Original Article

Risk Factors of Ambulatory Status in Metastatic Bone Disease of the Femur Treated with Intramedullary Device Fixation

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Background: New cancer managements have improved patient survival. However, these patients can develop metastatic bone disease and present with impending or pathologic fracture. Femur is a common metastatic site of the lower extremities. Bone stabilization is a commonly performed procedure in patients with metastatic bone at the shaft and subtrochanter of the femur. Intramedullary fixation is commonly performed due to mechanical benefit and less complications. Enhanced awareness of the factors that influence early postoperative ambulation may reduce complications and improve patient outcomes.

Objective: To identify risk factors of ambulatory status in patients with metastatic bone disease of the femur that were treated with intramedullary device fixation.

Materials and Methods: This retrospective study included patients with metastasis lesion at the shaft and subtrochanter of the femur that were treated with intramedullary nail fixation during 2007 to 2014 at the Department of Orthopaedic Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. Patients were categorized into either the early (ambulation within 3 days of surgery) or late (ambulation later than 3 days postoperatively) ambulation groups.

Results: Thirty-one patients (19 females, 12 males; mean age: 54.1 years) were included. The mean postoperative pain score was significantly lower in the early ambulation group (0.8±1.1 vs. 2.1±1.1; p = 0.015). There was no significant difference between groups for MSTS functional scoring, intra-operative bleeding, intraoperative blood transfusion, or operative time. Regarding postoperative care, the early ambulation group had a significantly shorter mean length of hospital stay (p = 0.016).

Conclusion: Intramedullary nailing fixation is a treatment of choice in patients with metastatic bone tumor of the femur. Lower postoperative pain score was found to be an important factor that may predict early ambulation. Early ambulation in these particular patients can provide better outcome with less complications.

Keywords: Fractures, Femur, Prognostic factors, Pathology, Intramedullary nailing, Ambulation

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Advancements in condition-specific management combined with a multidisciplinary team approach has improved the survivorship and quality of life of patients with cancer. However, the longer life expectancy now being observed in many types of cancer increases the likelihood of metastasis to other organs. Bone is the third most common metastatic site, and more than 50% of cancer patients will have at least one site of skeletal metastasis[1,2]. The femur is a common site of bone metastasis[2]. Patients with bone metastasis at the femur frequently present with impending or pathologic fracture[3]. These patients present with bone pain, deformity, and an inability to ambulate due to the effects of pathologic fracture[4]. Bone stabilization is a common procedure in patients with metastatic bone at the shaft and subtrochanter of the femur. Intramedullary fixation is commonly used in this setting due to its less invasive nature, and the fact that it facilitates early weight-bearing ambulation[5]. In addition to reduced ambulation due to pain, patients with bone metastasis are also at increased risk for developing fever, venous thromboembolism, urinary tract infection, and pneumonia. Early bone stabilization can minimize or prevent these complications. Patients can have early ambulation and weight-bearing with gait support, and they can return to their activities of daily living with good quality of life. Pile JC reported that the likelihood of postoperative fever due to bacterial infection is increased after the 3rd postoperative day[6]. Therefore, patients in this study were divided into 2 groups – those able and unable to ambulate within 3 days after surgery. The aim of this study was to investigate and identify factors that significantly predict ambulatory status in patients with metastatic bone

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disease of the femur treated with intramedullary device fixation.

Materials and Methods

The authors retrospectively studied patients with metastasis lesion at shaft and subtrochanter of the femur that were treated with intramedullary nail fixation during 2007 to 2014 at the Department of Orthopaedic Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. There were 25 pathologic fractures and 9 impending fractures with Mirel's scores ≥ 9[7] (Figure 1). Patients with preoperative bedridden status; early postoperative (within 24 hours) complication(s) that adversely affect ambulatory status; lesion extending to the femoral head, neck, or distal epiphyseal; and/or bone metastasis from solitary renal cell or thyroid carcinoma (because resection and prosthetic reconstruction are recommended in these cases) were excluded. All included patients had radiographic examination at the surgical site to ensure appropriate and adequate fixation without bone defect (Figure 2). All patients were allowed to ambulate with full weight-bearing with the help of a walker at or within 24 hours after surgery. Patients were categorized into either the early (within 3 days after surgery) or the late (later than 3 days after surgery) ambulation group. Collected data included age, gender, primary cancer, type of fracture, presence or not of preoperative hypercalcemia, location of bone metastasis, Musculoskeletal Tumor Society (MSTS) functional score, visual analog score (VAS) for pain, intraoperative bleeding and transfusion, operative time, and length of hospital stay. These factors were all compared between the early and late ambulation groups The protocol for this study was approved by the Siriraj Institution Review Board (SIRB) (COA No. 483/2557 [EC2]). The requirement to obtain written informed consent was waived due to the retrospective nature of the present study.

Statistical analysis

The present study used SPSS Statistics program version 18 (SPSS, Inc, Chicago, Illinois, USA) for statistical analysis[8]. Patient characteristics were summarized using descriptive statistics. Categorical data are presented as frequency and percentage, and continuous data are shown as mean $\pm$ standard deviation. Comparison of categorical data was performed using Chi-square test or Fisher's exact test, and continuous data were compared using Student's t-test or Mann-Whitney U test. A p-value <0.05 was considered statistically significant for all tests.

Results

Thirty-four patients were evaluated for inclusion eligibility. Of those, 2 patients were excluded due to their pre-operative bedridden status, and another patient died from

Figure 1. Radiographic evidence of impending fracture at left femur from lung cancer metastasis.

Figure 2. Radiographic demonstration of post-cephalomedullary nail fixation.

pulmonary complications within 24 hours after surgery. The remaining 31 patients (19 females, 12 males) were included. The mean age of patients was 54.1 years. Breast cancer and lung cancer were the two most common primary tumors. In the early group (7 patients), there were 3 breast cancers, 3 lung cancers, and 1 prostate cancer. In the late group (24 patients), there were 8 breast cancers, 8 lung cancers, 3 nasopharyngeal cancers, 2 unknown primary cancers, and one each of prostate cancer, cervical cancer, and bladder cancer. Twenty-two patients had complete pathologic fracture and 9 patients also had a contralateral lesion. The demographic data and clinical characteristics listed in Table 1 were not significantly different between groups. Seven patients with pathologic fracture were stabilized with intramedullary nail and augmented with polymethyl methacrylate (PMMA). Of those, one patient was in the early ambulation group and 6 patients were in the late ambulation group. Three patients in the late ambulation group had complication from upper urinary tract infection (UTI), and one patient had superficial wound infection that was successfully treated with antibiotics within the admission period. All patients were evaluated for hemodynamic status and had radiographic examination before ambulation. All patients received both non-narcotic and narcotic drugs to control pain. Data specific to MSTS score, VAS-pain, operative data, and length of hospital stay are shown in Table 2. Visual analog score (VAS) was used for postoperative pain evaluation[9]. The mean postoperative pain score was significantly lower in the early ambulation group than in the late ambulation group (0.8±1.1 vs. 2.1±1.1, respectively; $p = 0.015$). There was no significant difference between groups for MSTS functional score[10], intra-operative bleeding, intra-operative blood transfusion, or operative time. Regarding postoperative care, the early ambulation group had less postoperative complications and a significantly

Table 1. Demographic and clinical characteristics

Characteristics	Early (n = 7)	Late (n = 24)	*p*-value
Ages (years), mean ± SD	53.1±9.8	55.1±14.4	0.741
Gender			
Female	4 (57.1%)	15 (62.5%)	0.999
Male	3 (42.9%)	9 (37.5%)	
Primary cancer			
Breast	3 (42.9%)	8 (33.3%)	0.786
Lung	3 (42.9%)	8 (33.3%)	
Prostate	1 (14.3%)	1 (4.2%)	
Other	0 (0.0%)	7 (29.2%)	
Type of fracture			
Complete	5 (71.4%)	17 (70.8%)	0.999
Impending	2 (28.6%)	7 (29.2%)	
Preoperative hypercalcemia (serum calcium >10.5 mg/dL)			
Yes	0 (0.0%)	2 (8.3%)	0.99
No	7 (100.0%)	22 (91.7%)	
Metastasis at contralateral femur			
Yes	2 (28.6%)	7 (29.2%)	0.99
No	5 (71.4%)	17 (70.8%)	
Metastasis at other bone			
Yes	2 (28.6%)	18 (75.0%)	0.067
No	5 (71.4%)	6 (25.0%)	

Table 2. MSTS scoring, pain, and operative data

Factors	Early (n = 7)	Late (n = 24)	*p*-value
MSTS score (percent)	47.3±10.7	41.9±7.3	0.240
Visual analog score			
Preoperative	6.9±2.1	4.9±2.3	0.057
Postoperative (1 day)	0.8±1.1	2.1±1.1	0.015
Intraoperative bleeding (ml)	220±160.5	395±325.6	0.397
Intraoperative blood transfusion (ml)	96.3±164.6	388.7±320.9	0.650
Operative time (minutes)	111±36.8	131±42.1	0.329
Length of hospital stay (days)	9.9±2.3	21±13.6	0.016

ml = milliliter

shorter mean length of hospital stay ($p = 0.016$). Four patients in the late ambulation group had postoperative complications from UTI in 3 patients and superficial wound infection. One patient died from pulmonary embolism postoperatively.

Discussion

Advancements in medical treatment and a multidisciplinary team management approach can improve the survival of metastatic patients[11]. Patients with metastatic bone disease suffer from skeletal-related events, such as pain, impending or pathologic fracture, and spinal vertebra collapse with or without neurological deficit. Long bone metastasis can cause high risk of fracture, especially in weight-bearing bone such as femur[12]. Metastatic bone disease located at the subtrochanter or shaft of the femur can cause fracture-related complications, such as thromboembolism, urinary tract infection, pneumonia, muscle hypotrophy, and loss of strength[13]. These complications also increase the probability of a mortality outcome in this patient population.

Surgical treatment plays the major role in improving quality of life in patients with pathologic fracture at subtrochanter and shaft of the femur. Mirel's scoring system is used to estimate the risk of pathologic fracture. Impending fracture with a score ≥9 has high risk for fracture and should be considered for prophylactic fixation[7]. Intramedullary nail fixation is commonly used to treat and shore up the bone around these lesions in patients that meet the eligibility criteria for this treatment[13]. This type of fixation can provide less invasive whole bone stabilization, which facilitates early ambulation and less fracture-related complications[5]. Arvinius, et al reported that femoral intramedullary nailing of metastatic lesions provides satisfactory results, both clinically and radiologically. Early treatment of metastases prevents fractures, yields better results, and improves patient quality of life[13]. This study found significantly less postoperative pain in the early ambulation group compared to the late ambulation group. Although the difference in the VAS-pain score was 1.3, both groups were classified as mild pain (VAS 0 to 5). Pain in metastatic patients can be caused by many mechanisms. Physicians and team members should understand and observe for the characteristics of pain, and they should provide proper multimodal pain control for patients. This study showed the benefit of early ambulation, which could decrease the number of postoperative complications and could significantly shorten the length of hospital stay. There was 1 patient who died from pulmonary embolism that occurred immediately after the operation. Pre- and perioperative anticoagulant and closed intra-operative monitoring in patients at high risk for developing thromboemboli to prevent pulmonary embolism is important. This crucial complication is not uncommon and should be prophylactically managed.

Secure bone fixation, reconstruction of bone defect, and less invasive operation are important criteria in the surgical management of metastatic bone disease. Intramedullary nailing can satisfy all of these criteria with less complications. Significantly lower postoperative pain score and lower volume of intraoperative blood transfusion were observed among patients in the early ambulation group. Patients in the early ambulation group also had a shorter length of hospital stay. Good pre-operative planning and effective postoperative pain control can effectuate improved outcomes and quality of life in patients with metastatic bone disease of the femur that are treated with intramedullary device fixation.

Limitations

The present study has some limitations. First, the retrospective nature of the present study rendered its vulnerable to missing or incomplete data. Second, we enrolled a small number of patients, and all of them were treated at a single center. Third and last, our investigation did not include and compare the type of bone lesion, survival rate, or the duration of disease.

Conclusion

Surgical management of metastatic bone disease of the femur consisting of using intramedullary nail fixation and augmented with PMMA can yield good outcomes with less pain and early ambulation. Early ambulation in patients with impending or pathologic fracture is important for preventing postoperative complications.

What is already known on this topic?

The goal of surgery in metastatic bone disease in long bone is to perform whole bone fixation. Intramedullary nail fixation for metastatic bone disease at the subtrochanter and shaft of the femur can provide whole bone fixation that allows for early ambulation.

What this study adds?

Intramedullary nail fixation in the subtrochanter and shaft of the femur provides good bone stabilization. Adequate postoperative pain control facilitates early ambulation in both impending and pathologic fracture.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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