augmentation was not performed because the prognosis was estimated to be poor. This patient walked with full weight bearing against our recommendation and the stem was broken three weeks after surgery (Figure 2). A case with thyroid cancer metastasis underwent IM nail insertion and PMMA augmentation but the stem was broken 2 years after surgery. All other cases showed excellent clinical outcomes. Survival times were longer than the estimated prognosis demonstrating that the operative procedure was only marginally invasive and had little effect on the general condition. The mean PS improved from a preoperative score of 3.7 to a postoperative score of 1.9.

For the 12 patients with femoral shaft to supracondylar metastasis, the long type of gamma nail was inserted for bony fixation. Three cases did not undergo augmentation with PMMA due to estimation of poor prognosis but all could move themselves by wheelchair after surgery. One case with metastasis from lung cancer had bilateral femoral stabilization. The remaining 9 cases showed excellent clinical outcomes without any serious complications. All cases achieved daily living activities until the final periods. Breakage of long IM nails was not observed throughout the follow-up period. The mean PS improved from a

preoperative score of 3.4 to a postoperative score of 2.6. We could not confirm bony union in all cases. No revision surgery, because of local tumor recurrence or infection, was necessary.

Discussion

Operative indication for femoral metastasis. Over the past decade, the prognosis and quality of life for patients with disseminated cancer has significantly improved thanks to newly-introduced medical and radiation therapies. However, this has led to an increased incidence of skeletal-related metastatic events, particularly in the lower extremity (11, 12). The treatment of such events is not curative and serves only as local disease control for the cancer patient.

Femoral metastases are especially difficult to manage because the majority are osteolytic. The major problems associated with these events are pain and mechanical disruption. Different therapeutic approaches have been proposed for femoral metastasis. Nilsson and Gustafson reviewed 245 operations in 216 patients with this condition. (2) They concluded that patients can be operated safely and with an acceptable complication rate. Several authors have recommended surgical stabilization of femoral fractures to reduce pain and to improve quality of life (13-16). Pain can be controlled by pain-killer drugs but the mechanical

disruption of bone should be treated surgically (12). To date however, the operative indications for femoral metastasis have not been clear (1). Because these patients have a relatively short lifespan and their general condition deteriorates over time, the initial operative intervention should be definitive. The orthopedic surgeon must assume the fractures will not unite and the fixation must be durable so that it lasts for the remaining lifetime of the patient. The operative method should be adapted on a case by case basis to reflect the individual circumstances.

Cammasio *et al.* (17) used the management protocol proposed by Capanna (18) for the operative indication of long bone metastasis. Lesions were divided into 4 classes, with class 1 to 3 patients indicated for surgical treatment. However, this protocol did not consider the prognosis or the general condition of the patient. In the present study, the factors of metastatic site, uncontrollable pain, uncontrollable tumor growth and uncontrollable instability were all taken into consideration. If at least one of these conditions was met the doctor in charge was consulted for the next two general conditions, comprising an estimated prognosis of >3 months and a suitable patient condition for surgical intervention. These treatment guidelines seem rational for femoral metastasis.

Appropriate operative procedure. The rapid progression of internal fixation devices and endoprosthesis over the past 20 years has improved the prognosis following surgical management of metastatic long bone fractures. However, the best way to treat femoral metastasis is still uncertain and complication rates are high (19). FHP is suitable for lesions in the femoral head to neck region. The best approach for lesions in the proximal femoral to shaft region is less clear.

Prosthetic replacement is now used more commonly for proximal femoral metastasis (5-7) (Table I). When the metastasis is located in the metaphyseal region, a wide resection and reconstruction with megaprosthesis may be indicated. Cammasio *et al.* reviewed 154 patients treated with prosthesis for metastatic bone disease, with metastatic breast and renal carcinoma accounting for 66% of lesions (17). The complication rate was acceptable and functional results showed improvement in 73% of patients with a proximal femur lesion. Hwang *et al.* reported on 315 patients who underwent resection of renal cell carcinoma metastasis and reconstruction with massive endoprosthetic replacement (6). They concluded that patients with solitary bone lesions and with no visceral metastases should be considered for megaprosthesis reconstruction. However, these prosthetic devices are more invasive, more expensive and are associated with higher rates of complications, such as infection and massive bleeding requiring longer hospital stays. Moreover, the attached gluteal and iliopsoas muscles are resected, thus decreasing the abductor strength and favoring dislocation of the hip joint.

Wedin and Bauer presented a retrospective series of 146 operations in 142 cases with proximal femur metastasis (19). In their study, postoperative complications were seen amongst patients operated with hip prosthesis. On the other hand, the risk of re-operation due to implant failure was twice as high in the group treated by osteosynthesis.

Doorn and Stapert reviewed 101 patients with femoral metastasis and stabilized with a long gamma nail (12). They reported that 92% of patients became mobile and that pain was absent or acceptable in 93%. Only two nails broke after surgery. Samsani *et al.* also reported that stabilization using a long gamma nail for femoral metastasis due to breast carcinoma is a safe and effective method with acceptable risk (20). Rosa *et al.* treated 21 patients with IM nailing, of which 8 patients were also treated with acrylic cement (11). Only one patient in their series was re-operated due to tumor progression and cement failure. Giannoudis *et al.* treated 30 patients with pathological femoral fracture by unreamed IM nailing (16). Only one was revised for implant failure through a distal metastasis at 6 months.

Our results confirmed that use of IM interlocking nails reduces pain and improves the quality of life in patients with femoral metastasis. Hip prosthesis is recommended for the increasing number of patients with proximal femoral metastasis. However, endoprosthetic replacement involves invasive surgery and is associated with increased morbidity (19). Indications for prosthetic joint replacement in patients with femoral metastasis include the prospect of long survival, isolated lesions, extensive bone loss and failed conventional reconstruction with osteosynthetic devices (Table I).

Complications of IM nailing for femoral metastasis. The major complications of IM nail stabilization for femoral metastasis involve infection, bleeding, tumor recurrence, deep venous thrombosis and implant breakage (13-16). In our series the latter event occurred in two cases.

The results of our study demonstrate that intramedullary stabilization of femoral metastasis can achieve the goal of surgical palliation with an acceptable risk of complication. None of our cases experienced uncontrollable tumor recurrence or growth, infection or deep venous thrombosis. Bleeding could be controlled by preoperative arterial embolization. Implant breakage is, however, a major issue. As described above, implant failure is not uncommon with these lesions and a failure rate of 10% has been reported with intramedullary implants such as long gamma nails (13-16). The implant failure rate will increase with longer survival times, as seen in our breast cancer patients. Unfortunately, femoral metastatic fractures did not show bony union, even with an IM nail. A strong fixation device

is required so that it lasts for the remainder of the patient's life without the risk of implant failure.

The composition, diameter, rigidity and design of IM nails contribute to the strength of the implant. These should be able to withstand the strain of weight-bearing for the remainder of the patient's life. To prevent IM nail breakage, we recommend that patients use a T-cane and limit their weight-bearing activity. The level of activity following femoral stabilization should be set lower than full activity. Augmentation by PMMA is a beneficial tool to increase the durability of IM nails.

Removal of tumor and adjuvant procedures. The use of reaming prior to tumor curettage and insertion of the IM nail is a matter of debate (21, 22). Reaming is necessary because a mechanical advantage can be obtained using a larger nail diameter. However, reaming may increase the diffusion of carcinoma into the distal end of the femur. The removal of metastatic carcinoma is an essential part of the management of femoral metastasis and is usually achieved by intralesional curettage. The empty cavity is filled with PMMA, thus conferring improved stability to the fixation construct. Moreover, local adjuvant treatments such as cryosurgery and adriamycin-containing PMMA can help to prevent local progression. For patients with poor prognosis (3 months or less), the removal of carcinoma is an invasive process and is, therefore, not warranted.

As an alternative, Ogura *et al.* reported an interesting case with hepatocellular carcinoma metastasis to the proximal femur (23). This patient was treated with radiofrequency ablation and prophylactic internal fixation. His postoperative course was uneventful and the patient was almost asymptomatic without local progression when he died 14 months after surgery. This case shows that femoral metastasis can be controlled without aggressive wide resection and megaprosthesis reconstruction.

Conclusion

The femur is the most common long bone affected by metastatic carcinoma. The major problems arising from femoral metastasis are pain and mechanical disruption. Short-term improvements in pain and functional status are particularly important for patients with limited life expectancy. Several authors have recommended surgical stabilization of femoral metastasis. The aim of surgical treatment should be to prevent or to stabilize the pathological fracture, relieve pain and permit an acceptable quality of life for the remainder of the patient's life.

Life expectancy should be longer than the time to recover from surgery. FHP is indicated for metastases in the femoral head to neck region. IM nailing is best indicated when the lesion is located in the proximal to midshaft and the patient's life expectancy is <6 months, especially if associated with an aggressive carcinoma.

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