

Clinical Research

Is Total Femur Replacement a Reliable Treatment Option for Patients With Metastatic Carcinoma of the Femur?

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Abstract

Background The majority of metastatic bone lesions to the femoral bone can be treated without surgery or with minimally invasive intramedullary nailing. In rare patients with extensive metastatic disease to the femur, total femur replacement may be the only surgical alternative to amputation; however, little is known about this approach. **Questions/purposes** In a highly selected small group of patients with metastatic carcinoma of the femur, we asked: (1) What was the patient survivorship after this treatment?

(2) What was the implant survivorship free from all-cause revision and amputation, and what complications were associated with this treatment? (3) What functional outcomes were achieved by patients after total femur replacement for this indication?

Methods Eleven patients (three men, eight women) with a mean age of 64 years (range, 41-78 years) received total femur replacements between 1986 and 2016; none were lost to followup. The most common primary disease was breast cancer. In general, during this period, our indications for this procedure were extensive metastatic disease precluding internal fixation or isolated proximal or distal femur replacement, and an anticipated lifespan exceeding 6 months. Our contraindication for this procedure during this time was expected lifespan less than 6 months. Patient survival was assessed by Kaplan-Meier analysis; implant survival free from revision surgery and amputation were assessed by competing risk analysis. Function was determined preoperatively and 6 to 12 weeks postoperatively with the Musculoskeletal Tumor Society (MSTS) score normalized to a 100-point scale, with higher scores representing better function from a longitudinally maintained institutional database.

Results Eleven patients died at a median of 5 months (range, 1-31 months) after surgery. One-year revision-free and limb survival were 82% (95% CI, 51%-98%) and 91% (95% CI, 61%-99%), respectively. Reasons for reoperation were hip dislocation, infection and local recurrence in one patient each. The latter two complications resulted in amputation in two patients. The median MSTS score was 32 (range, 13-57).

Conclusions Despite attempts to select patients who might have anticipated greater life expectancy, eight of 11 patients died by 6 months after surgery, and an additional

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two patients had undergone an amputation at 8 and at 17 months postoperatively. Most patients undergoing total femur replacement in this series did not recover from the procedure by the time they died, despite our best attempts to perform the procedure in patients whom we thought would live at least 6 months. Based on this, we believe that most patients with extensive metastatic disease to the femur should be offered palliative care, rather than major reconstruction.
Level of Evidence Level IV, therapeutic study

Introduction

The most common site for extremity metastatic bone lesions from cancer is the femur [5, 26]. Most metastatic bone lesions are treated effectively with nonsurgical modalities such as radiation therapy, chemotherapy, hormonal therapy, or bisphosphonates [12]. The indications for surgical stabilization of an impending fracture are persistent pain or enlargement of the lesion after radiation and involvement of the cortex of at least 50% on biplanar radiographs [6, 8, 18]. Impending and pathologic fractures with minimal bone loss usually are treated with locking intramedullary nails [30], whereas open curettage and single- or double-plate fixation are indicated in pathologic fractures with considerable bone destruction [13, 15]. In patients with severe destruction of the proximal or distal part of the femur, with no chance of stable screw fixation, proximal or distal femur replacement can be indicated [10].

In some patients, the remaining femoral bone stock is too weak for adequate internal fixation or arthroplasty of the upper or lower portion of the femur; in those rare situations, the remaining reconstructive option should surgery be selected would be total femoral endoprosthetic replacement. However, prosthetic reconstruction is more expensive, more invasive, and associated with a longer operating time, greater blood loss, and a longer hospital stay compared with internal fixation [2]. When contemplating such an invasive treatment, it is crucial for the patient and the treating physicians to consider the expected remaining lifetime of the patient and balance it against the risk of complications. Although some authors state that patients with a life expectancy less than 3 months should not be considered for any operative treatment [29], others extend this group to approximately 6 months or less [27]. To the best of our knowledge, no studies have reported on total femur endoprosthetic replacement exclusively among patients with metastatic carcinoma of bone, which we have used occasionally in patients with extensive femoral metastases and a life expectancy estimated to be greater than 6 months.

In a highly selected small group of patients with metastatic carcinoma of the femur, we therefore asked: (1) What was the patient survivorship after this treatment? (2) What

was the implant survivorship free from all-cause revision and amputation, and what complications were associated with this treatment? (3) What functional outcomes were achieved (as measured by the Musculoskeletal Tumor Society [MSTS] score) by patients after total femur replacement for this indication?

Patients and Methods

Between 1986 and 2016, 11 patients (three men and eight women) with metastatic bone disease were treated with total femur replacement. Their mean age at the time of total femur replacement was 64 years (range, 41-78 years).

Information for this retrospective study was collected from a longitudinally maintained database and from chart review of medical records. Institutional review board approval was obtained before initiation of this study.

The main goals of the surgery were relief of pain and immediate mobilization postoperatively to increase quality of life for the remaining lifetime of the patients. All patients were unable to put weight on their leg and experienced extensive pain owing to a fracture or severe osteolysis. Bone loss was quantified on biplanar radiographs. Additional metastatic bone disease was assessed by bone scintigraphy. During this period, our indications for this procedure were extensive metastatic disease to the femur precluding adequate internal fixation or isolated proximal or distal femur replacement, and an anticipated lifespan exceeding 6 months and exclusion of disseminated cancer. Our contraindications for this procedure during this time were expected lifetime less than 6 months, disseminated cancer, and sufficient remaining bone stock allowing internal fixation or partial endoprosthetic replacement of the femur. We used internal fixation with either nail or plates in combination with cement, or isolated proximal or distal femur replacement when the remaining bone stock was adequate. During this time, palliative care was considered when patients were not approved for surgery owing to a limited general health state and had an expected lifespan less than 6 months with disseminated cancer. Estimation for remaining lifetime was done by an interdisciplinary treating team of an orthopaedic surgeon and an oncologist until 2005. Since then therapeutic strategy was discussed by the musculoskeletal tumor board, comprised of a radiologist, oncologist, pathologist, radiotherapist, and an orthopaedic surgeon. Although we have no documented numbers, we assume that approximately one of 10 patients with metastatic carcinoma underwent total femur replacement; the other nine received palliative care.

The most common primary disease was breast cancer and the most common indication for total femur replacement was pathologic fracture of a previously plated

femur (Table 1). Owing to metastatic bone destruction in 11 patients, no other bone-preserving surgery was feasible.

Total femur replacement was performed using the Howmedica modular reconstruction system (HMRS[®]; Stryker-Howmedica Inc, Mahwah, NJ, USA) in eight patients (between 1987 and 2002), in two with the Global modular reconstruction system (GMRS[®]; Stryker-Howmedica Inc) (between 2007 and 2010), and in one with the Kotz modular femur and tibia reconstruction system (KMFTR[®]; Stryker-Howmedica Inc) (1986).

Fixation of the tibial component was entirely cemented (stem and plateau) in seven patients, hybrid-cemented (cemented plateau and cementless stem) in three, and cementless in one patient with the KMFTR. Bone quality of the acetabulum was tested intraoperatively with a clamp. Six patients with adequate bone quality in the acetabulum received a bipolar head for hip reconstruction, whereas five patients with osteoporotic bone had acetabular reconstruction with a cup (three cemented and two uncemented).

We used a Watson-Jones approach to the hip with a long lateral incision that reached the anterolateral aspect of the patellar tendon and tibial tuberosity. For gluteus medius

fixation, a custom-made device (enhanced tendon attachment system, ETA[®]; Stryker-Howmedica Inc) was used in one patient, a ligament augmentation and reconstruction system (LARS[®]; Surgical Implants and Devices, Arc-sur-Tille, France) with reattachment of the tendon to the LARS ligament was used in two patients, and soft tissue fixation with the remaining gluteal tendon to the fascia lata in eight patients.

All patients died during the first 31 months after surgery; none have been lost to followup.

Patient survival was defined as the time from implantation to death, revision-free survival from implantation to first revision surgery with involvement of the prosthesis, or limb survival from implantation to amputation. For physical functioning, pain, and walking ability, we used the MSTS score normalized to 100, with higher scores being better [9]. Assessment of the MSTS score was performed preoperatively and between 6 and 12 weeks after surgery for all but one patient who died 2 weeks postoperatively. For patients treated before publication of the 1993 MSTS score [9], the score was calculated from the medical records.

Table 1. Primary diagnosis, indication, and outcome of total femur endoprosthetic replacement in patients with metastatic disease

Number of patients	Primary disease	Age (years)*	Previous surgery to femur	Indication	Time to total femur replacement		Time to amputation [#] (months) [#]	Time to death (months) [#]	Failure	MSTS Score
					(months) [§]	Followup (months)				
1	RCC	68	DO	Pathologic fracture	3	1		0.5		NA
2	Breast cancer	62	DO + THA	Recurrence	82	6		6		40
3	CML	41	None	Osteolysis	0	5		5		27
4	RCC	56	WFO	Pathologic fracture	34	16	8	16	Infection	57
5	BCC	63	PO	Recurrence	6	5		5		33
6	Breast cancer	66	DO + THA	Pathologic fracture	31	31		31	Hip dislocation	30
7	Breast cancer	60	DP	Pathologic fracture	23	3		3		43
8	Breast cancer	75	DO	Pathologic fracture	18	3		3		13
9	HCC	78	DO + THA	Pathologic fracture	1	5		5		33
10	Prostate cancer	71	DO	Pathologic fracture	11	18	17	18	Local recurrence	27
11	Breast cancer	62	PO	Pathologic fracture	7	3		3		27

*At total femur replacement; [§]time from initial operation to total femur replacement.

[#]no value means no event.

MSTS = Musculoskeletal Tumor Society; RCC = renal cell carcinoma; CML = chronic myeloid leukemia; BCC = basal cell carcinoma; HCC = hepatocellular carcinoma; DO = diaphyseal osteosynthesis; DP = distal prosthesis; WFO = whole femur osteosynthesis; PO = proximal osteosynthesis; NA = not applicable.

The Kaplan-Meier method was used for estimation of patient survival. To evaluate implant survival and revision-free survival, survival probabilities were estimated in a competing-risk framework. With respect to implant survival, death was considered a competing event. SAS Version 9.4 (SAS Institute Inc, Cary, NC, USA) was used for statistical calculations.

Results

Eleven patients died at a median of 5 months (range, 1-31 months) after surgery. One- and 2-year survival were 27% (95% CI, 7%-54%) and 9% (95% CI, 0.5%-33%) respectively, using the Kaplan Meier estimation (Fig. 1). One patient with renal cell cancer with lung metastases died 2 weeks after surgery owing to heart failure, leading to a 30-day mortality rate of 9% (95% CI, 1%-49%).

One-year revision-free implant survival (Fig. 2A) and limb survival (Fig. 2B) were estimated as 82% (95% CI, 51%-98%) and 91% (95% CI, 61%-99%), respectively, in the competing-risk analysis. One chronic hip dislocation, one infection, and one local recurrence occurred in three patients. Two amputations were performed owing to infection and local recurrence. Minor complications were transient peroneal palsy and a wound healing dehiscence leading to two revision procedures within 6 weeks post-operatively in one patient.

The median MSTS score for the 10 patients who could be assessed was 32 (range, 13-57) of 100, with higher

scores representing better function. All patients had pain relief between 6 and 12 weeks after surgery as measured by the MSTS (scale 0-5) score pre- and postoperatively, with medians of 0 and 3, respectively. Three patients were free of pain, and eight patients still had moderate pain. Eight patients were able to walk; five of them could walk only a short distance inside, and three could walk for a few hundred meters outside. All patients needed crutches for walking. Two patients were not able to walk owing to paraplegia and chronic hip dislocation, respectively. The longest period of a resilient limb was 8 months until the limb had to be amputated owing to infection.

Seven patients were able to leave the hospital after surgery after a mean stay of 5 weeks (range, 1-15 weeks). Four patients could not be discharged owing to early death, paraplegia, severe graft-versus-host disease, or ongoing radiotherapy with a reduced general health state, respectively. Their mean hospital stay until they died was 3 months (range, 1-5 months).

Discussion

Deciding when or whether to perform total femur replacement in patients with advanced metastatic disease is a challenge. While avoiding or promptly treating pathologic fractures is important [28], total femur replacement is a very large operation, and one from which not all patients with very short life expectancies will recover. While helping patients remain ambulatory and reasonably pain free during their remaining months or years of life is an important goal, for some patients palliative care is the better choice. While some patients in the current series benefited from total femur replacement, most did not recover from the procedure by the time they died, despite our best attempts to select patients whom we thought had a life expectancy of more than 6 months. Even though we were conservative in setting the indication for total femur replacement, we were wrong in terms of expected remaining lifetime in eight of 11 patients.

This study has some limitations. First, this study is retrospective; however, the data were drawn mainly from a longitudinal institutional database, and our indications were reasonably consistent during the time in question. We sought to select patients whom we thought had at least 6 months to live, although as is evident here, these estimates are extremely difficult to make. Unfortunately information for patients treated in our outpatient clinic without surgery are not included in our tumor registry, so we do not know exact numbers of patients who might have been considered for total femur replacement, but we believe that most such patients were treated with palliative care. Second, the cohort is small and with different primary tumors in different tumor stages, each with their own prognosis making it

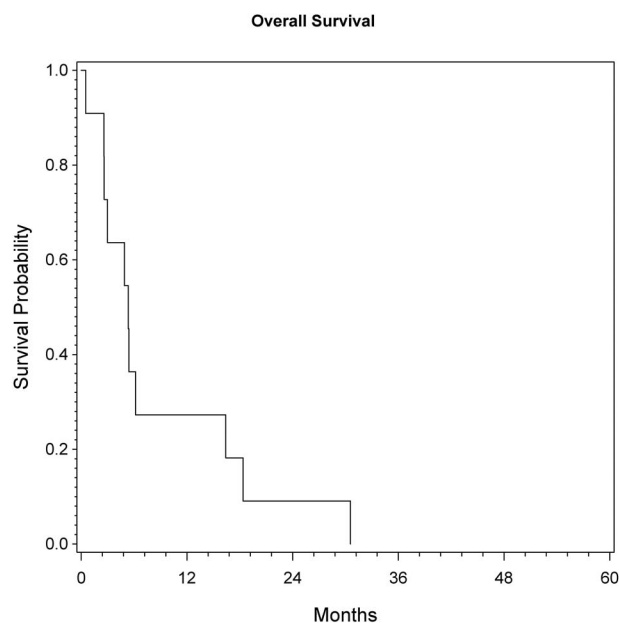


Fig. 1 The Kaplan-Meier estimation shows the overall probability of patient survival.

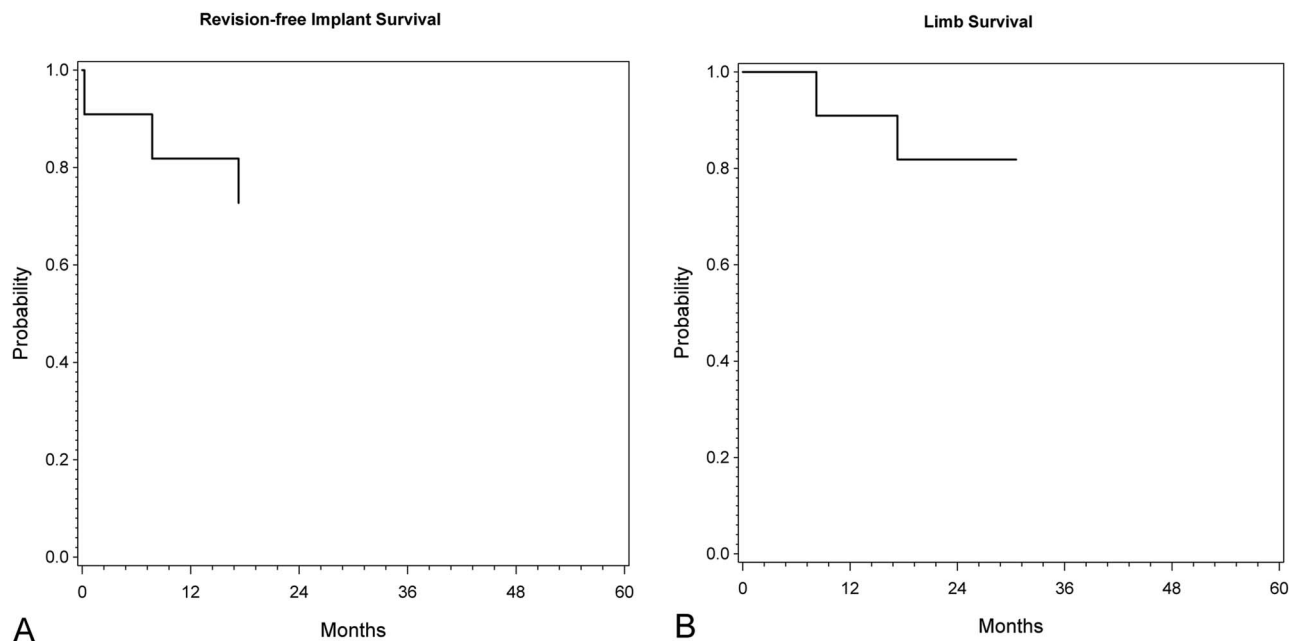


Fig. 2 A-B (A) Revision-free implant survival and **(B)** limb survival probability are shown using competing-risk analysis considering death as a competing event.

impossible to draw conclusions regarding which patients benefit from this procedure. Third, during the 30-year interval of our study, development of new anticancer agents and supportive palliative medicine have pushed back surgical treatment and enhanced nonsurgical treatment and palliative care. Therefore, we have not used total femur replacement for patients with metastatic carcinoma during the last 7 years.

We observed a median patient survival of 5 months. One patient died 2 weeks postoperatively owing to heart failure. Median survival in patients with metastatic disease treated with intramedullary nailing ranges from 5 to 14 months [4, 17, 19, 21]. Perioperative mortality of intramedullary nailing has been reported in 11% of patients [4], which is comparable to the 9% observed in our study. Patient survival after partial femur endoprosthesis replacement of metastatic bone lesions has been reported between 30% and 54% at 1 year [10, 31]. One case report of a total femur replacement in a patient with lung cancer showed survival of 12 months [7]. Hattori et al. [10] reported the problem of predicting the remaining lifetime in patients with metastatic carcinoma, and they could not find a substantial influence of a prognostic scoring system on patient survival.

Three of 11 patients with metastatic disease (27%) in our study underwent revision of total femur replacement, leading to amputation in two of them (18%). The reported revision rates of total femur replacement, mainly for primary bone tumor resection, range from 11% to 50% and

amputation rates range from 0% to 13% [1, 14, 16, 20, 22-25]. It might appear that we had a similar revision rate and slightly worse amputation rate in our patients with metastatic carcinoma compared with these studies reporting mainly on primary bone tumors. However, considering the much longer followup from 33 to 71 months in these studies [1, 14, 16, 20, 22-25] compared with 5 months in our study, the revision and amputation rate in our study is much worse than it appears at first glance. For this reason, we believe that reporting outcomes of these two medical conditions should be separated. Competing risk analysis for 1-year revision-free implant survival and limb survival for primary bone tumors has been reported as 73% and 97%, respectively [24]. In patients with metastatic cancer we showed 1-year revision-free survival and limb survival of 82% and 91%, respectively, using competing-risk analysis. The lower risk for revision in patients with metastatic cancer is a consequence of the much-shorter followup period in our study. Nevertheless, amputation is more frequent in patients with metastatic cancer. Even though incidence of aseptic loosening and periprosthetic fracture is higher in patients with primary bone tumors, this is likely attributable to longer patient survival; other causes for revision like infection, local recurrence, and hip dislocation are similar in patients with metastatic cancer [11, 24, 25]. The main complications from intramedullary nailing are local progression of the disease, nonunion, deep venous thrombosis, and implant failures in surgical treatment [19, 21, 31]. Postoperative thromboembolic

events have been reported, especially in patients treated with intramedullary nailing of pathologic fractures in up to 14% [3, 21], leading to immediate death after all procedures in 11% of patients [4]. Wedin and Bauer preferred endoprosthetic reconstruction to intramedullary nailing in proximal femur metastatic bone lesions owing to a lower reoperation rate during the first 2 years (8% versus 16%) [31].

We found that the main benefit of this procedure was pain relief as assessed by MSTTS scores. In addition, seven of 11 patients were able to ambulate after the procedure. However, our patients had a maximum of 8 months of functional improvement, owing to limited lifetime or early amputation. The mean MSTTS score of 32 is lower compared with total femur replacement after primary bone tumor resections, with values between 66% and 80% [1, 14, 16, 20, 22-25]. This difference may be explained by the reduced general health state of patients with metastatic cancer. Hattori et al. [10] reported a MSTTS score of 62% in patients with metastatic disease treated with modular femur megaprotheses. In contrast to our study with total femur replacement, their patients received only partial reconstruction of the femur. Eighty-two percent of our patients were able to walk using crutches for limited distances after surgery. In their patients with metastatic disease treated with lower extremity nailing, Moon et al. [19] reported the ability to walk using a walker in 60%, using a cane or crutches in 25%, and not able to walk in 15%.

Despite attempts to select patients who might have anticipated greater life expectancy, eight of our 11 patients died by 6 months after surgery, and an additional two patients had undergone an amputation at 8 and at 17 months postoperatively. Even though all patients achieved pain relief, most of the patients undergoing total femur replacement in our series did not recover from the procedure by the time they died, despite our best attempts to perform the procedure in patients whom we thought would live at least 6 months. Based on this, we believe that most patients with extensive metastatic disease of the femur should be offered palliative care, rather than major reconstruction.

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