Case series

Metastases of the femur: analysis of 124 patients

Dimitrios Serenidis, Ioannis Zafeiris, Fotini Soucacos, Vasileios Karampikas, Pavlos Altsitzioglou, Orestis Konstantas, Panayiotis J. Papagelopoulos, Andreas F. Mavrogenis

First Department of Orthopaedics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

Abstract

Background: There are several studies providing surgical indications for patients treated for femoral metastases. The purpose of this study is to highlight the survival rates of patients with femoral metastases and provide information concerning the treatment of patients suffering from femoral impending fractures and those treated for actual pathological fractures.

Materials and Methods: We retrospectively studied 124 patients with femoral metastases from different cancers. The patients were treated with intramedullary nailing, tumor excision and arthroplasty reconstruction, or tumor resection and megaprosthetic reconstruction from 2013 and 2023. The mean follow-up was 18 months. Analysis of patients' survival rates was done based on the cancer type, number and location of metastases, presence of a pathological fracture, and type of surgery.

Results: The overall survival of the patients at 60 months was 16%. The presence of an actual pathological fracture, as well as the type of surgery were the only univariate survival predictors, with the first being the only multivariate predictor. Survival was statistically significantly higher in patients treated with tumor excision and arthroplasty reconstruction and patients treated with tumor resection and megaprosthetic reconstruction compared to those treated with nailing ($p= 0.002$). The survival of the patients with an impending fracture was statistically significantly higher compared to those with an actual pathological fracture ($p= 0.001$). There was no difference in survival among males and females, cancer types or number and location of femoral metastases. The complications rate was 7.2%; the most common complication was infection.

Conclusions: Survival rates were higher in patients with femoral metastases treated with tumor excision and arthroplasty reconstruction, or tumor resection and megaprosthetic reconstruction compared to those treated with nailing. Patients with an impending fracture had higher survival rates compared to patients with an actual pathological fracture.

Keywords: Metastases; femur; survival; resection; nailing; reconstruction.

Corresponding author: Andreas F. Mavrogenis, afm@otenet.gr

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Introduction

Metastatic bone tumors are the most prevalent skeletal cancers; the skeleton is the third most common site of metastatic disease following the lung and liver.[1] Concerning the incidence of metastatic tumors in the extremities, the femur is the most common long bone to be affected. Patients with primary or metastatic bone tumors usually experience impending fractures or actual pathological fractures leading to significant disability, treatment and prognosis alterations, as well as compromised survival rates.[2-6]

Surgical intervention for bone metastases aims to prevent and adequately manage pathological fractures, along with achieving optimal joint function, bone stability, pain reduction, as well as substantial improvement of quality of life and local control of metastatic lesions.[7,8] In general, impending and pathological fractures require different surgical approaches for stabilization compared to non-pathological fractures. Fixation devices or prosthetic implants used to restore a bone with metastatic disease should be durable and stable for the remaining of patients' lives.[9] Various factors affecting patients' survival and quality of life should be taken into consideration in decision making concerning the time and the surgical technique, including the primary cancer type, the extent of metastatic disease and limb function.[3,10] However, accurate prediction of the postsurgical outcome in these patients remains a challenge, especially due to the paucity of prospective studies analyzing the correlation of the above-mentioned factors with patients' survival.[10,11]

The purpose of this retrospective study is to evaluate the survival and treatment of patients with femoral metastatic disease from various cancers.

Materials and Methods

We retrospectively studied the files of 124 patients with femoral metastases treated for impending or actual pathological fractures at the authors' institution from January 2013 to January 2023. There were 60 male and 64 female patients with a mean age of 69 years (range, 53-85 years) (Table 1). A pathological fracture was the first symptom to diagnose the primary cancer in 21 patients (34%). All patients or their relatives gave a written informed consent for their data to be included in the study.

All patients had histological confirmation of their metastatic lesion by a biopsy prior to surgery, and adjuvant therapy administered according to the primary cancer type. All patients underwent surgical treatment within 1 to 45 days (mean, 15 days) after admission to the hospital. Surgical treatment included marginal tumor resection and megaprosthetic reconstruction (16 patients), intralesional excision and cemented hip arthroplasty (28 patients), and closed antegrade intramedullary nailing (80 patients) with reconstruction-type long hip or femoral nails (Tables 1 and 2). Surgical selection of patients with impending pathological fractures was done according to the Mirels' criteria.[14] Indications for intramedullary nailing were: (1) impending or actual pathological intertrochanteric, diaphyseal, or distal femoral fractures without involvement of the distal femoral articular surface, and/or (2) nursing care and pain relief in bedridden patients or patients with deteriorated general health status, deep vein thrombosis, tumor thromboembolism, or short expected survival from widespread cancer. Reconstruction-type nails (interlocking hip or femoral nails) were used in all patients (Fig. 1). Indications for tumor excision and arthroplasty reconstruction were: (1) femoral head and neck metastatic lesions with an impending or actual pathological fracture (Fig. 2), and/or (2) failure of previous hip intramedullary nailing operations. Indications for tumor resection and megaprosthetic reconstruction were: (1) extensive bone loss and bone destruction precluding standard internal fixation or arthroplasty (Fig. 3), (2) prolonged expected survival and solitary metastases of breast, renal cell, or thyroid cancer, and/or (3) impending or actual pathological fracture of the proximal or distal femur involving the articular surface of the hip and knee joint, respectively. A bipolar hip prosthesis was used in all patients.

The mean follow-up was 18 months (range, 2 to 120 months; minimum, 6 months). Eight patients were lost to follow-up; there were one (2/16) patient with tumor resection and megaprosthetic reconstruction, three (4/28) patients with tumor excision

Table 1. Demographic data: presentation and treatment.	
Data	**Patients (n = 124)**
Age and gender	
Age	Mean 69 years (range, 53–85 years)
Gender (male/female)	60/64
Type of cancer	
Breast	36
Renal	28
Lung	28
Prostate	10
Gastrointestinal (oral, esophagus, stomach, pancreas, colon)	12
Bladder	6
Thyroid	4
Location of metastasis in femur	
Proximal	96
Diaphysis	20
Distal	8
Number of metastases	
Solitary	88
Multiple	36
Pathological fractures	
Impending	72
Actual	52
Surgical treatment	
Intramedullary nailing	80
Excision and arthroplasty reconstruction	28
Resection and megaprosthetic reconstruction	16

and arthroplasty reconstruction, and two (2/80) patients with nailing. Patients' survival was analyzed using the Kaplan–Meier survival analysis with respect to different modes of metastatic presentation regarding gender, femoral metastases' location, impending and actual pathological fracture, type of surgery type, type of primary cancer, and solitary or multiple metastases.[23] Comparison of the curves

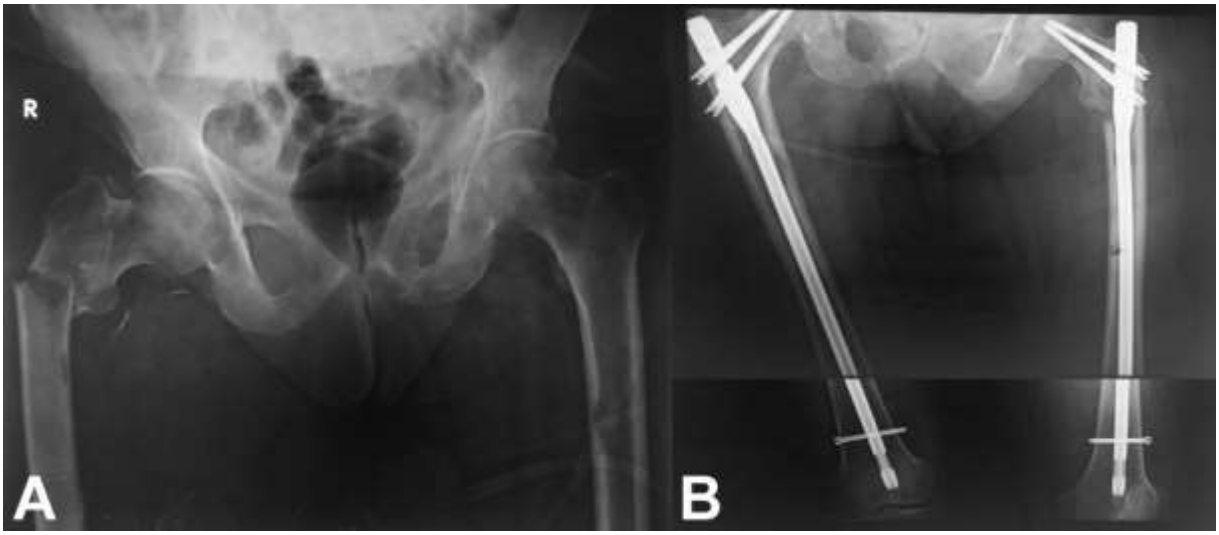

Figure 1. (A) *A 72-year-old woman with recently diagnosed breast cancer experienced an actual right proximal femoral pathological fracture, and an impending left femoral diaphysis pathological fracture.* ***(B)*** *Long reconstruction type intramedullary nailing was done for both fractures.*

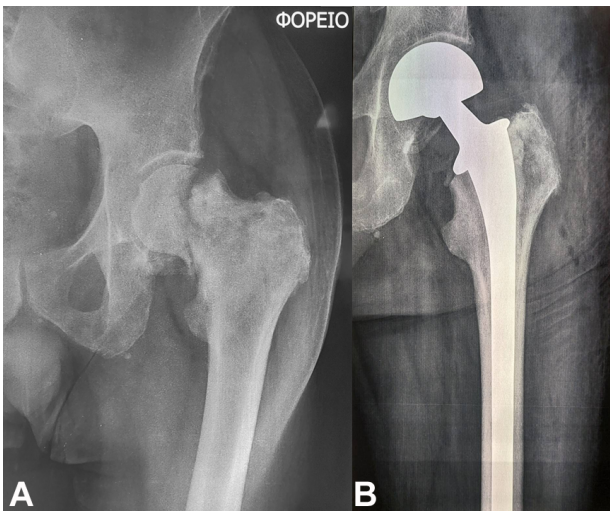

Figure 2. (A) *A 65-year-old man with urothelial cancer and left proximal femoral pathological fracture* ***(B)*** *treated with a long stem cemented hemiarthroplasty of the hip.*

was done with the log-rank test. The differences in survival were evaluated using the chi-square test. Multivariate analysis was performed using the Cox-regression analysis. Complications and death were recorded at routine clinical and imaging follow-up evaluations.

Results

Survival

The overall survival of the entire patient population with femoral metastases was 54% at 12 months, 30% at 24 months, 20% at 36 months, 18% at 48 months, and 16% at 60 months (mean survival time, 18 months) (Fig. 4). At the last follow-up, 20 patients were alive with disease and 96 patients were dead with disease. The 60-months survival of male patients was 14% (mean survival time, 12 months) compared to 19% of female patients (mean survival time, 16 months) (Fig. 5). The 60-months survival of patients with breast cancer was 22% compared to 7% of patients with renal cancer, 14% of patients with lung cancer, and 60% of patients with prostate cancer (Fig. 6). The 60-months survival of patients with solitary femoral metastases was 18% compared to 11% of patients with multiple metastases (Fig. 7). The 60-months survival of patients with proximal femoral metastases was 10% compared to 30% of patients with diaphyseal femoral metastases, and 50% of patients with distal femoral metastases (Fig. 8). The 60-months survival of patients with femoral metastases treated with nailing was 16% compared to 24% of patients treated with tumor excision and arthroplasty reconstruction, and 18% of patients treated with tumor resection and megaprosthetic reconstruc-

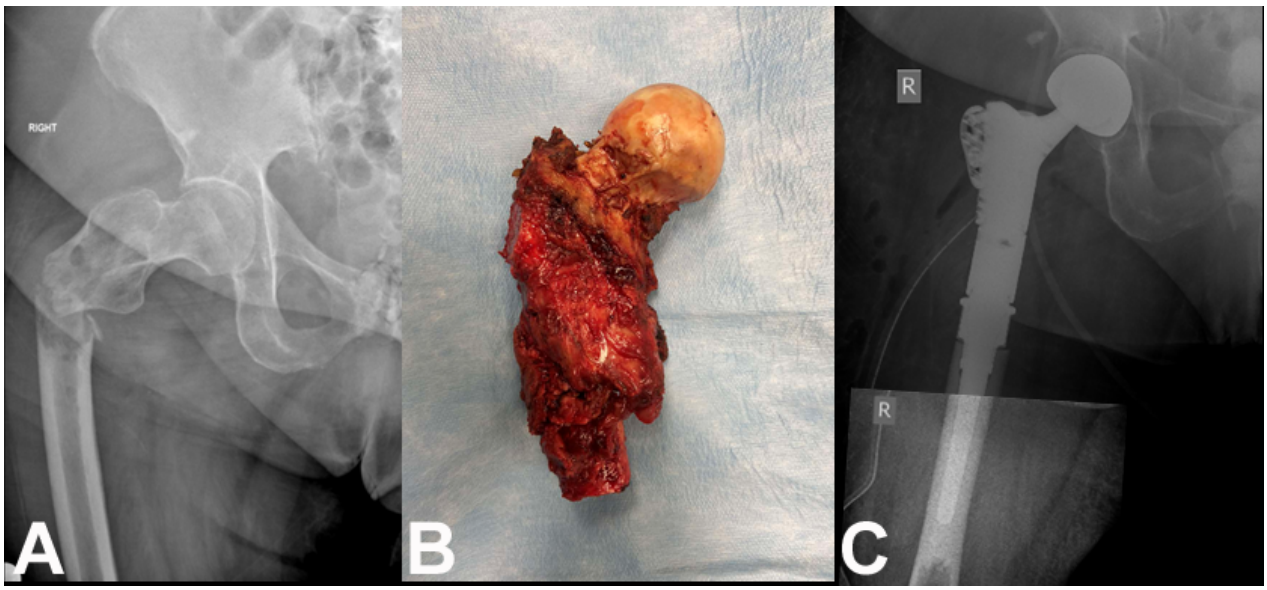

Figure 3. ***(A)*** *A 78-year-old woman with breast cancer and right proximal femoral pathological fracture treated with* ***(B)*** *resection and* ***(C)*** *proximal femoral megaprosthetic reconstruction.*

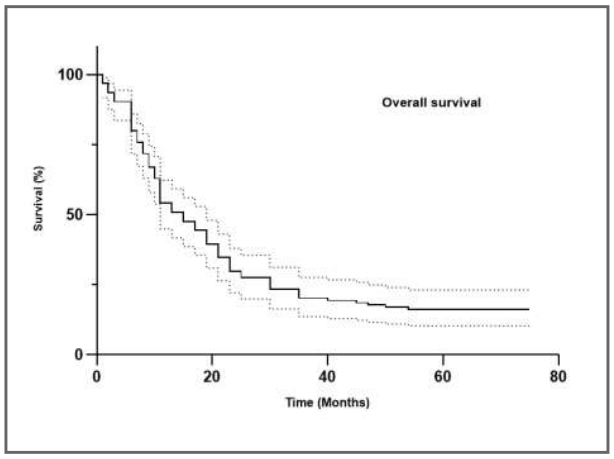

Figure 4. *A Kaplan–Meier survival curve shows the overall survival of patients with femoral metastases.*

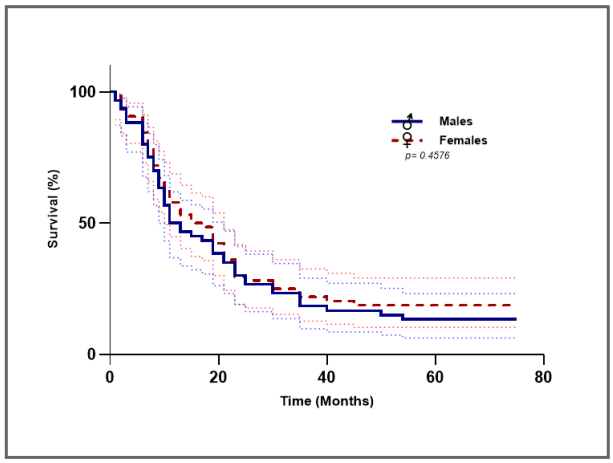

Figure 5. *A Kaplan–Meier survival curve shows that the survival of male and female patients with femoral metastases was not different among groups*

tion (Fig. 9). The 60-months survival of patients with impending pathological fractures was 28% compared to 0% survival of patients with actual fracture (Fig. 10; Table 3).

Univariate and Multivariate Predictors of Survival

The only factors found to be univariate survival predictors were the presence of a pathological fracture and the type of surgery. Survival was statistically significantly higher only in univariate analysis in patients treated with tumor excision/resection and reconstruction compared to nailing ($p= 0.002$), as well as in patients with impending pathological fractures compared to those with actual pathological fractures ($p= 0.001$). Gender, type of cancer, number and location of metastases were not important

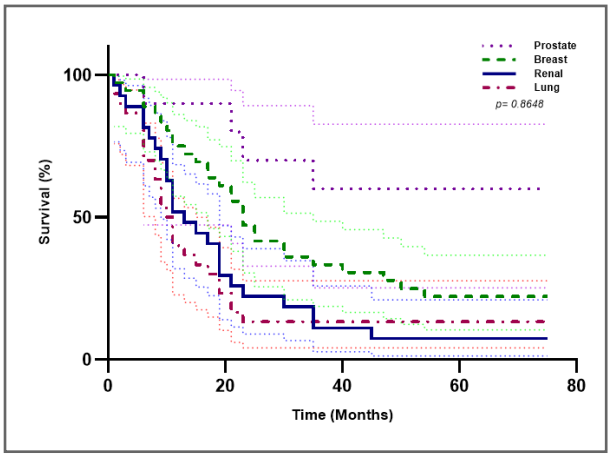

Figure 6. *A Kaplan–Meier survival curve shows that the survival of patients with breast, renal, lung and prostate cancer femoral metastases was not different among groups.*

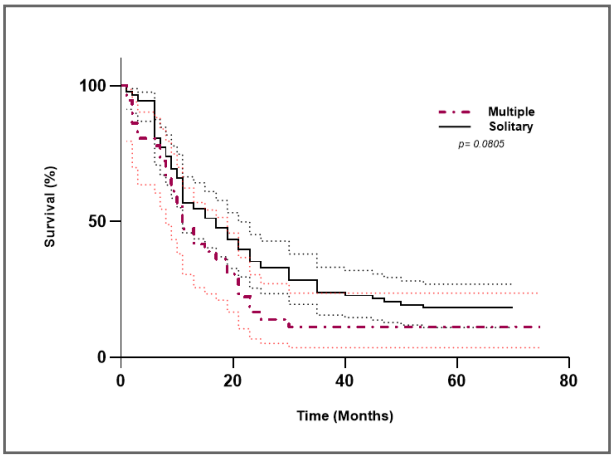

Figure 7. *A Kaplan–Meier survival curve shows that the survival of patients with solitary and multiple metastases was not different among groups.*

Table 2. Surgical treatment by location of femoral metastases.

Location of metastasis in femur and type of surgery	**Patients (n= 124)**
Proximal femur	
Standard and long trochanteric hip nails[a]	54
Proximal femoral excision and arthroplasty reconstruction[c]	28
Proximal femoral resection and megaprosthetic reconstruction[b]	14
Femoral diaphysis	
Long trochanteric hip nails[a]	20
Distal femur	
Long trochanteric hip nails[a]	6
Distal femoral megaprostheses[d]	2

[a] *Veronail®, Orthofix, Italy*
[b] *Mutars® Proximal Femoral Reconstruction, Implantcast, Germany*
[c] *Quadra®, Medacta International, Switzerland*
[d] *Mutars® Distal Femoral Reconstruction, Implantcast, Germany*

univariate survival predictors (Tables 3 and 4). The only factor found to be multivariate survival predictor was the presence of a pathological fracture (actual pathological fracture) ($p= 0.001$). Gender, type of cancer, number and location of metastases, as well as the type of surgery were not important multivar-

Table 3. Metastatic presentations and their significance for survival.

Metastatic presentation		**Patients (n)**	**Survival (*p- value*)**
Independent			
Gender	Male vs. female	60/64	No difference (0.457)
Type of cancer	Breast vs. renal, lung, prostate	36/28/28/10	No difference (0.865)
Number of metastases	Solitary vs. multiple	88/36	No difference (0.080)
Location of femoral metastasis	Proximal vs. distal	90/14	No difference (0.626)
Type of surgery	Nailing vs. excision/resection	80/44	Higher in patients treated with excision/resection (0.002)
Pathological fracture	Impending vs. actual	72/52	Higher in patients with impending fracture (0.001)
Associated with pathological fracture, type of surgery, and location of femoral metastasis			
Impending fracture	Nailing vs. excision (arthroplasty)	44/28	No difference (0.155)
Actual fracture	Nailing vs. resection (megaprosthesis)	36/16	Higher in patients with actual fracture treated with resection (0.039)
Solitary metastasis	Impending vs. actual fracture	54/34	Higher in patients with solitary metastasis and impending fracture (0.027)
Multiple metastasis	Impending vs. actual fracture	20/16	No difference (0.194)
Proximal femoral impending fracture	Nailing vs. excision (arthroplasty)	36/28	No difference (0.876)
Proximal femoral actual fracture	Nailing vs. resection (megaprosthesis)	18/14	Higher in patients with proximal femoral actual fracture treated with resection (0.002)

iate predictors of survival (Table 4).

Complications

The complications rate for the patients with femoral metastases included at the latest follow-up for the purpose of this study was 6.5% (8/124 patients) (Fig. 11). Infection was the most common complication. The mean survival of the patients with complications was 32 months (Table 5).

Discussion

Among published research, there is an abundance of studies reporting functional and oncological outcomes on surgical modalities for the management of femoral metastases.[6,8,12-18] Capanna and Campanacci et al. attempted to standardize the management of patients with bone metastases by determining which of the patients were suitable candidates for surgical intervention, as well as which of the reconstruction techniques had potentially more favorable outcomes in different clinical situations. Patients were divided into four classes based on several parameters including the metastatic site, life expec-

Table 4. Univariate and multivariate predictors of survival						
Variable	**Univariate association**	***p- value***	**Multivariate association**	***p- value***	**Odds ratio**	**95% CI**
Gender	-	0.457	-	0.224	1.3452	0.5107–1.4021
Type of cancer	-	0.865	-	0.986	1.0197	0.8697–1.1835
Number of metastases	-	0.080	-	0.126	0.7655	0.4267–0.9813
Location of metastasis	-	0.626	-	0.481	1.1212	0.7583–1.6383
Type of surgery	+	0.002[a]	-	0.072	0.6328	0.4156–1.0229
Actual Pathological fracture	+	0.001 [a]	+	0.002 [b]	2.0794	1.720–3.7110

The only significant factor in multivariate association was the occurrence of a pathological fracture (actual pathological fracture).

[a] *Statistically significant based on univariate analysis.*

[b] *Statistically significant based on multiple regression analysis (p= 0.008).*

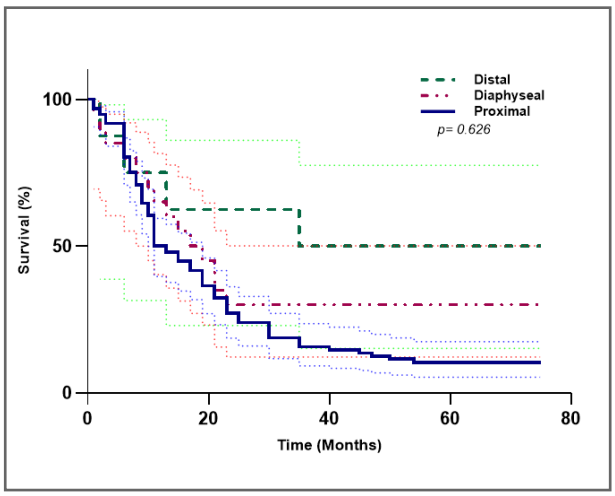

Figure 8. *A Kaplan–Meier survival curve shows that the survival of patients with proximal, diaphyseal and distal femoral metastases was not different among groups.*

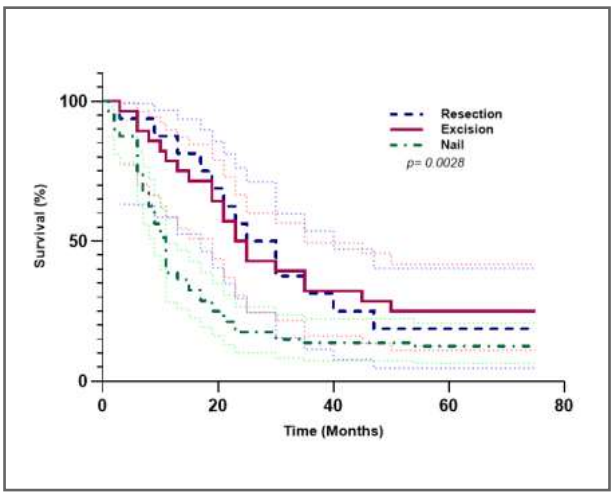

Figure 9. *A Kaplan–Meier survival curve shows the survival of patients treated with nailing or excision/ resection; survival was statistically significantly higher in patients treated with tumor excision and arthroplasty reconstruction or tumor resection and megaprosthetic reconstruction.*

tancy, tumor type and stage, risk for pathological fractures, presence of visceral metastases, and sensitivity to nonsurgical therapies. According to this protocol, patients are surgically treated with either prosthetic replacement or osteosynthesis with or without cement.[7,19] Due to extensive disease, a relative contraindication for operative treatment of any metastatic lesion in the extremities is considered to

Table 5. Complications of surgical treatment.

Patient no./ Gender	Metastatic presentation	Type of surgery	Complication	Outcome (months)
1/Female	Proximal femoral actual pathological fracture, gastrointestinal cancer	Intramedullary nailing	Tumor progression	DWD (28 months)
2/Female	Proximal femoral actual pathological fracture, breast cancer	Intramedullary nailing	Nail breakage (revision with a megaprosthesis)	DWD (52 months)
3/Male	Proximal femoral actual pathological fracture, lung cancer	Resection and megaprosthetic reconstruction	Dislocation (open reduction)	DWD (32 months)
4/Male	Proximal femoral actual pathological fracture, prostate cancer	Resection and megaprosthetic reconstruction	Breakage of neck of implant (revision of implant)	AWD (16 months)
5/Female	Proximal femoral actual pathological fracture, gastrointestinal cancer	Excision and arthroplasty reconstruction	Infection (debridement and antibiotics)	DWD (24 months)
6/Male	Proximal femoral actual pathological fracture, lung cancer	Resection and megaprosthetic reconstruction	Disassembly of the megaprosthesis	DWD (9 months)
7/Male	Proximal femoral actual pathological fracture, renal cancer	Excision and arthroplasty reconstruction	Infection (debridement and antibiotics)	AWD (26 months)
8/Female	Proximal femoral actual pathological fracture, breast cancer	Intramedullary nailing	Infection (debridement and antibiotics)	DWD (32 months)

DWD, dead with disease; AWD, alive with disease.

have expected survival of less than 4 - 6 weeks.[20] Less invasive surgery is preferable in patients with a life expectancy of 3 – 12 months, while in those with better prognosis and long-term expected survival (>12months) en bloc resection of the lesion and prosthetic reconstruction, which is more invasive but durable, should be attempted.[3,21,22] During the previous years, several preoperative survival prediction models were utilized with variability of accuracy power. Further development is necessary, so that these tools become reliably implemented in the daily decision-making of orthopaedic surgeons.[20]

Metastatic bone disease is a common complication of cancer with a wide variety of tumors metastasizing to bones.[23] Higher survival rates at 12 months have been recorded in patients with breast cancer, myeloma, lymphoma and kidney cancer while lung, prostate and unknown cancer as primary tumors are associated with lower patient survival.[24] Breast cancer has proven to be a positive predictor

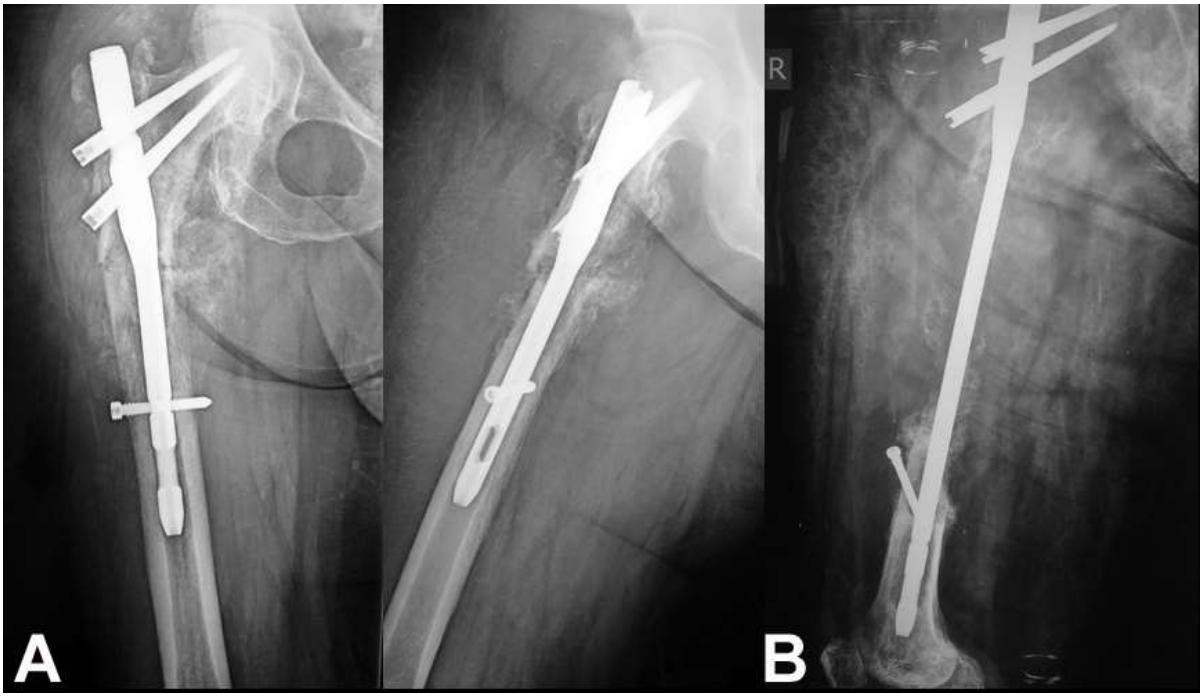

Figure 11. ***(A)*** *A 75 year-old woman with gastrointestinal cancer and right proximal femoral pathological fracture treated with intramedullary hip nailing and postoperative radiation therapy.* ***(B)*** *Tumor progression and revision operation with a long reconstruction type nail for palliation and nursing.*

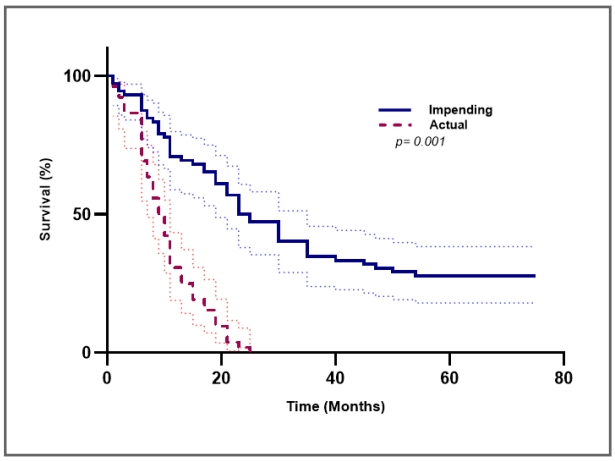

Figure 10. *A Kaplan–Meier survival curve shows the survival of patients with impending and actual fractures; survival was statistically significantly higher in patients with impending fractures.*

of survival, with 12-months survival rates ranging from 45% to 53% in the literature.[10,25] Ratasvuori et al. reported age under 65 years, Karnofsky score greater than 70 and solitary skeletal metastases as additional favorable prognostic factors in breast cancer patients.[4] Aggressive treatment of metastatic lesions and reconstruction with modular prostheses are related to prolonged survival, while en bloc resection of a solitary metastasis improves survival rates.[4,5,26,27] Patients affected by lung or gastrointestinal cancer are expected to have worse life expectancy and surgical treatment often plays a palliative role. These patients may benefit from less invasive procedures with durable internal fixation and adjuvant radiation therapy. Among authors, there is an agreement that the presence of visceral metastases is an independent negative prognostic factor for patients' survival.[4,5,28,29]

Concerning the location of the metastatic lesions in the proximal femur, 50% affect the femoral neck, 30% the subtrochanteric area and 20% the intertrochanteric area.[18,30] Overall, 12-months survival in patients with metastatic disease of the proximal femur ranges from 42% to 75%.[15] In a recent study

by Angelini et al. which included 40 patients with proximal femoral metastases, the postoperative survival rate of the patients was 70% at 6 months and 58% at 12 months. Higher survival was recorded in patients treated with resection and reconstruction with endoprostheses (EPR) or proximal femoral replacement (PFR) compared to those treated with intramedullary nailing (mean survival time 8 and 11 months for EPR and PFR respectively, mean survival time 5 months for nailing). However, the presence of pathological fracture and the number of metastases did not significantly affect the outcome in patients' survival.[15] Similarly, Guzik et al. analyzed 122 patients with mean follow-up 27 months and found mean survival of 860 days after modular endoprosthetic replacement and 360 days after bone fixation as surgical treatment for metastatic lesions of proximal femur.[18] On the contrary, metastatic lesions located in the femoral diaphysis are less common. In 25% of patients with diaphyseal femoral metastases and pathological fractures survival is critically affected.[31] Huang et al. conducted a study including 16 patients with diaphyseal pathological femoral fractures who were treated with resection and intercalary prosthetic reconstruction with 18.8% and 12.5% overall survival at 12 and 24 months, respectively.[16]

According to current literature, the presence of pathological fractures is a significant negative factor for patients' survival, as patients who have developed actual pathological fractures are related to worse mortality rates compared to those with impending pathological fractures.[4,13,32] Despite its prognostic value, the occurrence of a pathological fracture in the femur is an indication for surgery, as it may have a devastating effect on patients' quality of life with significant functional impairment and severe pain.[6,28] Internal fixation of pathological fractures in femoral diaphysis and metaphysis managed with intramedullary nailing should be reserved for patients with extensive disease, or those with well-expected response to nonsurgical therapies.[3,7,14,33,34] Survival rates of 40% at 12 months, 25% at 24 months and 15% at 36 months were observed in a study evaluating intramedullary nailing for treatment of patients with pathological fractures of the femur.[14] Prophylactic stabilization of the femoral bone with metastatic tumor lesions seems to improve patients' survival, as it may enable early postoperative mobilization and avoid treatment delay. Philipp et al. recently studied 950 patients with femoral metastatic lesions, of which 38% (362 patients) underwent prophylactic stabilization. This group of patients recorded lower mortality rates compared to those who were treated after the occurrence of a pathological fracture.[17]

We acknowledge several limitations in this study. First, it is a retrospective study with its inherent limitations. Conducting a research paper on patients with metastatic bone disease is a challenge as this group of patients is usually associated with poor prognosis due to advanced disease. However, useful information concerning prognostic variables and outcomes of surgical procedures can be drawn with well-designed retrospective studies on a topical topic. Yet, as a nonrandomized retrospective study potential selection bias may occur. Second, the standard adjuvant treatments that patients received, such as chemotherapy, hormonal and radiation therapy were not included. Third, the types of cancer varied. We preferred to include all patients with different primary tumors to femoral bone in order to investigate the prognosis and treatment outcome. High grade tumors with multiple metastases in older people appear to have a negative impact on survival. Nevertheless, none of these variables was found important predictor of survival in this study. Fourth, we did not include patients with myeloma even though the principles for pathological fracture management and myeloma have been similar. As a primary hemoproliferative malignancy, we consider myeloma a clinical entity with different prognosis and outcome from metastatic bone lesions.

In conclusion, this study showed variable survival of patients with metastases of the femur from various cancers. The survival was higher in patients with femoral metastases when treated for an impending fracture compared to those experiencing an actual pathological fracture. Additionally, the results of this study showed that patients with prox-

imal and distal femoral pathological fractures have higher survival although having a higher rate of complications when treated with metastatic tumor resection and reconstruction. The later may be biased by the relatively small sample size of the present study. Actual pathological fractures and type of surgery were the univariate predictors of survival; however, the only multivariate predictor of survival was the presence of a pathological fracture. The rate of complications should be acknowledged and kept to minimum in cancer patients.

Conflict of Interest

The authors declared no conflicts of interest.

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